

A novel green and Efficient Heterogeneous Acid Catalyst for the One-pot Synthesis of Benzopyrazine -Aminoimidazole hybrids with Antiproliferative Potential

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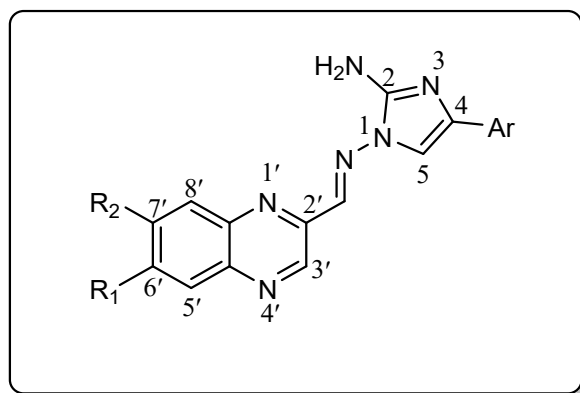
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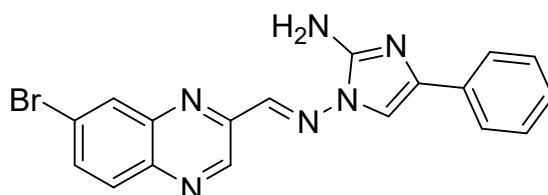
Materials and methods

All starting materials and chemicals used in this research were bought from the Sigma-Aldrich chemical company and applied without further purification. Melting points were measured using an Electrothermal 9200 apparatus and were uncorrected. Elemental analysis was performed on a Perkin–Elmer 2400 C, H, N analyzer. FT-IR spectra of all samples in our study were recorded in the sub-region 400-4000 cm⁻¹ using potassium bromide discs using a Perkin–Elmer 550 spectrometer. Mass spectra were obtained on an HP 5975 Mass Selective Detector at 70 eV. The ¹H NMR and ¹³C NMR were performed on Bruker advance spectrometer instrument using CDCl₃ and DMSO-d₆ as solvent and tetramethylsilane as internal standard. Thin layer chromatography (TLC) was used in silica gel polygram SILG/ V 254 nm plates. The X-ray diffraction (XRD) pattern related to the structural phases of the prepared catalyst was accomplished using a JEOL JSM-6100 microscope with (Cu K α radiation, $\lambda=1.54$ Å) in the region of $2\Theta = 10^\circ - 80^\circ$. The surface morphology of the MCFe₂O₄@Alginate@SAA nanocatalyst was studied by SEM (Hitachi S4160

scanning electron microscopy). The elemental mapping and compositional analysis were performed by energy-dispersive X-ray spectroscopy (EDX) by a KeveX, Delta Class I, equipped with the SEM instrument. A varying magnetic field from -10000 to 10000 Oe on a BHV-S5 vibrating sample magnetometer (VSM) was utilized at room temperature to characterize the magnetic measurement of modified and unmodified nanoparticles. The nanocatalyst's transmission electron microscope (TEM) images were performed using an FEI CM200 field emission at an accelerating voltage of 200 kV. The thermal gravimetric analysis (TGA) of the nano-magnetic solid acid catalyst was carried out on a Shimadzu Thermogravimetric Analyzer (TG-50) in the temperature range of 25-800 °C at a heating rate of 10 °C /min in the air under N₂ atmosphere.



(E)-1-(((6-bromoquinoxalin-2-yl)methylene)amino)-4-phenyl-1H-imidazol-2-amine (5a)



IR (KBr): 3424 and 33302 (NH str.), 3230, 3134 and 2920 (CH str.), 1642, 1466, 1171, 766, 694 cm⁻¹; ¹H NMR (600 MHz, DMSO-d₆) δ: 9.92 (s, 1H, CHN), 8.66 (s, 1H, 3'-H), 8.25 (s, 1H, 5-H), 8.19 (d, 1H, J = 2.2 Hz, 8'-H), 8.17 (d, 1H, J = 8.8 Hz, 5'-H), 7.91 (dd, 1H, J_{6',5'} = 8.8 and J_{6',8'} = 2.2 Hz, 6'-H), 7.74 (d, 2H, J = 7.8 Hz, 6''-H and 2''-H), 7.36 (t, 2H, J = 7.6 Hz, 3''-H and 5''-H), 7.22 (t, 1H, J = 7.4 Hz, 4''-H), 6.66 (s, 2H, NH₂); ¹³C NMR (100 MHz, DMSO-d₆) δ: 101.8 (C-5),

124.4 (C-2'' and C-6''), 126.8 (C-4''), 127.7 (C-3'' and C-5''), 128.4 (C-8'), 130.9 (C-5'), 131.2 (C-6'), 134.0 (C-1''), 135.0 (C-7'), 138.3 (C-4), 140.3 (C- 4'a), 141.7 (C-8'a), 144.5 (C-3'), 144.5 (CHN), 149.3 (C-2'), 150.5 (C-2); MS: (m/z) M⁺ calcd. for C₁₈H₁₃BrN₆: 393.0, Found: 393.0

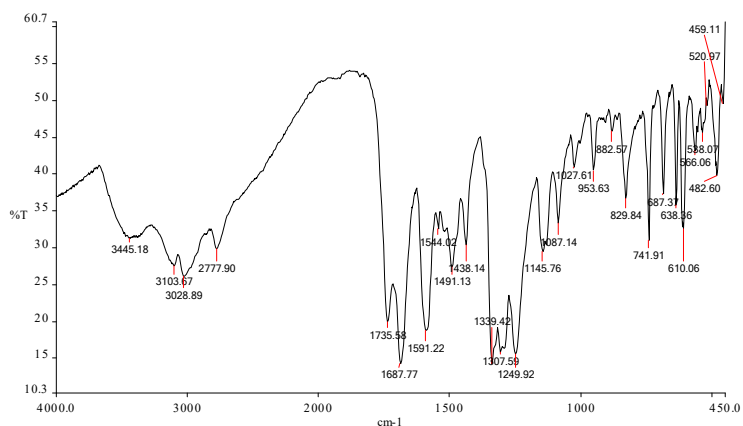


Figure S1. IR spectrum of 5a

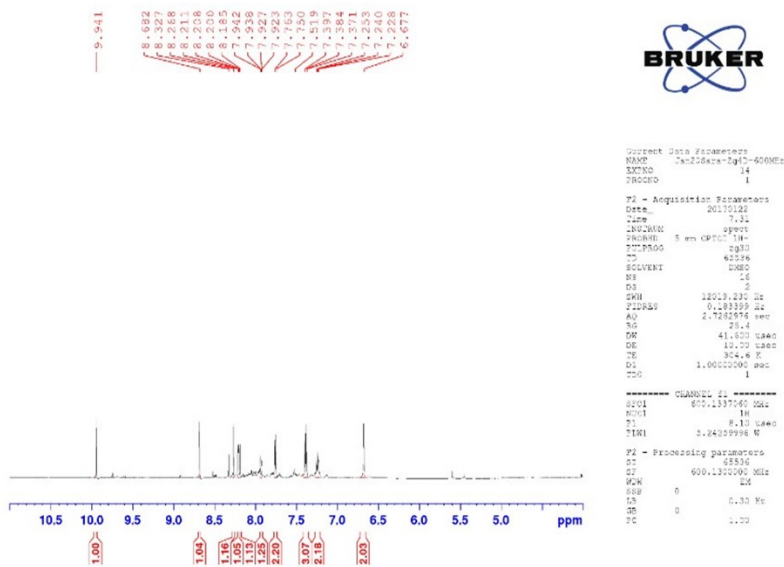


Figure S2. ¹H NMR spectrum (600 MHz, DMSO-d₆) of 5a

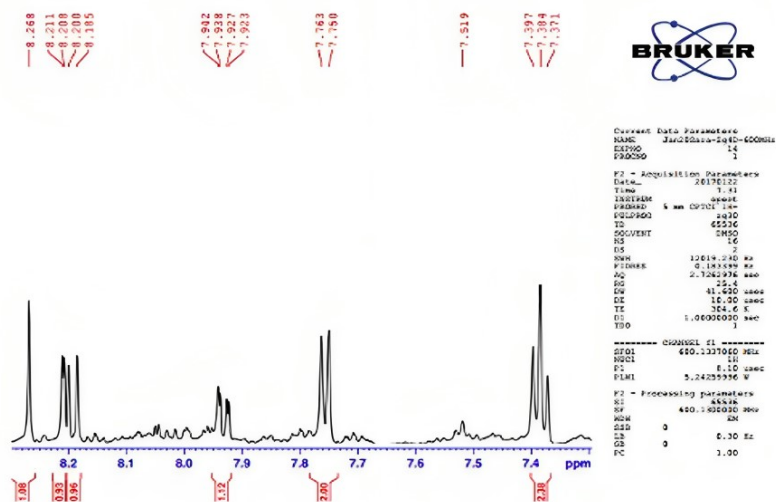


Figure S3. Expand ¹H NMR spectrum (600 MHz, DMSO-d₆) of 5a

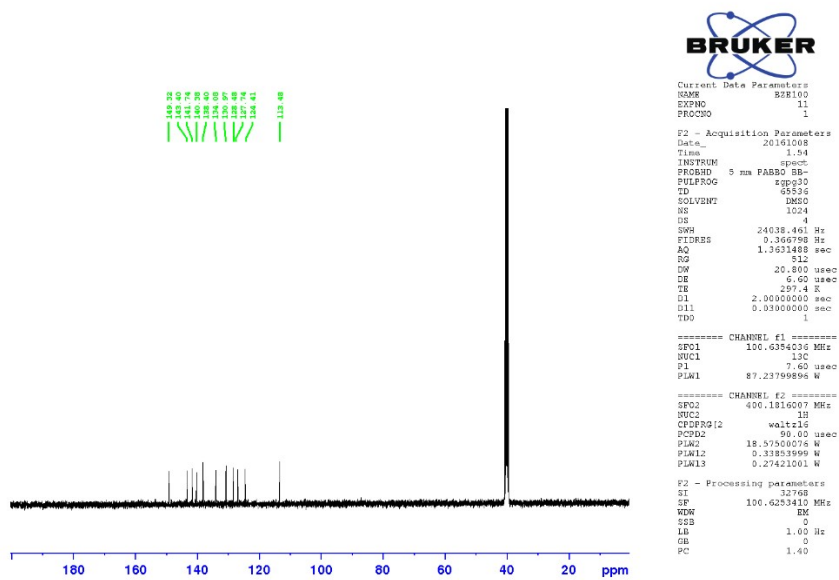


Figure S4. ¹³C NMR spectrum (100 MHz, DMSO-d₆) of 5a

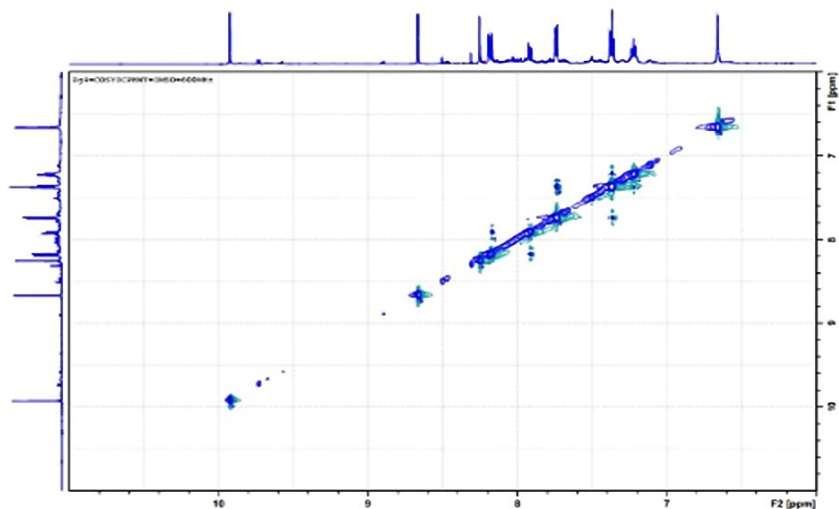


Figure S5. HH ROSY spectrum of 5a

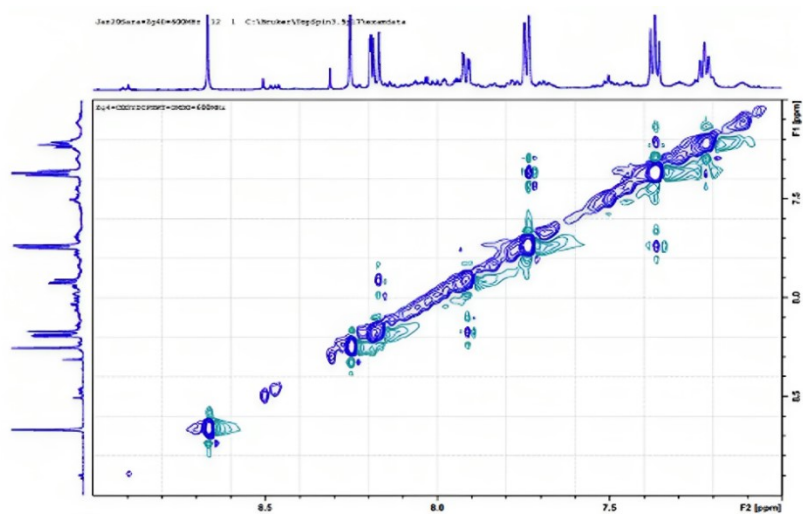


Figure S6. Expand HH ROSY spectrum of 5a

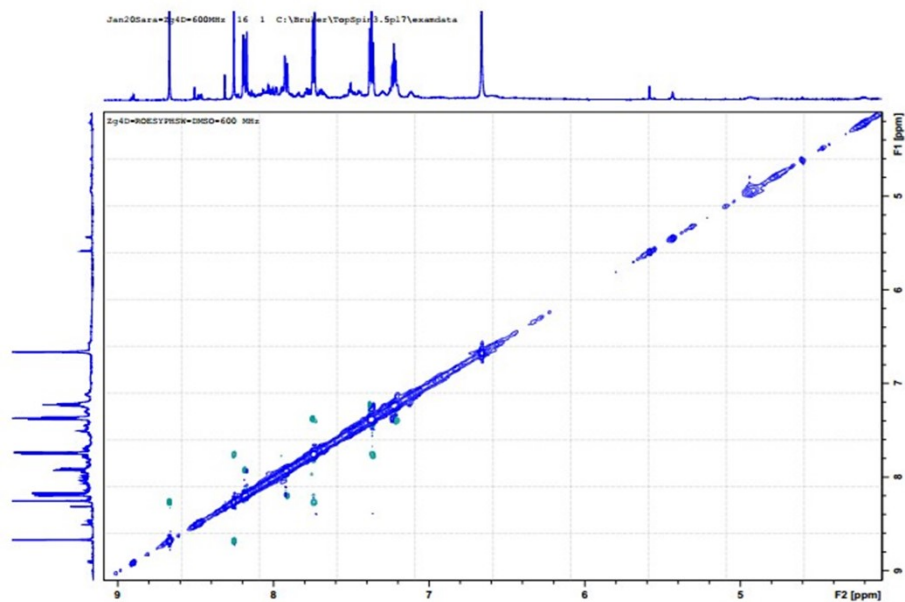


Figure S7. HH COSY spectrum of 5a

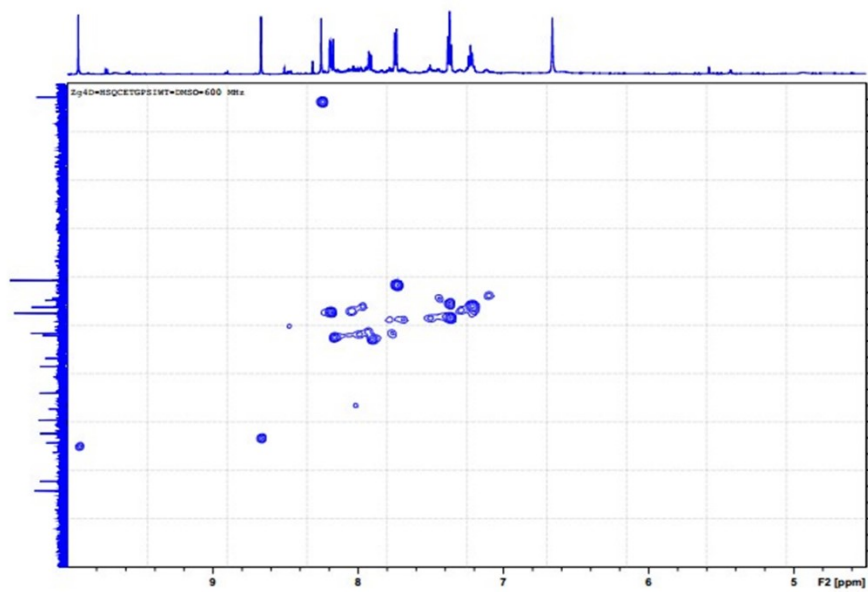


Figure S8. HSQC spectrum of 5a

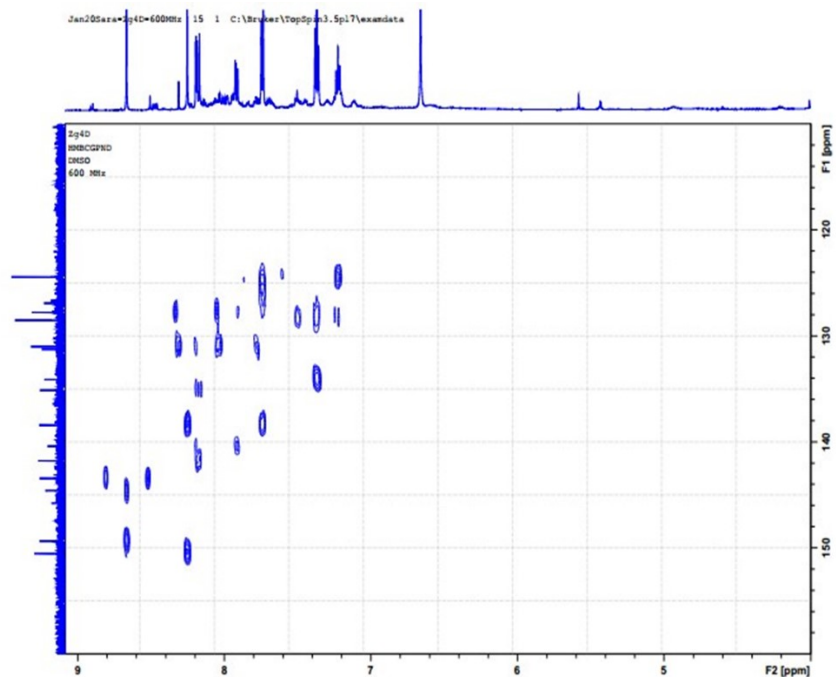


Figure S9. HMBC spectrum of **5a**

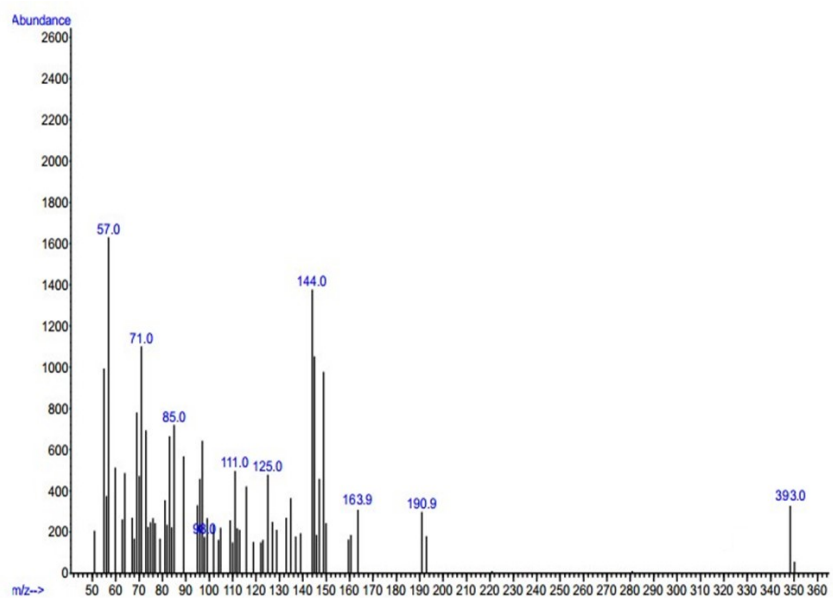
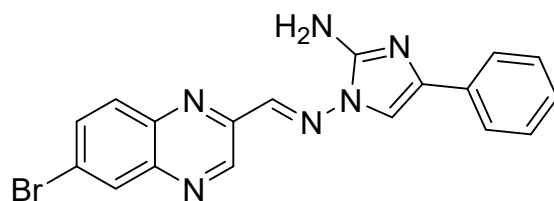


