New Method for the General Synthesis of [1,2,4]Triazolo[1,5-*a*]pyridines

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[1,2,4]Triazolo[1,5-*a*]pyridines without substituents on the 2-position have been prepared from 2-aminopyridines by cyclization of *N*-(pyrid-2-yl)formamidoximes with trifluoroacetic anhydride. Triazoles substituted at any position on the pyridine ring may be prepared in good yields and under mild reaction conditions.

Introduction

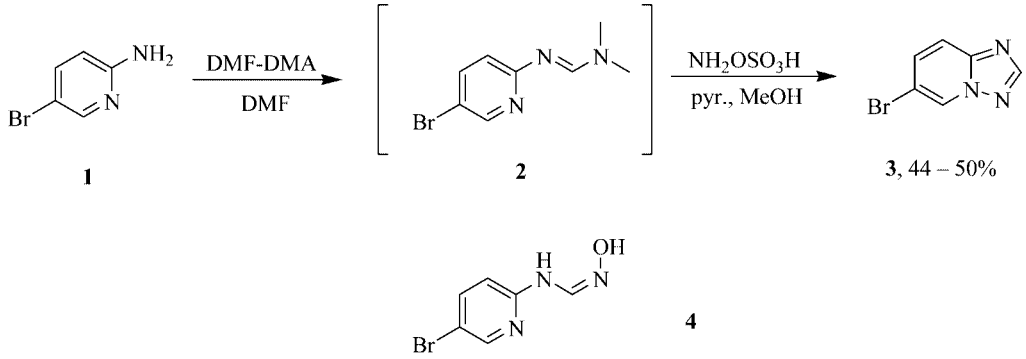
6-Bromo[1,2,4]triazolo[1,5-*a*]pyridine (**3**) is a key component of a larger molecule of pharmaceutical interest. The synthesis of this type of heterocycles has been previously reported in the literature by several synthetic methods such as amination of 2-aminopyridine with hydroxylamine-*O*-sulfonic acid (HSA), followed by cyclization with formic acid (18–27% overall yield);[1] reaction of 2-aminopyridines with DMF–dimethyl acetal, (DMF–DMA) followed by cyclization with HSA (26–87% yield);[2] cyclization of *N*-iminopyridine with HCN (2% yield);[3] isomerization of [1,2,4]-triazolo[4,3-*a*]pyridines in the presence of formic acid;[4] reaction of 2-aminopyridines with DMF–DMA and hydroxylamine, followed by cyclization with polyphosphoric acid (PPA) (54% overall yield);[5] and acetylation of formamidoximes followed by heating in aqueous solution (2 steps, 25% overall yield).[6]

There are a number of significant disadvantages to these methods, including low yields and scope limitation. In particular, triazoles prepared from 2-aminopyridines bearing a substituent on the 6 position are especially challenging and all the cyclization methods previously reported offer very limited success to prepare these types of compounds.[7]

Results and Discussion

The triazolo-pyridine **3** was successfully prepared by the method of Lin[2] (Scheme 1). However, yields were consistently lower than 50%.[8] While the formation of amidine intermediate **2** was nearly quantitative, subsequent cyclization to **3** proceeded poorly. Additionally, a substantial amount (10–30%) of *N*-hydroxy impurity **4**[9] was produced in the cyclization reaction.

The reaction is likely to proceed by replacing the dimethylamino moiety on **2** with HSA to form **5** (Scheme 2).[10] The sulfonyl moiety on intermediate **5** behaves as a leaving group, being displaced by the pyridine nitrogen during the cyclization that produces **3**.[2] However, if intermediate **5** is unstable to the reaction conditions, it could hydrolyze to produce **4**. We thought that the reaction could be improved by replacing the sulfonyl group with a different chemical entity that could stabilize intermediate **5** towards hydrolysis and behave as a better leaving group towards the pyridine nitrogen.



1 **2** **3**, 44 – 50% **4**

Scheme 1. HSA synthesis of **3**.

