

Supporting Information

Copper-catalyzed tandem azide-alkyne cycloaddition, Ullmann type C-N coupling and intramolecular direct arylation

Kasiviswanadharaju Pericherla,^{a,b} Amitabh Jha,^b Bharti Khungar^a and Anil Kumar^{a,*}

^aDepartment of Chemistry, Birla Institute of Technology and Science, Pilani 333 031, Rajasthan, India

^bDepartment of Chemistry, Acadia University, Wolfville, NS, B4P 2R6, Canada

Email: anilkumar@pilani.bits-pilani.ac.in

Contents

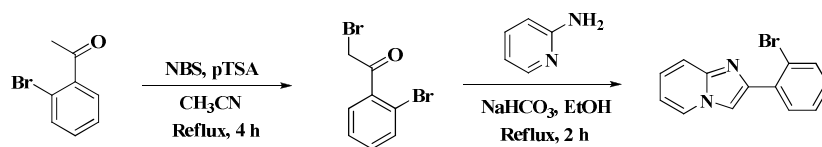
1. General information	S2
2. Experimental	S2
a. Preparation of 2-(2-bromophenyl)imidazo[1,2-a]pyridines	S2
b. Preparation of 3-bromo-2-(2-bromophenyl)imidazo[1,2-a]pyridines (1a-e).....	S3
c. Preparation of 1,2,3-triazole-fused imidazo[1,2-a]pyridines (5a-o).....	S4
d. Preparation of compounds 7-10	S8
3. Copies of ¹ H NMR and ¹³ C NMR spectra of 2-(2-bromophenyl)imidazo[1,2-a]pyridines, 1a-e , 5a-o , 7 and 9	S9

1. General information

Melting points were determined in open capillary tubes on a MPA120-Automated melting point apparatus and are uncorrected. Reactions were monitored by using thin layer chromatography (TLC) on 0.2 mm silica gel F254 plates (Merck). The chemical structures of final products were characterized by nuclear magnetic resonance spectra (^1H NMR, ^{13}C NMR) determined on a Bruker AV NMR 300 MHz spectrometer. ^{13}C NMR spectra are fully decoupled. Chemical shifts were reported in parts per million (ppm) using deuterated solvent peak or tetramethylsilane (internal) as the standard. The chemical structures of all the products were confirmed by a Bruker microTOF Mass spectrometer. 1-Ethynyl-3-methylbenzene was prepared by Sonagashira coupling between 3-iodotoluene and trimethylsilylacetylene followed by TMS deprotection using tetrabutylammonium fluoride. All other chemicals were obtained from commercial suppliers and used without further purification.

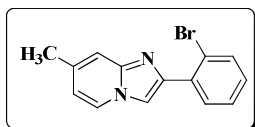
2. Experimental

2a. Preparation of 2-(2-bromophenyl)imidazo[1,2-a]pyridines :



2-(2-Bromophenyl)H-imidazo[1,2-a]pyridines were synthesized using previously reported procedures.¹ A solution of 2'-bromoacetophenone (5.0 g, 25 mmol), *N*-bromosuccinimide (4.5 g, 25 mmol) and *p*-toluenesulphonic acid (7.1 g, 37.5 mmol) in acetonitrile (40 mL) was stirred for 4 h at reflux temperature. On completion, the reaction mass was allowed to cool to ambient temperature and the volatiles were evaporated. The residue was diluted with water and the product was extracted into ethyl acetate. The organic layer was dried over anhydrous sodium sulfate and the solution was evaporated to dryness. The crude 2-bromo-1-(2-bromophenyl)ethanone (6.6 g, 95%, light brown liquid) was subjected to next step without further purifications.

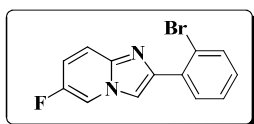
To a solution of 2-bromo-1-(2-bromophenyl)ethanone (6.50 g, 23.38 mmol) and sodium bicarbonate (2.9 g, 35.07 mmol) in ethanol (65 mL) was added 2-aminopyridine (2.19 g, 23.38 mmol) and the reaction mixture was stirred at reflux temperature for 2 h. After completion, the reaction mass was allowed to cool to ambient temperature and the volatiles were evaporated. The residue was diluted with water and extracted into ethyl acetate. The organic layer was dried over anhydrous sodium sulfate and the solution was evaporated to dryness. The crude residue was purified by column chromatography to get 2-(2-bromophenyl)H-imidazo[1,2-a]pyridine (4.15 g, 65%) as a pale yellow solid; mp 80-81 °C; ^1H NMR (500 MHz, CDCl_3): δ 8.28 (s, 1H), 8.17 – 8.13 (m, 2H), 7.68 – 7.62 (m, 2H), 7.41 (t, J = 7.6 Hz, 1H), 7.17 (t, J = 7.6 Hz, 2H), 6.78 (t, J = 6.7 Hz, 1H); ^{13}C NMR (126 MHz, CDCl_3) δ 144.5, 143.3, 134.5, 133.6, 131.7, 128.9, 127.5, 125.7, 124.7, 121.5, 117.7, 112.4, 112.0. HRMS calcd for $\text{C}_{13}\text{H}_{10}\text{BrN}_2$ 273.0022 found 273.0034 $[\text{M} + \text{H}]^+$.