Figure S10. Mas spectrum of **5a**

(E)-1-(((6-bromoquinolin-2-yl)methylene)amino)-4-phenyl-1H-imidazol-2-amine (5b)



IR (KBr): 3400 and 3288 (NH str.), 3225, 3135 and 3054 (CH str.), 1639, 1466, 1172, 769, 695 cm^{-1} . ^1H NMR (600 MHz, DMSO-d_6) δ : 6.64 (s, 1H, NH₂), 7.21 (t, 1H, J = 7.0 Hz, 4''-H), 7.36 (ab quartet, 2H, JH_{3''}H_{4''} or H_{5''}H_{4''} = 7.6 Hz, JH_{3''}H_{2''} or H_{5''}H_{6''} = 7.6, 3''-H and 5''-H), 7.73 (d, 2H, J = 7.6 Hz, 6''-H, 2''-H), 7.93 (dd, 1H, J_{7',8'} = 8.8 and J_{7',5'} = 2.2 Hz, 7'-H), 8.13 (d, 1H, J = 8.8 Hz, 8'-H), 8.23 (s, 1H, 5-H), 8.24 (d, 1H, J = 2.2 Hz, 5'-H), 8.66 (s, 1H, 3'-H), 9.92 (s, 1H, CHN). ^{13}C NMR (150 MHz, DMSO-d_6) δ : 101.5 (C-5), 124.2 (C-2'' and C-6''), 126.7 (C-4''), 127.8 (C-3'' and C-5''), 128.4 (C-5'), 130.7 (C-8'), 131.22 (C-7'), 133.9 (C-1''), 134.8 (C-6'), 138.1 (C-4), 139.9 (C-8'a), 141.7 (C-4'a), 143.3 (C-3'), 145.0 (CHN), 148.6 (C-2'), 150.3 (C-2); MS: (m/z) M⁺ calcd. for C₁₈H₁₃BrN₆: 393.0, Found: 393.0

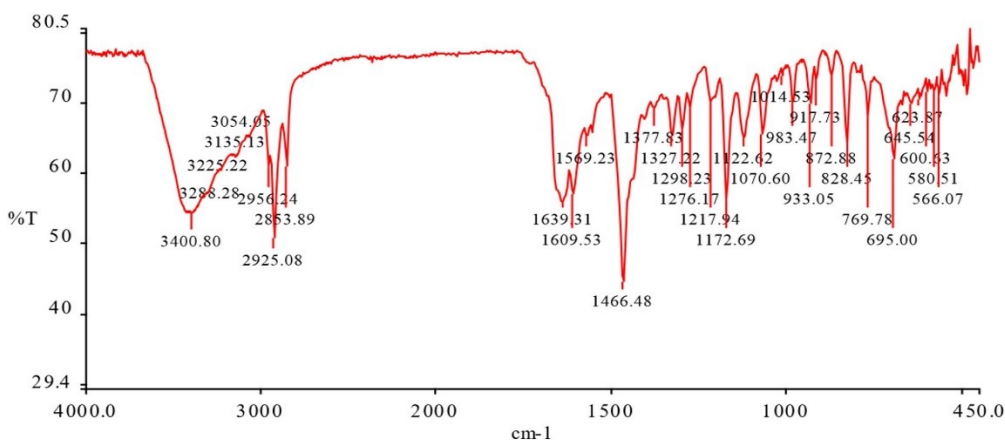


Figure S11. IR spectrum of **5b**

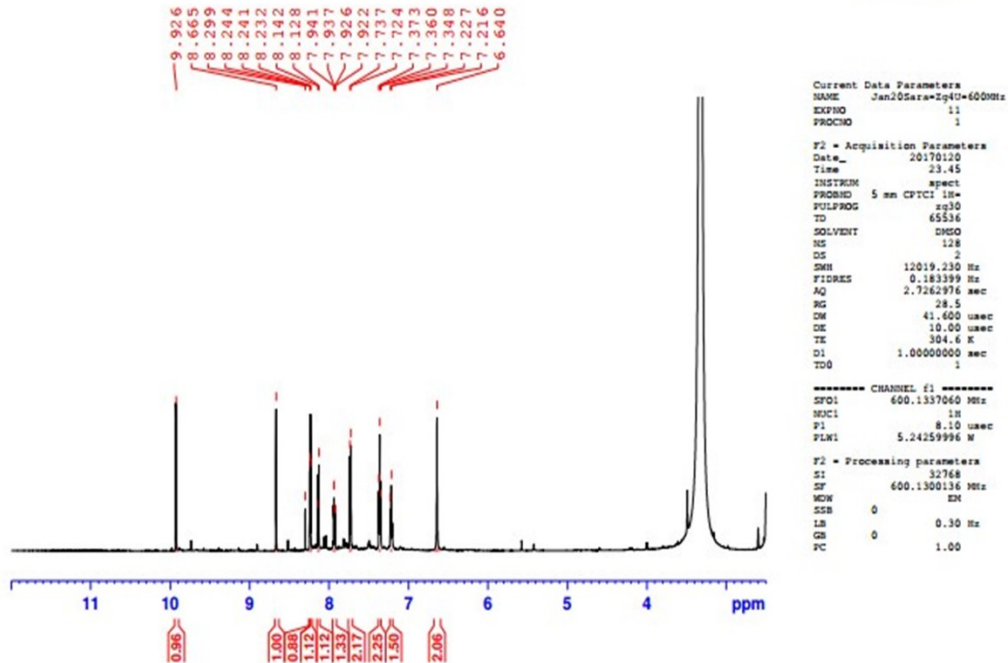


Figure S12. ¹H NMR spectrum (600 MHz, DMSO-d₆) of 5b

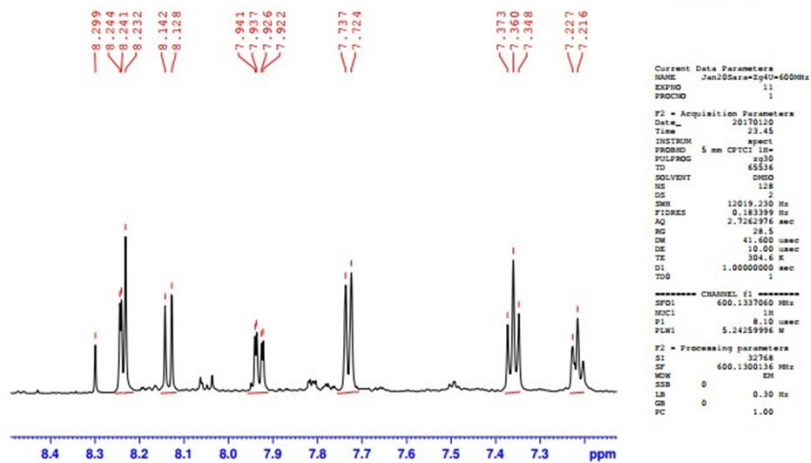


Figure S13. Expand ¹H NMR spectrum (600 MHz, DMSO-d₆) of 5b

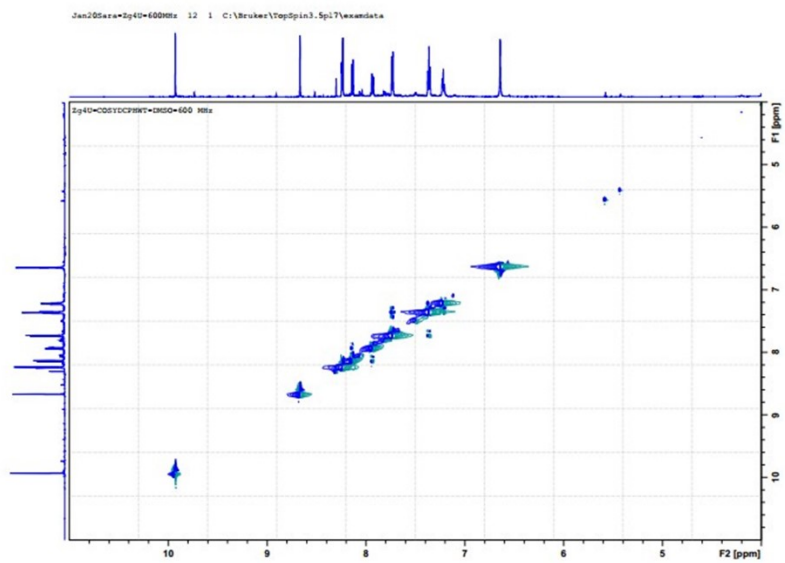


Figure S16. HH COSY spectrum of 5b

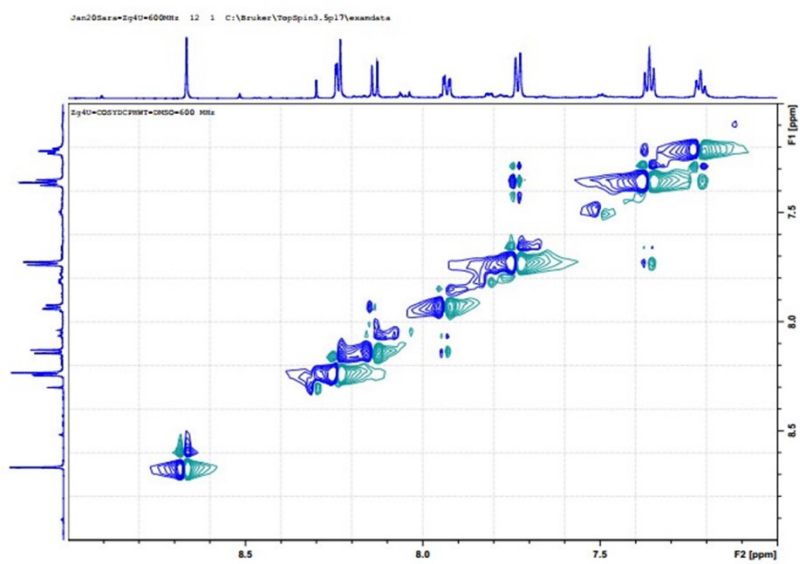


Figure S17. Expand HH COSY spectrum of 5b

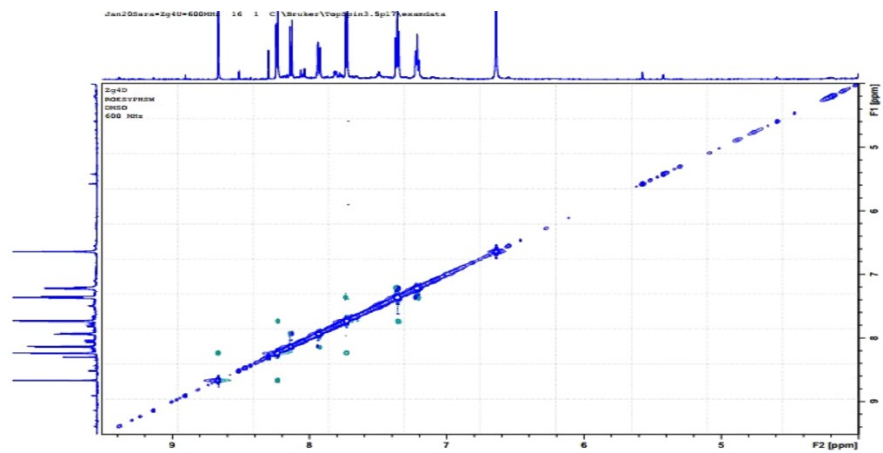


Figure S18. HH ROESY spectrum of 5b

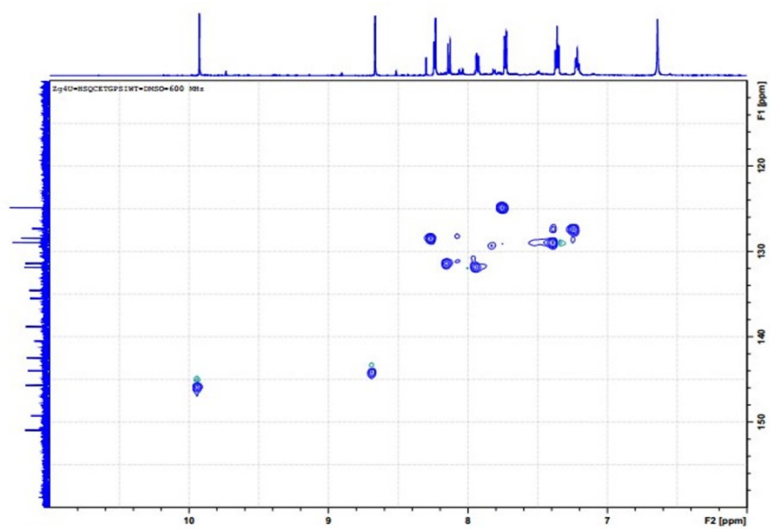


Figure S19. HSQC spectrum of 5b

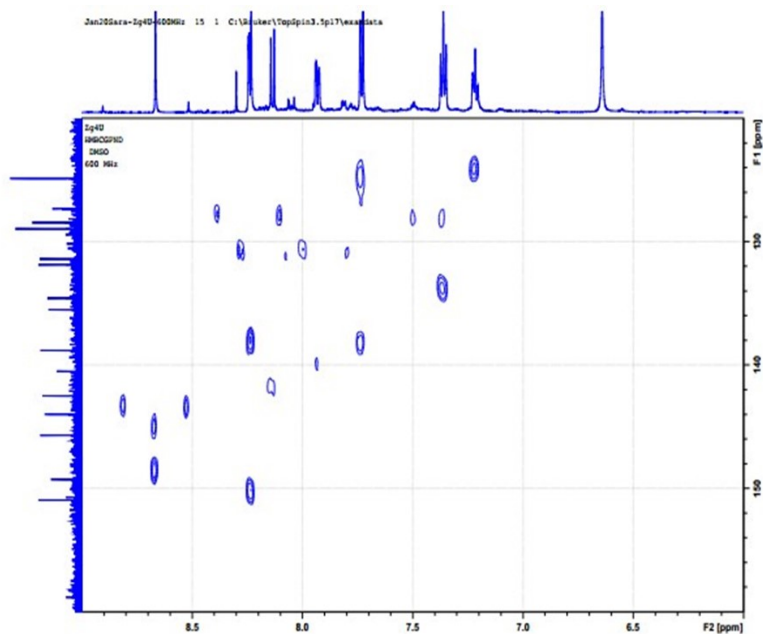


Figure S20. HMBC spectrum of 5b

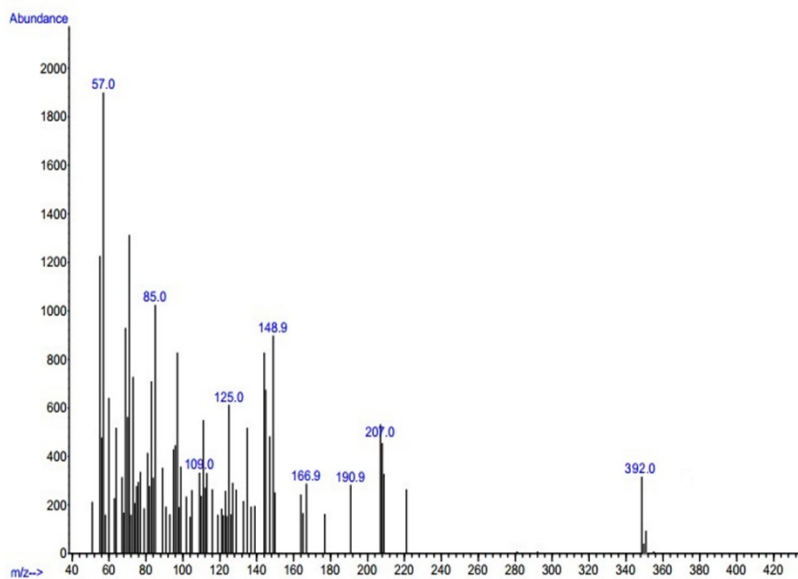


Figure S21. Mas spectrum of 5b

4.1.2.3. (E)-1-(((6-bromoquinoxalin-2-yl)methylene)amino)-4-(4-fluorophenyl)-1H-imidazol-2-amine (5c)

IR (KBr): 3420 and 3294 (NH str.), 3221, 3146 and 3061 (CH str.), 1644, 1470, 1172, 732, 675 cm^{-1} ; ^1H NMR (600 MHz, DMSO- d_6) δ : 9.92 (s, 1H, CHN), 8.64 (s, 1H, 3'-H), 8.24 (d, 1H, J =