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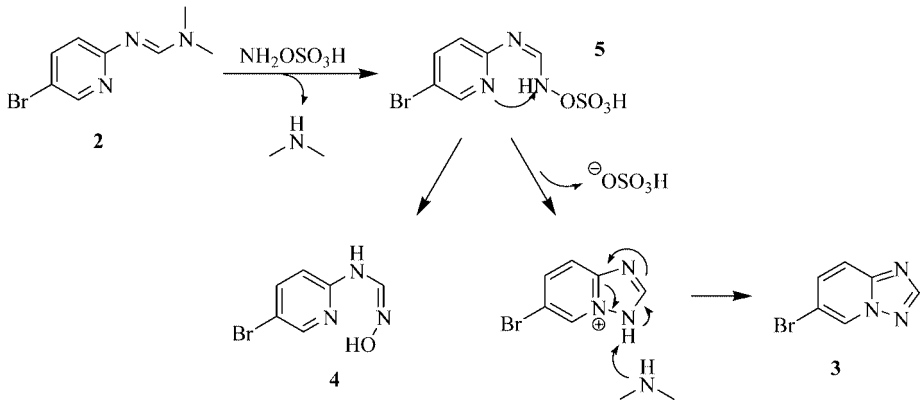
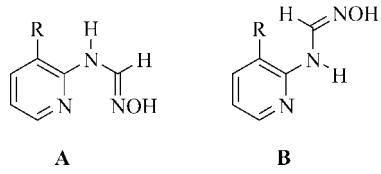


Scheme 2. Proposed mechanism in the HSA synthesis.

Intermediate **4** was easily prepared by treatment of amidine **2** with hydroxylamine.[5] Several dehydrating agents were screened as leaving groups to evaluate whether they could promote the cyclization reaction more efficiently (Table 1).

PPA was quite efficient at promoting the cyclization to **3** at elevated temperatures.[11] Other sulfur and phosphorus derived reagents afforded moderate yields of **3** at ambient temperature. Trifluoroacetic anhydride (TFAA), afforded the best results, cleanly promoting the desired reaction at ambient temperature. The presence of the electron withdrawing trifluoromethyl moiety is key to the reaction, as experiments conducted using acetyl chloride or acetic anhydride were unsuccessful. Under our optimized reaction conditions, the triazolo-pyridine **3** was obtained in 84% yield after crystallization.

The scope of this chemical transformation was then explored for other, more challenging, substituted 2-aminopyridines. Typically, 3-substituted 2-aminopyridines are the best substrates for the cyclization because of the predominance of the favorable geometrical isomer A over B (Scheme 3). While steric effects are minimal on 4 and 5-substituted 2-aminopyridines, the presence of a substituent on the 6 position of the pyridine ring strongly hinders the pyridine nitrogen making these types of substrates especially difficult to prepare.

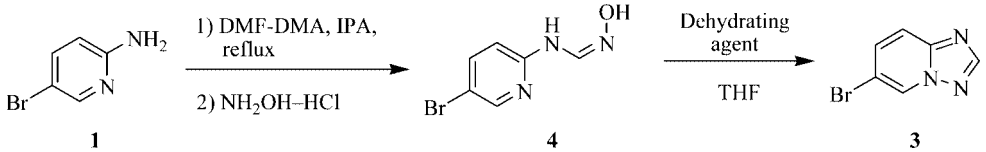


Scheme 3. The favorable effect of 3-substitution.

The TFAA-promoted synthesis of triazolo-pyridines is a very general method which provides access to triazolo-pyridines substituted on any position of the pyridine ring. The results obtained are summarized in Table 2. In most cases, both the intermediates **4a**–**i** and the products **3a**–**i** can be isolated by crystallization from the reaction mixture or workup solutions. No efforts were made to optimize yields in the crystallization process and the crude workup solutions were purified by chromatography in order to maximize the isolated yields.