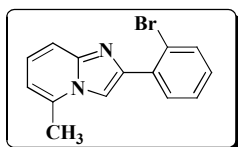
2-(2-Bromophenyl)-7-methylimidazo[1,2-a]pyridine: The reaction of 2-bromo-1-(2-bromophenyl)ethanone (6.5 g, 23.38 mmol), 2-amino-4-methylpyridine (2.52 g, 23.38 mmol), sodium bicarbonate (2.9 g, 35.07 mmol) in ethanol (65 mL) in the manner as described above afforded 4.16 g of 2-(2-Bromophenyl)-7-methylimidazo[1,2-a]pyridine (62%); colorless solid; mp 98-99 °C; ^1H NMR (300 MHz, CDCl_3) δ 8.21 (s, 1H), 8.17 (d, J = 7.8 Hz, 1H), 8.01 (d, J = 6.9 Hz, 1H), 7.67 (d, J = 8.0 Hz, 1H), 7.49 – 7.36 (m, 2H), 7.17 (t, J = 7.6 Hz, 1H),

¹ K. Pericherla, P. Khedar, B. Khungar and A. Kumar, *Chem. Commun.*, 2013, **49**, 2924-2926.

6.63 (d, $J = 6.8$ Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 145.28, 143.27, 136.09, 134.92, 133.96, 132.01, 129.02, 127.77, 125.25, 121.82, 116.27, 115.47, 111.73, 21.58. HRMS calcd for $\text{C}_{14}\text{H}_{12}\text{BrN}_2$ 287.0178 found 287.0169 $[\text{M} + \text{H}]^+$.

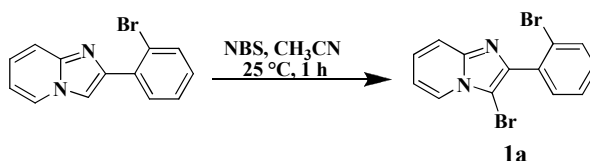


2-(2-Bromophenyl)-6-fluoroimidazo[1,2-a]pyridine: The reaction of 2-bromo-1-(2-bromophenyl)ethanone (6.5 g, 23.38 mmol), 2-amino-5-fluoropyridine (2.61 g, 23.38 mmol), sodium bicarbonate (2.9 g, 35.07 mmol) in ethanol (65 mL) in the manner as described above afforded 3.81 g of 2-(2-Bromophenyl)-6-fluoroimidazo[1,2-a]pyridine (56%); off-white solid; mp 109-110 °C; ^1H NMR (300 MHz, CDCl_3) δ 8.31 (s, 1H), 8.18 – 8.06 (m, 2H), 7.76 – 7.61 (m, 2H), 7.44 (t, $J = 7.6$ Hz, 1H), 7.31 – 7.09 (m, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 155.33, 152.18, 144.93, 142.61, 134.51, 134.02, 131.98, 129.40, 127.85, 121.85, 118.51, 118.39, 117.41, 117.07, 113.59, 112.84, 112.30. HRMS calcd for $\text{C}_{13}\text{H}_9\text{BrFN}_2$ 290.9928 found 290.9915 $[\text{M} + \text{H}]^+$.

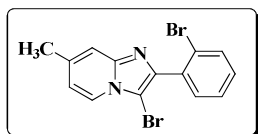


2-(2-Bromophenyl)-5-methylimidazo[1,2-a]pyridine: The reaction of 2-bromo-1-(2-bromophenyl)ethanone (6.5 g, 23.38 mmol), 2-amino-6-methylpyridine (2.52 g, 23.38 mmol), sodium bicarbonate (2.9 g, 35.07 mmol) in ethanol (65 mL) in the manner as described above afforded 2.81 g of 2-(2-Bromophenyl)-5-methylimidazo[1,2-a]pyridine (42%); pale yellow solid; mp 122-124 °C; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 8.30 (s, 1H), 8.07 (d, $J = 7.6$ Hz, 1H), 7.75 (d, $J = 7.8$ Hz, 1H), 7.50 (dd, $J = 13.9, 8.1$ Hz, 2H), 7.35 – 7.22 (m, 2H), 6.83 (d, $J = 6.3$ Hz, 1H), 2.65 (s, 3H); ^{13}C NMR (75 MHz, $\text{DMSO}-d_6$) δ 145.20, 143.39, 136.14, 135.50, 134.35, 132.42, 130.04, 128.45, 126.10, 121.74, 115.11, 112.24, 110.18, 18.97. HRMS calcd for $\text{C}_{14}\text{H}_{12}\text{BrN}_2$ 287.0178 found 287.0181 $[\text{M} + \text{H}]^+$.

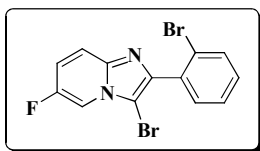
2b. Preparation of 3-bromo-2-(2-bromophenyl)imidazo[1,2-a]pyridine (**1a**):



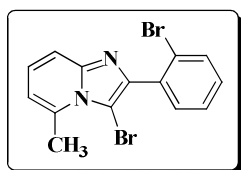
To a solution of 2-(2-bromophenyl)imidazo[1,2-a]pyridine (4.0 g, 14.76 mmol) in acetonitrile (40 mL) added *N*-bromosuccinimide (2.89 g, 16.23 mmol) and stirred at 25 °C for 1 h. On completion, the volatiles were evaporated. The residue was diluted with ethyl acetate and washed with saturated sodium thiosulfate solution and water. The ethyl acetate layer dried over anhydrous Na_2SO_4 and concentrated the solvent *in vacuo*. The crude residue was purified by column chromatography to yield 3-bromo-2-(2-bromophenyl)H-imidazo[1,2-a]pyridine (**1a**) (4.26 g, 82%) as yellow solid; mp 146-147 °C; ^1H NMR (300 MHz, CDCl_3) δ 8.24 (d, $J = 6.9$ Hz, 1H), 7.81 (d, $J = 9.1$ Hz, 1H), 7.74 (d, $J = 8.0$ Hz, 1H), 7.55 (d, $J = 7.5$ Hz, 1H), 7.49 – 7.30 (m, 3H), 7.07 (t, $J = 6.8$ Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 145.41, 144.17, 134.54, 133.37, 132.74, 130.46, 127.37, 125.38, 124.38, 124.13, 118.31, 113.62, 94.72. HRMS calcd for $\text{C}_{13}\text{H}_9\text{Br}_2\text{N}_2$ 350.9127 found 350.9116 $[\text{M} + \text{H}]^+$.



