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One-Pot Synthesis of *N*-(Imidazo[1,2-*a*]pyridin-3-yl)-Substituted Sulfonamides Using Catalytic Zinc Chloride

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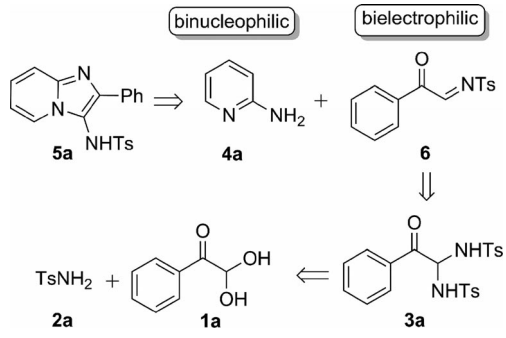
A one-pot two-step synthesis of *N*-(imidazo[1,2-*a*]pyridin-3-yl)sulfonamides from easily available arylglyoxal hydrates, 2-aminopyridines, and sulfonamides has been developed. The procedure, using zinc chloride as catalyst, is simple and inexpensive. The desired products were obtained in moderate to good yields under the optimized reaction conditions.

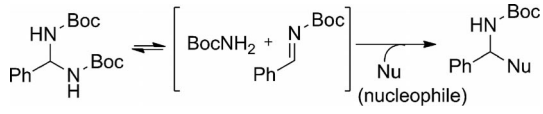
Introduction

The imidazopyridine nucleus, especially the imidazo[1,2-*a*]pyridine structure, is found in many pharmaceutical compounds.[1] These show a number of important properties, such as antifungal,[2] anti-inflammatory,[1c] antitumor,[3] antiviral,[4] antibacterial,[5] antiprotozoal,[6] antipyretic,[7] anti-HIV,[8] and antiapoptotic activities.[9] In addition, imidazo[1,2-*a*]pyridine is a substructure of several commercially available drugs, such as Alpidem[10] and Sarpidem (anxiolytic agents),[11] Olprinone (to treat acute heart failure),[12] and Zolimidine (used for the treatment of peptic ulcers).[13] Due to these important uses, imidazo[1,2-*a*]pyridines have received tremendous attention from synthetic organic and medicinal chemists. Numerous synthetic methods have been developed for the synthesis of imidazo[1,2-*a*]-pyridine derivatives, such as the condensation of 2-aminopyridine with α-halocarbonyl compounds,[14] three-component reactions of 2-aminopyridines, aldehydes, and isonitriles[15] or imidazoline-2,4,5-trione[16] or alkynes,[17] metal-catalyzed C–H activation,[18] Morita–Baylis–Hillman (MBH) reaction,[19] tetrabutylammonium iodide (TBAI)-catalyzed oxidative coupling,[20] and a recently reported iodine-promoted one-pot reaction.[21] Although much progress has been made in this field, further development of diverse methods for the construction of various imidazo[1,2-*a*]pyridines is still highly desirable.

Recently, the first synthesis of *N*-(imidazo[1,2-*a*]pyridin-3-yl)sulfonamides was reported. For this synthesis, *N*-(2,2-dichloro-2-phenylethylidene)arenesulfonamides, which are not easily accessible reagents, were used as starting materials.[22] Thus, it is necessary to find an easier and more economical method to synthesize this target molecule. As shown in Scheme 1, *N*-(imidazo[1,2-*a*]pyridin-3-yl)sulfonamide **5a** can be synthesized from the reaction of 2-aminopyridine (**4a**), a nucleophilic reagent bearing two nucleophilic sites, and α-keto imine **6**, a bielectrophilic reagent. According to the literature, *N*-Boc-(*tert*-butoxycarbonyl)-imines can be generated in situ from *N*-Boc-substituted aminals, and they can then undergo nucleophilic addition to form nitrogen-containing compounds (Scheme 2).[23] Inspired by this work, we planned to use *N*-tosyl aminal **3a** as a precursor to obtain α-keto imine **6**. Compound **3a** could be prepared from phenylglyoxal (**1a**), a versatile building block, containing both aldehyde and ketone func-



Scheme 1. Retrosynthesis of *N*-(imidazo[1,2-*a*]pyridin-3-yl)sulfonamides.



Scheme 2. Acid-catalyzed tandem *N*-Boc imine generation/Mannich-type reaction.

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tional groups, that has been widely used in the synthesis of a broad range of biologically active *N*-heterocyclic compounds.[24]

In this paper, we report an efficient and simple method to synthesize *N*-(imidazo[1,2-*a*]pyridin-3-yl)sulfonamides in a one-pot two-step process starting from readily available arylglyoxal hydrates, 2-aminopyridines, and sulfonamides.

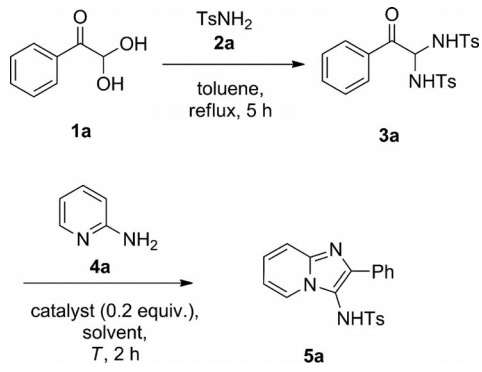
Results and Discussion

According to the literature for the preparation of *N*,*N*′-(2-oxo-2-phenylethane-1,1-diyl)dibenzamide,[25] *N*-tosyl-substituted aminal **3a** can be easily obtained by the reaction of phenylglyoxal hydrate (**1a**) and 4-methylbenzenesulfonamide (**2a**) in toluene at 110 °C for 5 h in almost quantitative yield. However, the purification of **3a** proved to be very tricky, due to the instability of the intermediate *N*-tosylaminal, which would partly revert to starting material when the solvent was evaporated. Therefore, a one-pot strategy that would avoid the isolation of compound **3a** was considered. Once the first step was complete, 2-aminopyridine (**4a**) was added to the reaction mixture, which was then stirred for a further 2 h at 90 °C, and imidazo[1,2-*a*]pyridine **5a** was obtained in 30% yield (Table 1, entry 1). Considering the poor solubility of **3a** and **5a** in the refluxing toluene, a polar solvent (CH_3CN) was added in the second step, and the yield of **5a** increased to 43% (Table 1, entry 2).

We briefly investigated the effects of various parameters in the second step in order to optimize the reaction conditions (Table 1). First, various catalysts were tested in the reaction (Table 1, entries 3–7). To our delight, when $ZnCl_2$ was used in the reaction in toluene/CH_3CN at 81 °C, compound **5a** was obtained in 60% yield (Table 1, entry 7). Next, different solvents, including dioxane, DMF, THF, MeOH, and EtOH, were tested. EtOH gave the best result, and **5a** was formed in 70% yield (Table 1, entry 14). When the ratio of **1a**/**2a**/**4a** was changed to 1:2.4:1.5, the yield of **5a** increased to 76% (Table 1, entry 16). The yield decreased when the temperature was changed to 65 or 55 °C (Table 1, entries 17–18). Interestingly, the yield of **5a** reached 81% when the volume ratio of toluene/EtOH was adjusted to 2:3 (Table 1, entry 20). The same result was achieved with only 0.1 equiv. of the catalyst. Therefore, the optimized conditions were identified (Table 1, entry 22).