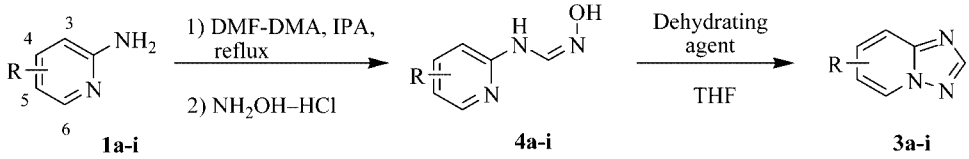
As expected, the presence of a C-3 substituent on the pyridine ring afforded excellent yields of the desired triazolo-pyridines (Entries b and f). Yields for the cyclization reaction were also high for pyridines with substituents on C-4 and C-5. A small methyl group was well tolerated on C-6, as the reaction proceeded with high yield at ambient temperature. Not surprisingly however, when a much larger

Table 1. Screening of dehydrating reagents.



Dehydrating agent	Conversion (time/temp.)	Isolated yield
PPA	100% (1 h/reflux in THF)	77%
$SOCl_2$	11% (3 d/room temp.)	15%
$POCl_3$	59% (3 d/room temp.)	34%
MsCl	95% (3 d/room temp.)	44%
TsCl	89% (3 d/room temp.)	69%
Ac_2O	46% (16 h/50 °C)	31%
AcCl	36% (16 h/50 °C)	18%
TFAA	100% (1 h/room temp.)	84%

Table 2. Synthesis of substituted triazoles.



1a-i **4a-i** **3a-i**

1a–i	R	**4a–i** isolated	reaction temperature	**3a–i** isolated
a	H	63%	room temperature	77%
b	3-CH_3	78%	room temperature	87%
c	4-CH_3	76%	room temperature	68%
d	5-CH_3	80%	room temperature	75%
e	6-CH_3	81%	room temperature	91%
f	3-Br	74%	room temperature	86%
g	5-Br	92%	room temperature	84%
h	6-Br	95%	reflux temperature	41%
i	5-COOMe	80%	reflux temperature	45%

bromine group was present on C-6 the reaction did not occur at room temperature. Running the reaction at elevated temperatures was necessary in order to promote the cyclization. Interestingly, the presence of a deactivating substituent on C-5 (Entry i) also slowed down the cyclization reaction and elevated temperatures were necessary to drive the reaction to completion.

Compounds **3f**–**h** are of particular interest as they can be used as building blocks of larger molecules through metal catalyzed cross-coupling reactions.[8]

In summary, a new general synthetic method for the preparation of [1,2,4]triazolo[1,5-*a*]pyridines has been developed, which requires inexpensive reagents and takes place under mild reaction conditions.

Experimental Section

General: ^{1}Hand ^{13}C NMR were recorded in [D_6]DMSO with a Bruker DPX400 spectrometer at a frequency of 400.13 MHz and 100.62 MHz, respectively. The chemical shifts (δ) are reported in ppm relative to residual [D_5]DMSO for proton (δ = 2.50 ppm) and [D_6]DMSO for carbon (δ = 39.5 ppm). Proton multiplicities are abbreviated as follows: Singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), and broad (b). All coupling constants (*J*) are reported in Hertz (Hz). Infrared spectra were recorded with a Nicolet 560 FT-IR spectrometer, using IR grade potassium bromide (Sigma, EC no. 231–830–3) pellets as the measurement medium. Peaks are reported in cm^{-1}. HPLC analysis were carried out with a Hewlett Packard 1100 system. Melting points were determined with a Buchi B-545 apparatus and are uncorrected. Combustion analysis was performed by Quantitative Technologies Inc., Whitehouse, NJ. Analytical thin-layer chromatography (TLC) was performed on Merck silica gel 60 plates, 0.25 mm thick with F-254 indicator. Visualization was accomplished by UV light, 5% phosphomolybdic acid solution in ethanol. Flash column chromatography was performed by the method of Still[12] with 32–63 μm silica gel (Woelm). Solvents for extraction and chromatography were reagent grade and used as received. All manipulations were carried out under an inert atmosphere of nitrogen. Reagents were purchased from Aldrich Chemical Co. unless otherwise noted and were used without prior purification. Yields reported are for isolated compounds judged pure by NMR or elemental analysis.