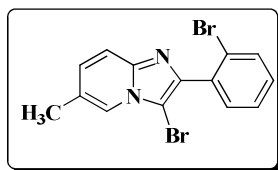
3-Bromo-2-(2-bromophenyl)-7-methylimidazo[1,2-a]pyridine (**1b**): The reaction of 2-(2-bromophenyl)-7-methylimidazo[1,2-a]pyridine (2.0 g, 6.96 mmol), *N*-bromosuccinimide (1.36 g, 7.66 mmol) in acetonitrile (20 mL) in the manner as described for compound **1a** above afforded 2.24 g of **1b** (88%); off-white solid; mp 131-133 °C; ^1H NMR (300 MHz, CDCl_3) δ 8.00 (dd, $J = 6.8, 1.9$ Hz, 1H), 7.65 (d, $J = 8.0$ Hz, 1H), 7.46 (d, $J = 7.6$ Hz, 1H), 7.41 – 7.29 (m, 2H), 7.24 (t, $J = 7.7$ Hz, 1H), 6.76 (d, $J = 5.4$ Hz, 1H), 2.40 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 145.43, 143.52, 136.09, 134.36, 132.94, 132.33, 130.12, 126.95, 123.70, 123.16, 116.31, 116.00, 93.52, 21.16. HRMS calcd for $\text{C}_{14}\text{H}_{11}\text{Br}_2\text{N}_2$ 364.9283 found 364.9278 $[\text{M} + \text{H}]^+$.



3-Bromo-2-(2-bromophenyl)-6-fluoroimidazo[1,2-a]pyridine (**1c**): The reaction of 2-(2-bromophenyl)-6-fluoroimidazo[1,2-a]pyridine (2.0 g, 6.87 mmol), *N*-bromo-succinimide (1.34 g, 7.56 mmol) in acetonitrile (20 mL) in the manner as described for compound **1a** above afforded 2.16 g of **1c** (85%); off-white solid; mp 211-213 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 8.68 – 8.61 (m, 1H), 7.84 – 7.73 (m, 2H), 7.58 – 7.47 (m, 3H), 7.47 – 7.37 (m, 1H). ¹³C NMR (75 MHz, DMSO-*d*₆) δ 155.56, 152.40, 145.23, 142.71, 133.91, 133.02, 132.21, 130.19, 127.01, 123.67, 118.66, 118.54, 117.24, 116.90, 111.26, 110.70, 95.62. HRMS calcd for C₁₃H₈Br₂FN₂ 368.9033 found 368.9049 [M + H]⁺.

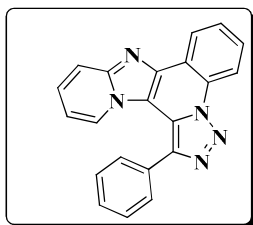
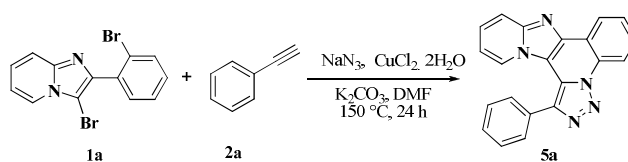


3-Bromo-2-(2-bromophenyl)-5-methylimidazo[1,2-a]pyridine (**1d**): The reaction of 2-(2-bromophenyl)-5-methylimidazo[1,2-a]pyridine (2.0 g, 6.96 mmol), *N*-bromo succinimide (1.36 g, 7.66 mmol) in acetonitrile (20 mL) in the manner as described for compound **1a** above afforded 1.65 g of **1d** (65%); pale yellow solid; mp 138-139 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.76 (d, *J* = 7.7 Hz, 1H), 7.57 – 7.34 (m, 4H), 7.24 (t, *J* = 7.8 Hz, 1H), 6.80 (d, *J* = 6.5 Hz, 1H), 3.04 (s, 3H). ¹³C NMR (75 MHz, DMSO-*d*₆) δ 146.99, 145.94, 137.44, 135.70, 133.37, 133.24, 131.28, 128.22, 126.38, 124.28, 116.86, 115.43, 93.36, 21.27. HRMS calcd for C₁₄H₁₁Br₂N₂ 364.9283 found 364.9279 [M + H]⁺.

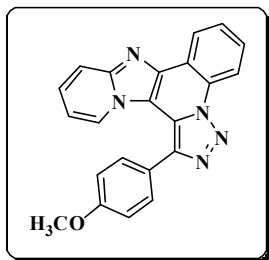


3-Bromo-2-(2-bromophenyl)-6-methylimidazo[1,2-a]pyridine (**1e**): The reaction of 2-(2-bromophenyl)-6-methylimidazo[1,2-a]pyridine (2.0 g, 6.96 mmol), *N*-bromo succinimide (1.36 g, 7.66 mmol) in acetonitrile (20 mL) in the manner as described for compound **1a** above afforded 1.97 g of **1e** (78%); off white solid; ¹H NMR (300 MHz, CDCl₃) δ 7.93 (s, 1H), 7.69 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.59 – 7.53 (m, 1H), 7.50 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.38 (td, *J* = 7.5, 1.3 Hz, 1H), 7.32 – 7.23 (m, 1H), 7.12 (dd, *J* = 9.2, 1.6 Hz, 1H), 2.39 (s, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 144.18, 143.55, 134.36, 132.98, 132.40, 130.07, 128.22, 127.07, 123.76, 123.12, 121.72, 117.27, 93.88, 18.37.