Having optimized the reaction conditions, we further examined the scope and limitations of this transformation. As summarized in Table 2, various arylglyoxal hydrates were found to participate in this reaction, and the electronic nature of arylglyoxal hydrates had little influence on the efficiency of the reaction. Arylglyoxal hydrates bearing electron-withdrawing (leading to **5e**–**5i**) as well as electron-donating groups (leading to **5b**–**5d**) gave the corresponding imidazo[1,2-*a*]pyridines in moderate to excellent yields (60–89%). A variety of functional groups, such as F (**5i**), Cl (**5f** and **5h**), Br (**5g**), and OH (**5j**), were unaffected under the reaction conditions, and the desired products were obtained in 68–79% yields. Much to our satisfaction, the heteroaryl

Table 1. Optimization of reaction conditions.[a]



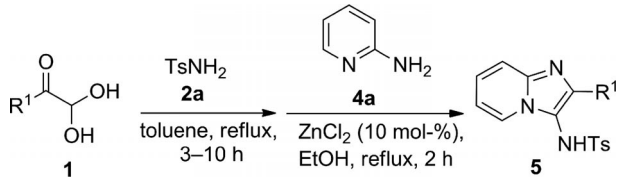
Entry	Catalyst	Solvent	*T* [°C]	Yield [%][b]
1	–	toluene	90	30
2	–	CH_3CN	81	43
3	$BF_3{\cdot}Et_2O$	CH_3CN	81	56
4	$AlCl_3$	CH_3CN	81	55
5	CuCl	CH_3CN	81	20
6	pTsOH·H_2O	CH_3CN	81	48
7	$ZnCl_2$	CH_3CN	81	60[c]
8	$ZnCl_2$	toluene	85	46
9	$ZnCl_2$	THF	78	55
10	$ZnCl_2$	DMF	85	59
11	$ZnCl_2$	MeOH	64	64
12	$ZnCl_2$	dioxane	85	36
13	$ZnCl_2$	*i*PrOH	81	56
14	$ZnCl_2$	EtOH	77	70
15	$ZnCl_2$	EtOH	77	77[d]
16	$ZnCl_2$	EtOH	77	76[e]
17	$ZnCl_2$	EtOH	65	64[e]
18	$ZnCl_2$	EtOH	55	60[e]
19	$ZnCl_2$	EtOH	77	51[e,f]
20	$ZnCl_2$	EtOH	77	81[e, g]
21	$ZnCl_2$	EtOH	77	82[e,h]
22	$ZnCl_2$	EtOH	77	81[e,i]

[a] Unless otherwise noted, reaction conditions were phenylglyoxal hydrate **1a** (1.0 mmol, 1.0 equiv.), 4-methylsulfonamide **2a** (2.4 mmol, 2.4 equiv.), 2-aminopyridine **4a** (1.2 mmol, 1.2 equiv.), toluene (10 mL), solvent (10 mL), catalyst (0.20 equiv.). [b] Isolated yield of **5a** based on **1a**. [c] Other Lewis acids, such as $CuCl_2{\cdot}H_2O$, I_2, $LiClO_4{\cdot}3H_2O$, $Cu(OAc)_2{\cdot}H_2O$, $Ni(OTf)_3$, and $FeCl_3$, were also tested, but the results were less satisfactory. [d] Molar ratio **1a**/**2a**/**4a** = 1:2.4:2.0. [e] Molar ratio **1a**/**2a**/**4a** = 1:2.4:1.5. [f] Volume ratio toluene/EtOH = 2:1. [g] Volume ratio toluene/EtOH = 2:3. [h] Volume ratio toluene/EtOH = 1:2. [i] Volume ratio toluene/EtOH = 2:3, $ZnCl_2$ (0.1 equiv.).

glyoxal hydrates 2-furanglyoxal hydrate and 2-thiopheneglyoxal hydrate performed smoothly to give the corresponding products (i.e., **5k** and **5l**) in 75 and 73% yields. Interestingly, methylglyoxal also gave the desired product (i.e., **5m**), albeit in a low yield of 28%.

Next, a few substituted sulfonamides were investigated in the reaction (Table 3). Generally, electron-rich aryl sulfonamides showed better reactivity and gave higher yields than electron-deficient ones (compare the results for **5n**–**5q**). To our surprise, the alkyl sulfonamides such as methanesulfonamide and cyclopropanesulfonamide also participated in this reaction to give the corresponding products (i.e., **5r** and **5s**) in 31 and 39% yields. Next, we investigated the scope of substituted aminopyridines (Table 3). Aminopyridines

Table 2. Substrate scope of arylglyoxal hydrates.[a]

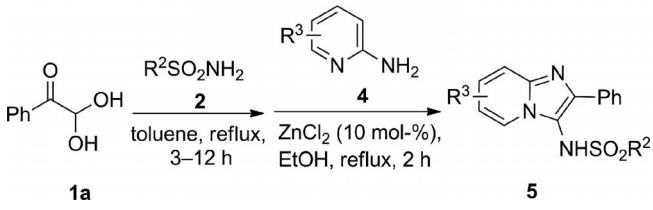


Entry	R^1	*t* [h][b]	Product	Yield [%][c]
1	Ph	5	**5a**	81
2	4-Me-C_6H_4	5	**5b**	70
3	4-MeO-C_6H_4	6	**5c**	89
4	3-MeO-C_6H_4	10	**5d**	64
5	4-NO_2–C_6H_4	3	**5e**	60
6	4-Cl-C_6H_4	5	**5f**	77
7	4-Br-C_6H_4	5	**5g**	79
8	3-Cl-C_6H_4	5	**5h**	76
9	4-F-C_6H_4	5	**5i**	76
10	4-OH-C_6H_4	7	**5j**	68
11	2-furanyl	6	**5k**	75
12	2-thienyl	6	**5l**	73
13[d]	Me	10	**5m**	28

[a] Molar ratio **1/2a/4a** = 1:2.4:1.5. [b] Reaction time for the first step. [c] Isolated yield based on **1**. [d] The second step required 8 h.

bearing methyl substituents at the 3- and 5-positions afforded the products (i.e., **5t** and **5u**) in 79 and 70% yields, respectively. When 2-amino-6-methylpyridine was subjected to the reaction conditions, only a trace amount of product was detected, which may be due to the steric hindrance on the pyridine ring. 2-Aminopyridines bearing halogen substituents on the aromatic ring, such as chloro (leading to **5v**) or bromo (leading to **5w**) groups, were tolerated, which provides the possibility for further functionalization through cross-coupling reactions. Furthermore, other 2-amino heterocycles, such as 2-aminopyrimidine and 2-aminothiozole, were also investigated. Unfortunately, none

Table 3. Substrate scope of aminopyridines and sulfonamides.[a]



Entry	R^2	R^3	*t* [h][b]	Product	Yield [%][c]
1	Ph	H	5	**5n**	80
2	4-MeO-C_6H_4	H	3	**5o**	90
3	4-Cl-C_6H_4	H	10	**5p**	75
4	4-NO_2–C_6H_4	H	10	**5q**	71
5[d]	Me	H	12	**5r**	31
6[d]	Cyclopropyl	H	12	**5s**	39
7	4-Me-C_6H_4	3-Me	5	**5t**	79
8	4-Me-C_6H_4	5-Me	5	**5u**	70
9[d]	4-Me-C_6H_4	5-Cl	5	**5v**	57
10	4-Me-C_6H_4	5-Br	5	**5w**	68

[a] Molar ratio **1a/2/4** = 1:2.4:1.5. [b] Reaction time for the first step. [c] Isolated yield based on **1a**. [d] Reaction time for the second step was 8 h.

of the desired products were isolated. The structure of target compound **5c** was further confirmed by X-ray crystallographic analysis (Figure 1).