***N*-(5-Bromopyrid-2-yl)formamidoxime (4g). General Procedure:** 2-Amino-5-bromopyridine (10.0 g, 58 mmol, 1.0 equiv.) was placed in a round-bottom flask equipped with magnetic stirrer, condenser, and nitrogen line, followed by 2-propanol (20 mL). To this mixture at room temperature was added dimethylformamide dimethyl acetal (8.95 g, 10.05 mL, 75 mmol, 1.3 equiv.). The reaction was heated to reflux and aged 3 h. It was then cooled to 50 °C, and hydroxylamine hydrochloride (5.21 g, 75 mmol, 1.3 equiv.) was added. The reaction was aged at 50 °C overnight. The volatile components were evaporated and the residue was purified by chromatography (silica gel, packed in 50% ethyl acetate/hexane, eluted with 50% to 75% ethyl acetate/hexane gradated elution) to obtain 11.51 g of **4g** (92% yield). M.p. 178–180 °C. LC-MS(ES+): *m*/*z* = 216 [M + H], 199 [M – OH], 198 [M – H_2O]. ^{1}H NMR (DMSO): δ (ppm) = 10.18 (s, 1 H), 9.53 (d, *J* = 10, 1 H), 8.21 (d, *J* = 2.40, 1 H), 7.81–7.74 (m, 2 H), 7.03 (dd, *J* = 8.8, 0.8, 1 H). ^{13}C NMR (DMSO): δ (ppm) = 151.9, 148.1, 140.8, 135.6, 112.7, 110.7. IR: $\tilde{\nu}$ = 3324, 3059, 2780, 1697, 1593, 1475, 1302, 1276, 940 cm^{-1}. $C_6H_6BrN_3O$ (216.04): calcd. C 33.36, H 2.80, N 19.45; found C 33.64, H 2.70, N 19.79.

6-Bromo[1,2,4]triazolo[1,5-*a*]pyridine (3g). General Procedure: The *N*-hydroxy intermediate (6.00 g, 27.8 mmol, 1.0 equiv.) was placed in a round-bottom flask equipped with magnetic stirrer and nitrogen line, followed by addition of THF (60 mL). The resulting mixture was cooled to 0 °C, and trifluoroacetic anhydride (6.41 g, 4.25 mL, 30.6 mmol, 1.1 equiv.) was added over 5–10 minutes, keeping the internal temperature below 20 °C. After the addition was complete, the reaction was warmed to room temperature and aged 3 h. at room temperature. The reaction was quenched with saturate aqueous $NaHCO_3$ (125 mL), then extracted with MTBE three times. The organic layers were combined, washed once with saturated aqueous $NaHCO_3$, dried with sodium sulfate, filtered, and concentrated. The residue was purified by column chromatography (silica gel, packed in 50% ethyl acetate/hexane, eluted with 50% ethyl acetate/hexane) to obtain 4.63 g of **3g** as an off-white solid (84% yield). M.p. 115–118 °C. LC-MS(ES+): *m*/*z* = 198 (M), 200 [M + 2]. ^{1}H NMR (DMSO): δ (ppm) = 9.37 (m, 1 H), 8.52 (s, 1 H), 7.84–7.78 (m, 2 H). ^{13}C NMR (DMSO): δ (ppm) = 154.5, 149.1, 133.8, 130.0, 117.3, 108.2. IR: $\tilde{\nu}$ = 3125, 3065, 3019, 1496, 1314, 1257, 1198, 1165, 809 cm^{-1}. $C_6H_4BrN_3$ (198.02): calcd. C 36.39, H 2.04, N 21.22; found C 36.27, H 1.79, N 20.86.