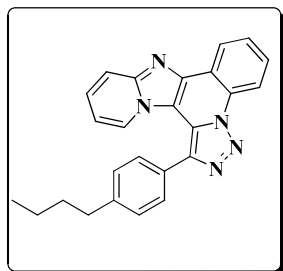
2c. General procedure for the regioselective synthesis of 1,2,3-triazole fused imidazo[1,2-a]pyridines (**5a-o**):



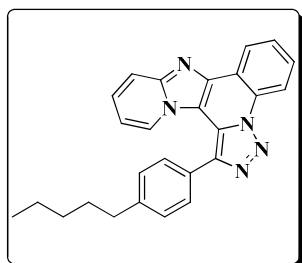
Compound 5a: Mixture of compound **1a** (175 mg, 0.5 mmol), phenylacetylene (61 mg, 0.6 mmol), sodium azide (40 mg, 0.6 mmol), CuCl₂·2H₂O (17 mg, 0.1 mmol), K₂CO₃ (172 mg, 1.25 mmol) were vigorously stirred in DMF (3 mL) at 150 °C for 24 h. After cooling to room temperature, the reaction mass was diluted with water and extracted into ethyl acetate. The organic layer was dried with anhydrous sodium sulfate and the solvent was evaporated. The crude compound was purified by flash chromatography on a short silica gel (ethyl acetate: hexanes) to afford 109 mg of compound **5a** (65%); yellow solid; mp 248-250 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.94 (d, *J* = 8.1 Hz, 1H), 8.71 (d, *J* = 7.6 Hz, 1H), 7.91 – 7.82 (m, 2H), 7.82 – 7.68 (m, 3H), 7.67 – 7.58 (m, 3H), 7.55 (d, *J* = 7.0 Hz, 1H), 7.45 – 7.35 (m, 1H), 6.69 (t, *J* = 6.8 Hz, 1H); ¹³C NMR (126 MHz, CDCl₃) δ 137.90, 131.84, 131.61, 131.36, 130.14, 129.55, 128.54, 128.30, 127.87, 124.46, 117.85, 117.44, 117.20, 113.24, 113.01; HRMS calcd for C₂₁H₁₃N₅Na 358.1063 found 358.1050 [M + Na]⁺.



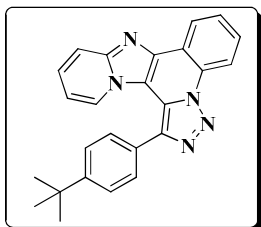
Compound 5b: The reaction of 3-bromo-2-(2-bromophenyl)H-imidazo[1,2-a]pyridine (**1a**, 175 mg, 0.5 mmol), 1-ethynyl-4-methoxybenzene (80 mg, 0.6 mmol), sodium azide (40 mg, 0.6 mmol), CuCl₂·2H₂O (17 mg, 0.1 mmol), K₂CO₃ (172 mg, 1.25 mmol) in DMF (3 mL) in the manner as described for compound **5a** above afforded 124 mg of **5b** (68%); white solid. mp 231-232 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.90 (d, *J* = 8.1 Hz, 1H), 8.69 (d, *J* = 7.6 Hz, 1H), 7.95 – 7.72 (m, 3H), 7.70 – 7.53 (m, 3H), 7.41 (t, *J* = 7.8 Hz, 1H), 7.13 (d, *J* = 8.3 Hz, 2H), 6.74 (t, *J* = 6.8 Hz, 1H), 3.97 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 161.03, 148.12, 139.77, 137.80, 132.94, 132.00, 129.96, 128.54, 127.78, 127.54, 124.72, 124.55, 122.65, 119.08, 118.01, 117.38, 114.29, 113.51, 113.02, 55.84; HRMS calcd for C₂₂H₁₅N₅NaO 388.1169 found 388.1171 [M + Na]⁺.



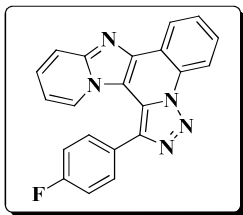
Compound 5c: The reaction of 3-bromo-2-(2-bromophenyl)H-imidazo[1,2-a]pyridine (**1a**, 175 mg, 0.5 mmol), 1-ethynyl-4-butylbenzene (95 mg, 0.6 mmol), sodium azide (40 mg, 0.6 mmol), CuCl₂·2H₂O (17 mg, 0.1 mmol), K₂CO₃ (172 mg, 1.25 mmol) in DMF (3 mL) in the manner as described for compound **5a** above afforded 116 mg of **5c** (59%); off-white solid; mp 169-170 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.97 (d, *J* = 8.2 Hz, 1H), 8.76 (d, *J* = 7.8 Hz, 1H), 7.96 – 7.72 (m, 3H), 7.68 – 7.50 (m, 3H), 7.50 – 7.33 (m, 3H), 6.67 (t, *J* = 6.8 Hz, 1H), 2.82 (t, *J* = 7.5 Hz, 3H), 1.83 – 1.69 (m, 2H), 1.57 – 1.38 (m, 2H), 1.03 (t, *J* = 7.3 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 148.19, 144.73, 139.90, 138.11, 131.96, 131.66, 129.95, 129.65, 128.78, 128.63, 127.79, 127.51, 124.52, 122.79, 119.14, 117.99, 117.40, 113.51, 112.80, 35.84, 33.89, 22.54, 14.19; HRMS calcd for C₂₅H₂₂N₅ 392.1870 found 392.1879 [M + H]⁺.