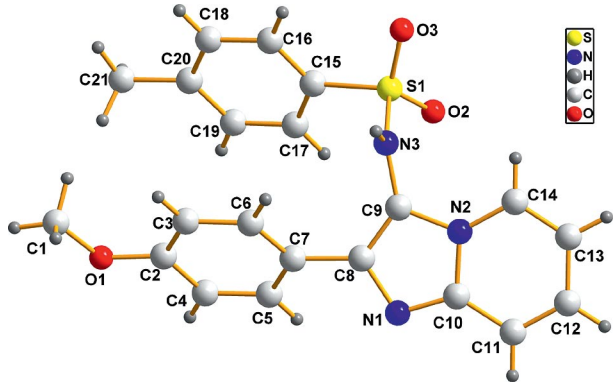
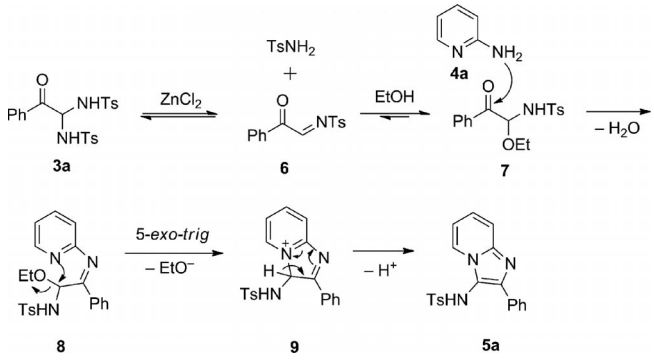


Figure 1. X-ray crystal structure of compound **5c**.

A plausible mechanism for this reaction is outlined in Scheme 3. The first step involves the $ZnCl_2$-catalyzed reversible elimination of $TsNH_2$ from *N*-tosyl-substituted aminal **3a** to produce imine **6**,[23] which reacts with ethanol to form adduct **7**.[26] Then the amino group of **4a** attacks the ketone group of **7** to obtain intermediate **8**. This is followed by an intramolecular nucleophilic substitution reaction to generate intermediate **9**. Finally, intermediate **9** loses a proton to give product **5a** (Scheme 3).



Scheme 3. Plausible reaction mechanism.

Conclusions

In conclusion, we have developed a zinc(II)-catalyzed one-pot method for the preparation of imidazo[1,2-*a*]pyridine derivatives bearing pharmacophoric sulfonylamino groups. Various functional groups are tolerated in this reaction system, and the products are formed in moderate to good yields. In this procedure, the starting materials are easily available, and the catalyst is nonhazardous and inexpensive. Further investigations into the scope of this reaction and its applications to the construction of biologically and medicinally active molecules are in progress.

Experimental Section

General Information: All reagents were obtained from commercial suppliers, and were used without further purification unless otherwise indicated. TLC analysis was carried out using precoated glass plates. Silica gel for column chromatography was purchased from Qingdao Haiyang Chemical Co., Ltd. IR spectra were recorded with a Thermo Nicolet AVATAR 370 spectrophotometer in KBr. Melting points were determined using a Büchi B-540 capillary melting-point apparatus. ^{1}H and ^{13}C NMR spectra were recorded with a Varian instrument at 400 and 100 MHz, respectively, and tetramethylsilane was used as internal standard. Mass spectra were measured with a Thermo Finnigan LCQ-Advantage instrument. High-resolution mass spectra (HRMS) were measured with a Bruker micrOTOF-Q II instrument using the ESI technique. Single-crystal diffraction data for compound **5c** were collected with an Xcalibur Eos Gemini-ultra diffractometer.

General Procedure (5a as an Example): A mixture of phenylglyoxal hydrate (**1a**; 152 mg, 1 mmol), $TsNH_2$ (**2a**; 410 mg, 2.4 mmol), and anhydrous toluene (10 mL) was heated at reflux. After the reactant had disappeared (3–5 h, monitored by TLC), 2-aminopyridine (**4a**; 141 mg, 1.5 mmol), $ZnCl_2$ (14 mg, 10 mol-%), and ethanol (15 mL) were added, and the resulting mixture was heated at reflux for 2 h. After that, the solvent was removed under reduced pressure, and CH_2Cl_2 (80 mL) was added to the residue. The mixture was washed with water (2× 30 mL), then the organic phase was dried with Na_2SO_4, and the solvents were evaporated in vacuo. The residue was purified by column chromatography on silica gel (petroleum ether/CH_2Cl_2/EtOAc, 2:1:1) to give compound **5a** (294 mg, 81%).

4-Methyl-*N*-(2-phenylimidazo[1,2-*a*]pyridin-3-yl)benzenesulfonamide (5a): White solid (294 mg, 81%), m.p. 211.4–213.3 °C. IR (KBr): ṽ = 3440 (NH), 3051, 3029, 2976, 2795, 2725, 1634 (C=N), 1597, 1501, 1446, 1427, 1334 (SO_2), 1238, 1204, 1164 (SO_2), 1092 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 10.52 (s, 1 H, NH), 8.16 (d, J = 6.8 Hz, 1 H, 5-H), 7.60 (d, J = 7.2 Hz, 2 H, Ar), 7.55 (d, J = 8.8 Hz, 1 H, 8-H), 7.36–7.28 (m, 3 H, 7-H, Ar), 7.19–7.08 (m, 3 H, Ar), 7.01 (d, J = 8.0 Hz, 2 H, Ar), 6.95 (t, J = 6.8 Hz, 1 H, 6-H), 2.21 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 143.0, 142.0, 139.6, 136.5, 132.3, 129.0, 127.4, 126.8, 126.6, 126.2, 125.6, 123.4, 116.5, 113.1, 112.0, 20.8 ppm. MS (ESI): m/z = 364.0 [M + H]$^+$. HRMS (ESI): calcd. for $C_{20}H_{18}N_3O_2S$ [M + H]$^+$ 364.1114; found 364.1097.

4-Methyl-*N*-(2-*p*-tolylimidazo[1,2-*a*]pyridin-3-yl)benzenesulfonamide (5b): White solid (263 mg, 70%), m.p. 225.6–226.7 °C. IR (KBr): ṽ = 3446 (NH), 3027, 2920, 2807, 2732, 1635 (C=N), 1597, 1509, 1498, 1449, 1352, 1328 (SO_2), 1243, 1203, 1161 (SO_2), 1091, 1020 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 10.48 (s, 1 H, NH), 8.15 (d, J = 6.8 Hz, 1 H, 5-H), 7.53 (d, J = 8.8 Hz, 1 H, 8-H), 7.48 (d, J = 8.0 Hz, 2 H, Ar), 7.32–7.28 (m, 3 H, Ar, 7-H), 7.02 (d, J = 8.8 Hz, 2 H, Ar), 6.95–6.92 (m, 3 H, Ar, 6-H), 2.27 (s, 3 H, CH_3), 2.23 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 143.1, 142.1, 139.8, 136.8, 136.4, 129.6, 129.1, 128.1, 126.6, 126.3, 125.6, 123.5, 116.5, 112.8, 112.1, 20.9, 20.8 ppm. MS (ESI): m/z = 378.0 [M + H]$^+$. HRMS (ESI): calcd. for $C_{21}H_{20}N_3O_2S$ [M + H]$^+$ 378.1271; found 378.1243.

***N*-[2-(4-Methoxyphenyl)imidazo[1,2-*a*]pyridin-3-yl]-4-methylbenzenesulfonamide (5c):** White solid (349 mg, 89%), m.p. 209.6–211.2 °C. IR (KBr): ṽ = 3428 (NH), 2978, 2840, 2809, 2728, 1633, 1613 (C=N), 1508, 1454, 1397, 1334 (SO_2), 1300, 1249, 1160 (SO_2), 1090, 1028 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 10.41 (s, 1 H, NH), 8.09 (d, J = 6.8 Hz, 1 H, 5-H), 7.51–7.45 (m, 3 H, Ar, 8-H), 7.28 (d, J = 8.0 Hz, 2 H, Ar), 7.23 (t, J = 7.6 Hz, 1 H, 7-H), 6.99 (d, J = 8.0 Hz, 2 H, Ar), 6.88 (t, J = 6.8 Hz, 1 H, 6-H), 6.63 (d, J = 8.8 Hz, 2 H, Ar), 3.72 (s, 3 H, OCH_3), 2.21 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 158.4, 143.0, 142.0, 139.7, 136.9, 129.1, 127.9, 126.3, 125.5, 125.0, 123.4, 116.4, 113.0, 112.4, 112.0, 55.0, 20.9 ppm. MS (ESI): m/z = 393.9 [M + H]$^+$. HRMS (ESI): calcd. for $C_{21}H_{20}N_3O_3S$ [M + H]$^+$ 394.1220; found 394.1219.