***N*-(Pyrid-2-yl)formamidoxime (4a):** Yield: 63%. M.p. 144–147 °C. LC-MS(ES+): *m/z* = 138 [M + H]. ^{1}H NMR (DMSO): δ (ppm) = 10.04 (s, 1 H), 9.30 (d, *J* = 10.0, 1 H), 8.12 (dq, *J* = 5.2, 0.7, 1 H), 7.85 (d, *J* = 10.0, 1 H), 7.61–7.55 (m, 1 H), 7.04 (dt, *J* = 8.4, 1.0, 1 H), 6.84–6.80 (m, 1 H). ^{13}C NMR (DMSO): δ (ppm) = 152.9, 147.8, 138.4, 136.0, 116.6, 110.7. IR: ṽ = 3209, 2755, 1688, 1607, 1580, 1442, 1213 cm^{-1}. $C_6H_7N_3O$ (137.14): calcd. C 52.55, H 5.14, N 30.64; found C 52.05, H 4.89, N 30.64.

[1,2,4]Triazolo[1,5-*a*]pyridine (3a): Yield: 77%. M.p. 110–112 °C. LC-MS(ES+): *m/z* = 120 [M + H]. ^{1}H NMR (DMSO): δ (ppm) = 8.95 (dt, *J* = 6.8, 1.2, 1 H), 8.49 (s, 1 H), 7.85 (dt, *J* = 8.8, 1.2, 1 H), 7.66 (dq, *J* = 6.8, 1.2, 1 H), 7.2 (td, *J* = 6.8, 1.2, 1 H). ^{13}C NMR (DMSO), δ (ppm): 154.2, 150.3, 130.6, 129.5, 116.6, 114.7. IR: ṽ = 3140, 3080, 3040, 1635, 1506, 1326, 1260, 1181, 770 cm^{-1}. $C_6H_5N_3$ (119.12): calcd. C 60.50, H 4.27, N 35.23; found C 60.22, H 3.98, N 35.27.

***N*-(3-Methylpyrid-2-yl)formamidoxime (4b):** Yield: 78%. M.p. 110–114 °C. LC-MS(ES+): *m/z* = 152 [M + H], 135 [M – OH], 134 [M – H_2O]. ^{1}H NMR (DMSO): δ (ppm) = 10.03 (s, 1 H), 8.04 (dd, *J* = 4.8, 1.2, 1 H), 7.96 (d, *J* = 9.6, 1 H), 7.73 (d, *J* = 9.6 Hz, 1 H), 7.50 (dd, *J* = 7.2, 0.8, 1 H), 6.85 (dd, *J* = 7.2, 4.8, 1 H), 2.19 (s, 3 H). ^{13}C NMR (DMSO): δ (ppm) = 150.4, 145.5, 139.1, 136.4, 118.6, 117.3, 16.3. IR: ṽ = 3434, 3078, 2780, 1663, 1599, 1506, 1471, 1245, 875 cm^{-1}. $C_7H_9N_3O$ (151.17): calcd. C 55.62, H 6.00, N 27.80; found C 55.36, H 5.80, N 27.69.

8-Methyl[1,2,4]triazolo[1,5-*a*]pyridine (3b): Yield: 87%. M.p. 56–57 °C. LC-MS(ES+): *m/z* = 134 [M + H]. ^{1}H NMR (DMSO): δ (ppm) = 8.76 (d, *J* = 6.8, 1 H), 8.43 (s, 1 H), 7.44–7.40 (m, 1 H), 7.07 (t, *J* = 7.0, 1 H), 3.34 (s, 3 H). ^{13}C NMR (DMSO), δ (ppm): 153.6, 150.7, 128.8, 127.0, 126.6, 114.4, 16.7. IR: ṽ = 3095, 3024, 2917, 1630, 1505, 1346, 1260, 1194, 761 cm^{-1}. $C_7H_7N_3$ (133.15): calcd. C 63.14, H 5.30, N 31.56; found C 62.73, H 4.97, N 31.29.