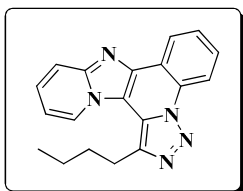
Compound 5d: The reaction of 3-bromo-2-(2-bromophenyl)H-imidazo[1,2-a]pyridine (**1a**, 175 mg, 0.5 mmol), 1-ethynyl-4-pentylbenzene (103 mg, 0.6 mmol), sodium azide (40 mg, 0.6 mmol), CuCl₂·2H₂O (17 mg, 0.1 mmol), K₂CO₃ (172 mg, 1.25 mmol) in DMF (3 mL) in the manner as described for compound **5a** above afforded 131.5 mg of **5d** (65%); pale yellow solid; mp 181-183 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.87 (d, *J* = 8.2 Hz, 1H), 8.62 (d, *J* = 8.0 Hz, 1H), 7.85 – 7.73 (m, 2H), 7.70 (t, *J* = 7.5 Hz, 1H), 7.61 (d, *J* = 7.7 Hz, 2H), 7.51 (d, *J* = 6.9 Hz, 1H), 7.40 (d, *J* = 8.0 Hz, 2H), 7.33 (dd, *J* = 17.3, 9.3 Hz, 1H), 6.61 (t, *J* = 7.0 Hz, 1H), 2.79 (t, *J* = 7.5 Hz, 2H), 1.88 – 1.63 (m, 2H), 1.53 – 1.31 (m, 4H), 0.96 (t, *J* = 6.7 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 148.26, 144.69, 140.04, 138.04, 131.92, 131.64, 129.82, 129.70, 128.74, 128.59, 127.69, 127.29, 124.42, 122.78, 119.23, 118.03, 117.35, 113.46, 112.63, 36.11, 31.69, 31.36, 22.81, 14.27; HRMS calcd for C₂₆H₂₃N₅Na 428.1840 found 428.1856 [M + Na]⁺.



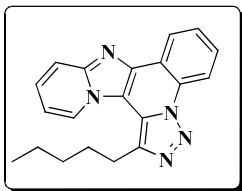
Compound 5e: The reaction of 3-bromo-2-(2-bromophenyl)H-imidazo[1,2-a]pyridine (**1a**, 175 mg, 0.5 mmol), 1-*tert*-butyl-4-ethynylbenzene (95 mg, 0.6 mmol), sodium azide (40 mg, 0.6 mmol), CuCl₂·2H₂O (17 mg, 0.1 mmol), K₂CO₃ (172 mg, 1.25 mmol) in DMF (3 mL) in the manner as described for compound **5a** above afforded 129 mg of **5e** (66%); colorless solid; mp 268-270 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.90 (d, *J* = 8.2 Hz, 1H), 8.65 (d, *J* = 7.7 Hz, 1H), 7.86 – 7.68 (m, 3H), 7.63 (s, 4H), 7.44 (d, *J* = 6.9 Hz, 1H), 7.35 (t, *J* = 8.0 Hz, 1H), 6.58 (t, *J* = 7.0 Hz, 1H), 1.47 (s, 9H); ¹³C NMR (75 MHz, CDCl₃) δ 153.15, 148.22, 139.97, 137.99, 131.95, 131.55, 129.88, 129.45, 128.59, 127.74, 127.38, 125.58, 124.48, 122.90, 119.20, 118.01, 117.38, 113.49, 112.66, 35.25, 31.71; HRMS calcd for C₂₅H₂₂N₅ 392.1870 found 392.1869 [M + H]⁺.



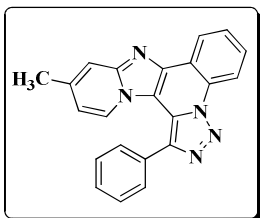
Compound 5f: The reaction of 3-bromo-2-(2-bromophenyl)H-imidazo[1,2-a]pyridine (**1a**, 175 mg, 0.5 mmol), 1-ethynyl-4-fluorobenzene (95 mg, 0.6 mmol), sodium azide (40 mg, 0.6 mmol), CuCl₂·2H₂O (17 mg, 0.1 mmol), K₂CO₃ (172 mg, 1.25 mmol) in DMF (3 mL) in the manner as described for compound **5a** above afforded 109 mg of **5f** (62%); colorless solid; mp 268-270 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.97 (d, *J* = 8.2 Hz, 1H), 8.76 (d, *J* = 8.0 Hz, 1H), 7.95 – 7.75 (m, 3H), 7.75 – 7.65 (m, 2H), 7.61 (d, *J* = 6.9 Hz, 1H), 7.44 (t, *J* = 8.0 Hz, 1H), 7.38 – 7.24 (m, 2H), 6.78 (t, *J* = 6.9 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 148.29, 136.91, 133.49, 133.38, 131.99, 130.13, 128.65, 128.20, 127.98, 127.71, 124.66, 122.79, 119.16, 118.29, 117.48, 116.01, 115.72, 113.16, 109.55; HRMS calcd for C₂₁H₁₃FN₅ 354.1150 found 354.1138 [M + H]⁺.