***N*-[2-(3-Methoxyphenyl)imidazo[1,2-*a*]pyridin-3-yl]-4-methylbenzenesulfonamide (5d):** White solid (251 mg, 64%), m.p. 188.5–190.5 °C. IR (KBr): ṽ = 3426 (NH), 3274 (NH), 3041, 2968, 2839, 1633 (C=N), 1602, 1500, 1425, 1382, 1349 (SO_2), 1252, 1232, 1162 (SO_2), 1090, 1037 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 10.53 (s, 1 H, NH), 8.17 (d, J = 6.8 Hz, 1 H, 5-H), 7.55 (dt, J = 8.8, 1.2 Hz, 1 H, 8-H), 7.34–7.28 (m, 3 H, 7-H, Ar), 7.21–7.18 (m, 1 H, Ar), 7.15–7.14 (m, 1 H, Ar), 7.04 (t, J = 8.0 Hz, 1 H, Ar), 7.00 (d, J = 7.6 Hz, 2 H, Ar), 6.95 (td, J = 6.8, 1.2 Hz, 1 H, 6-H), 6.73 (ddd, J = 8.0, 2.4, 0.8 Hz, 1 H, Ar), 3.71 (s, 3 H, OCH_3), 2.22 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 158.4, 142.8, 141.9, 139.5, 136.5, 133.7, 129.0, 128.4, 126.1, 125.5, 123.4, 119.2, 116.5, 113.1, 112.9, 112.0, 54.8, 20.8 ppm. MS (ESI): m/z = 394.0 [M + H]$^+$. HRMS (ESI): calcd. for $C_{21}H_{20}N_3O_3S$ [M + H]$^+$ 394.1220; found 394.1223.

4-Methyl-*N*-[2-(4-nitrophenyl)imidazo[1,2-*a*]pyridin-3-yl]benzenesulfonamide (5e): Pale yellow solid (245 mg, 60%), m.p. 226.6–229.0 °C. IR (KBr): ṽ = 3431 (NH), 2998, 2814, 2742, 1635 (C=N), 1602, 1520 (NO_2), 1445, 1346 (NO_2), 1245, 1206, 1161 (SO_2), 1092 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 10.76 (s, 1 H, NH), 8.29 (d, J = 6.8 Hz, 1 H, 5-H), 7.96 (d, J = 8.8 Hz, 2 H, Ar), 7.81 (d, J = 8.8 Hz, 2 H, Ar), 7.61 (d, J = 9.2 Hz, 1 H, 8-H), 7.40–7.36 (m, 1 H, 7-H), 7.29 (d, J = 8.0 Hz, 2 H, Ar), 7.03 (t, J = 6.8 Hz, 1 H, 6-H), 6.99 (d, J = 8.0 Hz, 2 H, Ar), 2.11 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 145.6, 143.1, 142.4, 138.9, 137.1, 136.3, 129.0, 127.2, 126.2, 123.7, 122.5, 116.7, 114.8, 112.6, 20.4 ppm. MS (ESI): m/z = 409.0 [M + H]$^+$. HRMS (ESI): calcd. for $C_{20}H_{17}N_4O_4S$ [M + H]$^+$ 409.0965; found 409.0955.

***N*-[2-(4-Chlorophenyl)imidazo[1,2-*a*]pyridin-3-yl]-4-methylbenzenesulfonamide (5f):** White solid (306 mg, 77%), m.p. 226.9–227.4 °C. IR (KBr): ṽ = 3443 (NH), 2986, 2813, 2737, 1635 (C=N), 1599, 1503, 1489, 1447, 1404, 1353, 1338 (SO_2), 1244, 1205, 1162 (SO_2), 1093, 1015 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 10.50 (s, 1 H, NH), 8.18 (d, J = 6.8 Hz, 1 H, 5-H), 7.5–7.48 (m, 3 H, 8-H, Ar), 7.32–7.23 (m, 3 H, 7-H, Ar), 7.14–7.08 (m, 2 H, Ar), 6.97 (d, J = 8.0 Hz, 2 H, Ar), 6.94 (td, J = 6.8, 0.8 Hz, 1 H, 6-H), 2.23 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 143.4, 142.3, 138.5, 136.5, 131.9, 131.3, 129.1, 128.3, 127.6, 126.4, 126.1, 123.7, 116.7, 113.4, 112.5, 21.0 ppm. MS (ESI): m/z = 397.9 [M + H]$^+$. HRMS (ESI): calcd. for $C_{20}H_{17}ClN_3O_2S$ [M + H]$^+$ 398.0725; found 398.0722.

***N*-[2-(4-Bromophenyl)imidazo[1,2-*a*]pyridin-3-yl]-4-methylbenzenesulfonamide (5g):** White solid (348 mg, 79%), m.p. 231.5–233.5 °C. IR (KBr): ṽ = 3440 (NH), 2982, 2812, 2734, 1635 (C=N), 1599, 1503, 1488, 1445, 1401, 1381, 1337 (SO_2), 1243, 1204, 1162 (SO_2), 1093, 1010 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 10.57 (s, 1 H, NH), 8.24 (d, J = 6.8 Hz, 1 H, 5-H), 7.56 (d, J = 9.2 Hz, 1 H, 8-H), 7.52–7.47 (m, 2 H, Ar), 7.37–7.32 (m, 1 H, 7-H), 7.29 (d, J = 8.4 Hz, 4 H, Ar), 7.02 (d, J = 8.4 Hz, 2 H, Ar), 6.98 (d, J = 6.8 Hz, 1 H, 6-H), 2.27 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 143.2, 142.2, 138.5, 136.5, 131.6, 130.4, 128.96, 128.4, 126.2, 125.8, 123.5, 120.4, 116.6, 113.3, 112.2, 20.9 ppm. MS (ESI): m/z = 441.9 [M + H]$^+$. HRMS (ESI): calcd. for $C_{20}H_{17}BrN_3O_2S$ [M + H]$^+$ 442.0219; found 442.0213.

_N_-[2-(3-Chlorophenyl)imidazo[1,2-*a*]pyridin-3-yl]-4-methylbenzenesulfonamide (5h): White solid (302 mg, 76%), m.p. 198.4–199.4 °C. IR (KBr): ṽ = 3437 (NH), 2977, 2800, 2728, 1634 (C=N), 1597, 1573, 1501, 1473, 1428, 1367, 1335 (SO_2), 1237, 1203, 1164 (SO_2), 1093 cm^{-1}. ^1H NMR (400 MHz, [D_6]DMSO): δ = 10.61 (s, 1 H, NH), 8.26 (d, J = 6.8 Hz, 1 H, 5-H), 7.60–7.53 (m, 3 H, 8-H, Ar), 7.38–7.32 (m, 1 H, 7-H), 7.30 (d, J = 8.4 Hz, 2 H, Ar), 7.20 (dt, J = 8.0, 1.6 Hz, 1 H, Ar), 7.19–7.14 (m, 1 H, Ar), 7.02–6.98 (m, 3 H, 6-H, Ar), 2.21 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, [D_6]-DMSO): δ = 143.0, 142.2, 138.0, 136.1, 134.4, 132.5, 129.2, 129.0, 126.7, 126.1, 125.9, 125.1, 123.6, 116.6, 113.5, 112.3, 20.8 ppm. MS (ESI): m/z = 398.0 [M + H]$^+$. HRMS (ESI): calcd. for $C_{20}H_{17}ClN_3O_2S$ [M + H]$^+$ 398.0725; found 398.0705.