2.2 Hz, 5'-H), 8.15 (d, 1H, J = 8.6 Hz, 8'-H), 8.23 (s, 1H, 5-H), 7.95 (dd, 1H, $J_{7',8'} = 8.6$ and $J_{7',5'} = 2.2$ Hz, 7'-H), 7.74 (ab quartet, 2H, $J_{HH} = 8.5$ Hz, $J_{HF} = 5.6$, 6''-H and 2''-H), 7.20 (ab quartet, 2H, $J_{HH} = 8.6$ Hz, $J_{HF} = 8.6$ Hz, 3''-H and 5''-H), 6.66 (s, 2H, NH₂); ¹³C NMR (150 MHz, DMSO-d₆) δ: 161.7 (C-4''), 160.4 (C-1''), 150.4 (C-2'), 148.4 (C-2), 145.0 (CH=N), 143.6 (C-3'), 141.7 (C-4'a), 139.8 (C-8'a), 137.2 (C-4), 134.9 (C-6'), 131.8 (C-7'), 130.7 (C-8'), 127.9 (C-5'), 125.8 (C-2'' and C-6''), 115.0 (C-3'' and C-5''), 101.3 (C-5); MS: (m/z) M⁺ calcd. for C₁₈H₁₂BrFN₆: 411.0, Found: 411.1

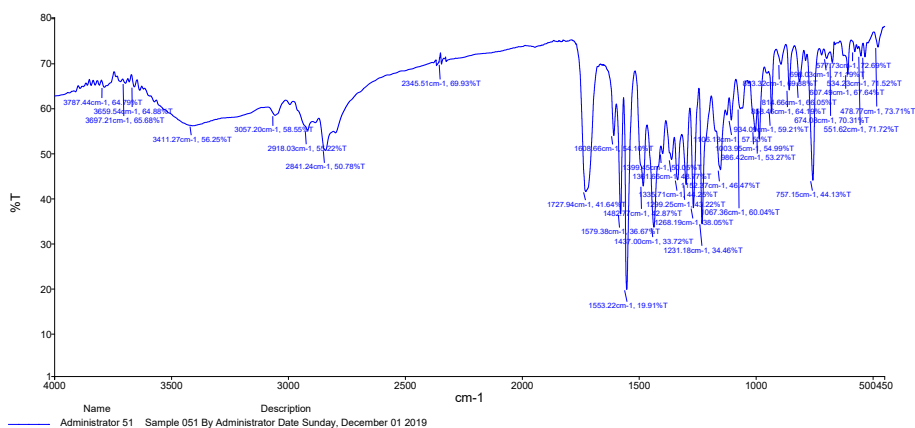
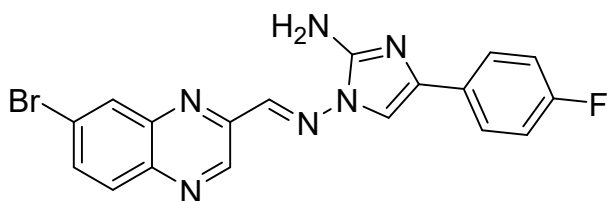


Figure S22. IR spectrum of 5c

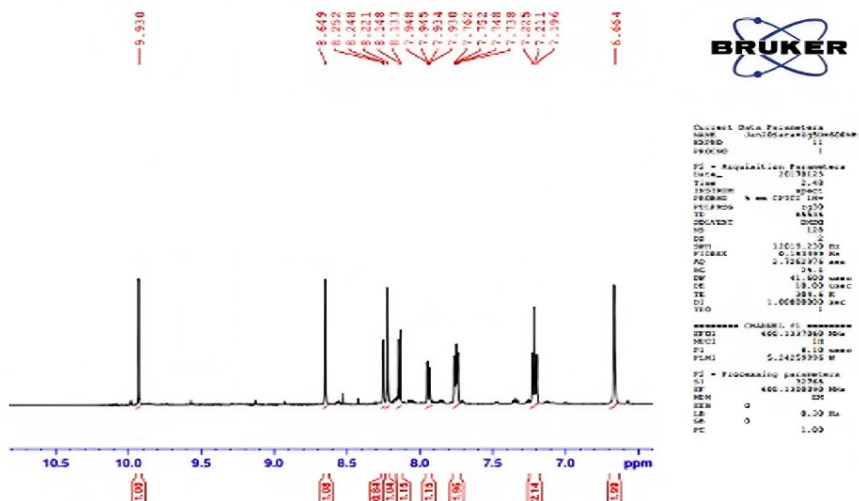


Figure S23. Expand ¹H NMR spectrum (600 MHz, DMSO-d₆) of 5c

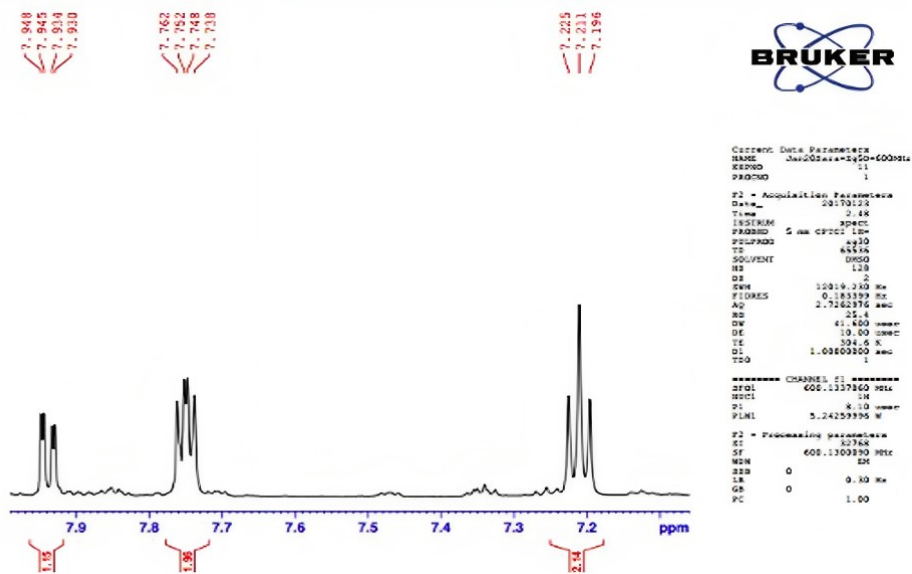
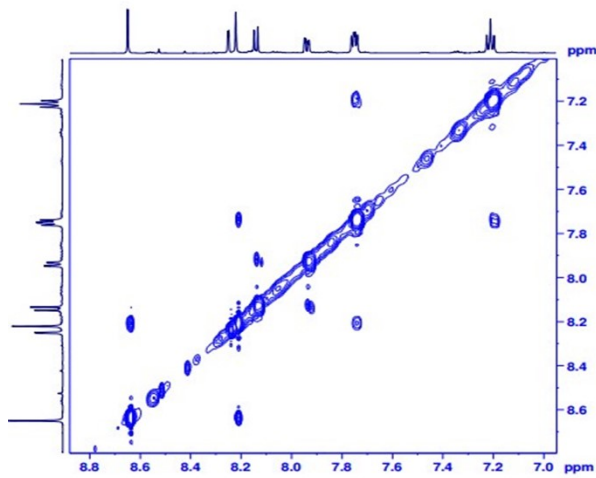


Figure S24. Expand ¹H NMR spectrum (600 MHz, DMSO-d₆) of 5c

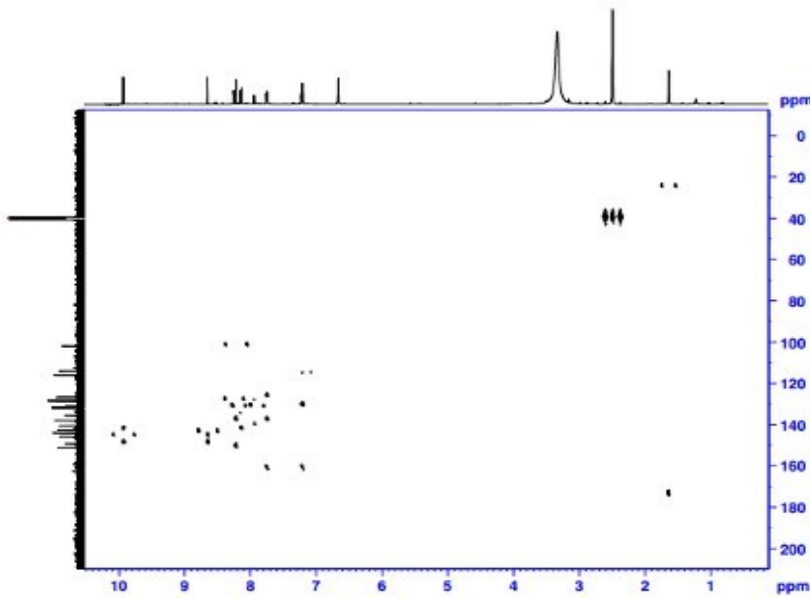


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SOLVENT: DMSO
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DS: 4
SWH: 4350.000 Hz
FIDRES: 3.051708 Hz
AQ: 0.143800 sec
RG: 655
AQ2: 10.000000 sec
RG2: 10.000000 sec
T0: 304.4 K
D1: 0.0001000 sec
d11: 0.0000000 sec
d12: 0.0000000 sec
TAS: 0.0001000 sec
L4: 1.00
F15: 200000.000000 sec
===== CHANNEL f1 =====
NUC1: 13
P1: 8.100000 sec
P17: 2000.000000 sec
P25: 84.000000 sec
PL12: 3.2433900 W
PL15: 0.50882000 W
PL17: 0.1478900 W
F1 - Acquisition parameters
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SFO: 400.1330000 MHz
F2RES: 18.828110 Hz
SF: 400.1300154 MHz
WDW: EM
SSB: 0 Hz
GB: 0
PC: 1.00
F2 - Processing parameters
SI: 32768
SF: 400.1300154 MHz
WDW: EM
SSB: 0 Hz
GB: 0
PC: 1.00
F1 - Processing parameters
SI: 65536
SF: 400.1300154 MHz
WDW: EM
SSB: 0 Hz
GB: 0
PC: 1.00
  
```

Figure S27. Expand ROSY spectrum of 5c

Figure S28. HSQC spectrum of 5c



```

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PROCNO: 1
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PROBHD: 5 mm cryoac 1H-
PULPROG: zgpg30
SOLVENT: DMSO
NS: 4
DS: 4
SWH: 4750.000 Hz
FIDRES: 3.140870 Hz
AQ: 0.14380000 sec
RG: 655
AQ2: 10.000000 sec
RG2: 10.000000 sec
T0: 304.4 K
D1: 0.0001000 sec
d11: 0.0000000 sec
d12: 0.0000000 sec
TAS: 0.0001000 sec
L4: 1.00
F15: 200000.000000 sec
===== CHANNEL f1 =====
NUC1: 13
P1: 8.100000 sec
P17: 2000.000000 sec
P25: 84.000000 sec
PL12: 3.2433900 W
PL15: 0.50882000 W
PL17: 0.1478900 W
F1 - Acquisition parameters
TD: 65536
SFO: 400.1330000 MHz
F2RES: 18.828110 Hz
SF: 400.1300154 MHz
WDW: EM
SSB: 0 Hz
GB: 0
PC: 1.00
F2 - Processing parameters
SI: 32768
SF: 400.1300154 MHz
WDW: EM
SSB: 0 Hz
GB: 0
PC: 1.00
F1 - Processing parameters
SI: 65536
SF: 400.1300154 MHz
WDW: EM
SSB: 0 Hz
GB: 0
PC: 1.00
  
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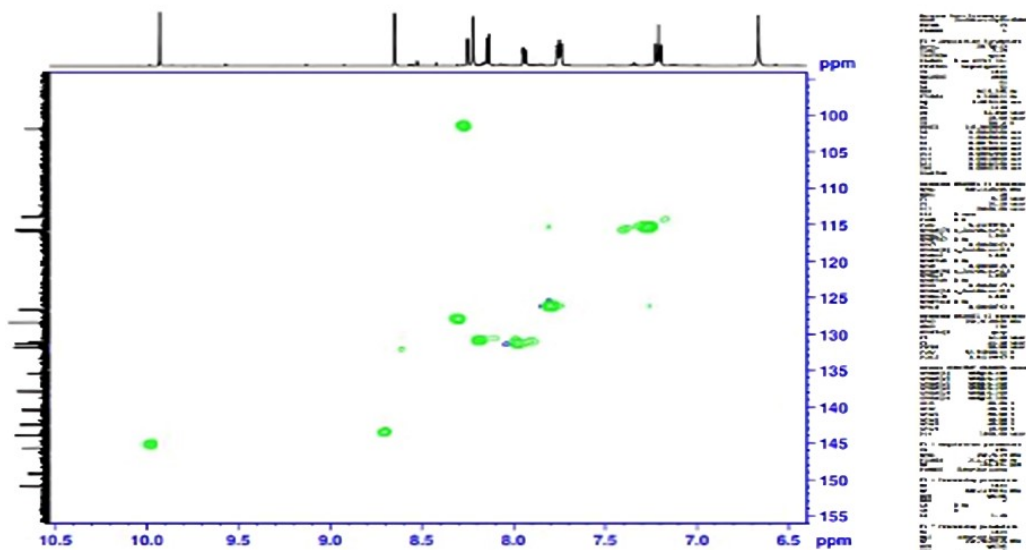


Figure S29. HMBC spectrum of 5c

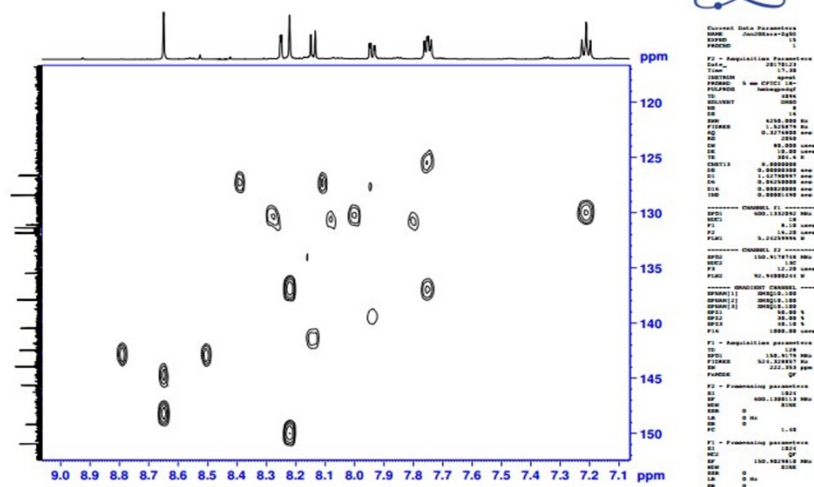


Figure S30. Expand HMBC spectrum of 5c

4.1.2.4. (E)-1-(((6-bromoquinoxalin-2-yl)methylene)amino)-4-(4-fluorophenyl)-1H-imidazol-2-amine (5d)

IR (KBr): 3420 and 3284 (NH str.), 3222, 3146 and 3062 (CH str.), 1648, 1472, 1170, 735, 676 cm^{-1} ; ^1H NMR (600 MHz, DMSO-d_6) δ : 9.93 (s, 1H, CHN), 8.65 (s, 1H, 3'-H), 8.26 (d, 1H, J = 2.2 Hz, 8'-H), 8.23 (s, 1H, 5-H), 8.15 (d, 1H, J = 8.8 Hz, 5'-H), 7.95 (dd, 1H, J_{6',5'} = 8.8 and J_{6',8'} = 2.2 Hz, 6'-H), 7.76 (ab quartet, 2H, J_{HH} = 8.4 Hz, J_{HF} = 5.7 Hz, 2''-H and 6''-H), 7.22 (ab quartet, 2H, J_{HH} = 8.8 Hz, J_{HF} = 8.8 Hz 3''-H and 5''-H), 6.66 (s, 2H, NH₂); ^{13}C NMR (150 MHz, DMSO-d_6) δ : 161.8 (C-4''), 160.4 (C-1''), 150.3 (C-2'), 148.7 (C-7'), 145.2 (CH=N), 143.3 (C-3'), 141.9 (C-8'a), 139.9 (C-4'a), 137.4 (C-4), 134.8 (C-7'), 131.3 (C-6'), 130.8 (C-5'), 127.6 (C-8'), 126.0 (C-2'' and C-6''), 115.2 (C-3'' and C-5''), 101.8 (C-5); MS: (m/z) M⁺ calcd. for $\text{C}_{18}\text{H}_{12}\text{BrFN}_6$: 410.0, Found: 410.1

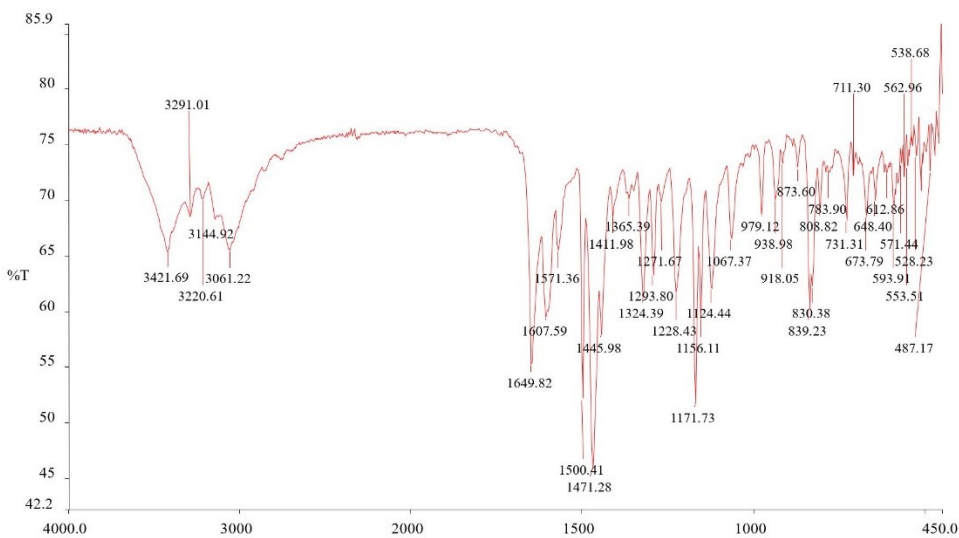
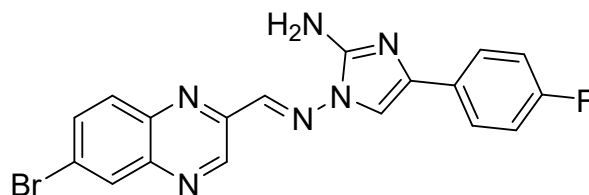