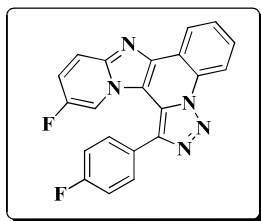
Compound 5g: The reaction of 3-bromo-2-(2-bromophenyl)H-imidazo[1,2-a]pyridine (**1a**, 175 mg, 0.5 mmol), hex-1-yne (51 mg, 0.6 mmol), sodium azide (40 mg, 0.6 mmol), CuCl₂·2H₂O (17 mg, 0.1 mmol), K₂CO₃ (172 mg, 1.25 mmol) in DMF (3 mL) in the manner as described for compound **5a** above afforded 113.5 mg of **5g** (72%); colorless solid; mp 176-177 °C; ¹H NMR (300 MHz, DMSO) δ 8.88 (d, *J* = 7.1 Hz, 1H), 8.69 (d, *J* = 8.2 Hz, 1H), 8.54 (t, *J* = 8.4 Hz, 1H), 7.97 – 7.71 (m, 3H), 7.60 (t, *J* = 8.1 Hz, 1H), 7.28 (t, *J* = 7.0 Hz, 1H), 3.45 (t, *J* = 7.7 Hz, 2H), 1.93 – 1.75 (m, 2H), 1.59 – 1.40 (m, 2H), 0.96 (t, *J* = 7.3 Hz, 3H). ¹³C NMR (75 MHz, DMSO) δ 147.55, 138.92, 137.02, 131.68, 129.40, 127.23, 126.98, 125.70, 123.98, 122.31, 118.65, 118.41, 116.93, 113.81, 113.23, 33.59, 28.07, 22.28, 13.72; HRMS calcd for C₁₉H₁₇N₅Na 338.1371 found 338.1364 [M + Na]⁺.



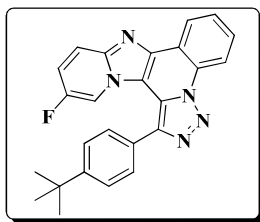
Compound 5h: The reaction of 3-bromo-2-(2-bromophenyl)H-imidazo[1,2-a]pyridine (**1a**, 175 mg, 0.5 mmol), hept-1-yne (58 mg, 0.6 mmol), sodium azide (40 mg, 0.6 mmol), CuCl₂·2H₂O (17 mg, 0.1 mmol), K₂CO₃ (172 mg, 1.25 mmol) in DMF (3 mL) in the manner as described for compound **5a** above afforded 125 mg of **5h** (76%); colorless solid; mp 182-184 °C; ¹H NMR (500 MHz, CDCl₃) δ 8.90 (d, *J* = 6.9 Hz, 1H), 8.88 (d, *J* = 8.3 Hz, 1H), 8.70 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.94 (d, *J* = 9.1 Hz, 1H), 7.83 – 7.79 (m, 1H), 7.77 – 7.71 (m, 1H), 7.56 – 7.50 (m, 1H), 7.14 (t, *J* = 6.8 Hz, 1H), 3.53 – 3.49 (m, 2H), 2.06 – 1.96 (m, 2H), 1.64 – 1.54 (m, 2H), 1.47 (dd, *J* = 14.9, 7.3 Hz, 2H), 0.97 (t, *J* = 7.3 Hz, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 137.23, 131.66, 131.60, 129.65, 127.48, 125.76, 124.06, 122.36, 118.40, 117.06, 113.93, 113.87, 113.60, 31.49, 28.46, 22.50, 14.10. HRMS calcd for C₂₀H₂₀N₅ 330.1713 found 330.1726 [M + H]⁺.



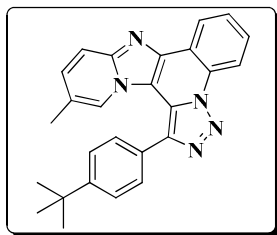
Compound 5i: The reaction of 3-bromo-2-(2-bromophenyl)-7-methylimidazo[1,2-a]pyridine (**1b**, 182 mg, 0.5 mmol), phenylacetylene (61 mg, 0.6 mmol), sodium azide (40 mg, 0.6 mmol), CuCl₂·2H₂O (17 mg, 0.1 mmol), K₂CO₃ (172 mg, 1.25 mmol) in DMF (3 mL) in the manner as described for compound **5a** above afforded 129 mg of **5i** (74%); colorless solid; mp 273-274 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.96 – 8.90 (m, 1H), 8.69 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.86 – 7.68 (m, 4H), 7.65 – 7.56 (m, 4H), 7.40 (d, *J* = 7.1 Hz, 1H), 6.52 (dd, *J* = 7.1, 1.5 Hz, 1H), 2.45 (s, 3H); ¹³C NMR (75 MHz, DMSO) δ 148.94, 140.01, 139.77, 137.65, 132.65, 131.88, 131.48, 130.48, 130.07, 129.21, 128.47, 127.64, 124.61, 123.26, 119.52, 117.25, 116.56, 115.98, 113.13, 21.60; HRMS calcd for C₂₂H₁₆N₅ 350.1400 found 350.1398 [M + H]⁺.



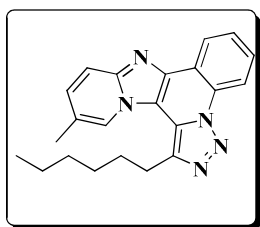
Compound 5j: The reaction of 3-bromo-2-(2-bromophenyl)-6-fluoroimidazo[1,2-a]pyridine(**1c**, 183.5 mg, 0.5 mmol), 1-ethynyl-4-fluorobenzene (72 mg, 0.6 mmol), sodium azide (40 mg, 0.6 mmol), $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (17 mg, 0.1 mmol), K_2CO_3 (172 mg, 1.25 mmol) in DMF (3 mL) in the manner as described for compound **5a** above afforded 126 mg of **5j** (68%); pale yellow solid; mp 288-289 °C; ^1H NMR (500 MHz, CDCl_3) δ 9.00 (d, $J = 8.3$ Hz, 1H), 8.76 (d, $J = 7.8$ Hz, 1H), 7.96 – 7.90 (m, 1H), 7.91 – 7.86 (m, 1H), 7.82 (t, $J = 7.5$ Hz, 1H), 7.77 – 7.70 (m, 2H), 7.51 (dd, $J = 4.4, 2.1$ Hz, 1H), 7.44 – 7.34 (m, 3H); HRMS calcd for $\text{C}_{21}\text{H}_{11}\text{F}_2\text{N}_5\text{Na}$ 394.0869 found 394.0880 $[\text{M} + \text{Na}]^+$.