_N_-[2-(4-Fluorophenyl)imidazo[1,2-*a*]pyridin-3-yl]-4-methylbenzenesulfonamide (5i): White solid (289 mg, 76%), m.p. 225.8–227.9 °C. IR (KBr): ṽ = 3446 (NH), 2977, 2799, 2730, 1635 (C=N), 1604, 1597, 1559, 1505, 1505, 1429, 1335 (SO_2), 1225, 1165 (SO_2), 1093, 1014 cm^{-1}. ^1H NMR (400 MHz, [D_6]DMSO): δ = 10.53 (s, 1 H, NH), 8.19 (d, J = 6.8 Hz, 1 H, 5-H), 7.64–7.57 (m, 2 H, Ar), 7.54 (d, J = 8.8 Hz, 1 H, 8-H), 7.35–7.28 (m, 3 H, 7-H, Ar), 7.03 (d, J = 8.0 Hz, 2 H, Ar), 6.99–6.91 (m, 3 H, 6-H, Ar), 2.23 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, [D_6]DMSO): δ = 162.46, 160.03, 143.0, 142.0, 138.7, 136.6, 129.0, 128.6, 126.2, 125.6, 123.5, 116.5, 114.4, 114.2, 112.9, 112.1, 20.7 ppm. MS (ESI): m/z = 382.0 [M + H]$^+$. HRMS (ESI): calcd. for $C_{20}H_{17}FN_3O_2S$ [M + H]$^+$ 382.1020; found 382.1018.

_N_-[2-(4-Hydroxyphenyl)imidazo[1,2-*a*]pyridin-3-yl]-4-methylbenzenesulfonamide (5j): White solid (258 mg, 68%), m.p. 242.8–243.6 °C. IR (KBr): ṽ = 3441 (NH), 3342 (OH), 3111, 1634 (C=N), 1615, 1596, 1515, 1447, 1370, 1356 (SO_2), 1274, 1235, 1165 (SO_2), 1091 cm^{-1}. ^1H NMR (400 MHz, [D_6]DMSO): δ = 10.39 (s, 1 H, NH), 9.41 (s, 1 H, OH), 8.09 (d, J = 6.8 Hz, 1 H, 5-H), 7.49 (d, J = 8.8 Hz, 1 H, 8-H), 7.41 (d, J = 8.8 Hz, 2 H, Ar), 7.35 (d, J = 8.4 Hz, 2 H, Ar), 7.30–7.24 (m, 1 H, 7-H), 7.07 (d, J = 8.0 Hz, 2 H, Ar), 6.90 (t, J = 6.8 Hz, 1 H, 6-H), 6.50 (d, J = 8.8 Hz, 2 H, Ar), 2.27 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, [D_6]DMSO): δ = 156.8, 143.2, 141.9, 140.0, 137.0, 129.1, 128.0, 126.3, 125.3, 123.3, 116.3, 114.4, 112.0, 111.8, 21.0 ppm. MS (ESI): m/z = 380.0 [M + H]$^+$. HRMS (ESI): calcd. for $C_{20}H_{18}N_3O_3S$ [M + H]$^+$ 380.1063; found 380.1044.

_N_-[2-(Furan-2-yl)imidazo[1,2-*a*]pyridin-3-yl]-4-methylbenzenesulfonamide (5k): White solid (265 mg, 75%), m.p. 208.0–208.9 °C. IR (KBr): ṽ = 3446 (NH), 3025, 2808, 2744, 1635 (C=N), 1558, 1540, 1506, 1353, 1336 (SO_2), 1255, 1204, 1163 (SO_2), 1093, 1067, 1013 cm^{-1}. ^1H NMR (400 MHz, [D_6]DMSO): δ = 10.47 (s, 1 H, NH), 8.17 (d, J = 6.8 Hz, 1 H, 5-H), 7.51 (d, J = 9.2 Hz, 1 H, 8-H), 7.45 (d, J = 8.4 Hz, 2 H, Ar), 7.35–7.28 (m, 2 H, 7-H, Furyl), 7.20 (d, J = 8.0 Hz, 2 H, Ar), 6.96 (t, J = 6.8 Hz, 1 H, 6-H), 6.51 (d, J = 2.8 Hz, 1 H, Furyl), 6.31 (dd, J = 3.2, 2.0 Hz, 1 H, Furyl), 2.30 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, [D_6]DMSO): δ = 147.2, 143.1, 142.4, 142.3, 136.9, 132.0, 129.1 126.5, 126.0, 123.6, 116.5, 112.6, 112.3, 110.7, 107.9, 21.0 ppm. MS (ESI): m/z = 354.0 [M + H]$^+$. HRMS (ESI): calcd. for $C_{18}H_{16}N_3O_3S$ [M + H]$^+$ 354.0907; found 354.0912.

4-Methyl-_N_-[2-(thiophen-2-yl)imidazo[1,2-*a*]pyridin-3-yl]benzenesulfonamide (5l): White solid (269 mg, 73%), m.p. 226.7–228.6 °C. IR (KBr): ṽ = 3446 (NH), 3025, 2808, 2744, 1635 (C=N), 1558, 1540, 1506, 1353, 1336 (SO_2), 1255, 1204, 1163 (SO_2), 1093, 1067, 1013 cm^{-1}. ^1H NMR (400 MHz, [D_6]DMSO): δ = 10.55 (s, 1 H, NH), 7.99 (d, J = 6.8 Hz, 1 H, 5-H), 7.52 (d, J = 8.8 Hz, 1 H, 8-H), 7.45 (d, J = 8.0 Hz, 2 H, Ar), 7.39 (d, J = 5.2 Hz, 1 H, Thienyl), 7.33–7.26 (m, 1 H, 7-H), 7.17 (d, J = 8.4 Hz, 2 H, Ar), 7.09 (d, J = 3.6 Hz, 1 H, Thienyl), 6.90 (t, J = 6.8 Hz, 1 H, 6-H), 6.80 (dd, J = 4.8, 3.6 Hz, 1 H, Thienyl), 2.29 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, [D_6]DMSO): δ = 147.2, 143.1, 142.4, 142.3, 136.9, 132.0, 129.1 126.5, 126.0, 123.6, 116.5, 112.6, 112.3, 110.7, 107.9, 21.0 ppm. MS (ESI): m/z = 370.0 [M + H]$^+$. HRMS (ESI): calcd. for $C_{18}H_{16}N_3O_2S_2$ [M + H]$^+$ 370.0678; found 370.0680.

4-Methyl-_N_-(2-methylimidazo[1,2-*a*]pyridin-3-yl)benzenesulfonamide (5m): White solid (84 mg, 28%), m.p.217.6–220.1 °C. IR (KBr): ṽ = 3434 (NH), 3026, 2964, 2809, 2707, 1637 (C=N), 1597, 1581, 1497, 1444, 1440, 1334 (SO_2), 1284, 1255, 1165 (SO_2), 1090 cm^{-1}. ^1H NMR (400 MHz, [D_6]DMSO): δ = 10.18 (s, 1 H, NH), 8.09 (dt, J = 6.8, 1.2 Hz, 1 H, 5-H), 7.58–7.48 (m, 2 H, Ar), 7.40–7.36 (m, 3 H, 8-H, Ar), 7.22 (ddd, J = 9.2, 6.8, 1.2 Hz, 1 H, 7-H), 6.87 (td, J = 6.8, 1.2 Hz, 1 H, 6-H), 2.39 (s, 3 H, CH_3), 1.59 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, [D_6]DMSO): δ = 143.5, 141.6, 138.3, 136.5, 129.6, 126.7, 124.7, 123.1, 115.9, 114.0, 111.6, 21.1, 11.92 ppm. MS (ESI): m/z = 301.9 [M + H]$^+$. HRMS (ESI): calcd. for $C_{15}H_{16}N_3O_2S$ [M + H]$^+$ 302.0958; found 302.0962.

