Electronic Supplementary Material (ESI) for Medicinal Chemistry Communications.
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Supporting information

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Design, Synthesis and Biological Evaluation of Imidazopyridine/imidazopyrimidine-Benzimidazole Conjugates as Potential Anticancer Agents

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Experimental Section

I. Biology

1. MTT Assay

The anticancer activity of the compounds was determined using MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide) reduction assay.[1] Around 1×10^4 cells/well were seeded in 100 µl DMEM (Dulbecco's Modified Eagle's Medium) supplemented with 10% FBS in each well of 96-well plates and were incubated for 24 h at 37 °µC in a CO_2 incubator. After 24 h of incubation, cells were treated with the test compounds for 48 h. After the treatment, 10 µl of MTT (5 mg/mL) was added to each well and the plates were further incubated for 4 h. After incubation, supernatant from each well was carefully removed and formazon crystals were dissolved in 100 µl of dimethyl sulfoxide (DMSO). Finally, the absorbance was measured at 570 nm.

2. Cell cycle analysis

Flow cytometric analysis (FACS) was performed to evaluate the distribution of the cells through the cell cycle phases. A549, Lung cancer cells were incubated with compounds (**11p** and **11i**) at 1 and 2 µM concentrations for 48 h. Nocodazole (1 µM for 48 h) was used as reference compound. Untreated and treated cells were harvested, washed with PBS, fixed in ice-cold 70% ethanol and stained with propidium iodide (Sigma Aldrich). Cell cycle was performed by flow cytometry (Becton Dickinson FACS Caliber) as earlier described.[2]

3. Tubulin polymerization assay

A fluorescence based *in vitro* tubulin polymerization assay was performed according to the manufacturer's protocol (BK011, Cytoskeleton, Inc.). Briefly, the reaction mixture in a total volume of 10 µl contained PEM buffer, GTP (1 µM) in the presence or absence of test compounds (final concentration of 3 µM). Tubulin polymerization was followed by a time dependent increase in fluorescence due to the incorporation of a fluorescence reporter into microtubules as polymerization proceeds. Fluorescence emission at 420 nm (excitation wavelength is 360 nm) was measured by using a Varioscan multimode plate reader (Thermo scientific Inc.). Nocodazole was used as positive control in each assay. The IC_{50} value was defined as the drug concentration required inhibiting 50% of tubulin assembly compared to control. The reaction mixture for these experiments include: tubulin (3 mg/ml) in PEM buffer, GTP (1 mM), in the presence or absence of test compounds at 2.5, 5, 10, and 15 µM concentrations. Polymerization was monitored by increase in the Fluorescence as mentioned above at 37 $^{\circ}$C.[3, 4]

4. Immunohistochemistry

A549 cells were seeded on glass cover slips, incubated for 48 h in the presence or absence of test compounds **11p, 11s** and **11i** (1 µM). Following the termination of incubation, cells were fixed with 3% paraformaldehyde, 0.02 % glutaraldehyde in PBS and permeabilized by dipping the cells in 100% methanol (-20 $^{\circ}$C). Later, cover slips were blocked with 1% BSA in phosphate buffered saline for 1 h followed by incubation with a primary anti tubulin (mouse monoclonal) antibody and FITC conjugated secondary mouse anti IgG antibody. Photographs were taken using the fluorescence microscope, equipped with FITC settings and the pictures were analyzed for the integrity of microtubule network. In parallel experiments, Nocodazole (1µM) was used as positive control for analyzing microtubule integrity.[4]

4. Hoechst staining

Cells were seeded at a density of 10,000 cells over 18-mm cover slips and incubated for 24 h. After incubation, cells were treated with the compounds **11p** and **11i** (1 µM) for 24 h. Hoechst 33342 (Sigma Aldrich) was added to the cells at a concentration of 0.5 mg/mL and incubated for 30 min at 37 $^{\circ}$C. Later, cells were washed with phosphate buffered saline (PBS). Cells from each cover slip were captured from randomly selected fields under fluorescent microscope (Leica,

Germany) to qualitatively determine the proportion of viable and apoptotic cells based on their relative fluorescence and nuclear fragmentation.[5]

5. Caspase-3

To determine the caspase-3 activity of the active compounds AFC conjugated Ac-DEVD substrate was used. Lung cancer cells (A- 549) were seeded in 6 well plates with the confluence of 2.5×10^5 per well and are treated with the compounds, **11p** and **11i** at 1 μM 2 μM concentration along with standard Nocodazole. After incubation for 48 h cell were washed with PBS and then cells were scraped in to the PBS and centrifuged at 2000 rpm for 10 min at 4 °C. Pellet was resuspended in 80 µl of lysis buffer, pellet was passed through insulin syringe followed by incubation of suspension on ice for 20-30 min centrifuged the lysate at 13,200 rpm for 20 min at 4 °C and transferred the supernatant to fresh tubes. In a 96 well black polystyrene plate, 50 µl of 2X assay buffer, 50 µl cell lysate and 2 µl of caspase-3 substrate were taken. The reactionwas allowed taking place for 1 h. The fluorescence generated by the release of the fluorogenic group AFC on cleavage by caspase-3 was measured by excitation at 400 nm and emission at 505 nm for every 5 min over 1 h. Protein was estimated by Bradford's method and normalized accordingly.[4, 6, 7]

6. DNA fragmentation assay

Cells were seeded (1×10^6) in six-well plates. After incubation of 24 h cells were treated with compounds **11p** and **11i** at 1 μM/ml concentration. After 48 h of treatment, cells were collected and centrifuged at 2500 rpm for 5 min at 4 °C. Pellet was collected and washed with Phosphate buffered saline (PBS). Then added 100 µl of Lysis buffer centrifuged at 3000 rpm for 5 min at 4 °C and collected supernant. And added 10 µl of 10% SDS and 10 µl of (50 mg/ml) RNase-A and incubated for 2 h at 56 °C. After incubation Proteinase K (25 mg/ml) was added and further incubated at 37 °C for 2 h. Then added 65 µl of 10 M Ammonium acetate and 500 µl of ice cold ethanol and mixed well. And these samples were incubated at -80 °C for 1 h. After incubatation samples were centrifuged at 12000 rpm for 20 min at 4 °C. After centrifuge pellet was washed with 80% ethanol and air dried for 10 min at room temperature. Dissolved the pellet in 50 µl of TE buffer and DNA laddering was determined by using 2% agarose gel electrophoresis in TE Buffer.[8]

7. Annexin V–FITC assay:

A549 cells (1×10^6) were seeded in six-well lates and incubated for 24 h. The cells were then treated with compounds 26 and 36 at concentrations of 50 and 100 nm for 48 h. After 48 h of treatment, the cells were harvested by trypsinization and washed with PBS by centrifuging at 3000 rpm for 5 min at 48C. The cells (1×10^6) were then stained with Annexin V–FITC and propidium iodide (PI) by using the Annexin-V–PI apoptosis detection kit (Invitrogen). Flow cytometry was performed by using a FACScan instrument (Becton Dickinson) equipped with a single 488 nm argon laser.