Figure S31. IR spectrum of 5d

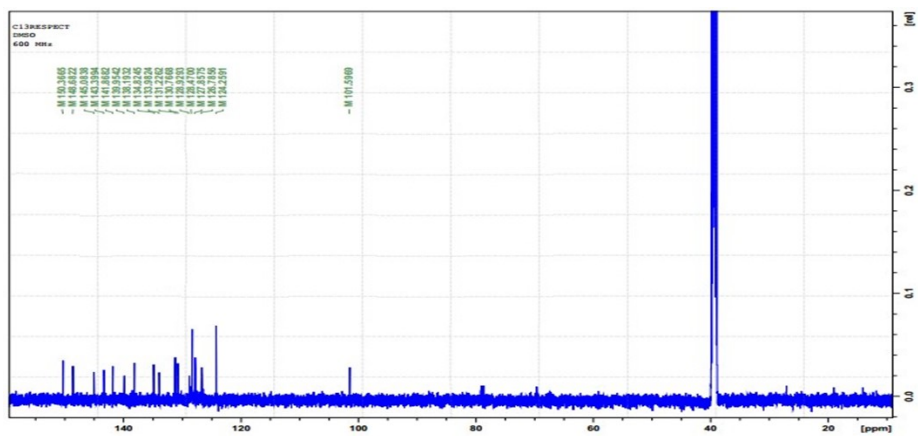


Figure S34. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 5d

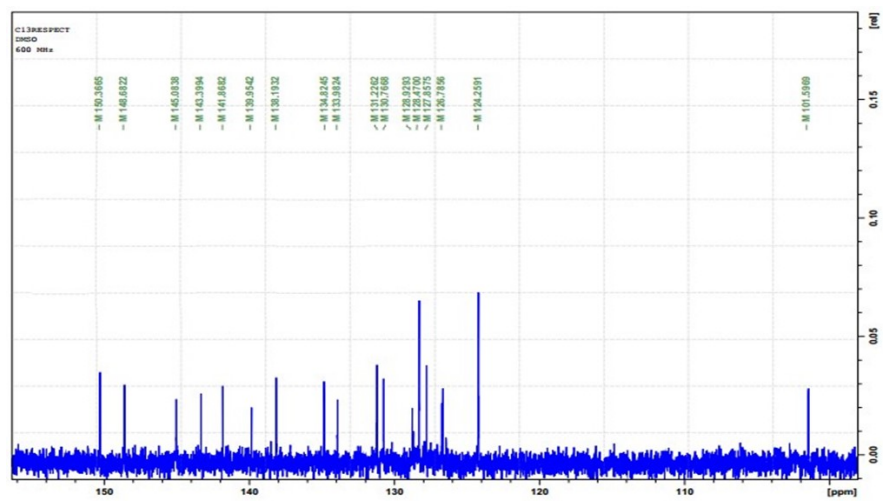
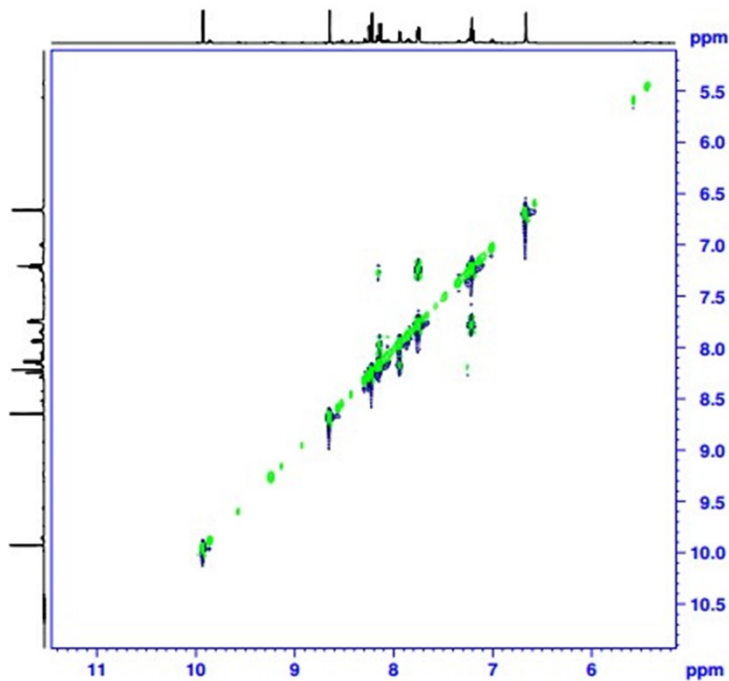


Figure S35. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 5d



```

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PROCNO: 1

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PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 4
DS 32
SWH 6329.114 Hz
FIDRES 0.1617920 Hz
AQ 0.1617920 sec
RG 32
SW 79.000 usec
DE 10.00 usec
TE 304.6 K
D0 0.0005684 sec
D1 2.0000000 sec
D11 0.0300000 sec
D12 0.0000000 sec
INQ 0.0001500 sec
L4 11.90
P15 200000.00 usec

===== CHANNEL f1 =====
NUC1 13C
P1 8.10 usec
P15 2500.00 usec
P25 84.00 usec
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PLM2 0.50883001 Hz
PLM3 0.18498999 Hz

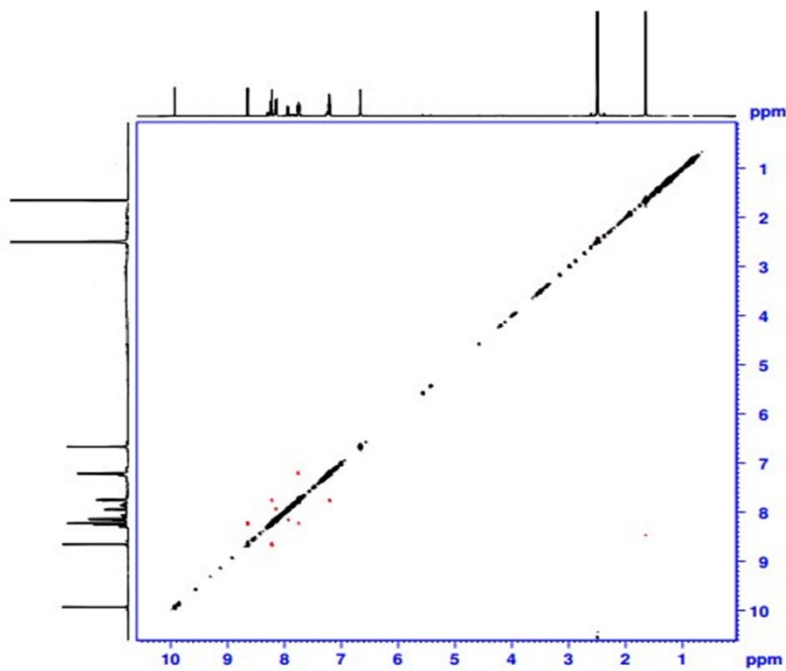
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F2 - Processing parameters
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SF 600.1300104 MHz
WDW GSINE
SSB 2
GB 0 Hz
PC 1.00

F1 - Processing parameters
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MC2 States-TPP1
SF 600.1300104 MHz
WDW GSINE
SSB 2
GB 0 Hz

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Figure S36. COSY spectrum of 5d



```

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PROCNO: 1

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PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 4
DS 32
SWH 6329.114 Hz
FIDRES 0.1617920 Hz
AQ 0.1617920 sec
RG 32
SW 79.000 usec
DE 10.00 usec
TE 304.6 K
D0 0.0005684 sec
D1 2.0000000 sec
D11 0.0300000 sec
D12 0.0000000 sec
INQ 0.0001500 sec
L4 11.90
P15 200000.00 usec

===== CHANNEL f1 =====
NUC1 13C
P1 8.10 usec
P15 2500.00 usec
P25 84.00 usec
PLM1 5.2425996 Hz
PLM2 0.50883001 Hz
PLM3 0.18498999 Hz

F1 - Acquisition parameters
TD 256
SF 600.1332 MHz
FIDRES 49.444201 Hz
SW 10.546 ppm
FIRMODE States-TPP1

F2 - Processing parameters
SI 1024
SF 600.1300104 MHz
WDW GSINE
SSB 2
GB 0 Hz
PC 1.00