***N*-(4-Methylpyrid-2-yl)formamidoxime (4c):** Yield: 76%. M.p. 137–142 °C. LC-MS(ES+): *m/z* = 152 [M + H], 135 [M – OH], 134 [M – H_2O]. ^{1}H NMR (DMSO): δ (ppm) = 10.00 (s, 1 H), 9.16 (d, *J* = 10.0, 1 H), 7.98 (d, *J* = 5.2, 1 H), 7.82 (d, *J* = 10.0, 1 H), 6.86 (S, 1 H), 6.68 (d, *J* = 5.2, 1 H), 2.20 (s, 3 H). ^{13}C NMR (DMSO): δ (ppm) = 153.1, 149.0, 147.5, 136.2, 118.0, 110.7, 21.0. IR: ṽ = 2847, 1618, 1579, 1426, 1308, 1213, 904 cm^{-1}. $C_7H_9N_3O$ (151.17): calcd. C 55.62, H 6.00, N 27.80; found C 55.37, H 5.79, N 27.69.

7-Methyl[1,2,4]triazolo[1,5-*a*]pyridine (3c): Yield: 68%. M.p. 83–85 °C. LC-MS(ES+): *m/z* = 134 [M + H]. ^{1}H NMR (DMSO): δ (ppm) = 8.80 (d, *J* = 6.8, 1 H), 8.39 (s, 1 H), 7.60 (br. s, 1 H), 7.02 (dd, *J* = 6.8, 1.6, 1 H), 2.42 (s, 3 H). ^{13}C NMR (DMSO): δ (ppm) = 154.2, 150.5, 141.5, 128.4, 116.9, 114.9, 21.2. IR: ṽ = 3130, 3045, 1642, 1501, 1344, 1260, 1210, 1192, 796 cm^{-1}. $C_7H_7N_3$ (133.15): calcd. C 63.14, H 5.30, N 31.56; found C 62.89, H 5.11, N 31.51.

***N*-(5-Methylpyrid-2-yl)formamidoxime (4d):** Yield: 80%. M.p. 165–169 °C. LC-MS(ES+): *m/z* = 152 [M + H], 135 [M – OH], 134 [M – H_2O]. ^{1}H NMR (DMSO): δ (ppm) = 9.96 (s, 1 H), 9.16 (d, *J* = 10.0, 1 H), 7.95 (br. s, 1 H), 7.80 (d, *J* = 10.0, 1 H), 7.41 (dd, *J* = 8.4, 2.4, 1 H), 6.95 (d, *J* = 8.4, 1 H), 2.16 (s, 3 H). ^{13}C NMR (DMSO): δ (ppm) = 151.0, 147.3, 139.1, 136.3, 125.1, 110.3, 17.4. IR: ṽ = 3370, 3013, 2771, 1680, 1613, 1496, 1283, 886 cm^{-1}. $C_7H_9N_3O$ (151.17): calcd. C 55.62, H 6.00, N 27.80; found C 55.65, H 5.76, N 27.38.

6-Methyl[1,2,4]triazolo[1,5-*a*]pyridine (3d): Yield: 75%. M.p. 74–77 °C. LC-MS(ES+): *m/z* = 134 [M + H]. ^{1}H NMR (DMSO): δ (ppm) = 8.76 (br. s, 1 H), 8.40 (s, 1 H), 7.73 (d, *J* = 9.2, 1 H), 7.50 (dd, *J* = 9.2, 1.6, 1 H), 2.35 (s, 3 H). ^{13}C NMR (DMSO): δ (ppm) = 153.8, 149.0, 133.2, 127.2, 124.4, 115.7, 17.6. IR: ṽ = 3071, 3029, 2957, 1519, 1441, 1324, 1258, 1186, 821 cm^{-1}. $C_7H_7N_3$ (133.15): calcd. C 63.14, H 5.30, N 31.56; found C 62.89, H 5.04, N 31.54.