8. Molecular Docking Procedure

The optimization of all the compounds were carried out in Gaussian 09 using PM3 semi-empirical method.[9] The protein co-crystal structure was downloaded from RSCB-Protein Data Bank with ligand colchicine (PDB ID 3E22).[10] Autodock 4.2 software [11] were used to perform the docking studies. The visualization and analysis of interactions has been performed using Pymol, v. 0.99.[12]

II. Chemistry

All chemicals and reagents were obtained from Sigma–Aldrich (St. Louis, MO, USA), Lancaster (Alfa Aesar, Johnson Matthey Company, Ward Hill, MA, USA) or Spectrochem Pvt. Ltd. (Mumbai, India), and were used without further purification. Reactions were monitored by TLC performed on silica gel coated glass plates containing 60 GF254 with visualization achieved by UV light or iodine indicator. Column chromatography was performed with Merck 60–120 mesh silica gel. ^{1}H and ^{13}C spectra were recorded on Bruker UXNMR/ XWIN-NMR (300 MHz) or Inova Varian-VXR-unity (400, 500 MHz) instruments. Chemical shifts (δ) are reported in ppm downfield from an internal TMS standard. ESI spectra were recorded on a Micromass Quattro LC using ESI+ software with capillary voltage 3.98 kV and ESI mode positive ion trap detector. High-resolution mass spectra (HRMS) were recorded on a QSTAR XL Hybrid MS–MS mass spectrometer. Melting points were determined with an Electro thermal melting point apparatus, and are uncorrected.

2-(4-methoxyphenyl)imidazo[1,2-a]pyridine (8a)

2-Aminopyridine (**5a,** 2.5 g, 26 mmol) was dissolved in acetone (100 mL) and treated with 2-bromo-1-(4-methoxyphenyl)ethanone (**6b,** 6.08 g, 26 mmol). The reaction mixture was reflux for

6–8 h, and the resulting salt (**7a**) was collected by filtration, washed with acetone, and then dissolved in 2N HCl (300 mL) and heated at reflux for 2 h. Before complete cooling, the solution was cautiously basified by drop wise addition of 15% aq NH_4OH to pH-8. The resulting base was collected by filtration and crystallised from EtOH to afford 2-(4-methoxyphenyl)imidazo[1,2-a]pyridine **(8a)** as a white solid (4.5 g, 87% yield); Mp 130–132 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.06 (d, *J* = 6.8 Hz, 1H), 7.84 (d, *J* = 8.9 Hz, 2H), 7.72 (s, 1H), 7.59 (d, *J* = 9.0 Hz, 1H), 7.11 (t, *J* = 8.3 Hz, 1H), 6.93 (d, *J* = 8.7 Hz, 2H), 6.72 (t, *J* = 6.8 Hz, 1H), 3.83 (s, 3H); MS (ESI): *m/z* 225 $(M+1)^+$.

2-(4-methoxyphenyl)imidazo[1,2-a]pyrimidine (8b)

Compound **8b** was prepared according to the method described for compound **8a**, employing 2-bromo-1-(4-methoxyphenyl)ethanone (**6b**, 6.026 g, 26 mmol) and 2-aminopyrimidine (**5b**, 2.5 g, 26 mmol) to obtain the pure product **8b** as a white solid (4.5 g, 87% yield); Mp: 187-189 ºC;^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 8.54 (d, *J* = 7.3 Hz, 1H), 8.46 (m, 1H), 7.92 (d, *J* = 6.2 Hz, 2H), 7.82 (d, *J* = 4.1 Hz, 1H), 6.94 (d, *J* = 6.2 Hz, 2H), 6.85 (d, *J* = 4.1 Hz, 1H), 3.85 (s, 3H); MS (ESI): m/z 226 $(M+1)^+$.

2-(4-fluorophenyl)imidazo[1,2-a]pyrimidine (8c)

Compound **8c** was prepared according to the method described for compound **8a**, employing 2-bromo-1-(4-fluorophenyl)ethanone (**6c**, 5.7 g, 26 mmol) and 2-aminopyrimidine (**5b**, 2.5 g, 26 mmol) to obtain the pure product **8c** as a white solid (4.1 g, 73% yield); Mp: 228-230 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 8.55-8.53 (m, 1H), 8.42 (dd, *J* = 1.9 Hz, 8.3 Hz, 1H), 8.00 (dd, *J* = 5.5 Hz, 8.7 Hz, 2H), 7.78 (s, 1H), 7.14 (t, *J* = 8.7 Hz, 17.3 Hz, 2H), 6.86 (dd, *J* = 2.6 Hz, 6.8 Hz, 1H); MS (ESI): m/z 214 $(M+1)^+$.

2-phenylimidazo[1,2-a]pyrimidine (8d):

Compound **8d** was prepared according to the method described for compound **8a**, employing 2-bromo-1-(4-fluorophenyl)ethanone (**6c**, 5.7g, 26 mmol) and 2-aminopyrimidine (**5b**, 2.5 g, 26 mmol) to obtain the pure product **8d** as a white solid (4.5 g, 87% yield); Mp: 144–46 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 8.51-8.50 (m, 1H), 8.42 (d, *J* = 6.1 Hz, 1H), 8.01 (d, *J* = 7.4 Hz, 2H), 7.81-7.80 (m, 1H), 7.44 (t, *J* = 7.2 Hz, 14.7 Hz, 2H), 7.35 (d, *J* = 7.17 Hz, 1H), 6.85-6.82 (m, 1H); MS (ESI): m/z 195 $[M+1]^+$.

General procedure for the synthesis of aldehydes (9)

The Vilsmeier reagent was prepared at 0–5 °C by dropping $POCl_3$ (5 mL, 21 mmol) into a stirred solution of DMF (4 mL, 20 mmol) in $CHCl_3$ (10 mL). Compound **8** (1 g, 5 mmol) in $CHCl_3$ (60 mL) was added dropwise to the Vilsmeier reagent while maintaining stirring and cooling. The reaction mixture was kept at room temperature for 3 h and later refluxed for 8–24 h (according to a TLC test). $CHCl_3$ was removed under reduced pressure, and the resulting oil was poured onto ice. The crude aldehyde **9** thus obtained was collected by filtration and crystallized from ethanol with a yield of 70–80%.

2-(4-methoxyphenyl)imidazo[1,2-a]pyridine-3-carbaldehyde (9a)

Compound **9a** was prepared according to the method described for compound **9**, employing 2-(4-methoxyphenyl)imidazo[1,2-a]pyridine (**8a,** 1.0 g, 4.46 mmol) to obtain the pure product **9a** as a white solid (980 mg, 87% yield); Mp 146–148 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 10.04 (s, 1H), 9.66 (d, *J* = 6.4 Hz, 2H), 7.77 (d, *J* = 8.0 Hz, 2H), 7.55 (t, *J* = 8.0 Hz, 1H), 7.10 (t, *J* = 6.4 Hz, 1H), 7.03 (d, *J* = 8.0 Hz, 2H,), 3.88 (s, 3H); MS (ESI): *m/z* 253 $(M+1)^+$.