F1 - Processing parameters
SI 1024
MC2 States-TPP1
SF 600.1300104 MHz
WDW GSINE
SSB 2
GB 0 Hz

```

Figure S37. ROSY spectrum of 5d

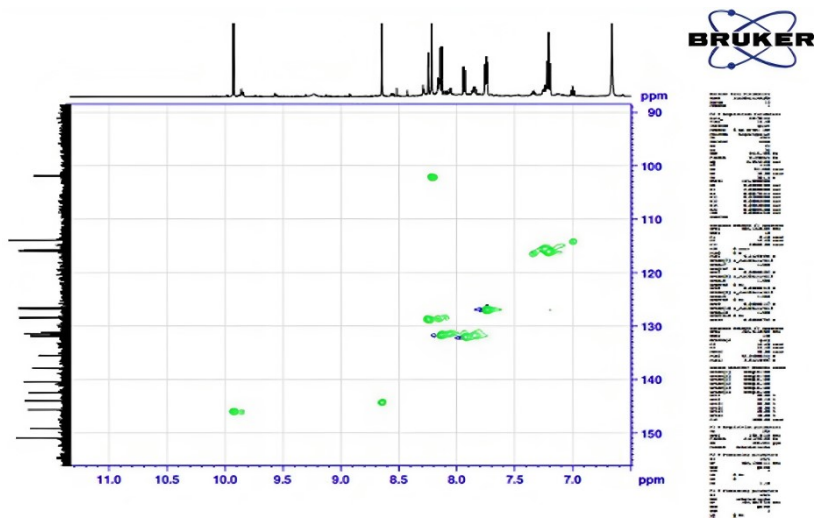


Figure S38. HMBC spectrum of 5d

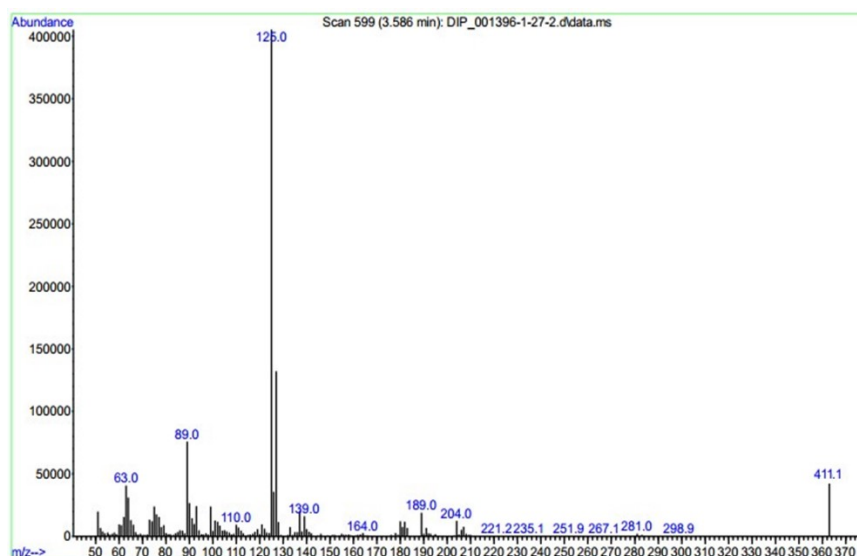


Figure S39. Mas spectrum of 5d

4.1.2.6. (E)-4-(4-bromophenyl)-1-(((7-bromoquinoxalin-2-yl)methylene)amino)-1H-imidazol-2-amine (5e)

IR (KBr): 3412 and 3317 (NH str.), 3212, 3135 and 3061 (CH str.), 1638, 1472, 1177, 725, 678 cm^{-1} ; ^1H NMR (400 MHz, DMSO-d_6) δ : 9.93 (s, 1H, CHN), 8.66 (s, 1H, 3'-H), 8.33 (s, 1H, 5-H) 8.19 (d, 1H, $J = 2.4$, 8'-H), 8.16 (d, 1H, 5'-H, $J = 8.4$ Hz), 7.92 (dd, 1H, $J_{6',5'} = 8.6$, $J_{6',8'} = 2.4$ Hz, 6'-H), 7.58 (d, 2H, $J = 8.4$ Hz, 2''-H, 6''-H), 7.55 (d, 2H, $J = 8.4$ Hz, 3''-H and 5''-H), 6.70 (s,

2H, NH₂); ¹³C NMR (100 MHz, DMSO-d₆) δ: 102.6 (C-5), 119.9 (C-4''), 128.1 (C-8'), 126.7 (C-2'' and C-6''), 131.3 (C-5'), 131.8 (C-3'' and C-5''), 132.6 (C-7'), 133.8 (C-1''), 135.5 (C-6'), 137.6 (C-4), 140.4 (C-4'a), 142.1 (C-8'a), 144.2 (C-3'), 145.6 (CHN), 149.1 (C-2'), 150.9 (C-2); MS: (m/z) M⁺ calcd. for C₁₈H₁₂ Br₂N₆: 426.0, Found: 472.0

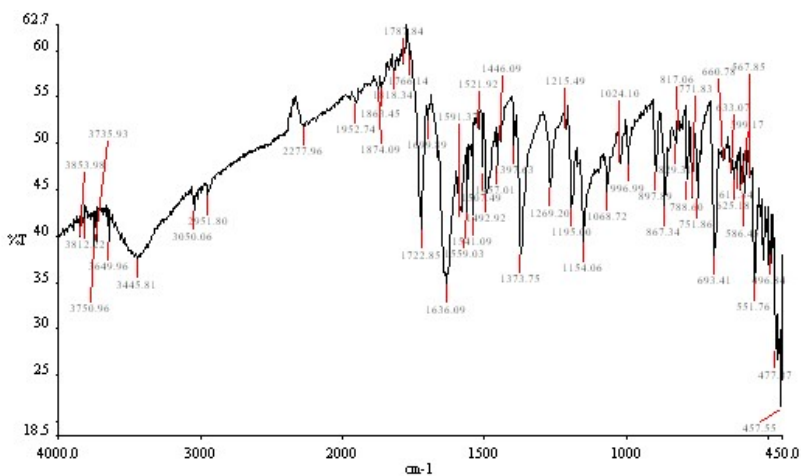
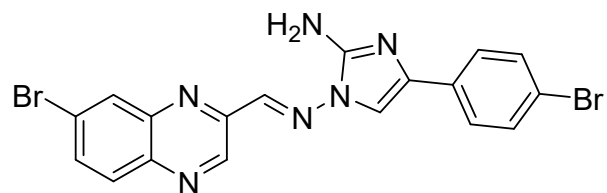


Figure S40. IR spectrum of 5e

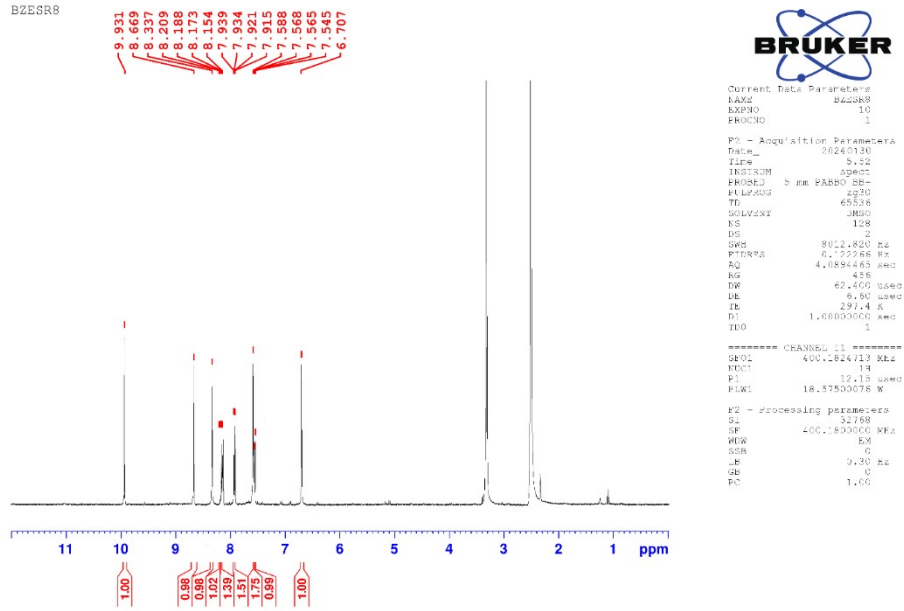


Figure S41. ¹H NMR spectrum (400 MHz, DMSO-d₆) of 5e

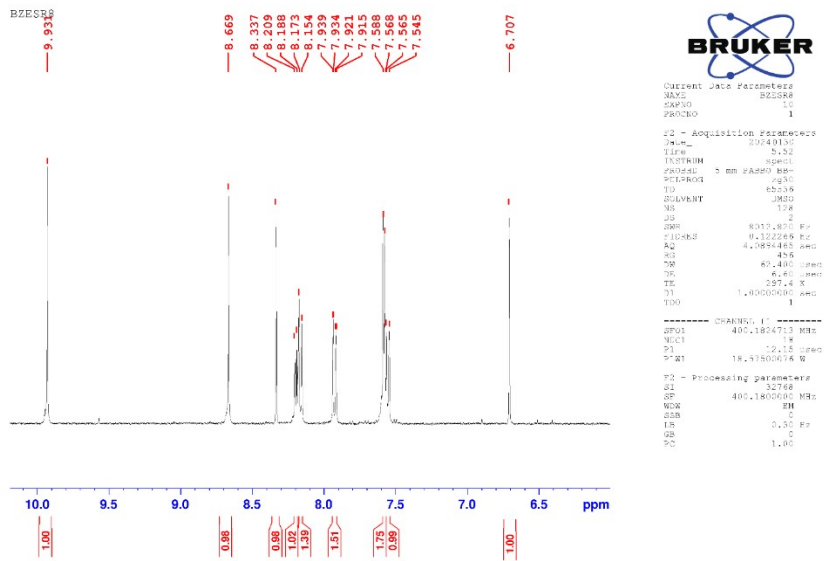


Figure S42. Expand ¹H NMR spectrum (400 MHz, DMSO-d₆) of 5e

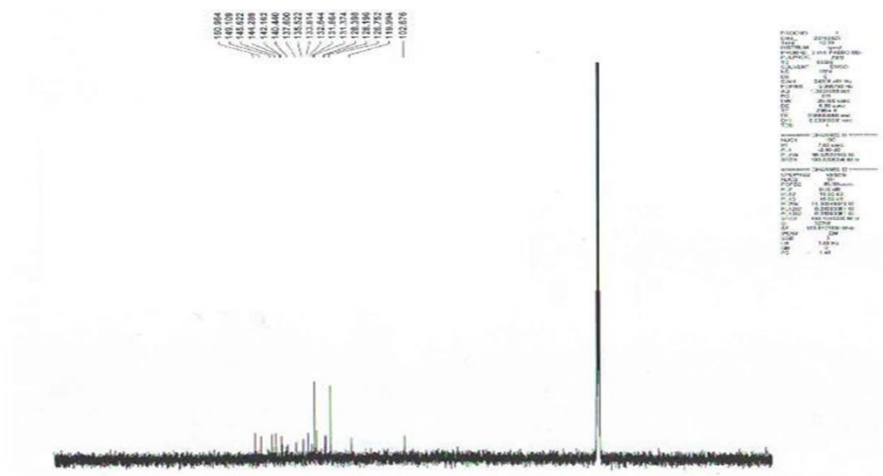


Figure S43. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of **5e**

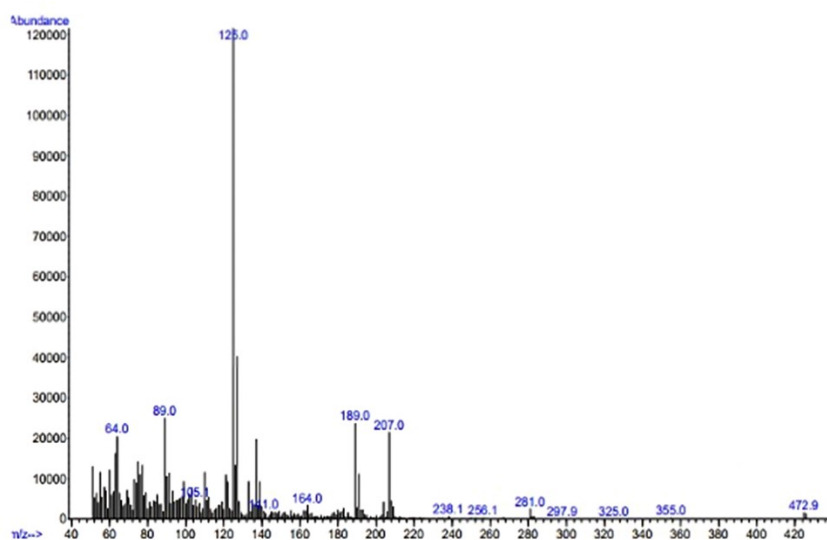


Figure S44. Mass spectrum of **5e**

4.1.2.5. (E)-4-(4-bromophenyl)-1-(((7-bromoquinoxalin-2-yl)methylene)amino)-1H-imidazol-2-amine (**5f**)

IR (KBr): 3414 and 3310 (NH str.), 3214, 3132 and 3066 (CH str.), 1635, 1472, 1174, 726, 676 cm^{-1} ; ^1H NMR (600 MHz, DMSO-d_6) δ : 9.93 (s, 1H, CHN), 8.66 (s, 1H, 3'-H), 8.31 (s, 1H, 5-H), 8.25 (d, 1H, $J = 2.4$, 5'-H), 8.14 (d, 1H, 8'-H, $J = 8.6$ Hz), 7.94 (dd, 1H, $J_{7'-8'} = 8.6$, $J_{7'-5'} = 2.4$, 7'-H), 7.58 (d, 2H, $J = 8.4$ Hz, 2''-H, 6''-H), 7.55 (d, 2H, $J = 8.4$ Hz, 3''-H and 5''-H), 6.70 (s, 2H,

NH₂); ¹³C NMR (150 MHz, DMSO-d₆) δ: 150.9 (C-2), 149.1 (C-2'), 145.6 (CHN), 144.2 (C-3'), 142.4 (C-4'a), 140.4 (C-8'a), 137.6 (C-4), 135.5 (C-6'), 133.4 (C-1''), 131.8 (C-7'), 131.4 (C-4''), 131.3 (C-8'), 129.3 (C-5'), 128.9 (C-3'' and C-5''), 126.4 (C-2'' and C-6''), 102.6 (C-5); MS: (m/z) M⁺ calcd. for C₁₈H₁₂Br₂N₆: 426.0, Found: 472.0

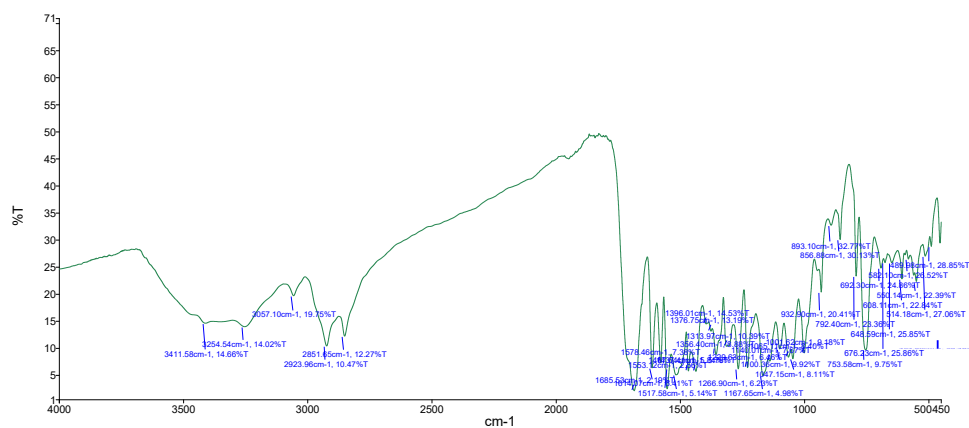
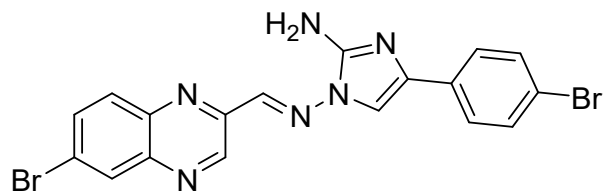


Figure S45. IR spectrum of 5f

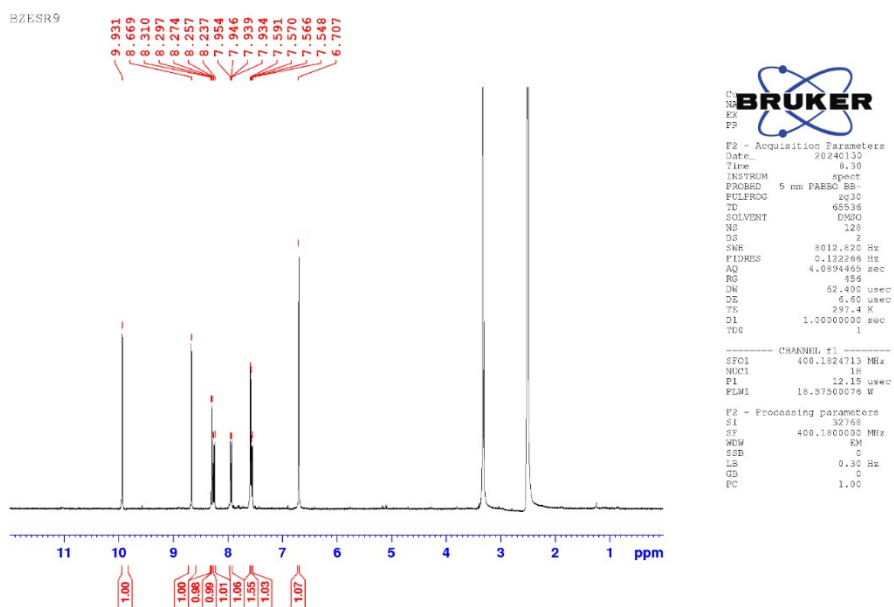


Figure S46. ¹H NMR spectrum (600 MHz, DMSO-d₆) of 5f

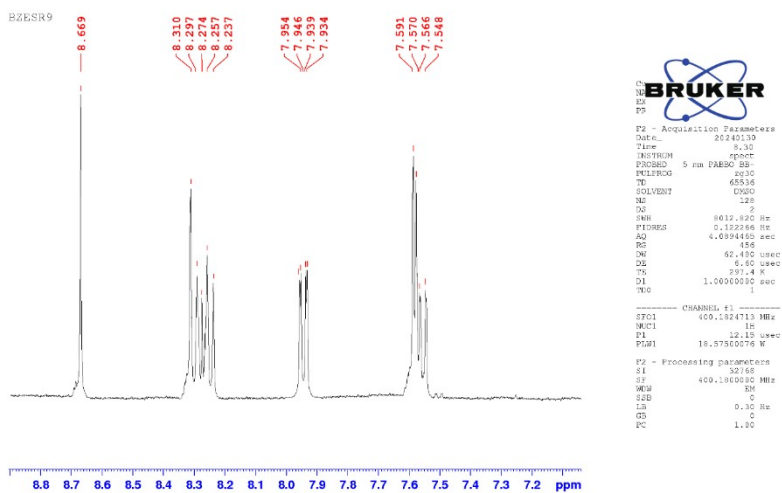


Figure S47. Expand ¹H NMR spectrum (600 MHz, DMSO-d₆) of 5f

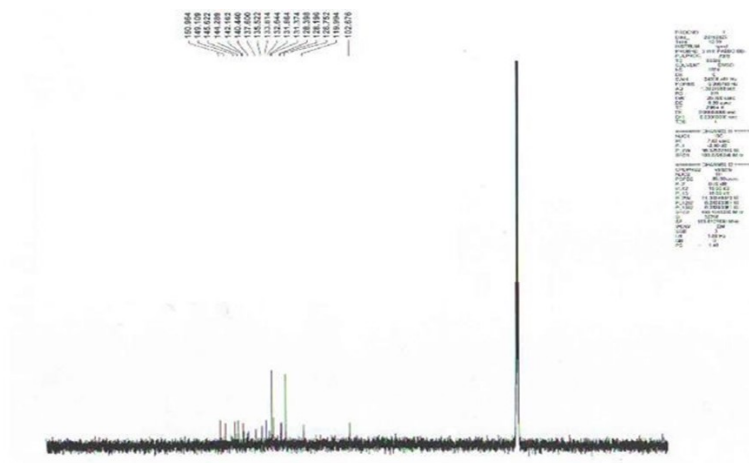


Figure S48. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of **5f**

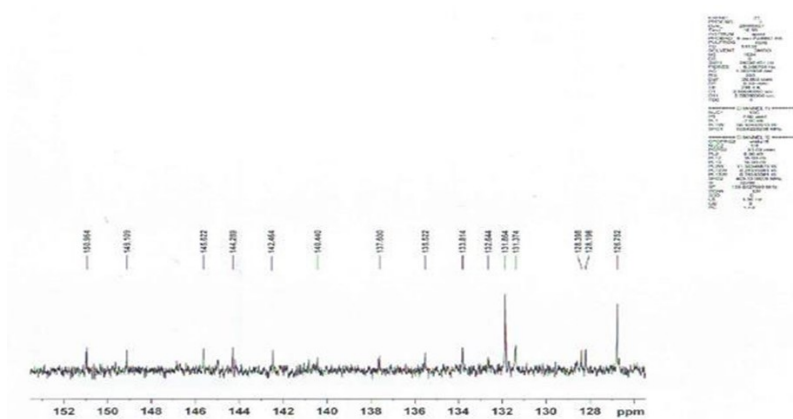


Figure S49. Expand ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of **5f**

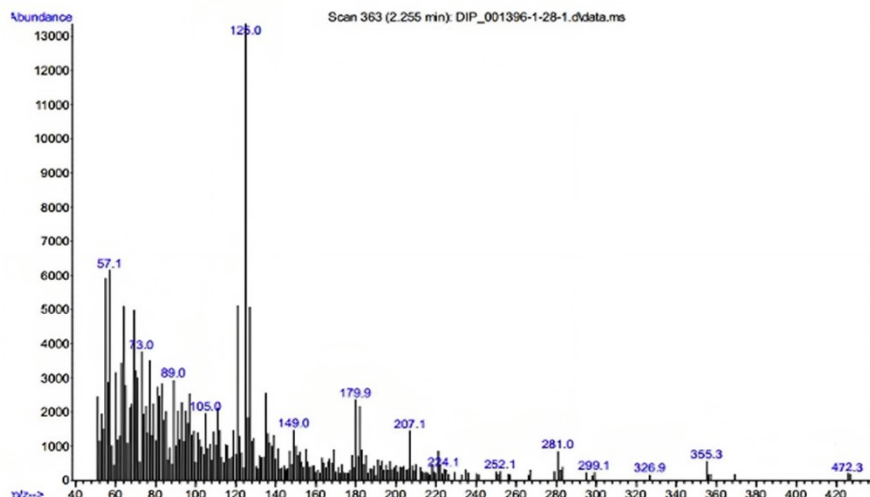
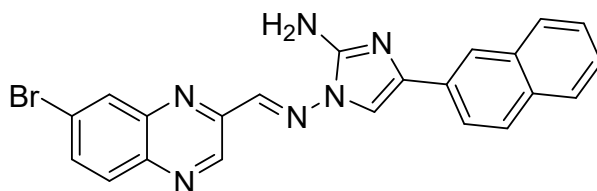


Figure S50. Mass spectrum of 5f

4.1.2.8. **(E)-1-(((7-bromoquinoxalin-2-yl)methylene)amino)-4-(naphthalen-2-yl)-1H imidazol-2-amine (5g)**

IR (KBr): 3396 and 3295 (NH str.), 3216, 3135 and 3055 (CH str.), 1627, 1466, 1169, 747, 670 cm^{-1} . ^1H NMR (400 MHz, DMSO-d_6) δ : 6.73 (s, 2H, NH_2), 7.44–7.56 (m, 2H, H-6'', H-7''), 7.86–7.94 (m, 4H, H-3'', H-4'', H-5'', H-8''), 7.96 (dd, 1H, H-6', $J_{6',5'} = 13.38$, $J_{6',8'} = 3.36$ Hz, H-6'), 8.20 (d, 1H, $J = 13.38$ Hz, 5'-H), 8.22 (d, 1H, $J = 3.36$ Hz, 8'-H), 8.26 (s, 1H, 1''-H), 8.72 (s, 1H, 3'-H), 9.96 (s, 1H, CHN). ^{13}C NMR (100 MHz, DMSO-d_6) δ : 103.1 (C-5), 122.8 (C-3''), 123.8 (C-1''), 126.0 (C-6''), 126.7 (C-7''), 128.0 (C-4''), 128.3 (C-5'' and C-8''), 128.4 (C-8'), 131.4 (C-5'), 132.0 (C-6'), 133.7 (C-1'), 135.4 (C-7'), 138.7 (C-4), 139.9 (C-4'a), 141.7 (C-8'a), 143.3 (C-3'), 146.7 (CHN), 149.4 (C-2'), 151.0 (C-2). MS: (m/z) M^+ calcd. for $\text{C}_{22}\text{H}_{15}\text{BrN}_6$: 442.0, Found: 398.



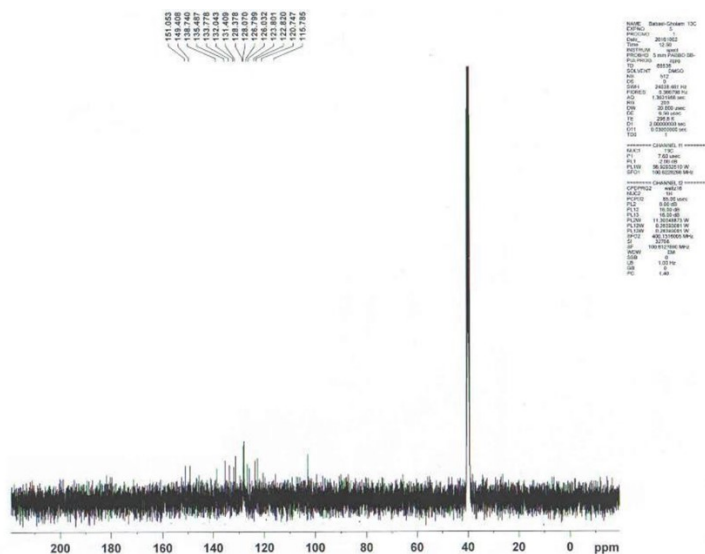


Figure S54. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of **5f**

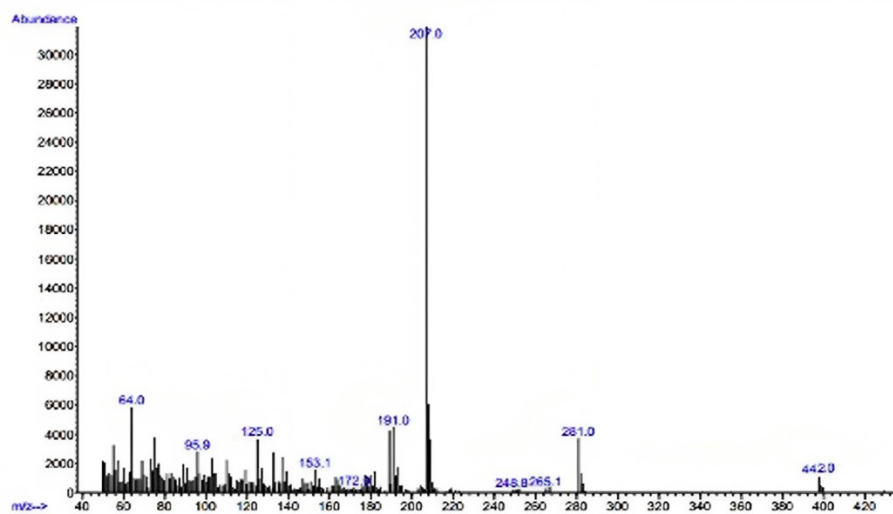