***N*-(6-Methylpyrid-2-yl)formamidoxime (4e):** Yield: 81%. M.p. 185–188 °C. LC-MS(ES+): *m/z* = 152 [M + H], 135 [M – OH], 134 [M – H_2O]. ^{1}H NMR (DMSO): δ (ppm) = 9.99 (s, 1 H), 9.19 (d, *J* = 10.0, 1 H), 7.85 (d, *J* = 10.0, 1 H), 7.46 (t, *J* = 7.8, 1 H), 6.83 (d, *J* = 8.4, 1 H), 6.68 (d, *J* = 7.2, 1 H), 2.33 (s, 3 H). ^{13}C NMR (DMSO): δ (ppm) = 156.3, 152.3, 138.7, 136.1, 115.6, 107.5, 24.4. IR: ṽ = 2848, 1683, 1604, 1467, 1317, 1220, 1166, 904 cm^{-1}. $C_7H_9N_3O$ (151.17): calcd. C 55.62, H 6.00, N 27.80; found C 55.67, H 5.85, N 27.40.

5-Methyl[1,2,4]triazolo[1,5-*a*]pyridine (3e): Yield: 91%. M.p. 54–59 °C. LC-MS(ES+): *m/z* = 134 [M + H]. ^{1}H NMR (DMSO): δ (ppm) = 8.48 (s, 1 H), 7.69 (d, *J* = 9.0, 1 H), 7.57 (dd, *J* = 8.8, 7.2, 1 H), 7.05 (d, *J* = 7.2, 1 H), 2.71 (s, 3 H). ^{13}C NMR (DMSO): δ (ppm) = 153.7, 150.4, 139.1, 130.2, 113.8, 113.5, 17.4. IR: ṽ = 3080, 2985, 1638, 1556, 1515, 1307, 1197, 785 cm^{-1}. $C_7H_7N_3$ (133.15): calcd. C 63.14, H 5.30, N 31.56; found C 62.80, H 5.23, N 31.17.

***N*-(3-Bromopyrid-2-yl)formamidoxime (4f):** Yield: 74%. M.p. 151–155 °C. LC-MS(ES+): *m/z* = 216 [M + H], 199 [M – OH], 198 [M – H_2O]. ^{1}H NMR (DMSO): δ (ppm) = 10.68 (s, 1 H), 8.21 (dd, *J* = 4.8, 1.6, 1 H), 8.14 (bd, *J* = 9.6, 1 H), 8.02 (dd, *J* = 8.0, 1.6, 1 H), 7.92 (d, *J* = 9.6, 1 H), 6.91 (dd, *J* = 7.6, 4.8, 1 H). ^{13}C NMR (DMSO): δ (ppm) = 148.3, 147.4, 141.8, 135.6, 118.7, 105.8. IR: ṽ = 3414, 3075, 2912, 1666, 1591, 1453, 1265, 1016 cm^{-1}. $C_6H_6BrN_3O$ (216.04): calcd. C 33.36, H 2.80, N 19.45; found C 33.38, H 2.74, N 18.99.

8-Bromo[1,2,4]triazolo[1,5-*a*]pyridine (3f): Yield: 86%. M.p. 150–152 °C. LC-MS(ES+): *m/z* = 198 [M], 200 [M + 2]. ^{1}H NMR (DMSO): δ (ppm) = 9.00 (d, *J* = 6.8, 1 H), 8.57 (s, 1 H), 8.00 (d, *J* = 8.0, 1 H), 7.14 (t, *J* = 7.2, 1 H). ^{13}C NMR (DMSO): δ (ppm) = 154.2, 149.2, 133.3, 129.3, 115.1, 109.1. IR: ṽ = 3101, 3080, 1628, 1498, 1337, 1260, 1206, 752 cm^{-1}. $C_6H_4BrN_3$ (198.02): calcd. C 36.39, H 2.04, N 21.22; found C 36.37, H 1.87, N 21.11.