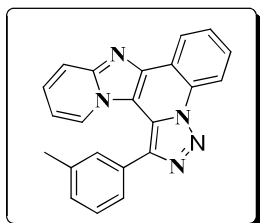
Compound 5k: The reaction of 3-bromo-2-(2-bromophenyl)-6-fluoroimidazo[1,2-a]pyridine(**1c**, 183.5 mg, 0.5 mmol), 1-*tert*-butyl-4-ethynylbenzene (95 mg, 0.6 mmol), sodium azide (40 mg, 0.6 mmol), $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (17 mg, 0.1 mmol), K_2CO_3 (172 mg, 1.25 mmol) in DMF (3 mL) in the manner as described for compound **5a** above afforded 159.5 mg of **5k** (78%); off-white solid; mp 294-295 °C; ^1H NMR (500 MHz, CDCl_3) δ 8.99 (d, $J = 8.3$ Hz, 1H), 8.73 (d, $J = 7.9$ Hz, 1H), 7.89 – 7.83 (m, 2H), 7.80 (t, $J = 7.6$ Hz, 1H), 7.70 – 7.62 (m, 4H), 7.35 – 7.31 (m, 1H), 7.26 (dd, $J = 4.7, 2.3$ Hz, 1H), 1.49 (s, 9H). ^{13}C NMR (126 MHz, CDCl_3) δ 153.55, 153.47, 151.65, 137.99, 131.60, 131.31, 130.36, 129.90, 128.56, 127.72, 125.47, 124.06, 119.41, 119.20, 117.93, 117.86, 117.20, 115.48, 115.13, 35.01, 31.36. HRMS calcd for $\text{C}_{25}\text{H}_{21}\text{FN}_5$ 410.1776 found 410.1770 $[\text{M} + \text{H}]^+$.



Compound 5l: The reaction of 3-bromo-2-(2-bromophenyl)-6-methylimidazo[1,2-a]pyridine(**1e**, 182 mg, 0.5 mmol), 1-*tert*-butyl-4-ethynylbenzene (95 mg, 0.6 mmol), sodium azide (40 mg, 0.6 mmol), $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (17 mg, 0.1 mmol), K_2CO_3 (172 mg, 1.25 mmol) in DMF (3 mL) in the manner as described for compound **5a** above afforded 154 mg of **5l** (76%); colorless solid; mp 299-301 °C; ^1H NMR (300 MHz, CDCl_3) δ 8.88 (dd, $J = 8.2, 0.9$ Hz, 1H), 8.61 (dd, $J = 7.8, 1.3$ Hz, 1H), 7.80 – 7.64 (m, 3H), 7.62 (s, 4H), 7.20 (s, 1H), 7.15 (dd, $J = 9.2, 1.5$ Hz, 1H), 1.96 (s, 3H), 1.46 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 152.68, 146.92, 139.45, 137.42, 131.37, 131.33, 130.12, 129.30, 129.13, 127.39, 126.16, 125.15, 123.87, 122.71, 122.07, 118.97, 117.01, 116.71, 112.74, 34.93, 31.47, 17.93. HRMS calcd for $\text{C}_{26}\text{H}_{24}\text{N}_5$ 406.2026 found 406.2035 $[\text{M} + \text{H}]^+$.

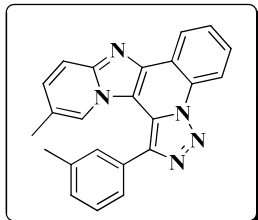


Compound 5m: The reaction of 3-bromo-2-(2-bromophenyl)-6-methylimidazo[1,2-a]pyridine(**1e**, 182 mg, 0.5 mmol), oct-1-yne (66 mg, 0.6 mmol), sodium azide (40 mg, 0.6 mmol), $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (17 mg, 0.1 mmol), K_2CO_3 (172 mg, 1.25 mmol) in DMF (3 mL) in the manner as described for compound **5a** above afforded 127 mg of **5m** (71%); colorless solid; mp 155-156 °C; ^1H NMR (300 MHz, CDCl_3) δ 8.79 (dd, $J = 8.1, 1.0$ Hz, 1H), 8.60 – 8.55 (m, 1H), 8.54 (s, 1H), 7.76 – 7.62 (m, 3H), 7.27 – 7.22 (m, 1H), 3.50 – 3.37 (m, 2H), 2.43 (s, 3H), 2.01 – 1.85 (m, 2H), 1.66 – 1.52 (m, 2H), 1.50 – 1.25 (m, 4H), 0.91 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 146.69, 138.80, 137.04, 131.44, 130.21, 129.22, 127.27, 123.78, 123.26, 123.13, 122.42, 118.79, 117.53, 116.94, 113.48, 32.23, 31.73, 29.22, 28.62, 22.63, 18.55, 14.06. HRMS calcd for $\text{C}_{22}\text{H}_{24}\text{N}_5$ 358.2026 found 358.2011 $[\text{M} + \text{H}]^+$.