2-(4-methoxyphenyl)imidazo[1,2-a]pyrimidine-3-carbaldehyde (9b)

Compound **9b** was prepared according to the method described for compound **9**, employing 2-(4-methoxyphenyl)imidazo[1,2-a]pyrimidine (**8b,** 1.0 g, 4.44 mmol) to obtain the pure product **9b** as a white solid (1 g, 88% yield); Mp: 178-180 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 10.13 (s, 1H), 9.88 (dd, *J* = 1.8 Hz, 6.7 Hz, 1H), 8.82-8.81 (m, 1H), 7.89 (d, *J* = 8.7 Hz, 2H), 7.16 (dd, *J* = 2.3 Hz, 6.7 Hz, 1H), 7.05 (d, *J* = 8.7 Hz, 2H), 3.89 (s, 3H); MS (ESI): m/z 254 $(M+1)^+$.

2-(4-fluorophenyl)imidazo[1,2-a]pyrimidine-3-carbaldehyde (9c)

Compound **9c** was prepared according to the method described for compound **9**, employing 2-(4-fluorophenyl)imidazo[1,2-a]pyrimidine (**8c,** 1.0 g, 4.69 mmol) to obtain the pure product **9c** as a white solid (990 mg, 87% yield); Mp: 208-210 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 10.12 (s, 1H), 9.90 (d, *J* = 7.2 Hz, 1H), 8.84 (dd, *J* = 6.1 Hz, 4.2 Hz, 1H), 7.92 (dd, *J* = 8.8 Hz, 5.6 Hz, 2H), 7.28−7.22 (m, 3H); MS (ESI): m/z 242 $(M+1)^+$.

2-phenylimidazo[1,2-a]pyrimidine-3-carbaldehyde (9d)

Compound **9d** was prepared according to the method described for compound **9**, employing 2-phenylimidazo[1,2-a]pyrimidine (**8d,** 1.0 g, 5.12 mmol) to obtain the pure product **9d** as a white

solid (900 mg, 78% yield); Mp: 155–158 ºC;^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 10.14 (s, 1H), 9.89 (dd, *J* = 1.9 Hz, 8.7 Hz, 1H), 8.86-8.84 (m, 1H), 7.93-7.90 (m, 2H), 7.56-7.54 (m, 3H), 7.20 (dd, J = 2.5 Hz, 8.7 Hz, 1H); MS (ESI): m/z 224 $[M+1]^+$

2-(2-(4-methoxyphenyl)imidazo[1,2-a]pyridin-3-yl)-1H-benzo[d]imidazole (11a)

To the stirred solution of 2-(4-methoxyphenyl)imidazo[1,2-a]pyridine-3-carbaldehyde (**9a,** 200 mg, 0.793 mmol) in ethanol (10 mL), benzene-1,2-diamine (**10a,** 85.7 mg, 0.793 mmol) and sodium metabisulfite (301.7 mg, 1.58 mmol) were added. The reaction mixture was allowed to stir at 80 °C for 8 h, and was monitored by TLC using ethyl acetate/hexane (7:3) as a solvent system. After completion of the reaction the solution was cooled to room temperature. The obtained precipitate was filtered and washed with ethanol. The crude product was purified by using column chromatography using EtOAc/hexane (6:4) as the eluent to afford compound **11a** as a yellow solid. (yield: 212 mg, 78.5 %); Mp: 214-216 ºC; IR (KBr): $\bar{\upsilon}_{max}/cm^{-1}$- 3425, 3052, 3002, 2952, 2834, 2776, 2772, 2637, 1636, 1612, 1584, 1532, 1503, 1470, 1445, 1420, 1401, 1356, 1338, 1302, 1271, 1249, 1224, 1172, 1156, 1107, 1051, 1031, 1002, 925; ^{1}H NMR (DMSO, 500 MHz) δ (ppm): 11.91 (brs, 1H), 9.27 (d, *J* = 6.9 Hz, 1H), 7.81-7.78 (m, 1H), 7.67 (d, *J* = 8.9 Hz, 2H), 7.63 (d, *J* = 8.9 Hz, 1H), 7.33 (t, *J* = 8.9 Hz, 2H), 7.20-7.18 (m, 2H), 6.96-6.90 (m, 3H), 3.82 (s, 3H); ^{13}C NMR (DMSO, 75 MHz) δ (ppm): 159.5, 145.1, 143.5, 142.8, 134.2, 129.3, 126.7, 125.8, 122.9, 121.8, 118.9, 116.6, 114.0, 113.9,113.2, 111.8, 111.5, 55.18; MS (ESI): m/z 341 $[M+1]^+$; HRMS (ESI) calcd for $C_{21}H_{17}N_4O$ $[M+1]^+$ 341.13969; found: 341.13948.

6-fluoro-2-(2-(4-methoxyphenyl)imidazo[1,2-a]pyridin-3-yl)-1H-benzo[d]imidazole (11b)

Compound **11b** was prepared according to the method described for compound **11a**, employing 2-(4-methoxyphenyl)imidazo[1,2-a]pyridine-3-carbaldehyde (**9a,** 200 mg, 0.793 mmol) and 4-fluorobenzene-1,2-diamine (**10b**, 100.1 mg, 0.793 mmol) and sodium metabisulfite (301.7 mg, 1.58 mmol) to obtain the pure product **11b** as a yellow solid. (yield: 221 mg, 77.8 %); Mp: 232-235 ºC; IR (KBr): $\bar{\upsilon}_{max}/cm^{-1}$- 3423, 3076, 2954, 2833, 1630, 1611, 1582, 1529, 1497, 1453, 1437, 1351, 1334, 1296, 1278, 1250, 1173, 1152, 1137, 1106, 1046, 1030, 961; ^{1}H NMR (DMSO, 500 MHz) δ (ppm): 11.91 (brs, 1H), 9.29 (d, *J* = 5.9 Hz, 1H), 7.75 (d, *J* = 5.9 Hz, 1H), 7.68 (d, *J* = 8.9 Hz, 2H), 7.61 (d, *J* = 8.9 Hz, 1H), 7.33 (t, *J* = 7.9 Hz, 2H), 6.97-6.90 (m, 4H), 3.83 (s, 3H); ^{13}C NMR (DMSO, 75 MHz) δ (ppm): 159.5, 145.2, 143.8, 129.4, 126.8, 125.9, 119.9, 116.8,

116.6, 114.1, 113.3, 112.5, 111.1, 110.5, 110.1, 55.2; MS (ESI): m/z 359 $(M+1)^+$; HRMS (ESI) calcd for $C_{21}H_{16}FN_4O$ $[M+H]^+$ 359.13027; found: 359.13018.