Figure S55. Mass spectrum of **5g**

4.1.2.7. (E)-1-(((7-bromoquinoxalin-2-yl)methylene)amino)-4-(naphthalen-2-yl)-1H-imidazol-2-amine (**5h**)

IR (KBr): 3394 and 3296 (NH str.), 3218, 3134 and 3052 (CH str.), 1628, 1466, 1168, 745, 671 cm^{-1} ; ^1H NMR (400 MHz, DMSO-d_6) δ : 9.97 (s, 1H, CHN), 8.72 (s, 1H, 3'-H), 8.41 (s, 1H, 5-H), 8.27 (d, 1H, $J = 3.42$ Hz, 5'-H), 8.25 (s, 1H, 1''-H), 8.17 (d, 1H, $J = 13.44$ Hz, 8'-H), 7.96 (dd,

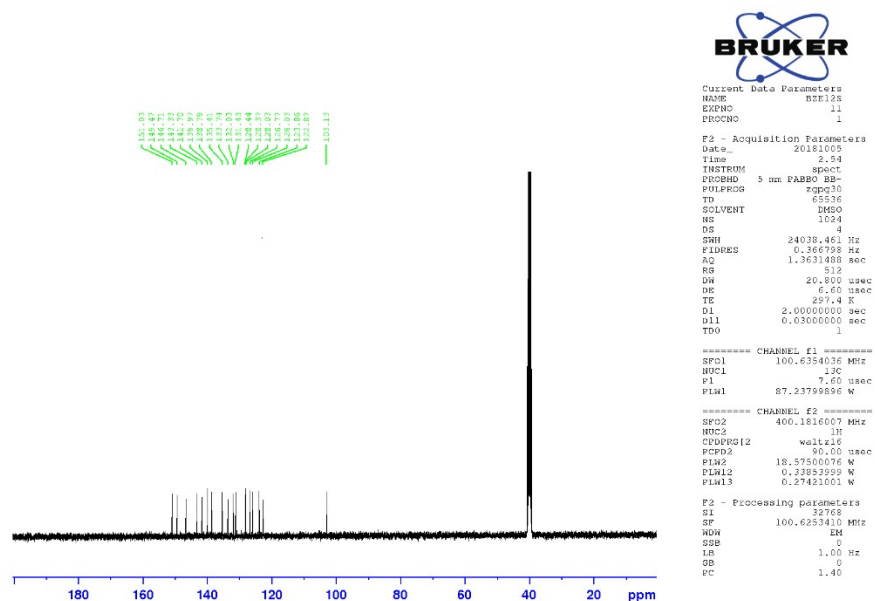


Figure S58. ^{13}C NMR spectrum (100 MHz, DMSO-d_6) of **5f**

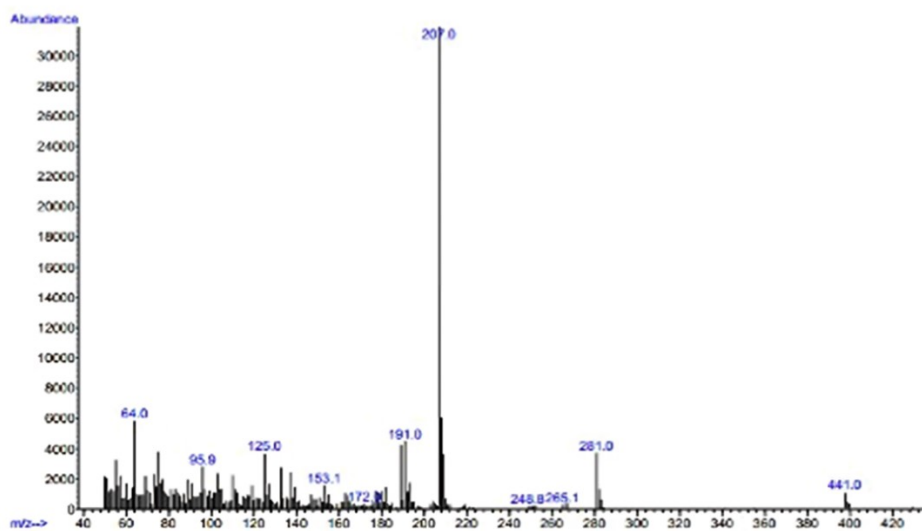


Figure S59. Mass spectrum of **5h**

4.1.2.10. (E)-1-(((7-bromoquinoxalin-2-yl)methylene)amino)-4-(4-methoxyphenyl)-1H-imidazol-2-amine (**5i**)

IR (KBr): 3434 and 3250 (NH str.), 3136 and 3082 (CH str.), 1626, 1463, 1170, 736, 670 cm^{-1} ;
 ^1H NMR (400 MHz, DMSO-d_6) δ : 9.93 (s, 1H, CHN), 8.62 (s, 1H, 3'-H), 8.19 (s, 1H, 5-H), 8.08 (d, 1H, $J = 2.3$ Hz, 8'-H), 7.97 (d, 1H, $J = 8.8$ Hz, 5'-H), 7.92 (dd, 1H, $J_{6',8'} = 2.3$ and $J_{6',5'} = 8.8$

Hz, 6'-H), 7.68 (d, 2H, J = 8.8, 2''-H and 6''-H), 6.96 (d, 2H, J = 8.8, 3''-H and 5''-H), 6.62 (s, 2H, NH₂), 3.78 (s, 3H, Me); ¹³C NMR (100 MHz, DMSO-d₆) δ: 158.8 (C-4''), 150.8 (C-2), 149.2 (C-2'), 144.9 (C-3'), 143.2 (C-8'a), 145.6 (CHN), 142.3 (C-7'), 140.4 (C-4), 135.4 (C-6'), 138.8 (C-4'a), 131.7 (C-5'), 128.3 (C-8'), 127.1 (C-1''), 126.1 (C-2'' and C-6''), 114.3 (C-3'' and C-5''), 100.6 (C-5), 55.5 (C-Me); MS: (m/z) M⁺ calcd. for C₁₉H₁₅BrN₆O: 378.1, Found: 423.0

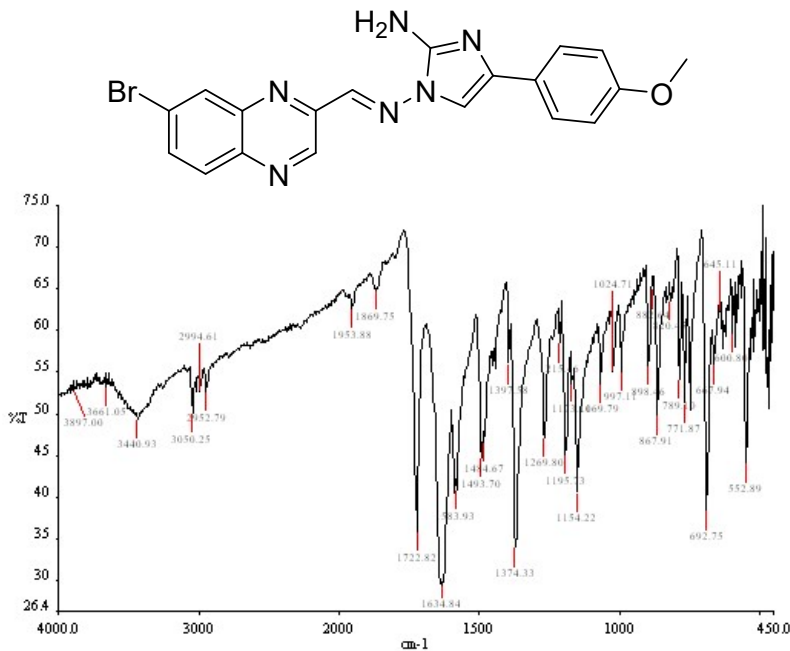
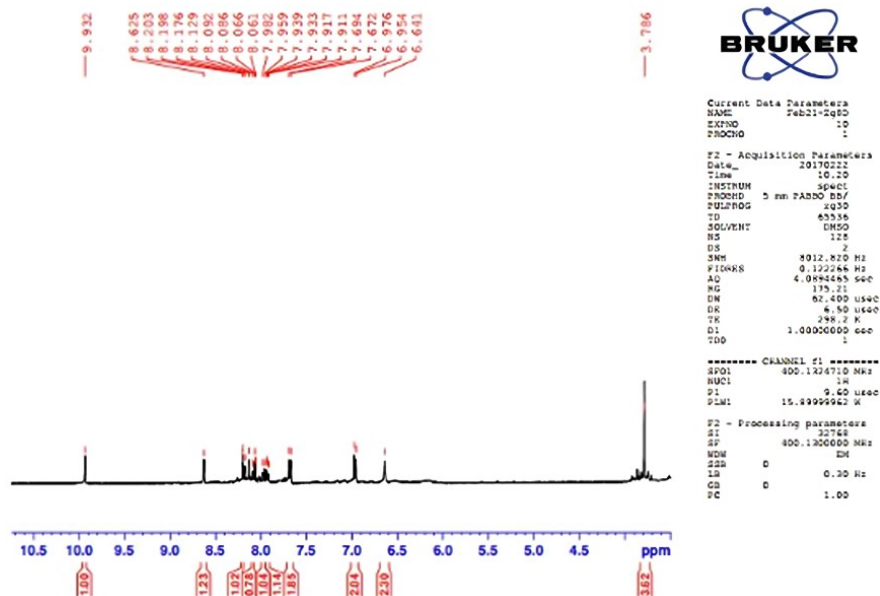


Figure S60. IR spectrum of 5h



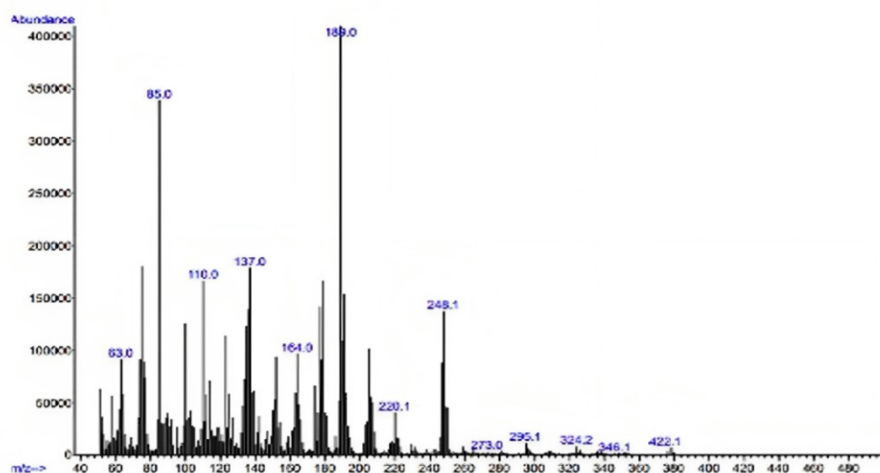
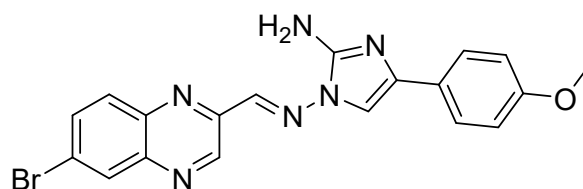


Figure S64. Mass spectrum of 5i

4.1.2.9.(E)-1-(((7-bromoquinoxalin-2-yl)methylene)amino)-4-(4-methoxyphenyl)-1H-imidazol-2-amine (5j)

IR (KBr): 3434 and 3250 (NH str.), 3136 and 3080 (CH str.), 1626, 1463, 1174, 737, 676 cm^{-1} ; ^1H NMR (600 MHz, DMSO-d_6) δ : 9.93 (s, 1H, CHN), 8.63 (s, 1H, 3'-H), 8.26 (d, 1H, $J = 2.2$ Hz, 5'-H), 8.15 (d, 1H, $J = 8.9$ Hz, 8'-H), 8.11 (s, 1H, 5-H), 7.95 (dd, 1H, $J_{7',8'} = 8.9$ Hz and $J_{7',5'} = 2.2$ Hz, 7'-H), 7.68 (d, 2H, $J = 8.8$, 2''-H and 6''-H), 6.96 (d, 2H, $J = 8.8$, 3''-H and 5''-H), 6.63 (s, 2H, NH_2), 3.78 (s, 3H, Me); ^{13}C NMR (150 MHz, DMSO-d_6) δ : 158.8 (C-4''), 150.8 (C-2), 149.2 (C-2'), 145.6 (CHN), 144.9 (C-3'), 143.2 (C-4'a), 142.1 (C-6'), 140.4 (C-4), 138.8 (C-8'a), 135.4 (C-7'), 131.5 (C-8'), 128.1 (C-5'), 127.1 (C-1''), 126.1 (C-2'' and C-6''), 114.3 (C-3'' and C-5''), 100.6 (C-5), 55.5 (C-Me); MS: (m/z) M^+ calcd. For $\text{C}_{19}\text{H}_{15}\text{BrN}_6\text{O}$: 378.1, Found: 423.0



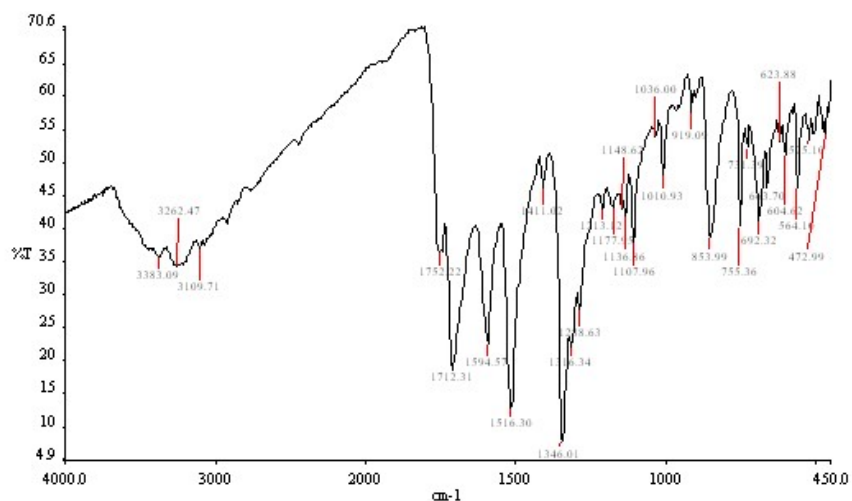


Figure S65. IR spectrum of 5j

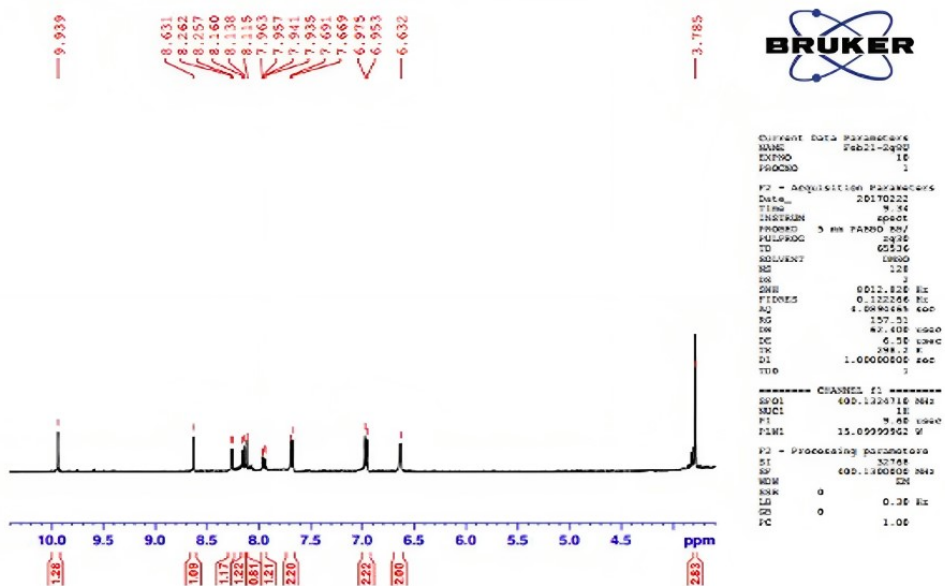


Figure S66. Expand ¹H NMR spectrum (600 MHz, DMSO-d₆) of 5j

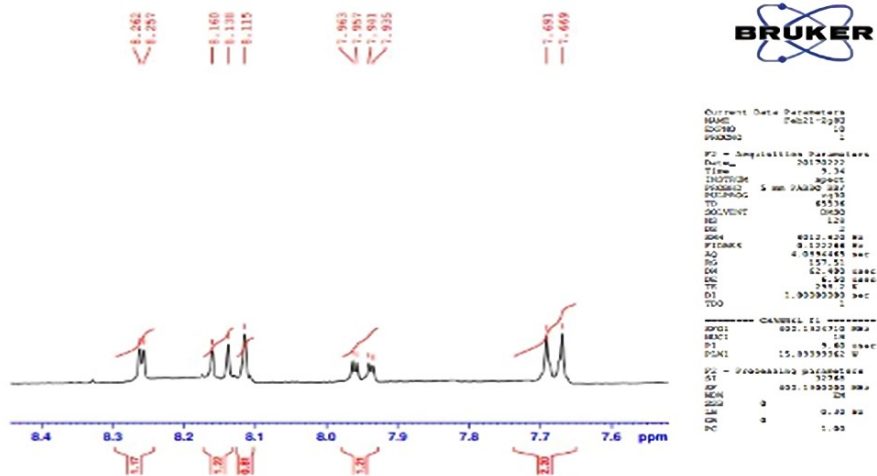


Figure S67. Expand ¹H NMR spectrum (600 MHz, DMSO-d₆) of 5j

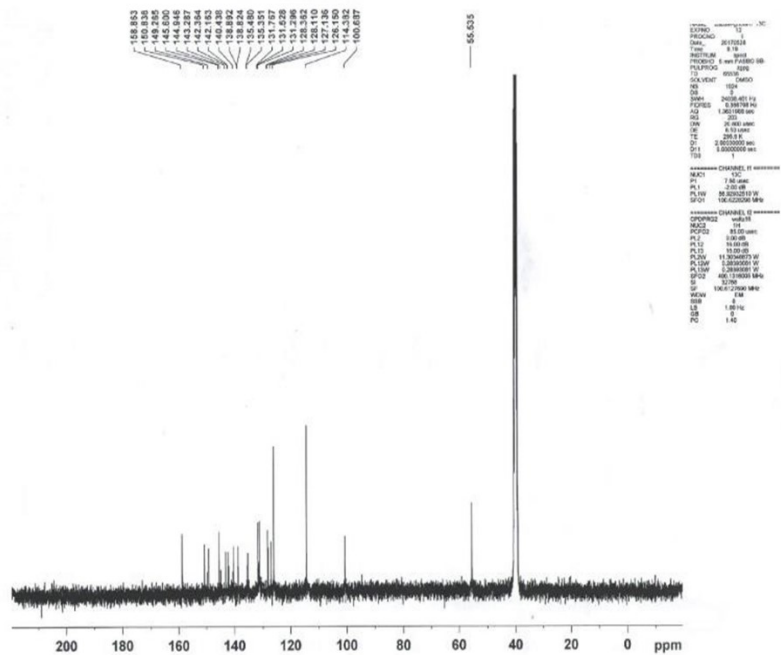


Figure S68. ¹³C NMR spectrum (100 MHz, DMSO-d₆) of 5f

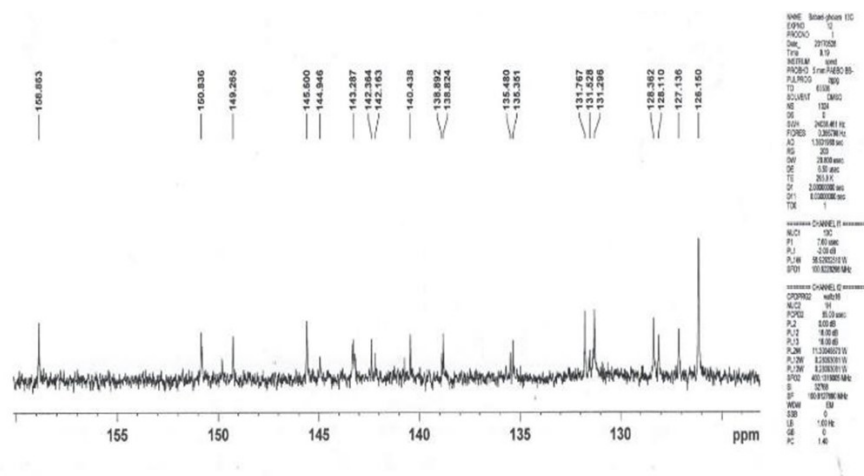


Figure S69. ^{13}C NMR spectrum (100 MHz, DMSO-d_6) of **5f**

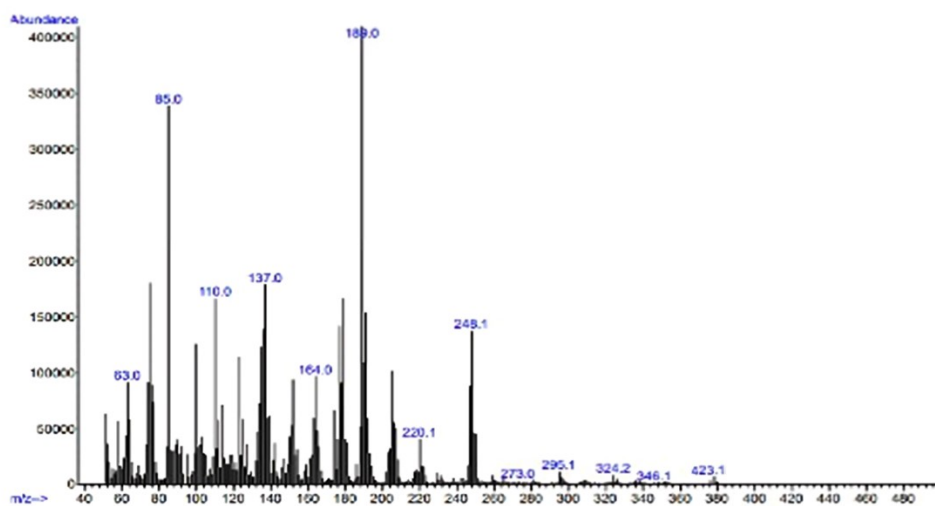


Figure S70. Mass spectrum of **5j**

4.1.2.12. (E)-4-(4-chlorophenyl)-1-(((7-bromoquinoxalin-2-yl)methylene)amino)-1H-imidazol-2-amine (**5k**)

IR (KBr): 3434 and 3302 (NH str.), 3226, 3138 and 3034 (CH str.), 1662, 1468, 1174, 828, 729 cm^{-1} ; ^1H NMR (400 MHz, DMSO-d_6) δ : 9.94 (s, 1H, CHN), δ : 8.67 (s, 1H, 3'-H), δ : 8.32 (s, 1H, 5-H), 8.21 (d, 1H, $J = 3.42$ Hz, 8'-H), 8.19 (d, 1H, $J = 13.38$ Hz, 5'-H), 7.93 (dd, 1H, $J_{6',5'} = 13.38$, $J_{6',8'} = 3.42$ Hz, 6'-H), 7.75 (d, 2H, $J = 12.76$ Hz, 2''-H, 6''-H), 7.44 (d, 2H, $J = 12.76$ Hz, 3''-H and 5''-H), 6.71 (s, 2H, NH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ : 150.9 (C-2), 149.1 (C-

2'), 145.6 (CHN), 144.2 (C-3'), 142.4 (C-8'a), 140.4 (C-4'a), 137.6 (C-4), 135.5 (C-7'), 133.4 (C-1'), 131.8 (C-6'), 131.4 (C-4''), 131.3 (C-5'), 130.7 (C-8'), 128.9 (C-3'' and C-5''), 126.4 (C-2'' and C-6''), 102.6 (C-5); MS: (m/z) M⁺ calcd. for C₁₈H₁₂BrClN₆: 382.0, Found: 425.0

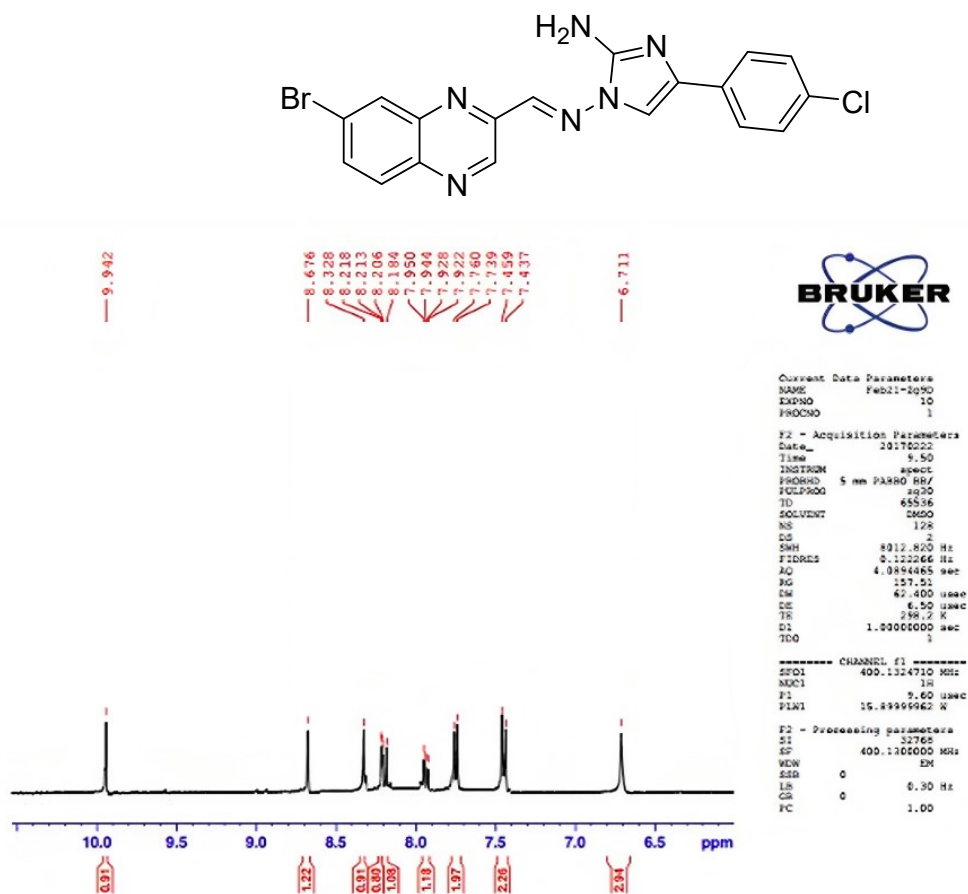
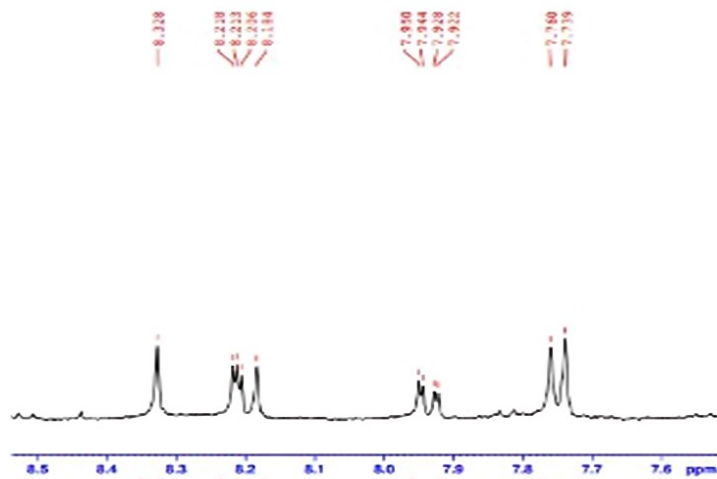


Figure S71. Expand ¹H NMR spectrum (400 MHz, DMSO-d₆) of 5k