_N_-(2-Phenylimidazo[1,2-*a*]pyridin-3-yl)benzenesulfonamide (5n): White solid (279 mg, 80%), m.p. 222.7–223.6 °C. IR (KBr): ṽ = 3428 (NH), 3054, 2966, 2792, 2720, 1635 (C=N), 1558, 1506, 1447, 1333 (SO_2), 1168 (SO_2), 1093, 1027 cm^{-1}. ^1H NMR (400 MHz, [D_6]DMSO): δ = 10.68 (s, 1 H, NH), 8.12 (d, J = 6.8 Hz, 1 H, 5-H), 7.71–7.65 (m, 2 H, Ar), 7.56 (dt, J = 9.2, 0.8 Hz, 1 H, 8-H), 7.51 (dd, J = 8.4, 1.2 Hz, 2 H, Ar), 7.4–7.39 (m, 1 H, 7-H), 7.35–7.25 (m, 3 H, Ar), 7.17–7.12 (m, 3 H, Ar), 6.94 (td, J = 6.8, 0.8 Hz, 1 H, 6-H) ppm. ^{13}C NMR (100 MHz, [D_6]DMSO): δ = 142.0, 139.8, 139.4, 132.5, 132.3, 128.6, 127.5, 127.1, 126.5, 126.1, 125.5, 123.3, 116.5, 113.0, 112.0 ppm. MS (ESI): m/z = 350 [M + H]$^+$. HRMS (ESI): calcd. for $C_{19}H_{16}N_3O_2S$ [M + H]$^+$ 350.0958; found 350.0960.

4-Methoxy-_N_-(2-phenylimidazo[1,2-*a*]pyridin-3-yl)benzenesulfonamide (5o): White solid (341 mg, 90%), m.p. 209.6–211.2 °C. IR (KBr): ṽ = 3436 (NH), 2966, 2941, 2840, 1635 (C=N), 1596, 1579, 1496, 1322 (SO_2), 1262, 1245, 1156 (SO_2), 1093, 1028 cm^{-1}. ^1H NMR (400 MHz, [D_6]DMSO): δ = 10.45 (s, 1 H, NH), 8.18 (d, J = 6.8 Hz, 1 H, 5-H), 7.65–7.62 (m, 2 H, Ar), 7.55 (d, J = 9.2 Hz, 1 H, 8-H), 7.37–7.30 (m, 3 H, 7-H, Ar), 7.19–7.10 (m, 3 H, Ar), 6.96 (t, J = 6.8 Hz, 1 H, 6-H), 6.72 (d, J = 8.8 Hz, 2 H, Ar), 3.71 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, [D_6]DMSO): δ = 162.3, 142.1, 139.6, 132.4, 130.9, 128.5, 127.6, 127.1, 126.7, 125.7, 123.6, 116.6, 113.9, 113.2, 112.2, 55.4 ppm. MS (ESI): m/z = 380.0 [M + H]$^+$. HRMS (ESI): calcd. for $C_{20}H_{18}N_3O_3S$ [M + H]$^+$ 380.1063; found 380.1075.

4-Chloro-_N_-(2-phenylimidazo[1,2-*a*]pyridin-3-yl)benzenesulfonamide (5p): White solid (287 mg, 75%), m.p. 224.2–225.0 °C. IR (KBr): ṽ = 3445 (NH), 2983, 2808, 2736, 1634 (C=N), 1585, 1503, 1476, 1447, 1434, 1343 (SO_2), 1236, 1204, 1166 (SO_2), 1093 cm^{-1}. ^1H NMR (400 MHz, [D_6]DMSO): δ = 10.80 (s, 1 H, NH), 8.29 (d, J = 6.8 Hz, 1 H, 5-H), 7.62–7.52 (m, 3 H, 8-H, Ar), 7.42–7.38 (m, 2 H, Ar), 7.38–7.32 (m, 1 H, 7-H), 7.26–7.10 (m, 5 H, Ar), 7.01 (t, J = 6.8 Hz, 1 H, 6-H) ppm. ^{13}C NMR (100 MHz, [D_6]DMSO): δ = 1421, 139.4, 138.1, 137.7, 132.1, 128.6, 128.0, 127.5, 127.0, 126.6, 125.8, 123.5, 116.5, 113.0, 112.3 ppm. MS (ESI): m/z = 384.0 [M + H]$^+$. HRMS (ESI): calcd. for $C_{19}H_{15}ClN_3O_2S$ [M + H]$^+$ 384.0568; found 384.0580.

4-Nitro-_N_-(2-phenylimidazo[1,2-*a*]pyridin-3-yl)benzenesulfonamide (5q): Yellow solid (279 mg, 71%), m.p. 237.5–238.4 °C. IR (KBr): ṽ = 3439 (NH), 3205, 3109, 3065, 1648 (C=N), 1605, 1591, 1520, 1499, 1443, 1347 (SO_2), 1267, 1234, 1142 (SO_2), 1091 cm^{-1}. ^1H NMR (400 MHz, [D_6]DMSO): δ = 11.40 (s, 1 H, NH), 8.39 (d, J = 6.0 Hz, 1 H, 5-H), 7.93 (d, J = 8.4 Hz, 2 H, Ar), 7.71–7.56 (m,

3 H, 8-H, Ar), 7.51 (d, J = 5.6 Hz, 2 H, Ar), 7.46–7.36 (m, 1 H, 7-H), 7.13–6.99 (m, 4 H, 6-H, Ar) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 149.0, 145.5, 141.5, 137.5, 131.7, 127.7, 127.5, 126.8, 126.5, 123.8, 123.7, 115.9, 114.23, 112.7 ppm. MS (ESI): m/z = 395.0 [M + H]$^+$. HRMS (ESI): calcd. for $C_{19}H_{15}N_4O_4S$ [M + H]$^+$ 395.0809; found 395.0808.

***N*-(2-Phenylimidazo[1,2-*a*]pyridin-3-yl)methanesulfonamide (5r):** White solid (89 mg, 31%), m.p. 206.4–208.1 °C. IR (KBr): $\tilde{\nu}$ = 3428 (NH), 3080, 2973, 2689, 1633 (C=N), 1568, 1498, 1445, 1411, 1398, 1329 (SO_2), 1244, 1206, 1157 (SO_2) cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 10.20 (s, 1 H, NH), 8.34 (dd, J = 6.8, 1.2 Hz, 1 H, 5-H), 8.12–8.05 (m, 2 H, Ar), 7.60 (dd, J = 8.8, 1.0 Hz, 1 H, 8-H), 7.50–7.44 (m, 2 H, Ar), 7.41–7.31 (m, 2 H, 7-H, Ar), 7.02 (t, J = 6.8 Hz, 1 H, 6-H), 2.79 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 142.2, 139.4, 132.7, 128.2, 127.8, 127.0, 125.7, 123.6, 116.7, 113.2, 112.3, 41.2 ppm. MS (ESI): m/z = 287.9 [M + H]$^+$. HRMS (ESI): calcd. for $C_{14}H_{14}N_3O_2S$ [M + H]$^+$ 288.0801; found 288.0805.