6-chloro-2-(2-(4-methoxyphenyl)imidazo[1,2-a]pyridin-3-yl)-1H-benzo[d]imidazole (11c)

Compound **11c** was prepared according to the method described for compound **11a**, employing 2-(4-methoxyphenyl)imidazo[1,2-a]pyridine-3-carbaldehyde (**9a,** 200 mg, 0.793 mmol) and 4-chlorobenzene-1,2-diamine (**10c**, 113.1 mg, 0.793 mmol) and sodium metabisulfite (301.7 mg, 1.58 mmol) to obtain the pure product **11c** as a yellow solid. (yield: 225 mg, 75.7 %); Mp: 223-225 ºC; IR (KBr): $\bar{\upsilon}_{max}/cm^{-1}$- 3426, 2931, 2834, 1612, 1574, 1529, 1484, 1455, 1428, 1401, 1354, 1302, 1279, 1248, 1174, 1154, 1049, 834; ^1H NMR (DMSO, 500 MHz) δ (ppm): 11.98 (brs, 1H), 9.31 (d, *J* = 5.9 Hz, 1H), 7.81-7.80 (m, 1H), 7.66 (d, *J* = 7.9 Hz, 2H), 7.61 (d, *J* = 8.9 Hz, 1H), 7.34 (t, *J* = 7.9 Hz, 2H), 7.17 (d, *J* = 7.9 Hz, 1H), 6.97-6.88 (m, 3H), 3.83 (s, 3H); ^{13}C NMR (DMSO, 75 MHz) δ (ppm): 159.5, 145.5, 144.2, 129.4, 126.8, 126.1, 125.7, 122.7, 118.2, 116.6, 114.1, 113.3, 110.4, 109.8, 55.2; MS (ESI): m/z 375 $(M+1)^+$; HRMS (ESI) calcd for $C_{21}H_{16}ClN_4O$ $[M+H]^+$ 375.10072; found: 375.10144.

2-(2-(4-methoxyphenyl)imidazo[1,2-a]pyridin-3-yl)-6-methyl-1H-benzo[d]imidazole (11d)

Compound **11d** was prepared according to the method described for compound **11a**, employing 2-(4-methoxyphenyl)imidazo[1,2-a]pyridine-3-carbaldehyde (**9a,** 200 mg, 0.793 mmol) and 4-methylbenzene-1,2-diamine (**10d**, 96.9 mg, 0.793 mmol) and sodium metabisulfite (301.7 mg, 1.58 mmol) to obtain the pure product **11d** as a yellow solid. (yield: 225 mg, 80.1 %); Mp: 210-212 ºC; IR (KBr): $\bar{\upsilon}_{max}/cm^{-1}$- 3433, 3049, 2923, 2853, 2733, 2628, 1613, 1534, 1507, 1460, 1446, 1391, 1354, 1330, 1305, 1279, 1248, 1224, 1174, 1158, 1050, 1035, 926; ^1H NMR (DMSO, 500 MHz) δ (ppm): 9.19 (d, *J* = 4.9 Hz, 1H), 7.86 (s, 1H), 7.68 (d, *J* = 8.9 Hz, 2H), 7.63-7.61 (m, 1H), 7.36-7.31 (m, 2H), 7.02 (d, *J* = 7.9 Hz, 1H), 6.95-6.91 (m, 3H), 3.83 (s, 3H), 2.49 (s, 3H); ^{13}C NMR (DMSO, 75 MHz) δ (ppm): 158.1, 147.2, 143.5, 141.7, 133.2, 128.2, 127.4, 126.5, 122.1, 121.9, 119.7, 119.4, 117.6, 114.6, 112.1, 110.8, 108.9, 55.6, 21.7; MS (ESI): m/z 355 $(M+1)^+$; HRMS (ESI) calcd for $C_{22}H_{19}N_4O$ $[M+H]^+$ 355.15534; found: 355.15501.

6-methoxy-2-(2-(4-methoxyphenyl)imidazo[1,2-a]pyridin-3-yl)-1H-benzo[d]imidazole (11e)

Compound **11e** was prepared according to the method described for compound **11a**, employing 2-(4-methoxyphenyl)imidazo[1,2-a]pyridine-3-carbaldehyde (**9a,** 200 mg, 0.793 mmol) and 4-

methoxybenzene-1,2-diamine (**10e**, 109.6 mg, 0.793 mmol) and sodium metabisulfite (301.7 mg, 1.58 mmol) to obtain the pure product **11e** as a light brown solid. (yield: 221mg, 75.3 %); Mp: 202-204 ºC; IR (KBr): $\bar{\upsilon}_{max}/cm^{-1}$- 3432, 2999, 2923, 2851, 2828, 2734, 2632, 1629, 1612, 1535, 1507, 1458, 1394, 1356, 1336, 1298, 1282, 1272, 1250, 1224, 1201, 1181, 1162, 1050, 1028; ^{1}H NMR (DMSO, 500 MHz) δ (ppm): 9.21 (d, *J* = 8.3 Hz, 1H), 7.89 (s, 1H), 7.71-7.69 (m, 1H), 7.68 (d, *J* = 6.3 Hz, 2H), 7.41-7.39 (m, 2H), 7.13-7.11 (m, 2H), 6.99-6.96 (m, 2H), 3.96 (s, 3H), 3.89 (s, 3H); MS (ESI): m/z 371 $(M+1)^{+}$; ^{13}C NMR (DMSO, 75 MHz) δ (ppm): 159.7, 148.5, 143.5, 135.8, 132.2, 129.1, 122.3, 122.1, 120.5, 118.7, 117.7, 117.5, 113.2, 110.1, 108.9, 55.9, 55.6; HRMS (ESI) calcd for $C_{22}H_{19}N_4O_2$ $[M+H]^{+}$ 371.15025; found: 371.14980.

3-(1H-benzo[d]imidazol-2-yl)-2-(4-methoxyphenyl)imidazo[1,2-a]pyrimidine (11f)

Compound **11f** was prepared according to the method described for compound **11a**, employing 2-(4-methoxyphenyl)imidazo[1,2-a]pyrimidine-3-carbaldehyde (**9b,** 200 mg, 0.789 mmol) and benzene-1,2-diamine (**10a,** 85.3 mg, 0.789mmol) and sodium metabisulfite (300.3 mg, 1.57 mmol) to obtain the pure product **11f** as a light brown solid. (yield: 210 mg, 77.8 %); Mp: 210-212 ºC; IR (KBr): $\bar{\upsilon}_{max}/cm^{-1}$- 3423, 3289, 3107, 1589, 1502, 1497, 1424, 1415, 1388, 1358, 1336, 1289, 1247, 1236, 1157, 849; ^{1}H NMR (DMSO, 300 MHz) δ (ppm): 12.61 (brs, 1H), 8.83-8.79 (m, 2H), 7.89 (d, *J* = 8.87 Hz, 2H), 7.37 (dd, *J* = 2.45 Hz, 6.79 Hz, 1H), 7.17 (d, *J* = 7.5 Hz, 1H), 7.06-7.03 (m, 1H), 6.99 (dd, *J* = 1.32 Hz, 7.79 Hz, 1H), 6.78 (dd, *J* = 6.79 Hz, 1.32 Hz, 2H), 6.59 (dd, J = 1.32 Hz, 7.79 Hz, 1H), 3.89 (s, 3H); ^{13}C NMR (DMSO, 75 MHz) δ (ppm): 163.1, 162.2, 154.8, 142.7, 138.7, 136.2, 124.6, 119.7, 118.6, 117.5, 117.1, 116.8, 114.4, 113.1, 112.9, 110.1, 56.2; MS (ESI): m/z 342 $(M+1)^{+}$; HRMS (ESI) calcd for $C_{20}H_{16}N_5O[M+H]^{+}$ 342.1355; found: 342.1349.