```

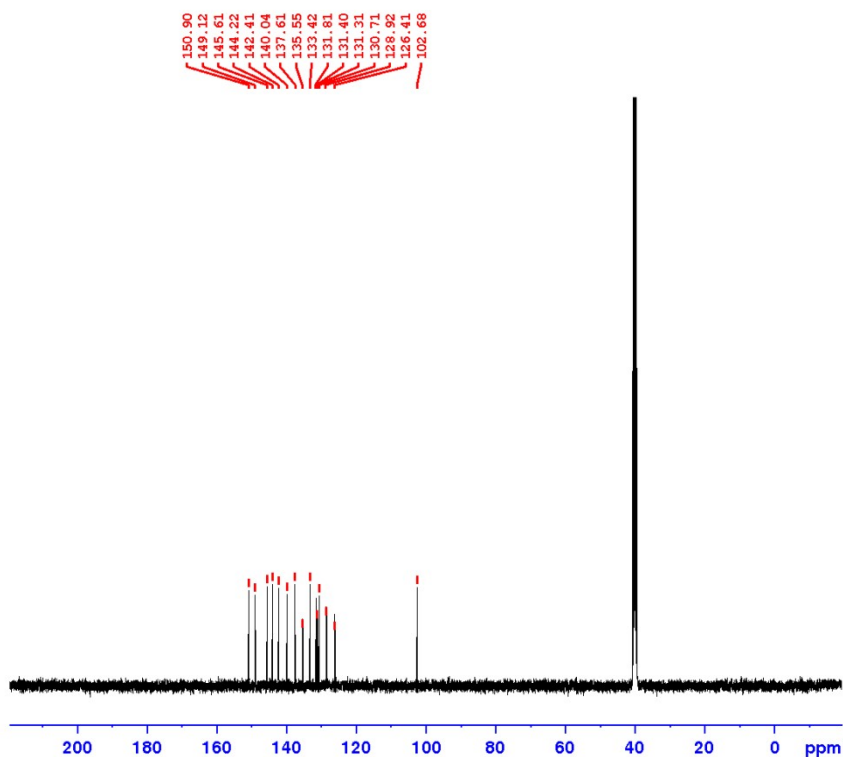
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EXPNO    10
PROCNO   1

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DS        4
SWH       24038.461 Hz
FIDRES    0.366798 Hz
AQ        1.3631488 sec
RG        1030
DW        20.800 usec
DE        6.60 usec
TE        297.4 K
D1        2.0000000 sec
D11       0.0300000 sec
TD0       1

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SFO1     400.1424710 MHz
NUC1     1H
PCPD2    waltz16
PCPD2    90.00 usec
PLW1     18.57500076 W
PLW2     0.33853999 W
PLW3     0.27421001 W

F2 - Processing parameters
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SF        400.1424710 MHz
WDW       EM
SSB       0
LB        1.00 Hz
GB        0
PC        1.40
  