***N*-(6-Bromopyrid-2-yl)formamidoxime (4h):** Yield: 95%. M.p. 172–175 °C. LC-MS(ES+): *m/z* = 216 [M + H], 199 [M – OH], 198 [M – H_2O]. ^{1}H NMR (DMSO): δ (ppm) = 10.25 (s, 1 H), 9.64 (d, *J* = 9.6, 1 H), 7.67 (d, *J* = 9.6, 1 H), 7.52 (t, *J* = 7.8, 1 H), 7.04 (dd, *J* = 7.8, 5.0, 2 H). ^{13}C NMR (DMSO): δ (ppm) = 153.3, 141.3, 139.3, 135.2, 119.6, 109.6. IR: ṽ = 3427, 3279, 3080, 2783, 1683, 1598, 1566, 1457, 1305, 780 cm^{-1}. $C_6H_6BrN_3O$ (216.04): calcd. C 33.36, H 2.80, N 19.45; found C 32.91, H 2.99, N 19.45.

5-Bromo[1,2,4]triazolo[1,5-*a*]pyridine (3h): Reaction was performed at reflux temperature for 13 hours. Yield: 41%. M.p. 164–167 °C. LC-MS(ES+): *m/z* = 198 [M], 200 [M + 2] peak. ^{1}H NMR (DMSO): δ (ppm) = 8.60 (s, 1 H), 7.89 (dd, *J* = 7.8, 2.2, 1 H), 7.64–7.57 (m, 2 H). ^{13}C NMR (DMSO): δ (ppm) = 153.7, 151.1, 131.3, 118.8, 117.9, 115.7. IR: ṽ = 3084, 3029, 1624, 1491, 1297, 1193, 784 cm^{-1}. $C_6H_4BrN_3$ (198.02): calcd. C 36.39, H 2.04, N 21.22; found C 36.28, H 1.80, N 20.97.

Methyl 6-{[(1*Z*)-(Hydroxyamino)methylene]amino}nicotinate (4i): Yield: 80%. M.p. 193–196 °C. LC-MS(ES+): *m/z* = 196 [M + H], 179 [M – OH], 178 [M – H_2O]. ^{1}H NMR (DMSO): δ (ppm) = 10.37 (s, 1 H), 9.91 (d, *J* = 10.0, 1 H), 8.68 (d, *J* = 2.4, 1 H), 8.05 (dd, *J* = 8.8, 2.4, 1 H), 7.90 (d, *J* = 9.6, 1 H), 7.12 (d, *J* = 8.8, 1 H), 3.80 (s, 3 H). ^{13}C NMR (DMSO): δ (ppm) = 165.6, 155.8, 150.2, 139.0, 135.2, 118.3, 110.3, 52.2. IR: ṽ = 3322, 3079, 3023, 1704, 1608, 1505, 1280, 1121, 880 cm^{-1}. $C_8H_9N_3O_3$ (195.18): calcd. C 49.23, H 4.65, N 21.53; found C 48.89, H 4.84, N 21.29.

Methyl [1,2,4]Triazolo[1,5-*a*]pyridine-6-carboxylate (3i): Reaction was performed at reflux temperature for 20 h. Yield: 45%. M.p.

166–170 °C. LC-MS(ES+): *m*/*z* = 178 [M + 1]. ^{1}H NMR (DMSO): δ (ppm) = 9.46 (s, 1 H), 8.67 (s, 1 H), 8.04 (d, *J* = 9.6, 1 H), 7.93 (d, *J* = 9.6, 1 H), 3.91 (s, 3 H). ^{13}C NMR (DMSO): δ (ppm) = 164.6, 156.2, 151.6, 132.5, 129.7, 118.0, 116.4, 53.1. IR: $\tilde{\nu}$ = 3071, 3034, 1725, 1635, 1443, 1312, 1165, 776 cm^{-1}. $C_8H_7N_3O_2$ (177.16): calcd. C 54.24, H 3.98, N 23.72; found C 53.84, H 3.71, N 23.33.

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