***N*-(2-Phenylimidazo[1,2-*a*]pyridin-3-yl)cyclopropanesulfonamide (5s):** White solid (122 mg, 39%), m.p. 205.0–206.2 °C. IR (KBr): $\tilde{\nu}$ = 3437 (NH), 3054, 3012, 2789, 2732, 1631 (C=N), 1497, 1446, 1326 (SO_2), 1237, 1142 (SO_2), 1069, 1042 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 10.19 (s, 1 H, NH), 8.34 (dt, J = 6.8, 1.0 Hz, 1 H, 5-H), 8.16–8.08 (m, 2 H, Ar), 7.59 (dt, J = 9.2, 1.0 Hz, 1 H, 8-H), 7.49–7.40 (m, 2 H, Ar), 7.39–7.30 (m, 2 H, 7-H, Ar), 7.01 (td, J = 6.8, 1.2 Hz, 1 H, 6-H), 2.45–2.38 (m, 1 H, CH), 0.74 (d, J = 3.6 Hz, 2 H, CH_2), 0.66 (d, J = 7.2 Hz, 2 H, CH_2) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 142.0, 139.6, 132.9, 128.0, 127.7, 127.1, 125.6, 123.6, 116.6, 113.4, 112.2, 31.1, 5.7 ppm. MS (ESI): m/z = 314.0 [M + H]$^+$. HRMS (ESI): calcd. for $C_{16}H_{16}N_3O_2S$ [M + H]$^+$ 314.0958; found 314.0952.

4-Methyl-*N*-(8-methyl-2-phenylimidazo[1,2-*a*]pyridin-3-yl)benzenesulfonamide (5t): White solid (298 mg, 79%), m.p.173.1–174.6 °C. IR (KBr): $\tilde{\nu}$ = 3436 (NH), 3034, 2972, 2925, 2727, 1631 (C=N), 1598, 1563, 1495, 1446, 1390, 1356 (SO_2), 1332, 1260, 1205, 1157 (SO_2), 1092 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.11 (d, J = 6.8 Hz, 1 H, 5-H), 7.31–7.20 (m, 4 H, 7-H, Ar), 7.04–7.01 (m, 2 H, Ar), 6.97 (t, J = 7.3 Hz, 2 H, Ar), 6.79 (d, J = 8.2 Hz, 2 H, Ar), 6.72 (t, J = 6.8 Hz, 1 H, 6-H), 2.61 (s, 3 H, CH_3), 2.19 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 142.9, 142.3, 139.1, 136.6, 132.5, 129.0, 127.4, 126.7, 126.6, 126.2, 126.0, 124.0, 121.2, 113.4, 112.0, 20.8, 16.0 ppm. MS (ESI): m/z = 378.0 [M + H]$^+$. HRMS (ESI): calcd. for $C_{21}H_{20}N_3O_2S$ [M + H]$^+$ 378.1271; found 378.1275.

4-Methyl-*N*-(6-methyl-2-phenylimidazo[1,2-*a*]pyridin-3-yl)benzenesulfonamide (5u): White solid (264 mg, 70%), m.p. 230.4–231.8 °C. IR (KBr): $\tilde{\nu}$ = 3436 (NH), 2975, 2923, 2800, 2734, 1597, 1511, 1490, 1433 (SO_2), 1412, 1381, 1337, 1214, 1164 (SO_2), 1094 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 10.45 (s, 1 H, NH), 7.72 (s, 1 H, 5-H), 7.70–7.63 (m, 2 H, Ar), 7.45 (d, J = 9.2 Hz, 1 H, 8-H), 7.35 (d, J = 8.0 Hz, 2 H, Ar), 7.18–7.11 (m, 4 H, 7-H, Ar), 7.05 (d, J = 8.0 Hz, 2 H, Ar), 2.24 (s, 3 H, CH_3), 2.23 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 143.0, 141.0, 139.5, 136.9, 132.5, 129.1, 128.3, 127.4, 126.8, 126.5, 126.2, 121.1, 120.7, 115.9, 112.8, 20.8, 17.5 ppm. MS (ESI): m/z = 378.0 [M + H]$^+$. HRMS (ESI): calcd. for $C_{21}H_{20}N_3O_2S$ [M + H]$^+$ 378.1271; found 378.1270.

***N*-(6-Chloro-2-phenylimidazo[1,2-*a*]pyridin-3-yl)-4-methylbenzenesulfonamide (5v):** White solid (226 mg, 57%), m.p. 216.6–218.2 °C. IR (KBr): $\tilde{\nu}$ = 3435 (NH), 3095, 2993, 2924, 2802, 2735, 1597, 1556, 1500, 1446, 1416, 1382, 1338 (SO_2), 1328, 1229, 1199, 1163 (SO_2), 1094 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 10.61 (s, 1 H, NH), 7.99–7.89 (m, 1 H, 5-H), 7.73–7.66 (m, 2 H, Ar), 7.61 (d, J = 9.6 Hz, 1 H, 8-H), 7.36–7.33 (m, 3 H, 7-H, Ar), 7.23–7.15 (m, 3 H, Ar), 7.07 (d, J = 8.0 Hz, 2 H, Ar), 2.24 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 143.5, 140.8, 140.5, 136.4, 132.0, 129.4, 127.7, 127.4, 126.7, 126.5, 126.3, 121.2, 119.3, 117.7, 113.9, 21.0 ppm. MS (ESI): m/z = 398.0 [M + H]$^+$. HRMS (ESI): calcd. for $C_{20}H_{17}Cl\,N_3O_2S$ [M + H]$^+$ 398.0725; found 398.0728.

***N*-(6-Bromo-2-phenylimidazo[1,2-*a*]pyridin-3-yl)-4-methylbenzenesulfonamide (5w):** Pale yellow solid (300 mg, 68%), m.p. 220.6–222.4 °C. IR (KBr): $\tilde{\nu}$ = 3435 (NH), 3090, 2991, 2923, 2801, 2734, 1733, 1625, 1597, 1552, 1498, 1431, 1409, 1381, 1338 (SO_2), 1327, 1227, 1195, 1163 (SO_2), 1092, 1071, 1050 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 10.56 (s, 1 H, NH), 7.94 (d, J = 1.2 Hz, 1 H, 5-H), 7.78–7.71 (m, 2 H, Ar), 7.54 (dd, J = 9.2, 0.8 Hz, 1 H, 8-H), 7.40 (dd, J = 9.2, 2.0 Hz, 1 H, 7-H), 7.37 (d, J = 8.4 Hz, 2 H, Ar), 7.22–7.20 (m, 3 H, Ar), 7.09 (d, J = 8.0 Hz, 2 H, Ar), 2.26 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 143.6, 140.5, 136.5, 131.9, 129.4, 128.5, 127.7, 127.4, 126.7, 126.3, 123.2, 117.9, 113.6, 106.2, 21.0 ppm. MS (ESI): m/z = 442.0 [M + H]$^+$. HRMS (ESI): calcd. for $C_{20}H_{17}BrN_3\,O_2S$ [M + H]$^+$ 442.0219; found 442.0209.

CCDC-957561 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif

Supporting Information (see footnote on the first page of this article): ^{1}H and ^{13}C NMR spectra of all compounds, crystal data and details of X-ray experiments for compounds **5c**.

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[1] a) K. S. Gudmundsson, J. D. Williams, J. C. Drach, L. B. Townsend, *J. Med. Chem.* **2003**, *46*, 1449–1455; b) J. J. Kaminski, A. M. Doweyko, *J. Med. Chem.* **1997**, *40*, 427–436; c) R. B. Lacerda, C. K. F. de Lima, L. L. da Silva, N. C. Romeiro, A. L. P. Miranda, E. J. Barreiro, C. A. M. Fraga, *Bioorg. Med. Chem.* **2009**, *17*, 74–84; d) N. M. Shukla, D. B. Salunke, E. Yoo, C. A. Mutz, R. Balakrishna, S. A. David, *Bioorg. Med. Chem.* **2012**, *20*, 5850–5863; e) K. A. Wafford, M. B. van Niel, Q. P. Ma, E. Horridge, M. B. Herd, D. R. Peden, D. Belelli, J. J. Lambert, *Neuropharmacology* **2009**, *56*, 182–189; f) M. H. Wiegand, *Drugs* **2008**, *68*, 2411–2417.