3-(6-fluoro-1H-benzo[d]imidazol-2-yl)-2-(4-methoxyphenyl)imidazo[1,2-a]pyrimidine (11g)

Compound **11g** was prepared according to the method described for compound **11a**, employing 2-(4-methoxyphenyl)imidazo[1,2-a]pyrimidine-3-carbaldehyde (**9b,** 200 mg, 0.789 mmol) and 4-fluorobenzene-1,2-diamine (**10b**, 99.7 mg, 0.789 mmol) and sodium metabisulfite (300.3 mg, 1.57 mmol) to obtain the pure product **11g** as a yellow solid. (yield: 220 mg, 77.4 %); Mp: 226-228 ºC; IR (KBr): $\bar{\upsilon}_{max}/cm^{-1}$- 3429, 3298, 3177, 3052, 1599, 1520, 1499, 1444, 1405, 1356, 1336, 1292, 1274, 1233, 1175, 871; ^{1}H NMR (DMSO, 300 MHz) δ (ppm): 12.59 (brs, 1H), 8.76-8.73 (m, 2H), 7.79 (d, *J* = 8.78 Hz, 2H), 7.62 (d, *J* = 7.1 Hz, 1H), 7.29 (dd, *J* = 3.15 Hz, 7.12 Hz, 1H), 7.10 (dd, *J* = 7.1 Hz, 2.5 Hz, 1H), 6.95 (d, *J* = 8.78 Hz, 1H), 6.77 (d, *J* = 2.5 Hz, 1H), 6.49 (dd, *J* = 2.5 Hz, 8.78

Hz, 1H), 3.83 (s, 3H); ^{13}C NMR (DMSO, 75 MHz) δ (ppm): 164.3, 161.9, 155.9, 144.7, 139.8, 136.7, 125.9, 119.8, 119.6, 117.1, 116.9, 115.9, 114.1, 112.6, 112.8, 110.1, 56.2; MS (ESI): m/z 360 $(M+1)^+$; HRMS (ESI) calcd for $C_{20}H_{15}FN_5O[M+H]^+$ 360.1261; found: 360.1257.

3-(6-chloro-1H-benzo[d]imidazol-2-yl)-2-(4-methoxyphenyl)imidazo[1,2-a]pyrimidine (11h)

Compound **11h** was prepared according to the method described for compound **11a**, employing 2-(4-methoxyphenyl)imidazo[1,2-a]pyrimidine-3-carbaldehyde (**9b,** 200 mg, 0.789 mmol) and 4-chlorobenzene-1,2-diamine (**10c**, 112.5 mg, 0.789 mmol) and sodium metabisulfite (300.3 mg, 1.57 mmol) to obtain the pure product **11h** as a yellow solid. (yield: 225mg, 75.7 %); Mp: 194-196 ºC; IR (KBr): $\bar{\upsilon}_{max}/cm^{-1}$- 3423, 3296, 3052, 2924, 1611, 1596, 1520, 1503, 1472, 1444, 1426, 1407, 1355, 1333, 1265, 1232, 1173, 1128, 1107, 1074, 910, 890; ^{1}H NMR (DMSO, 500 MHz) δ (ppm): 12.46 (brs, 1H), 8.79-8.74 (m, 2H), 7.82 (d, *J* = 8.3 Hz, 2H), 7.59 (d, *J* = 6.79 Hz, 1H), 7.32 (dd, *J* = 2.45 Hz, 6.79 Hz, 1H), 7.11 (d, *J* = 2.5 Hz, 1H), 6.97 (d, *J* = 8.31 Hz, 1H), 6.78 (d, *J* = 2.5 Hz, 1H), 6.52 (dd, *J* = 2.3 Hz, 8.3 Hz, 1H), 3.86 (s, 3H) ^{13}C NMR (DMSO, 75 MHz) δ (ppm): 164.1, 158.6, 151.4, 145.8, 138.6, 136.4, 126.4, 118.9, 118.5, 116.9, 115.9, 114.9, 113.7, 112.9, 110.1, 56.2; MS (ESI): m/z 376 $(M+1)^+$; HRMS (ESI) calcd for $C_{20}H_{15}ClN_5O[M+H]^+$ 376.09596; found: 376.09677.

2-(4-methoxyphenyl)-3-(6-methyl-1H-benzo[d]imidazol-2-yl)imidazo[1,2-a]pyrimidine (11i)

Compound **11i** was prepared according to the method described for compound **11a**, employing 2-(4-methoxyphenyl)imidazo[1,2-a]pyrimidine-3-carbaldehyde (**9b,** 200 mg, 0.789 mmol) and 4-methylbenzene-1,2-diamine (**10d**, 96.5 mg, 0.789mmol) and sodium metabisulfite (300.3 mg, 1.57 mmol) to obtain the pure product **11i** as a yellow solid. (yield: 220 mg, 78.3 %); Mp: 205-208 ºC; IR (KBr): $\bar{\upsilon}_{max}/cm^{-1}$- 3421, 3209, 2921, 1616, 1588, 1566, 1522, 1482, 1458, 1441, 1354, 1312, 1286, 1266, 1221, 1189, 1166, 847; ^{1}H NMR (DMSO, 300 MHz) δ (ppm): 8.84 (d, *J* = 2.1 Hz, 1H), 8.74-8.68 (m, 1H), 7.80 (d, *J* = 8.68 Hz, 2H), 7.49 (d, *J* = 6.7 Hz, 1H), 7.15 (dd, *J* = 4.5 Hz, 6.6 Hz, 1H), 7.06 (d, *J* = 8.68 Hz, 2H), 6.88-6.83 (m, 1H), 6.56-6.49 (m, 1H), 3.89 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (DMSO, 75 MHz) δ (ppm): 164.1, 159.8, 151.4, 148.8, 145.7, 145.1, 138.7, 136.9 132.6, 128.4, 118.2, 117.9, 115.6, 115.1, 109.9, 56.2, 21.9; MS (ESI): m/z 356 $(M+1)^+$; HRMS (ESI) calcd for $C_{22}H_{18}N_5O[M+H]^+$ 356.15059; found: 356.15050.