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Figure S72. Expand ¹H NMR spectrum (400 MHz, DMSO-d₆) of 5k



```

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PROCNO   1

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NS        1024
DS        4
SWH       24038.461 Hz
FIDRES    0.366798 Hz
AQ        1.3631488 sec
RG        1030
DW        20.800 usec
DE        6.60 usec
TE        297.4 K
D1        2.0000000 sec
D11       0.0300000 sec
TD0       1

===== CHANNEL f1 =====
SFO1     100.6254036 MHz
NUC1     13C
F1       7.60 usec
PLW1     87.23799896 W

===== CHANNEL f2 =====
SFO2     400.1816007 MHz
NUC2     1H
CPDPRG2  waltz16
PCPD2    90.00 usec
PLW2     18.57500076 W
PLW12    0.33853999 W
PLW13    0.27421001 W

F2 - Processing parameters
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SF        100.6253410 MHz
WDW       EM
SSB       0
LB        1.00 Hz
GB        0
PC        1.40
  
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Figure S73. ¹³C NMR spectrum (100 MHz, DMSO-d₆) of 5k

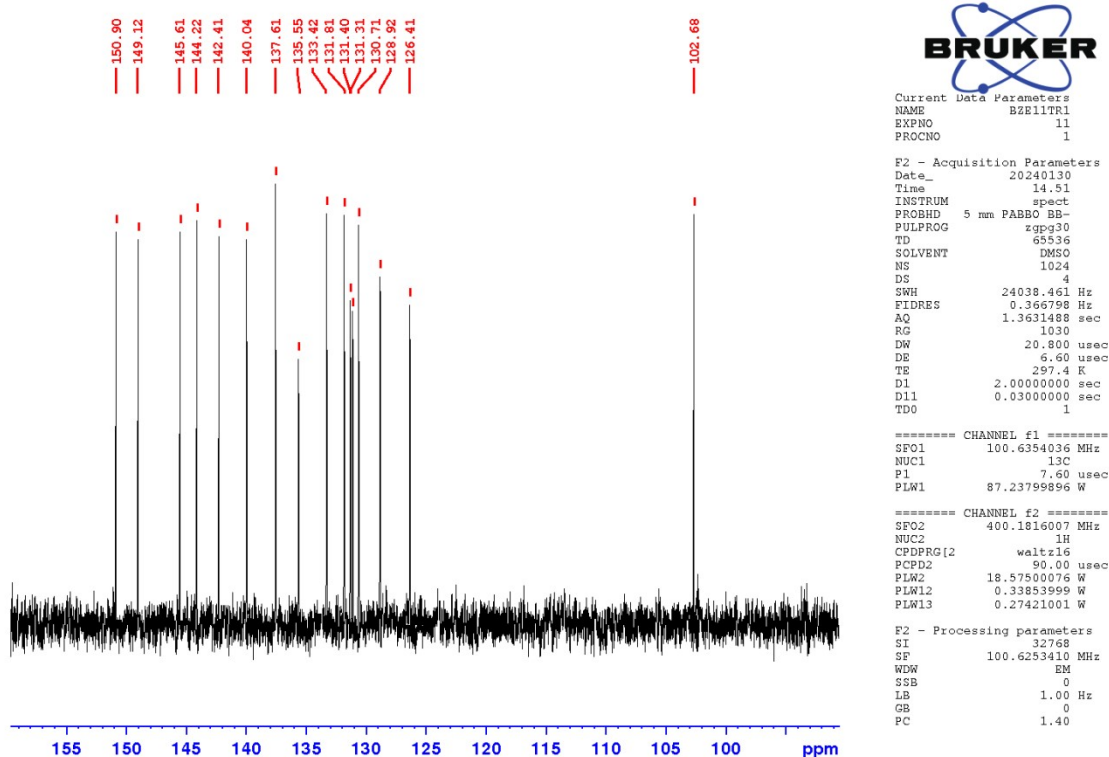


Figure S74. Expand ^{13}C NMR spectrum (100 MHz, DMSO-d_6) of **5k**

(E)-4-(4-chlorophenyl)-1-(((6-bromoquinoxalin-2-yl)methylene)amino)-1H-imidazol-2-amine(5l**)**

IR (KBr): 3436 and 3300 (NH str.), 3224, 3139 and 3035 (CH str.), 1660, 1465, 1171, 827, 727 cm^{-1} ; ^1H NMR (400 MHz, DMSO-d_6) δ : 9.94 (s, 1H, CHN), δ : 8.68 (s, 1H, 3'-H), δ : 8.31 (s, 1H, 5-H), 8.26 (d, 1H, $J = 3.42$, 5'-H), 8.16 (d, 1H, $J = 13.36$ Hz, 8'-H), 7.95 (dd, 1H, $J_{7',8'} = 13.38$, $J_{7',5'} = 3.42$ Hz, 7'-H), 7.74 (d, 2H, $J = 12.78$ Hz, 2''-H and 6''-H), 7.44 (d, 2H, $J = 12.78$ Hz, 3''-H and 5''-H), 6.69 (s, 2H, NH₂). ^{13}C NMR (100 MHz, DMSO-d_6) δ : 102.6 (C-5), 126.4 (C-2'' and C-6''), 128.9 (C-3'' and C-5''), 129.3 (C-5'), 131.3 (C-8'), 131.4 (C-4''), 131.8 (C-7'), 133.4 (C-1''), 135.5 (C-6'), 137.6 (C-4), 140.4 (C-8'a), 142.4 (C-4'a), 144.2 (C-3'), 145.6 (CHN), 149.1 (C-2'), 150.9 (C-2). $\text{C}_{18}\text{H}_{12}\text{Cl}_2\text{N}_6$; MS: (m/z) M⁺ calcd. for $\text{C}_{18}\text{H}_{12}\text{BrCl}_2\text{N}_6$: 382.0, Found: 425.0

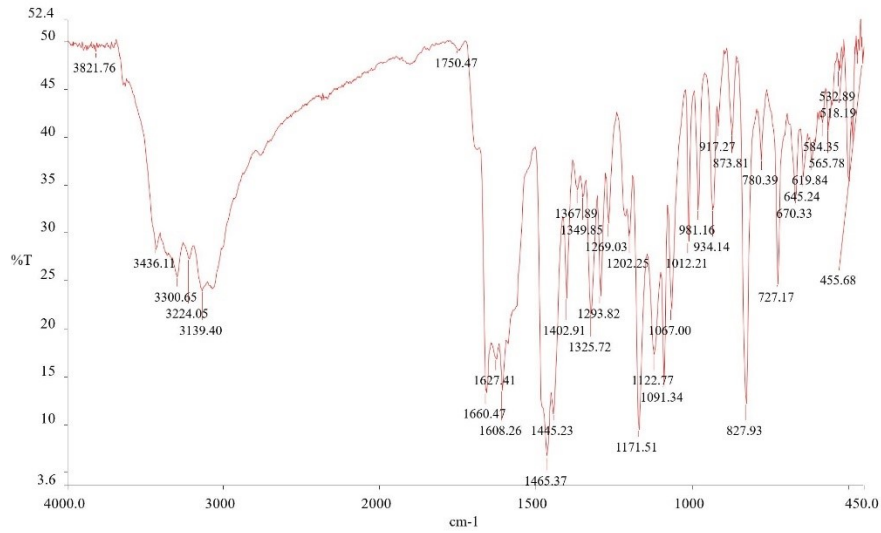
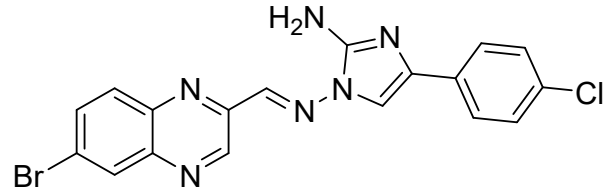


Figure S75. IR spectrum of 51

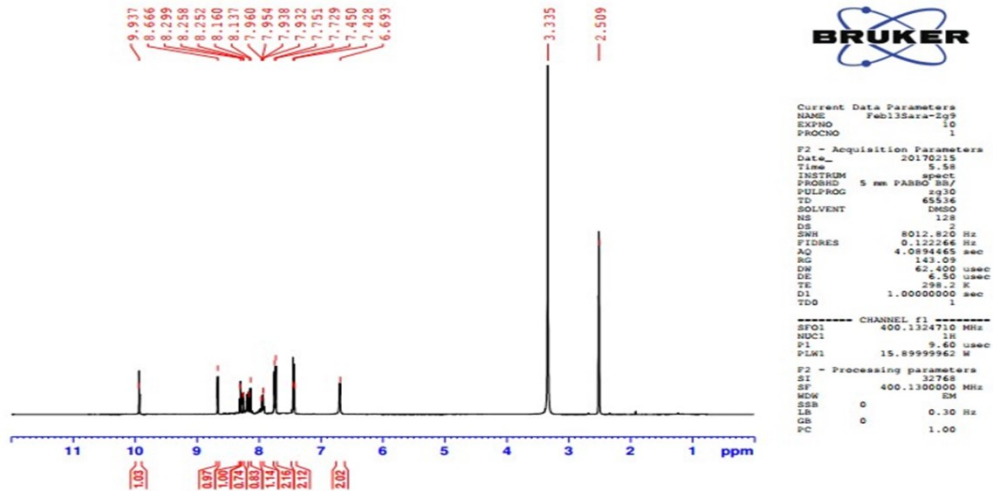


Figure S76. ¹H NMR spectrum (400 MHz, DMSO-d₆) of 51

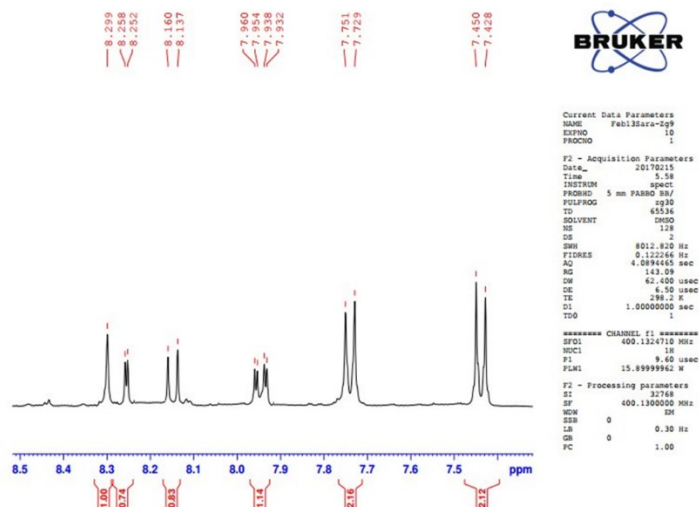


Figure S77. Expand ¹H NMR spectrum (400 MHz, DMSO-d₆) of 5I

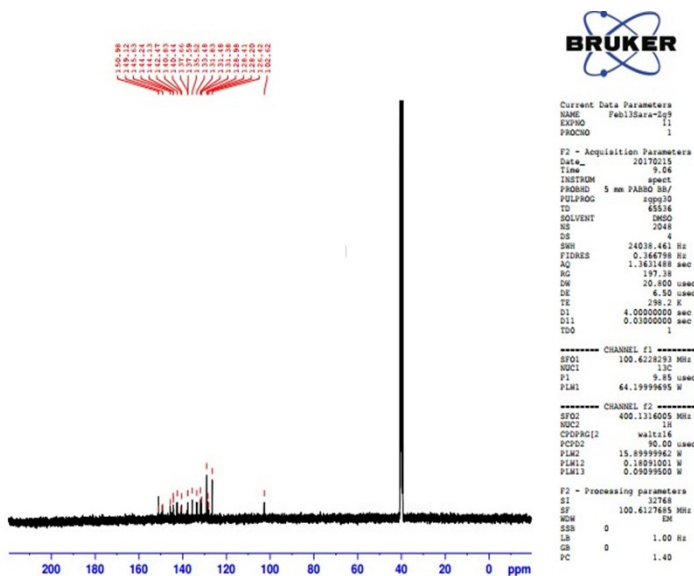
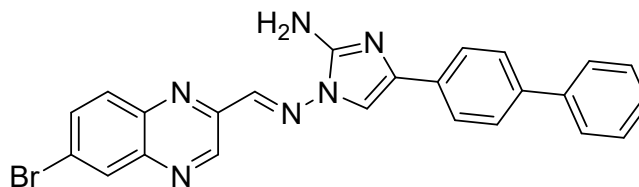


Figure S78. ¹³C NMR spectrum (100 MHz, DMSO-d₆) of 5I

4.1.2.13. (E)-4-([1,1'-biphenyl]-4-yl)-1-(((7-bromoquinoxalin-2-yl)methylene)amino) 1Himidazol-2-amine (5m)



IR (KBr): 3404 and 3276 (NH str.), 3204, 3064 and 2920 (CH str.), 1639, 1442, 1171, 736, 698 cm^{-1} ; ^1H NMR (400 MHz, DMSO-d_6) δ : 9.93 (s, 1H, CHN), 8.68 (s, 1H, 3'-H), 8.32 (s, 1H, 5-H), 8.24 (d, 1H, $J = 2.4$ Hz, 5'-H), 8.14 (d, 1H, $J = 8.8$ Hz, 8'-H), 7.93 (dd, 1H, $J_{7',8'} = 8.8$ and $J_{7',5'} = 2.4$ Hz, 7'-H), 7.83 (d, 2H, $J = 8.4$ Hz, 2''-H and 6''-H), 7.67-7.73 (m, 4H, 3''-H, 5''-H, H-2 phenyl and H-6 phenyl), 7.46 (t, 2H, $J = 7.4$ Hz, H-3 phenyl and H-5 phenyl), 7.35 (t, 1H, $J = 7.4$ Hz, H-4 phenyl), 6.69 (s, 2H, NH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ : 150.9 (C-2), 149.1 (C-2'), 145.6 (CHN), 143.9 (C-3'), 142.4 (C-6') 140.4 (C-8'a), 140.2 (C-4'a), 138.7 (C-4), 138.4 (C-4''), 135.4 (C-1 phenyl), 133.6 (C-1''), 131.3 (C-7'), 129.6 (C-8'), 129.3 (C-3 and C-5 phenyl), 128.3 (C-5'), 127.7 (C-4 phenyl), 127.1 (C-2'' and C-6''), 126.8 (C-2 and C-6 phenyl), 125.3 (C-3'' and C-5''), 102.3 (C-5); MS: (m/z) M^+ calcd. For $\text{C}_{24}\text{H}_{17}\text{BrN}_6$: 424.1, Found: 469.0

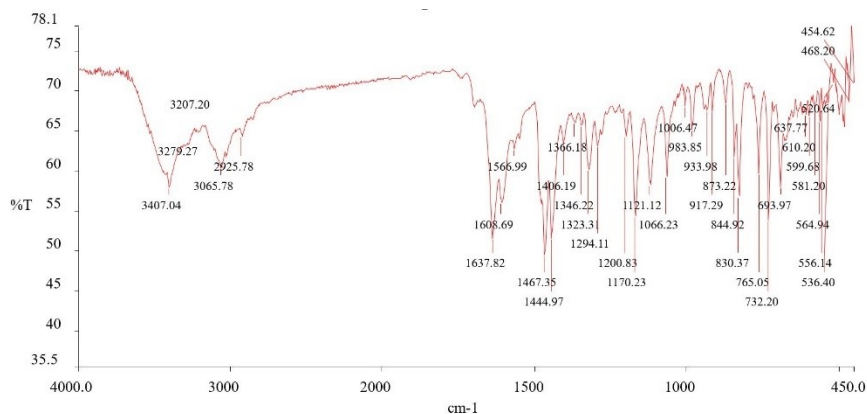
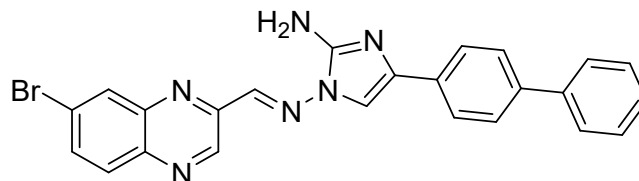


Figure S79. IR spectrum of 5m

4.1.2.14. (E)-4-([1,1'-biphenyl]-4-yl)-1-(((7-bromoquinoxalin-2-yl)methylene)amino)-1Himidazol-2-amine (5n)



IR (KBr): 3405 and 3289 (NH str.), 3204, 3076 and 2922 (CH str.), 1639, 1442, 1173, 738, 697 cm^{-1} ; ^1H NMR (400 MHz, DMSO-d_6) δ : 9.93 (s, 1H, CHN), 8.68 (s, 1H, 3'-H), 8.33 (d, 1H, $J = 2.2$ Hz, 8'-H), 8.32 (s, 1H, 5-H), 8.18 (d, 1H, $J = 8.8$ Hz, 5'-H), 7.91 (dd, 1H, $J_{6',5'} = 8.8$ and $J_{6',8'} = 2.2$ Hz, 6'-H), 7.83 (d, 2H, $J = 8.4$ Hz, 2''-H and 6''-H), 7.67-7.73 (m, 4H, 3''-H, 5''-H, H-2 phenyl and H-6 phenyl), 7.46 (t, 2H, $J = 7.4$ Hz, H-3 phenyl and H-5 phenyl), 7.35 (t, 1H, $J = 7.4$ Hz, H-4 phenyl), 6.69 (s, 2H, NH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ : 149.1 (C-2'), 150.9 (C-2), 145.6 (CHN), 143.9 (C-3'), 142.4 (C-7'), 140.4 (C-8'a), 140.2 (C-4'a), 138.7 (C-4), 138.4 (C-4''), 135.4 (C-1 phenyl), 133.6 (C-1''), 131.7 (C-6'), 129.3 (C-3 and C-5 phenyl), 129.6 (C-8'), 128.3 (C-5'), 127.5 (C-4 phenyl), 127.1 (C-2'' and C-6''), 126.8 (C-2 and C-6 phenyl), 125.3 (C-3'' and C-5''), 102.3 (C-5); MS: (m/z) M^+ calcd. For $\text{C}_{24}\text{H}_{17}\text{BrN}_6$: 424.1, Found: 469.0

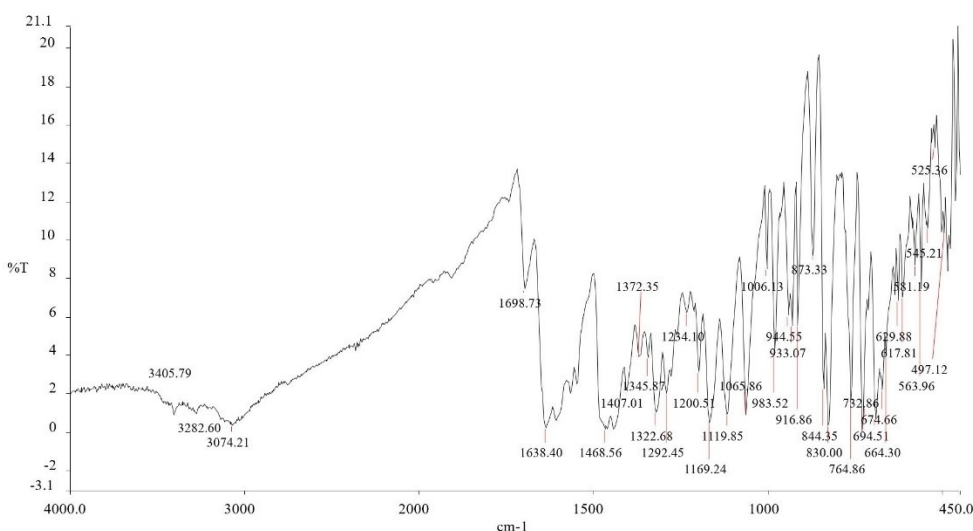


Figure S84. IR spectrum of **5n**

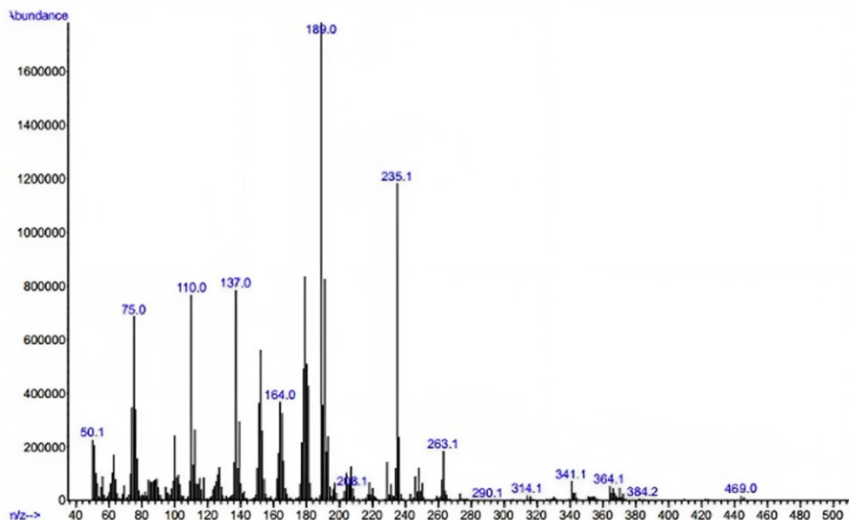
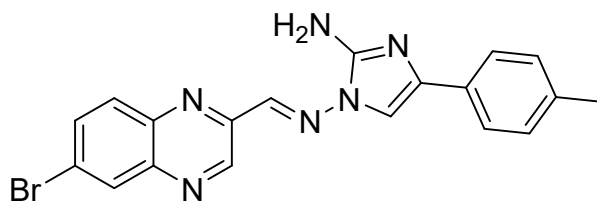


Figure S88. Mass spectrum of 5n

(*E*)-1-(((6-bromoquinoxalin-2-yl)methylene)amino)-4-(4-methoxyphenyl)-1*H*-imidazol-2-amine (5i)

IR (KBr): 3440 and 3251 (NH str.), 3134 and 3080 (CH str.), 1622, 1466, 1170, 732, 670 cm^{-1} . ^1H NMR (400 MHz, DMSO-d_6) δ : 9.93 (s, 1H, CHN), 8.63 (s, 1H, 3'-H), 8.26 (d, 1H, $J = 2.2$ Hz, 5'-H), 8.15 (d, 1H, $J = 8.9$ Hz, 8'-H), 8.11 (s, 1H, 5-H), 7.95 (dd, 1H, $J_{7',8'} = 8.9$ Hz and $J_{7',5'} = 2.2$ Hz, 7'-H), 7.68 (d, 2H, $J = 8.8$, 2''-H and 6''-H), 6.96 (d, 2H, $J = 8.8$, 3''-H and 5''-H), 6.63 (s, 2H, NH_2), 3.78 (s, 3H, Me). ^{13}C NMR (100 MHz, DMSO-d_6) δ : 158.8 (C-4''), 150.8 (C-2), 149.2 (C-2'), 145.6 (CHN), 144.9 (C-3'), 143.2 (C-4'a), 142.1 (C-6') 140.4 (C-4), 138.8 (C-8'a), 135.4 (C-7'), 131.5 (C-8'), 128.1 (C-5'), 127.1 (C-1''), 126.1 (C-2'' and C-6''), 114.3 (C-3'' and C-5''), 100.6 (C-5), 23.5 (C-Me); MS: (m/z) M^+ calcd. For $\text{C}_{19}\text{H}_{15}\text{BrN}_6$: 424.1, Found: 406.0



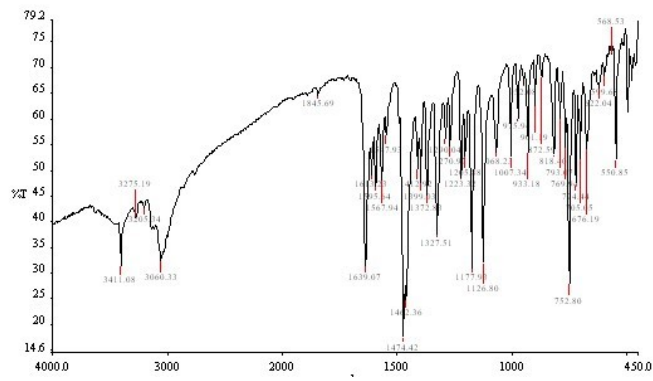


Figure S90. IR spectrum of 50

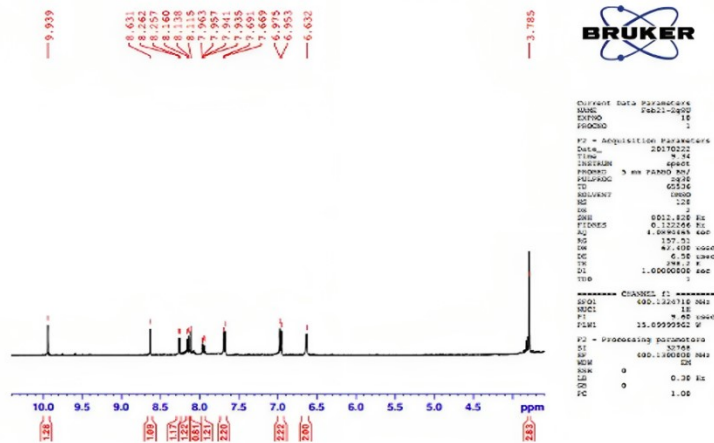


Figure S91. ¹H NMR spectrum (400 MHz, DMSO-d₆) of 50

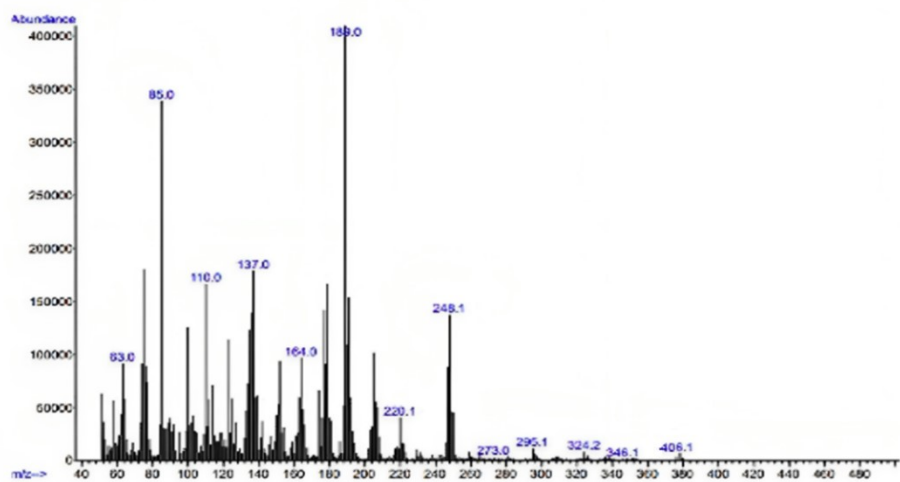


Figure S94. Mass spectrum of **50**