[2] Y. Rival, G. Grassy, A. Taudou, R. Ecalle, *Eur. J. Med. Chem.* **1991**, *26*, 13–18.

[3] a) E. Badawey, T. Kappe, *Eur. J. Med. Chem.* **1995**, *30*, 327–332; b) M. Hranjec, M. Kralj, N. Piantanida, M. Sedic, L. Suman, K. Pavelic, G. Karminski-Zamola, *J. Med. Chem.* **2007**, *50*, 5696–5711; c) M. Hranjec, I. Piantanida, M. Kralj, L. Suman, K. Pavelic, G. Karminski-Zamola, *J. Med. Chem.* **2008**, *51*, 4899–4910.

[4] a) A. Gueiffier, M. Lhassani, A. Elhakmaoui, R. Snoeck, G. Andrei, O. Chavignon, J. C. Teulade, A. Kerbal, E. M. Essassi, J. C. Debouzy, M. Witvrouw, Y. Blache, J. Balzarini, E. De Clercq, J. P. Chapat, *J. Med. Chem.* **1996**, *39*, 2856–2859; b) A. Gueiffier, S. Mavel, M. Lhassani, A. Elhakmaoui, R. Snoeck, G. Andrei, O. Chavignon, J. C. Teulade, M. Witvrouw, J. Balzarini, E. De Clercq, J. P. Chapat, *J. Med. Chem.* **1998**, *41*, 5108–5112; c) M. Lhassani, O. Chavignon, J. M. Chezal, J. C. Teulade, J. P. Chapat, R. Snoeck, G. Andrei, J. Balzarini,

E. De Clercq, A. Gueiffier, *Eur. J. Med. Chem.* **1999**, *34*, 271–274.
[5] M. H. Fisher, A. Lusi, *J. Med. Chem.* **1972**, *15*, 982–985.
[6] T. Biftu, D. Feng, M. Fisher, G. B. Liang, X. X. Qian, A. Scribner, R. Dennis, S. Lee, P. A. Liberator, C. Brown, A. Gurnett, P. S. Leavitt, D. Thompson, J. Mathew, A. Misura, S. Samaras, T. Tamas, J. F. Sina, K. A. McNulty, C. G. McKnight, D. M. Schmatz, M. Wyvratt, *Bioorg. Med. Chem. Lett.* **2006**, *16*, 2479–2483.
[7] L. Almirante, L. Polo, A. Mugnaini, E. Provinciali, P. Rugarli, A. Biancotti, A. Gamba, W. Murmann, *J. Med. Chem.* **1965**, *8*, 305–312.
[8] M. L. Bode, D. Gravestock, S. S. Moleele, C. W. van der Westhuyzen, S. C. Pelly, P. A. Steenkamp, H. C. Hoppe, T. Khan, L. A. Nkabinde, *Bioorg. Med. Chem.* **2011**, *19*, 4227–4237.
[9] C. Enguehard-Gueiffier, F. Fauvelle, J. C. Debouzy, A. Peinnequin, I. Thery, V. Dabouis, A. Gueiffier, *Eur. J. Pharm. Sci.* **2005**, *24*, 219–227.
[10] S. Z. Langer, S. Arbilla, J. Benavides, B. Scatton, *Adv. Biochem. Psychopharmacol.* **1990**, *46*, 61–72.
[11] R. J. Boerner, H. J. Moller, *Psychopharmakotherapie* **1997**, *4*, 145–148
[12] T. Ueda, K. Mizushige, K. Yukiiri, T. Takahashi, M. Kohno, *Cerebrovasc. Dis.* **2003**, *16*, 396–401.
[13] C. Enguehard-Gueiffier, A. Gueiffier, *Mini-Rev. Med. Chem.* **2007**, *7*, 888–899.
[14] E. S. Hand, W. W. Paudler, *J. Org. Chem.* **1978**, *43*, 2900–2906.
[15] H. Bienayme, K. Bouzid, *Angew. Chem.* **1998**, *110*, 2349–2352; *Angew. Chem. Int. Ed.* **1998**, *37*, 2234–2237.
[16] M. Abid, E. Sheibani, H. R. Bijanzadeh, L. G. Zhu, *Tetrahedron* **2008**, *64*, 10681–10686.
[17] a) N. Chernyak, V. Gevorgyan, *Angew. Chem.* **2010**, *122*, 2803–2806; *Angew. Chem. Int. Ed.* **2010**, *49*, 2743–2746; b) P. Liu, L. S. Fang, X. S. Lei, G. Q. Lin, *Tetrahedron Lett.* **2010**, *51*, 4605–4608.
[18] a) A. K. Bagdi, M. Rahman, S. Santra, A. Majee, A. Hajra, *Adv. Synth. Catal.* **2013**, *355*, 1741–1747; b) C. He, J. Hao, H. Xu, Y. P. Mo, H. Y. Liu, J. J. Han, A. W. Lei, *Chem. Commun.* **2012**, *48*, 11073–11075; c) P. Liu, C. L. Deng, X. S. Lei, G. Q. Lin, *Eur. J. Org. Chem.* **2011**, 7308–7316; d) H. G. Wang, Y. Wang, D. D. Liang, L. Y. Liu, J. C. Zhang, Q. Zhu, *Angew. Chem. Int. Ed.* **2011**, *50*, 5677–5680; e) H. G. Wang, Y. Wang, C. L. Peng, J. C. Zhang, Q. A. Zhu, *J. Am. Chem. Soc.* **2010**, *132*, 13217–13219; f) J. Zeng, Y. J. Tan, M. L. Leow, X. W. Liu, *Org. Lett.* **2012**, *14*, 4386–4389; g) R. L. Yan, H. Yan, C. Ma, Z. Y. Ren, X. A. Gao, G. S. Huang, Y. M. Liang, *J. Org. Chem.* **2012**, *77*, 2024–2028; h) H. Huang, X. Ji, X. Tang, M. Zhang, X. Li, H. Jiang, *Org. Lett.* DOI: 10.1021/ol403105p.
[19] D. K. Nair, S. M. Mobin, I. N. N. Namboothiri, *Org. Lett.* **2012**, *14*, 4580–4583.
[20] L. J. Ma, X. P. Wang, W. Yu, B. Han, *Chem. Commun.* **2011**, *47*, 11333–11335.
[21] Z. A. Fei, Y. P. Zhu, M. C. Liu, F. C. Jia, A. X. Wu, *Tetrahedron Lett.* **2013**, *54*, 1222–1226.
[22] I. B. Rozentsveig, V. Y. Serykh, G. N. Chernysheva, K. A. Chernyshev, E. V. Kondrashov, E. V. Tretyakov, G. V. Romanenko, *Eur. J. Org. Chem.* **2013**, 368–375.
[23] T. Kano, T. Yurino, D. Asakawa, K. Maruoka, *Angew. Chem. Int. Ed.* **2013**, *52*, 5532–5534.
[24] B. Eftekhari-Sis, M. Zirak, A. Akbari, *Chem. Rev.* **2013**, *113*, 2958–3043.
[25] E. E. Gilbert, *J. Chem. Eng. Data* **1974**, *19*, 182–183.
[26] V. Lucchini, M. Prato, G. Scorrano, P. Tecilla, *J. Org. Chem.* **1988**, *53*, 2251–2258.

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