3-(6-methoxy-1H-benzo[d]imidazol-2-yl)-2-(4-methoxyphenyl)imidazo[1,2-a]pyrimidine (11j)

Compound **11j** was prepared according to the method described for compound **11a**, employing 2-(4-methoxyphenyl)imidazo[1,2-a]pyrimidine-3-carbaldehyde (**9b,** 200 mg, 0.789 mmol) and 4-methoxybenzene-1,2-diamine (**10e**, 109.2 mg, 0.789mmol) and sodium metabisulfite (300.3 mg, 1.57 mmol) to obtain the pure product **11j** as a yellow solid. (yield: 221 mg, 75.2 %); Mp: 213-215 ºC; IR (KBr): $\bar{\upsilon}_{max}/cm^{-1}$- 3423, 3213, 3011, 2915, 1616, 1598, 1514, 1493, 1468, 1444, 1415, 1347, 1322, 1292, 1236, 1214, 1159, 805; ^{1}H NMR (DMSO, 300 MHz) δ (ppm): 8.81-8.78 (m, 2H), 7.83 (d, *J* = 8.7 Hz, 2H), 7.51 (d, *J* = 7.9 Hz, 1H), 7.19 (dd, *J* = 2.4 Hz, 7.9 Hz, 1H), 7.05-7.03 (m, 1H), 7.01 (d, *J* = 8.7 Hz, 2H), 6.68-6.65 (m, 1H), 3.92 (s, 3H), 3.81 (s, 3H); MS (ESI): m/z 372 $(M+1)^{+}$; HRMS (ESI) calcd for $C_{21}H_{18}N_5O_2$ $[M+H]^{+}$372.14550; found: 372.14545.

3-(1H-benzo[d]imidazol-2-yl)-2-(4-fluorophenyl)imidazo[1,2-a]pyrimidine (11k)

Compound **11k** was prepared according to the method described for compound **11a**, employing 2-(4-fluorophenyl)imidazo[1,2-a]pyrimidine-3-carbaldehyde (**9c,** 200 mg, 0.829 mmol) and benzene-1,2-diamine (**10a**, 89.5 mg, 0.829mmol) and sodium metabisulfite (315.2 mg, 1.66 mmol) to obtain the pure product **11k** as a yellow solid. (yield: 200 mg, 73.2 %); Mp: 190-192 ºC; IR (KBr): $\bar{\upsilon}_{max}/cm^{-1}$- 3388, 3212, 3104, 3059, 2925, 1605, 1579, 1519, 1503, 1466, 1444, 1407, 1371, 1349, 1325, 1274, 1222, 1157, 847; ^{1}H NMR (DMSO, 300 MHz) δ (ppm): 11.59 (brs, 1H), 8.85 (d, *J* = 4.6 Hz, 1H), 8.68-8.65 (m, 1H), 7.89-7.85 (m, 2H), 7.29-7.25 (m, 2H), 7.15 (d, *J* = 8.87 Hz, 1H), 6.95 (dd, *J* = 0.95 Hz, 7.9 Hz, 1H), 6.83 (d, *J* = 8.8 Hz, 2H), 6.69 (t, *J* = 7.9 Hz, 1H); ^{13}C NMR (DMSO, 75 MHz) δ (ppm): 164.1, 159.8, 151.4, 148.8, 145.7, 145.1, 138.7, 136.9 132.6, 128.4, 118.2, 117.9, 115.6, 115.1, 109.9; MS (ESI): m/z 330 $(M+1)^{+}$; HRMS (ESI) calcd for $C_{19}H_{13}FN_5$ $[M+H]^{+}$ 330.11495; found: 330.11475.

3-(6-fluoro-1H-benzo[d]imidazol-2-yl)-2-(4-fluorophenyl)imidazo[1,2-a]pyrimidine (11l)

Compound **11l** was prepared according to the method described for compound **11a**, employing 2-(4-fluorophenyl)imidazo[1,2-a]pyrimidine-3-carbaldehyde (**9c,** 200 mg, 0.829 mmol) and 4-fluorobenzene-1,2-diamine (**10b**, 104.5 mg, 0.829mmol) and sodium metabisulfite (315.2 mg, 1.66 mmol) to obtain the pure product **11l** as a yellow solid. (yield: 220 mg, 76.4 %); Mp: 219-221 ºC; IR (KBr): $\bar{\upsilon}_{max}/cm^{-1}$- 3425, 3298, 3056, 1603, 1520, 1504, 1445, 1408, 1363, 1327, 1289,

1273, 1230, 1176, 1157, 1129, 841; ^{1}H NMR (DMSO, 300 MHz) δ (ppm): 11.62 (brs, 1H), 8.71-8.68 (m, 2H), 7.89-7.86 (m, 2H), 7.72 (dd, *J* = 5.93 Hz, 1.6 Hz, 1H), 7.17 (d, *J* = 5.9 Hz, 1H), 7.09-7.05 (m, 1H), 6.89 (dd, *J* = 1.54 Hz, 7.79 Hz, 1H), 6.82-6.84 (m, 1H), 6.72 (d, *J* = 7.79 Hz, 1H); ^{13}C NMR (DMSO, 75 MHz) δ (ppm): 164.3, 161.2, 152.8, 151.4, 148.8, 145.7, 145.1, 137.1, 131.6, 129.2, 118.2, 116.6, 115.9, 115.6, 110.7; MS (ESI): m/z 348 $(M+1)^+$; HRMS (ESI) calcd for $C_{19}H_{12}F_2N_5$ $[M+H]^+$ 348.10553; found: 348.10562.

3-(6-chloro-1H-benzo[d]imidazol-2-yl)-2-(4-fluorophenyl)imidazo[1,2-a]pyrimidine (11m)

Compound **11m** was prepared according to the method described for compound **11a**, employing 2-(4-fluorophenyl)imidazo[1,2-a]pyrimidine-3-carbaldehyde (**9c,** 200 mg, 0.829 mmol) and 4-chlorobenzene-1,2-diamine (**10c**, 118.2 mg, 0.829mmol) and sodium metabisulfite (315.2 mg, 1.66 mmol) to obtain the pure product **11m** as a light yellow solid. (yield: 230 mg, 77.9 %); Mp: 209-211 ºC; IR (KBr): $\bar{\upsilon}_{max}/cm^{-1}$- 3419, 3292, 3053, 2925, 1613, 1599, 1519, 1503, 1477, 1426, 1408, 1358, 1332, 1320, 1263, 1230, 1156, 1110, 1096, 1060, 892; ^{1}H NMR (DMSO, 300 MHz) δ (ppm): 11.78 (brs, 1H), 8.79 (d, *J* = 1.5 Hz, 1H), 8.69-8.68 (m, 1H), 7.86 (d, *J* = 6.8 Hz, 2H), 7.56 (d, *J* = 7.7 Hz, 1H), 7.18 (t, *J* = 7.7 Hz, 1H), 6.98-6.96 (m, 2H), 6.84 (dd, *J* = 0.94 Hz, 8.3 Hz, 1H), 6.72-6.68 (m, 1H); ^{13}C NMR (DMSO, 75 MHz) δ (ppm): 164.1, 159.9, 151.3, 145.6, 145.1, 137.1, 133.4, 131.6, 129.2, 118.2, 116.6, 114.5, 112.5, 115.9, 115.6, 110.7; MS (ESI): m/z 364 $(M+1)^+$; HRMS (ESI) calcd for $C_{19}H_{12}FClN_5$ $[M+H]^+$ 364.0765; found: 364.0761.

2-(4-fluorophenyl)-3-(6-methyl-1H-benzo[d]imidazol-2-yl)imidazo[1,2-a]pyrimidine (11n)

Compound **11n** was prepared according to the method described for compound **11a**, employing 2-(4-fluorophenyl)imidazo[1,2-a]pyrimidine-3-carbaldehyde (**9c,** 200 mg, 0.829 mmol) and 4-methylbenzene-1,2-diamine (**10d**, 101.3 mg, 0.829mmol) and sodium metabisulfite (315.2 mg, 1.66 mmol) to obtain the pure product **11n** as a pale yellow solid. (yield: 210 mg, 73.7 %); Mp: 205-207 ºC; IR (KBr): $\bar{\upsilon}_{max}/cm^{-1}$- 3414, 3246, 3060, 2920, 2856, 1617, 1605, 1518, 1500, 1474, 1449, 1417, 1322, 1238, 1216, 1158, 850; ^{1}H NMR (DMSO, 500 MHz) δ (ppm): 11.01 (brs, 1H), 8.61-8.57 (m, 2H), 7.79 (d, *J* = 1.67 Hz, 1H), 7.68 (dd, *J* = 3.3 Hz, 8.4 Hz, 2H), 7.34 (d, *J* = 1.67 Hz, 8.4 Hz, 1H), 7.23 (d, *J* = 8.4 Hz, 1H), 7.05 (d, *J* = 8.4 Hz, 2H), 6.82 (dd, *J* = 7.5 Hz, 2.5 Hz, 1H), 2.32 (s, 3H); ^{13}C NMR (DMSO, 75 MHz) δ (ppm): 164.1, 160.8, 151.9, 148.1, 144.6, 134.4, 130.3, 129.5, 123.5, 118.6, 115.7, 115.4, 111.5, 110.2, 109.8, 23.2; MS (ESI): m/z 344 $(M+1)^+$; HRMS (ESI) calcd for $C_{20}H_{15}FN_5$ $[M+H]^+$ 344.1311; found: 344.1295.

2-(4-fluorophenyl)-3-(6-methoxy-1H-benzo[d]imidazol-2-yl)imidazo[1,2-a]pyrimidine (11o)

Compound **11o** was prepared according to the method described for compound **11a**, employing 2-(4-fluorophenyl)imidazo[1,2-a]pyrimidine-3-carbaldehyde (**9c,** 200 mg, 0.829 mmol) and 4-methoxybenzene-1,2-diamine (**10e**, 114.5 mg, 0.829mmol) and sodium metabisulfite (315.2 mg, 1.66 mmol) to obtain the pure product **11o** as a yellow solid. (yield: 220mg, 73.8 %); Mp: 195-198 ºC; IR (KBr): $\bar{\upsilon}_{max}/cm^{-1}$- 3424, 3303, 3096, 1611, 1530, 1519, 1500, 1466, 1453, 1434, 1410, 1328, 1300, 1269, 1229, 1217, 1157, 1033, 841; ^{1}H NMR (DMSO, 500 MHz) δ (ppm): 12.6 (brs, 1H), 8.81 (d, *J* = 1.5 Hz, 1H), 8.77-8.79 (m, 1H), 7.93 (d, *J* = 8.7 Hz, 2H), 7.68-7.62 (m, 2H), 7.29 (d, *J* = 8.71 Hz, 1H), 7.14 (dd, *J* = 2.26 Hz, 6.67 Hz, 1H), 7.05 (dd, *J* = 2.26 Hz, 6.67 Hz, 1H), 6.86-6.84 (m, 1H), 4.02 (s, 3H); ^{13}C NMR (DMSO, 75 MHz) δ (ppm): 164.1, 161.0, 152.8, 148.8, 139.1, 138.5, 133.2, 132.8, 132.7, 131.8, 126.0, 124.7, 120.8, 116.9, 113.1, 109.8; MS (ESI): m/z 360 $(M+1)^+$; HRMS (ESI) calcd for $C_{20}H_{15}FN_5O$ $[M+H]^+$ 360.12551; found: 360.12550.

3-(1H-benzo[d]imidazol-2-yl)-2-phenylimidazo[1,2-a]pyrimidine(11p)

Compound **11p** was prepared according to the method described for compound **11a**, employing 2-phenylimidazo[1,2-a]pyrimidine-3-carbaldehyde (**9d,** 200 mg, 0.896 mmol) and benzene-1,2-diamine (**10a,** 96.8 mg, 0.896 mmol) and sodium metabisulfite (340.9 mg, 1.79 mmol) to obtain the pure product **11p** as a yellow solid. (yield: 220mg, 73.8 %); Mp: 214-216 ºC; IR (KBr): $\bar{\upsilon}_{max}/cm^{-1}$- 3430, 3293, 3059, 2933, 2834, 1607, 1520, 1502, 1454, 1404, 1352, 1326, 1302, 1251, 1229, 1174, 1109, 1027, 838; ^{1}H NMR (300 MHz, DMSO)δ (ppm): 12.36 (s, 1H), 8.86 (d, *J* = 1.8 Hz, 1H), 8.76-8.78 (m, 1H), 7.85 (d, *J* = 7.17 Hz, 2H), 7.62-7.60 (m, 1H), 7.52 (d, *J* = 6.98 Hz, 1H), 7.21 (t, *J* = 10.7 Hz, 1H), 7.04 (t, *J* = 7.74 Hz, 2H), 6.93 (d, *J* = 7.74 Hz, 1H), 6.81 (d, *J* = 7.14 Hz, 1H), 6.70 (t, *J* = 7.74 Hz, 1H); ^{13}C NMR (DMSO, 75 MHz) δ (ppm): 163.7, 162.9, 159.8, 144.6, 141.9, 133.3, 129.8, 122.7, 119.7, 118.9, 118.7, 118.1, 117.5, 112.9, 110.8, 109.7; MS (ESI): m/z 312 $(M+1)^+$; HRMS (ESI) calcd for $C_{19}H_{14}N_5$ $[M+H]^+$ 312.12437; found: 312.12405.

3-(6-fluoro-1H-benzo[d]imidazol-2-yl)-2-phenylimidazo[1,2-a]pyrimidine (11q)

Compound **11q** was prepared according to the method described for compound **11a**, employing 2-phenylimidazo[1,2-a]pyrimidine-3-carbaldehyde (**9d,** 200 mg, 0.896 mmol) and 4-fluorobenzene-1,2-diamine (**10b,** 113.1 mg, 0.896mmol) and sodium metabisulfite (340.9 mg, 1.79 mmol) to

obtain the pure product **11q** as a light yellow solid .(yield: 210mg, 71.2%); Mp: 210-212 ºC; IR (KBr): $\bar{\upsilon}_{max}$/cm^{-1}- 3434, 3289, 2923, 1609, 1519, 1503, 1444, 1412, 1361, 1329, 1289, 1253, 1230, 1172, 1109, 1029, 972, 892; ^{1}H NMR (300 MHz, DMSO)δ (ppm): 8.82 (d, *J* = 2.8 Hz, 1H), 8.76-8.74 (m, 1H), 7.84 (dd, *J* = 1.7 Hz, 7.7 Hz, 1H), 7.67(d, *J* = 1.5 Hz, 1H), 7.55-7.51 (m, 2H),7.22 (dd, *J* = 2.6 Hz, 6.98 Hz, 1H), 6.91 (dd, *J* = 2.8 Hz, 8.68 Hz, 1H), 6.54 (dd, *J* = 2.6 Hz, 7.7 Hz, 2H), 6.34 (ddd, *J* = 2.8 Hz, 8.68 Hz, 11.1 Hz, 1H); ^{13}C NMR (DMSO, 75 MHz) δ (ppm): 164.1, 162.9, 159.8, 141.9, 139.8, 139.2, 133.3, 127.2, 125.2, 118.7, 117.9, 117.7, 116.5, 114.2, 113.2, 110.2, 107.5;MS (ESI): m/z 330 $(M+1)^{+}$; HRMS (ESI) calcd for $C_{19}H_{12}FN_5$ $[M+H]^{+}$ 330.1155; found: 330.1149.

3-(6-chloro-1H-benzo[d]imidazol-2-yl)-2-phenylimidazo[1,2-a]pyrimidine (11r)

Compound **11r** was prepared according to the method described for compound **11a**, employing 2-phenylimidazo[1,2-a]pyrimidine-3-carbaldehyde (**9d,** 200 mg, 0.896 mmol) and 4-chlorobenzene-1,2-diamine (**10c,** 127.8 mg, 0.896mmol) and sodium metabisulfite (340.9 mg, 1.79 mmol) to obtain the pure product **11r** as a yellow solid.(yield: 245mg, 79.2%); Mp: 202-204 ºC; IR (KBr): $\bar{\upsilon}_{max}$/cm^{-1}- 3424, 3291, 2923, 2851, 1630, 1596, 1518, 1493, 1412, 1358, 1333, 1267, 1229, 1203, 1059, 1034, 1014, 891; ^{1}H NMR (DMSO, 300 MHz) δ (ppm): 8.83 (d, *J* = 4.2 Hz, 1H), 8.77-8.74 (m, 1H), 7.87 (dd, *J* = 1.9 Hz, 6.04 Hz, 2H), 7.52 (d, *J* = 7.17 Hz, 2H), 7.16 (dd, *J* = 4.3 Hz, 6.98 Hz, 1H), 6.87 (d, *J* = 8.49 Hz, 1H), 6.81 (d, *J* = 2.07 Hz, 1H), 6.73-6.71(m, 1H), 6.68 (dd, *J* = 2.07 Hz, 7.36 Hz, 1H); MS (ESI): m/z 346 $(M+1)^{+}$; HRMS (ESI) calcd for $C_{19}H_{12}ClN_5$ $[M+H]^{+}$ 346.08591; found: 346.08461.

3-(6-methyl-1H-benzo[d]imidazol-2-yl)-2-phenylimidazo[1,2-a]pyrimidine (11s)

Compound **11s** was prepared according to the method described for compound **11a**, employing 2-phenylimidazo[1,2-a]pyrimidine-3-carbaldehyde (**9d,** 200 mg, 0.896 mmol) and 4-methylbenzene-1,2-diamine (**10d,** 109.5 mg, 0.896mmol) and sodium metabisulfite (340.9 mg, 1.79 mmol) to obtain the pure product **11s** as a light yellow solid. (yield: 210 mg, 71.9%); Mp: 206-208 ºC; IR (KBr): $\bar{\upsilon}_{max}$/cm^{-1}- 3429, 3198, 2917, 2862, 1611, 1524, 1504, 1456, 1416, 1403, 1326, 1303, 1276, 1252, 1223, 1175, 1042, 1026, 835; ^{1}H NMR (300 MHz, DMSO)δ (ppm): 8.79-8.76 (m, 2H), 7.93 (dd, *J* = 8.3 Hz, 4.2 Hz, 2H), 7.72 (dd, *J* = 2.1 Hz, 6.81 Hz, 1H), 7.49 (d, *J* = 4.2 Hz, 7.71 Hz, 1H), 7.19-7.16 (m, 2H), 7.01 (t, *J* = 8.3 Hz, 1H), 6.83-6.80 (m, 1H), 6.58 (d, *J* = 8.3 Hz, 1H), 2.83 (s, 3H);MS (ESI): m/z 326 $(M+1)^{+}$; ^{13}C NMR (DMSO, 75 MHz) δ (ppm):163.9, 159.9, 149.8, 141.2,

139.1, 133.8, 133.3, 128.4, 126.4, 120.3, 117.7, 115.4, 113.1, 111.9, 111.5, 108.9; HRMS (ESI) calcd for $C_{20}H_{16}N_5$ $[M+H]^+$326.14002; found: 326.13954.

3-(6-methoxy-1H-benzo[d]imidazol-2-yl)-2-phenylimidazo[1,2-a]pyrimidine (11t)

Compound **11t** was prepared according to the method described for compound **11a**, employing 2-phenylimidazo[1,2-a]pyrimidine-3-carbaldehyde (**9d,** 200 mg, 0.896 mmol) and 4-methoxybenzene-1,2-diamine (**10e,** 123.9 mg, 0.896mmol) and sodium metabisulfite (340.9 mg, 1.79 mmol) to obtain the pure product **11t** as a yellow solid.(yield: 215 mg, 70.2%); Mp: 197-199 ºC; IR (KBr): $\bar{\upsilon}_{max}/cm^{-1}$- 3425, 2996, 2936, 2835, 1617, 1529, 1507, 1455, 1433, 1417, 1405, 1389, 1292, 1273, 1253, 1223, 1197, 1177, 1157, 1148, 1111, 1041, 1025, 936, 833; ^{1}H NMR (300 MHz, DMSO)δ (ppm): 8.85-8.82 (m, 2H), 7.87 (d, *J* = 1.67 Hz, 1H), 7.85 (d, *J* =1.22 Hz, 1H), 7.55-7.52 (m, 2H), 7.09 (dd, *J* = 2.74 Hz, 6.86 Hz, 2H), 6.95 (d, *J* = 8.54 Hz, 1H), 6.81-6.79 (m, 1H), 6.61 (d, *J* = 2.74 Hz, 1H), 3.83 (s, 3H). ^{13}C NMR (DMSO, 75 MHz) δ (ppm): 164.1, 159.8, 157.6, 141.9, 133.7, 126.9, 121.5, 118.6, 116.9, 114.9, 113.9, 113.8, 113.1, 111.9, 111.7, 110.1, 56.2; MS (ESI): m/z 342 $(M+1)^+$; HRMS (ESI) calcd for $C_{20}H_{16}N_5O[M+H]^+$ 342.13494; found: 342.13452.

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