Compound 5n: The reaction of 3-bromo-2-(2-bromophenyl)H-imidazo[1,2-a]pyridine(**1a**, 175 mg, 0.5 mmol), 1-ethynyl-3-methylbenzene (70 mg, 0.6 mmol), sodium azide (40 mg, 0.6 mmol), $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (17 mg, 0.1 mmol), K_2CO_3 (172 mg, 1.25 mmol) in DMF (3 mL) in the manner as described for compound **5a** above afforded 119 mg of **5n** (68%); pale yellow solid; mp 218-219 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.97 (dd, $J = 8.3, 0.7$ Hz, 1H), 8.73 (dd, $J = 7.9, 1.2$ Hz, 1H), 7.88 (d, $J = 9.1$ Hz, 1H), 7.86 – 7.81 (m,

1H), 7.80 – 7.74 (m, 1H), 7.62 (d, $J = 7.0$ Hz, 1H), 7.55 (s, 1H), 7.53 – 7.46 (m, 2H), 7.46 – 7.38 (m, 2H), 6.71 (td, $J = 6.9, 1.1$ Hz, 1H), 2.50 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 148.10, 139.90, 138.28, 137.86, 131.94, 131.80, 131.55, 130.08, 129.67, 128.41, 128.32, 128.30, 127.59, 127.26, 124.11, 122.42, 118.95, 117.79, 117.16, 113.09, 112.53, 21.50. HRMS calcd for $\text{C}_{23}\text{H}_{16}\text{N}_5$ 350.1400 found 350.1403 $[\text{M} + \text{H}]^+$.



Compound 5o: The reaction of 3-bromo-2-(2-bromophenyl)-6-methylimidazo[1,2-a]pyridine (**1e**, 182 mg, 0.5 mmol), 1-ethynyl-3-methylbenzene (70 mg, 0.6 mmol), sodium azide (40 mg, 0.6 mmol), $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (17 mg, 0.1 mmol), K_2CO_3 (172 mg, 1.25 mmol) in DMF (3 mL) in the manner as described for compound **5a** above afforded 133 mg of **5o** (73%); pale yellow solid; mp 275–276 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.93 (d, $J = 8.0$ Hz, 1H), 8.67 (dd, $J = 7.9, 1.3$ Hz, 1H), 7.84 – 7.77 (m, 1H), 7.77 – 7.69 (m, 2H), 7.54 (s, 1H), 7.53 – 7.50 (m, 2H), 7.49 – 7.45 (m, 1H), 7.26 (s, 1H), 7.23 (dd, $J = 9.2, 1.5$ Hz, 1H), 2.50 (s, 3H), 2.04 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 147.06, 139.65, 138.09, 137.61, 132.32, 132.03, 131.40, 130.22, 129.95, 129.39, 128.81, 128.15, 127.48, 126.26, 123.95, 122.76, 122.18, 119.07, 117.11, 116.84, 112.78, 21.46, 17.95. HRMS calcd for $\text{C}_{23}\text{H}_{18}\text{N}_5$ 364.1557 found 364.1548 $[\text{M} + \text{H}]^+$.

General procedure for the synthesis of 7, 9 and 10: Mixture of compound **6** or **8** (1 mmol), phenylacetylene (1.2 mmol), sodium azide (1.2 mmol), $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (0.2 mmol), K_2CO_3 (2.5 mmol) were vigorously stirred in DMF (4 mL) at 150 °C for 24 h. After cooling to room temperature, the reaction mass was diluted with water and extracted into ethyl acetate. The organic layer was dried with anhydrous sodium sulfate and the solvent was evaporated. The crude compound was purified by flash chromatography on a short silica gel (ethyl acetate: hexanes).

2-(2-(4-Phenyl-1H-1,2,3-triazol-1-yl)phenyl)H-imidazo[1,2-a]pyridine (7): yield 78%; off-white solid; mp 189–192 °C; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 8.89 (s, 1H), 8.43 (d, $J = 6.8$ Hz, 1H), 8.29 (d, $J = 7.8$ Hz, 1H), 7.93 (d, $J = 7.3$ Hz, 2H), 7.79 – 7.69 (m, 1H), 7.59 (d, $J = 3.1$ Hz, 2H), 7.51 (d, $J = 4.8$ Hz, 1H), 7.46 (d, $J = 7.7$ Hz, 2H), 7.36 (t, $J = 7.3$ Hz, 1H), 7.27 – 7.15 (m, 1H), 6.93 (s, 1H), 6.80 (t, $J = 6.7$ Hz, 1H); ^{13}C NMR (75 MHz, $\text{DMSO}-d_6$) δ 147.98, 145.06, 140.34, 134.62, 131.26, 130.65, 130.56, 130.40, 128.86, 128.44, 128.29, 127.47, 126.15, 125.84, 125.00, 122.05, 117.55, 112.53, 110.39. HRMS calcd for 338.1400, found 338.1405 $[\text{M} + \text{H}]^+$.

2-phenylimidazo[1,2-a]pyridine (9): yield 35%; off-white solid; mp 134–136 °C; ^1H NMR (300 MHz, CDCl_3) δ 8.11 (d, $J = 6.6$ Hz, 1H), 7.96 (d, $J = 7.6$ Hz, 2H), 7.85 (s, 1H), 7.65 (d, $J = 9.1$ Hz, 1H), 7.44 (t, $J = 7.5$ Hz, 2H), 7.35 – 7.30 (m, 1H), 7.17 (t, $J = 7.9$ Hz, 1H), 6.78 (t, $J = 6.6$ Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 145.74, 137.95, 133.65, 128.69, 127.99, 126.11, 125.59, 124.76, 117.55, 112.51, 108.19; ESI–MS(m/z): 195.1 ($\text{M} + \text{H}$) $^+$.

2-phenyl-3-(phenylethynyl)imidazo[1,2-a]pyridine (10): yield 22%; viscous liquid; ^1H NMR (300 MHz, CDCl_3) δ 8.66 (d, $J = 6.8$ Hz, 1H), 8.32 (d, $J = 7.2$ Hz, 2H), 7.76 – 7.73 (m, 2H), 7.56 – 7.44 (m, 8H), 7.15 (t, $J = 6.8$ Hz, 1H); ESI–MS(m/z): 295.1 ($\text{M} + \text{H}$) $^+$.

2. ^1H NMR and ^{13}C NMR spectra of 1a-e, 5a-o, 7 and 9:

