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Novel 1-(azacyclyl)-3-arylsulfonyl-1*H*-pyrrolo[2,3-*b*]pyridines as 5-HT$_6$ agonists and antagonists

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Abstract—1-Aminoethyl-3-arylsulfonyl-1*H*-indoles **1** are 5-HT$_6$ receptor ligands with modest activity in a 5-HT$_6$ cyclase assay. Introduction of an additional nitrogen in the indole ring provides 1-aminoethyl-3-arylsulfonyl-1*H*-pyrrolo[2,3-*b*]pyridines **2** with both enhanced 5-HT$_6$ affinity and cyclase activity, many acting as 5-HT$_6$ agonists. We constrained the basic side chain as part of a ring to make 1-(azacyclyl)-3-arylsulfonyl-1*H*-pyrrolo[2,3-*b*]pyridines incorporating a pyrrolidinyl **3** or piperidinyl **4** ring system. Preparation of compounds **3** and **4** required synthesis of the key intermediates, 1-(pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridines **7** and 1-(piperidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridines **8**, respectively. Intermediates **7** were prepared through alkylation of 7-azaindole while the intermediates **8** required an alternate synthesis. The compounds of both series **3** and **4** were shown to have high binding affinities for the 5-HT$_6$ receptor. The in vitro functional activity at the 5-HT$_6$ receptor varied depending on various functionalities including the selection of the arylsulfonyl, the substitution on the arylsulfonyl group, the ring size, and the substitution on the basic amine moiety producing either 5-HT$_6$ receptor agonists or antagonists.

1. Introduction

Identification of ligands for the 5-HT$_6$ receptor has been the focus of several reports in the last decade.[1–4] Ligands for the 5-HT$_6$ receptor may be useful in the treatment of CNS disorders such as schizophrenia, depression, and impairment of learning and memory in diseases such as Alzheimer's disease (AD).[5–10] Efforts have led to the discovery of several classes of selective high affinity 5-HT$_6$ receptor ligands.[11–14] A common feature in many of these compound classes is the presence of a basic amine group and a requisite aryl sulfonyl moiety. As is the case with monoamine ligands, the necessity of the basic moiety for potent binding to the receptor was expected. However, among these classes it has been demonstrated that the presence of the aryl sulfonyl group was crucial for selectivity. Earlier we identified a series of 1-(2-aminoethyl)-3-arylsulfonyl-1*H*-indoles (**1**) (Fig. 1) with modest functional activity at the 5-HT$_6$ receptor (Table 1).[15] Continuing work expanding the scope led to a related series of 1-aminoethyl-3-arylsulfonyl-1*H*-pyrrolo[2,3-*b*]pyridines (**2**) with enhanced 5-HT$_6$ binding affinity and functional activity (Table 1).[16,17] In an effort to further expand the SAR around structure **2**, we sought to constrain the basic amine side chain as part of a ring to make 1-(azacyclyl)-3-arylsulfonyl-1*H*-pyrrolo[2,3-*b*]pyridines incorporating either a pyrrolidinyl (**3**) or piperidinyl (**4**) ring in the side chain (Fig. 1). The results of these efforts are the subject of this report.

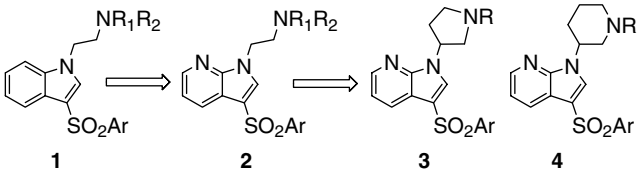

Figure 1. Genesis of leads.

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Table 1. Biological data for representative leads **1** and **2**, hydrochlorides[18,19]

Compound	Ar	R_1	R_2	5-HT_6 K_i (nM)	5-HT_6 cAMP Assay	
					Agonist	
					EC_{50} (nM)	E_{max} (%)
1a	Ph	Me	Me	20 ± 0.2	Weak partial	Agonist
2a	Ph	Me	Me	23 ± 2	25	94

2. Chemistry

2.1. Synthesis of pyrrolidine analogs (3)

Conversion of N-substituted hydroxypyrrolidines (**5**, R = Me or Et) into the chloro derivatives (**6a**) or the tosylates (**6b**) afforded substrates for N-substitution reactions. Reaction of 7-azaindole with either **6a** or **6b** under basic conditions efficiently furnished the desired pyrrolidinyl-7-azaindoles (**7**). Subsequent sulfonylation of **7** with sulfonyl chlorides in the presence of a Lewis acid in nitrobenzene afforded the target analogs **3** (R = Me or Et). In a similar manner, compounds **3** where R = benzyl were prepared. In an effort to prepare additional analogs, dealkylation of **3** with α-chloroethylchloroformate (ACE–Cl)[20] yielded secondary amines **3** (R = H) (Scheme 1).

2.2. Synthesis of piperidine analogs (4)

To prepare the piperidine analogs (**4**), we attempted alkylation of 7-azaindole with either 1-ethyl-3-chloropiperidine (**11a**), 1-benzyl-3-chloro-piperidine (**11b**), or the corresponding tosylates (**12a** and **12b**), under the same conditions used for the preparation of pyrrolidinyl derivatives (**7**). Instead of the desired piperidinyl-7-azaindoles (**8**), the reactions consistently gave the ring-contracted products (**9**) (Fig. 2). It is proposed that this transformation proceeds through the latent aziridinium species (**10**). Nucleophilic attack by the azaindole on the secondary carbon of the aziridinium system is preferred to attack on the tertiary center affording the pyrrolidinylmethyl derivatives (**9**). Furthermore, attempted alkylation of 7-azaindole with halopiperidine derivatives incapable of forming aziridinium cations (i.e., **13**–**16**) yielded no detectable alkylation product under similar reaction conditions, thus supporting the proposed mechanism. A variety of other routes were tried but were unsuccessful in yielding **8**. These included reactions of 7-azaindole with 1-benzyl-3-piperidinone under standard reductive amination conditions and reactions of 7-azaindole with 1-benzyl-3-piperidinol under Mitsunobu conditions.

An alternate route was required to access the desired analogs. The approach we envisioned (Scheme 2) utilizes conversion of the piperidinyl aminopicoline (**19**, R = benzyl), readily available from aminopyridine **17**, to piperidinyl-7-azaindole **8** following the procedure of Hands and coworkers.[21] Toward that end, reaction of 2-amino-picoline with 1-benzyl-3-piperidinone under one-pot reductive amination conditions[22,23] was attempted. Although the direct conversion failed to furnish **19**, a 2-step process in which imine (**18**) was preformed followed by a hydride reduction step afforded the required picoline. Subsequent treatment of **19** (R = benzyl) with *n*-BuLi followed by DMF[16] furnished piperidinyl 7-azaindole **8** system (R = Bn), albeit in poor yield due to formylation of the benzyl group. However, the desired *N*-ethyl analogs of **8** were obtained from **19** (R = ethyl) in significantly better yields under these conditions. Sulfonylation to final targets **4** (R = Et) was readily accomplished as previously described in Scheme 1. Removal of the ethyl using α-chloroethylchloroformate (ACE–Cl)[20] furnished the secondary unsubstituted amine **4** (R = H). Reaction of this free amine **4** (R = H) with aldehydes or ketones under standard reductive amination conditions furnished N-substituted analogs **4** (R = alkyl).

3. Biological data

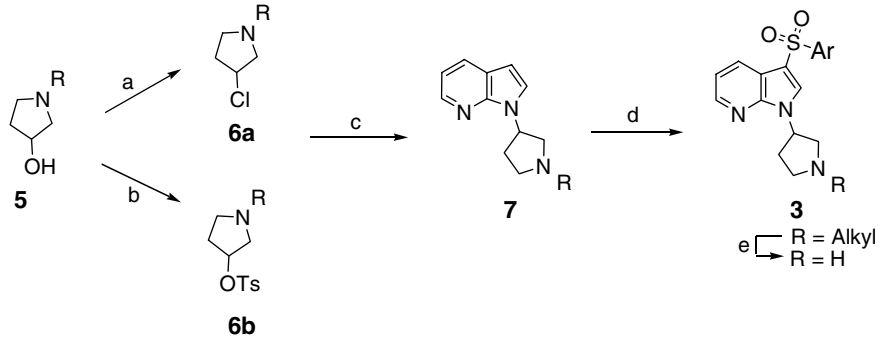
3.1. 5-HT_6 binding studies

All final compounds were tested in a standard radioligand binding assay[18] using human-cloned 5-HT_6 receptors stably transfected in HeLa cells (Tables 2 and 3) to determine affinity for the 5-HT_6 receptor. In pyrrolidinyl series **3**, essentially all the analogs, with the exception of **3q**, were high affinity ligands with K_i values <10 nM. This impressive and consistently high affinity shows that the constrained basic side chain locks the amine in a conformation that binds favorably to the receptor. However, within this series, a few subtle differences can still be discerned. For example, while a fluoro, chloro, bromo, or trifluoromethyl substitution at any position on the phenylsulfonyl ring is surprisingly well tolerated, there is a slight preference for *meta*-substitution (**3b**, **3d**, **3f**, and **3h**). Other sites of variation, however, had little impact on affinity. For example, both secondary and tertiary amine analogs (e.g., **3b** vs **3k** and **3d** vs **3n**) had comparable affinities. Interestingly, certain arylsulfonyl derivatives, in particular 5-chlorothien-2-yl (**3t**) and 6-Cl-imidazo[2,1-*b*]thiazol-5-yl (**3v**, **3w**, **3x**), were amongst the most potent at the 5-HT_6 receptor with K_i values around 1 nM.

Among the piperidinyl analogs (**4**), high 5-HT_6 affinity was observed with almost all derivatives as well with only four compounds (**4f**–**4h** and **4u**) having K_i values >10 nM. As in the first series, a minor preference for *meta*-substituted derivatives was observed (**4c**–**4e**). Among the aromatic derivatives, superior affinity for the receptor was achieved with **4y** and **4aa** which contain the bicyclic aromatic 6-Cl-imidazo[2,1-*b*]thiazol-5-yl moiety. In general, there was no direct correlation between the size of substituent on the amine (H, Me, Et, *i*-Pr) and the binding affinity (e.g., **4n**–**4q** or **4y**, **4z**, **4aa**, **4ab**).

3.2. 5-HT_6 functional assays

Functional efficacy of these ligands was determined for both series in a cAMP RIA in HeLa cells stably transfected with the h5-HT_6 receptor,[19] to determine



Scheme 1. Synthesis of compounds **3**. Reagents and conditions: (a) $POCl_3$, toluene, reflux; (b) tosylchloride, Et_3N, CH_2Cl_2; (c) 7-azaindole, Cs_2CO_3, DMSO, 80 °C; (d) $ArSO_2Cl$, AgOTf, $PhNO_2$, 140 °C; (e) i—ACE–Cl, DCE, reflux; ii—EtOH, reflux.

the correlation between receptor affinity and functional activity (Tables 2 and 3). Among the derivatives in series **3**, *meta*-substituted phenylsulfonyl compounds such as **3b**, **3d**, **3f**, and **3h** were generally partial agonists with moderate to weak potency in the functional assay. With the exception of compound **3c**, moving the phenyl substituent to the *ortho*- or *para*-positions provided compounds with antagonist efficacy. In addition, while alkylating the basic amine did not impact binding affinity, it did change the functional activity of the compounds (**3j**, **3l**–**3s**, **3w**, and **3x**) from agonist to antagonist. Among these, compounds **3p**, **3t**, and **3x** were nearly full antagonists with IC_{50} values of 23, 11, and 10 nM, respectively. A higher proportion of the compounds in series **4** demonstrated potent partial agonism with compounds **4c** and **4n** being nearly full agonists with moderate potency (EC_{50} = 50 and 67 nM, respectively). The functional SAR of this series is difficult to define, as there are instances of significant differences in efficacy with relatively small changes in the substitution pattern. For example, while the 3-fluorophenyl analog **4n** is nearly a full agonist, the closely related 2-fluorophenyl derivative (**4m**) possesses full antagonist efficacy with an IC_{50} = 50 nM. In addition, *meta*-substituted phenylsulfonyl derivatives were generally functionally agonists regardless of the substitution on the basic nitrogen, while the *para*-substituted analogs were generally antagonists.

Several of the racemic compounds in each series were separated into their enantiomers and tested separately in the binding assays but a significant eudismic ratio was not evident among the corresponding enantiomeric pairs. Similarly, in the functional assay, the enantiomers maintained functional activity and potency similar to that of the corresponding racemate.

4. Conclusions

Two series of 3-arylsulfonyl-7-azaindoles with constrained basic amine side chains were prepared. The basic amine was constrained in a five-membered ring, pyrrolidines (**3**), or six-membered ring, piperidines (**4**).

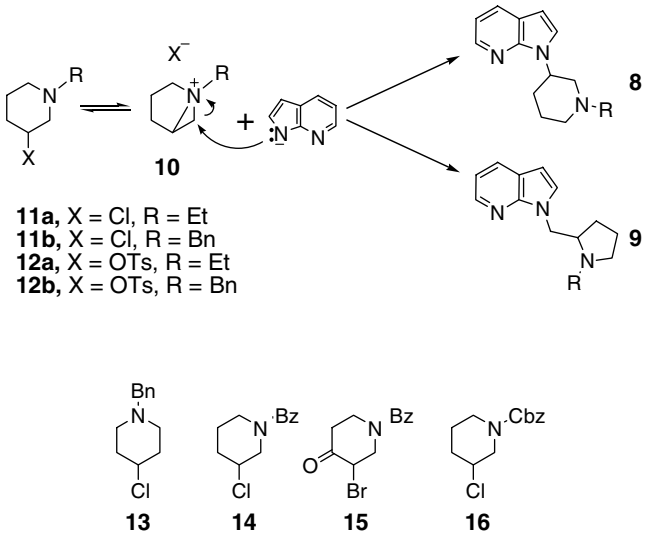
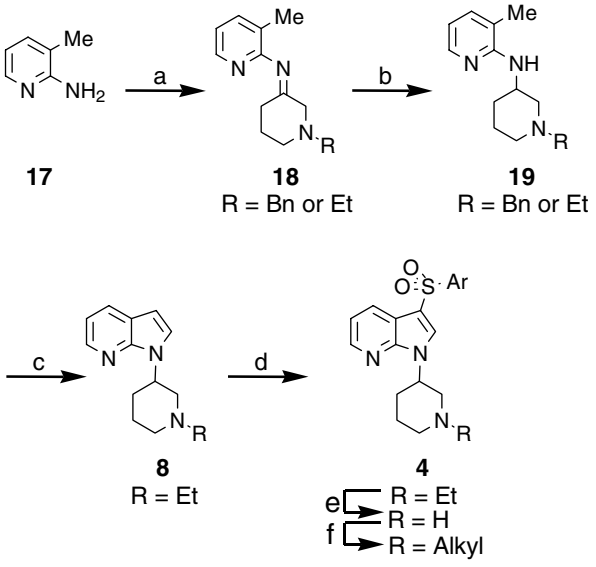


Figure 2. Alkylation of 7-azaindole with 3-piperidinyl halides or tosylates.



Scheme 2. Synthesis of compounds **4**. Reagents and conditions: (a) 1-benzyl-3-piperidinone, TsOH, benzene, reflux, 16 h; (b) MeOH, $NaBH_4$; (c) *n*-BuLi, DMF, THF, −78 °C; (d) $ArSO_2Cl$, AgOTf, $PhNO_2$, heat; (e) i—ACE–Cl, DCE, reflux; ii—EtOH, reflux; (f) aldehydes or ketones, $NaBH(OAc)_3$, THF.

Table 2. Biological data for compound **3** hydrochlorides[18,19]

Compound	Ar	R	5-HT$_6$ K_i[a] (nM)	5-HT$_6$ cAMP assay[a]			
				Agonist		Antagonist	
				EC_{50} (nM)	E_{max} (%)	IC_{50} (nM)	I_{max} (%)
3a	2-FPh	H	2.0 ± 0.1	—	—	50	100
3b	3-FPh	H	2.7 ± 0.1	278	44	—	—
3c	4-FPh	H	8.5 ± 0.5	1645	50	—	—
3d	3-ClPh	H	1.5 ± 0.1	1680	47	—	—
3e	4-ClPh	H	5.5 ± 0.4	—	—	340	94
3f	3-BrPh	H	1.3 ± 0.1	35	49	—	—
3g	4-BrPh	H	4.3 ± 0.3	—	—	135	96
3h	3-CF_3Ph	H	1.3 ± 0.1	520	41	—	—
3i	Ph	Me	2.5 ± 0.6	2035	61	—	—
3j	2-FPh	Me	5.6 ± 1	—	—	186	69
3k	3-FPh	Me	1.4 ± 0.3	231	54	—	—
3l	4-FPh	Me	5.0 ± 0.1	—	—	213	85
3m	2-ClPh	Me	2.2 ± 0.6	—	—	91	91
3n	3-ClPh	Me	1.5 ± 0.5	—	—	142	85
3o	4-ClPh	Me	4.2 ± 0.3	—	—	95	98
3p	3-BrPh	Me	0.9 ± 0.1	—	—	23	98
3q	Ph	Et	11 ± 1	—	—	56	75
3r	3-FPh	Et	8.3 ± 1.3	—	—	132	89
3s	3-ClPh	Et	3.3 ± 1	—	—	120	93
3t	5-Cl-thien-2-yl	H	1.0 ± 0.1	—	—	11	94
3u	8-Quinolyl	H	5.7 ± 0.5	—	—	643	100
3v	6-Cl-imidazo[2,1-*b*]thiazol-5-yl	H	1.0 ± 0.1	80	32	—	—
3w	6-Cl-imidazo[2,1-*b*]thiazol-5-yl	Me	0.8 ± 0.2	—	—	26	69
3x	6-Cl-imidazo[2,1-*b*]thiazol-5-yl	Et	1.4 ± 0.1	—	—	10	93

Displacement of [^{3}H]-LSD binding to cloned h5-HT$_6$ receptors stably expressed in HeLa cells.
[a] K_i, EC_{50}, IC_{50}, E_{max}, and I_{max} values were determined in triplicate.

Alkylation of 7-azaindole with 3-chloro-pyrrolidine or 3-tosyl-pyrrolidine furnished pyrrolidinyl-7-azaindoles (**7**) that were subsequently elaborated to targets **3**. On the other hand, alkylation of 7-azaindole with 1-benzyl-3-chloro-piperidine proceeded through an aziridinium intermediate to furnish a ring-contracted pyrrolidinylmethyl product **9**. An alternate facile synthetic route to the piperidinyl analogs **4** was designed and successfully utilized in the preparation of the compounds in this novel series.

All analogs were shown to have high binding affinity to the 5-HT$_6$ receptor. All the analogs in series **3** and **4**, with the exception of five compounds (90% of the compounds), exhibited high 5-HT$_6$ receptor binding affinity with K_i values <10 nM. Among compounds of the earlier series **2**, 17 out of 24 compounds (70%) were high potency ligands with K_i values <10 nM. Most compounds in series **4** functioned as partial agonists, while the majority of compounds in series **3** were identified as antagonists. In both series, *meta*-substitution on the phenylsulfonyl generally corresponded with partial agonism while *para*-substitution favored antagonism. Alkylation of the basic nitrogen shifted the functional activity to antagonism only in series **3**.

5. Experimental

5.1. General methods

Melting points were determined on a Thomas–Hoover capillary or an Electrothermal melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Varian Unity Plus 400 spectrometer. The chemical shifts (δ) are reported in parts per million (ppm) downfield from zero relative to the residual DMSO signal (2.49 ppm), chloroform (7.26 ppm), or TMS (0 ppm). Coupling constants are reported in Hertz (Hz). Solvate, hydrate, and HCl protons are not included. Mass spectra were recorded on either a Hewlett–Packard 5995A, a Finnigan Trace MS or a Micromass LCT spectrometer. C,H,N combustion analyses were determined on either a Perkin-Elmer 2400 analyzer or were performed by Robertson Microlit (Madison, NJ). All analyzed compounds are within ±0.4% of the theoretical value unless otherwise indicated. Unless otherwise noted, reagents were obtained from commercial sources and were used without further purification. Solvents for extraction and chromatography (dichloromethane, ethyl acetate) were HPLC-grade OmniSolv. Reagents purchased from EM Science. Chromatographic purifications were performed by flash chromatography using Baker 40-μm silica gel. Analytical high pressure liquid chromatography (HPLC) was performed on a Prodigy ODS 3 150, 4.6 mm id column using a 0.2% trifluoroacetic acid/water/acetonitrile gradient with a flow rate of 1 mL/min and UV detection at 215 nm. Chiral HPLC was performed on a Chiracel AD, 0.46 × 25 cm column.

5.2. General method for preparation of compounds 3 from compounds 7

A suspension of **7** (R = benzyl, methyl or ethyl) (4.0 mmol), arylsulfonylchloride (4 mmol) and silver trifluoromethanesulfonate (9.3 mmol) in nitrobenzene

Table 3. Biological data for compound **4** hydrochlorides[18,19]

Compound	Ar	R	5-HT$_6$ K_i [a] (nM)	5-HT$_6$ cAMP assay[a]			
				Agonist		Antagonist	
				EC_{50} (nM)	E_{max} (%)	IC_{50} (nM)	I_{max} (%)
4a	Ph	H	4.9 ± 0.5	47	56		
4b	Ph	Et	3.6 ± 0.2			26	58
4c	2-ClPh	H	3.7 ± 0.3	50	84		
4d	3-ClPh	H	1.3 ± 0.1	30	49		
4e	4-ClPh	H	7.6 ± 0.1			682	76
4f	4-ClPh	Me	11.5 ± 0.5			28	63
4g	4-ClPh	Et	33.5 ± 0.5			70	71
4h	4-ClPh	*i*-Pr	11.1 ± 0.2			338	74
4i	3-CF_3Ph	H	4.6 ± 0.4	273	65		
4j	4-CF_3Ph	H	12 ± 0.1	414	72		
4k	3-CF_3Ph	Me	2.1 ± 0.2	49	66		
4l	3-BrPh	H	3.8 ± 0.2	72	49		
4m	2-FPh	H	2.0 ± 0.1			50	100
4n	3-FPh	H	2.4 ± 0.1	67	84		
4o	3-FPh	Me	4.7 ± 0.5	306	75		
4p	3-FPh	Et	4.4 ± 0.1	60	63		
4q	3-FPh	*i*-Pr	3.4 ± 0.2	172	67		
4r	3-BrPh	*i*-Pr	9.4 ± 0.2			492	77
4s	3,5-diClPh	H	6.1 ± 0.2	297	62		
4t	3,5-diClPh	Me	3.9 ± 0.4	38.7	56		
4u	3,5-diClPh	Et	13.5 ± 0.5	67	50		
4v	5-Cl-thien-2-yl	H	1.2 ± 0.1	98	49		
4w	5-Cl-thien-2-yl	Me	1.9 ± 0.4	71	62		
4x	5-Cl-thien-2-yl	Et	3.2 ± 0.2	50	46		
4y	6-Cl-imidazo[2,1-*b*]thiazol-5-yl	H	0.7 ± 0.2	66	47		
4z	6-Cl-imidazo[2,1-*b*]thiazol-5-yl	Me	2.0 ± 0.4	25	68		
4aa	6-Cl-imidazo[2,1-*b*]thiazol-5-yl	Et	0.7 ± 0.1	34	44		
4ab	6-Cl-imidazo[2,1-*b*]thiazol-5-yl	*i*-Pr	1.7 ± 0.1			8	65

Displacement of [^{3}H]-LSD binding to cloned h5-HT$_6$ receptors stably expressed in HeLa cells.
[a] K_i, EC_{50}, IC_{50}, E_{max}, and I_{max} values were determined in triplicate.

(2.1 mL) was stirred at 140 °C under nitrogen for 17.5 h. The mixture was subjected to aqueous work-up and purified by flash chromatography or HPLC to afford compounds **3**. α-Chloroethylchloroformate (0.2 mL, 2 mmol) was added to a solution of **3** (R = benzyl) (0.644 mmol) in 1,2-dichloroethane (6 mL). The reaction mixture was refluxed under nitrogen for 4.5 h, concentrated, and diluted with ethanol (5 mL). The mixture was refluxed for 1.5 h followed by aqueous work-up and purification by flash chromatography to give **3** (R = H).

5.3. General method for preparation of compounds 4 from compound 8

A mixture of **8** (R = Et, 1.74 mmol), arylsulfonylchloride (1.92 mmol), and silver trifluoromethanesulfonate (3.5 mmol), in nitrobenzene (0.8 mL) was heated at 130 °C for 20 h in a pressure vessel. After cooling, the mixture was purified by column chromatography to afford compounds **4** (R = Et). α-Chloroethylchloroformate (2.2 mmol) was added to a solution of **4** (R = Et, 0.43 mmol) and proton-sponge (0.22 mmol) in 1,2-dichloroethane (7 mL). The mixture was heated at 100 °C for 8 h. The solvent was evaporated, and 10% water in dioxane (7 mL) was added and the mixture was again heated at 100 °C for 5 h. Purification by flash column chromatography furnished compounds **4** (R = H) (50–79% yield). An aldehyde or a ketone (0.35 mmol) was added to 0.1 mmol of **4** (R = H) and sodium triacetoxyborohydride (0.4 mmol) in acetonitrile (2.1 mL). The reaction mixture was stirred at room temperature for 3 h. followed by aqueous work-up, organic phase extraction, and treatment with ethereal HCl. Compounds **4** (R = alkyl) were obtained as hydrochloride salts.

5.3.1. 3-(2-Fluoro-benzenesulfonyl)-1-pyrrolidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine (3a)

5.3.1.1. Step 1. 1-(1-Benzyl-pyrrolidin-3-yl)-3-(2-fluoro-benzenesulfonyl)-1*H*-pyrrolo[2,3-*b*]pyridine was prepared from 1-(1-benzyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (1.7 g, 6.1 mmol), 2-fluorobenzenesulfonyl chloride (0.79 mL, 6.0 mmol) and silver trifluoromethanesulfonate (2.9 g, 11 mmol) in nitrobenzene as described in Step 1 for compound **3t** to give a yellow gum (0.233 g. 9.0%); mass spectrum (+EI, $[M+H]^+$) *m*/*z* 436. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.50 (s, 1H), 8.37 (dd, 1H, J = 4.64 Hz and 1.48 Hz), 8.06-8.10 (m, 2H), 7.65–7.71 (m, 1H), 7.40–7.44 (m, 1H), 7.26–7.36 (m, 6H), 7.18–7.23 (m, 1H), 5.43–5.48 (m, 1H), 3.72 (d, 1H, J = 13.05 Hz), 3.61 (d, 1H, J = 13.06 Hz), 3.04–3.10 (m, 1H), 2.78–2.81 (m, 1H), 2.66–2.70 (m, 1H), 2.36–2.43 (m, 1H), 1.96–2.04 ppm (m, 1H).

5.3.1.2. Step 2. α-Chloroethylchloroformate (0.13 mL, 1.2 mmol) was added to a solution of 1-(1-benzyl-pyrrolidin-3-yl)-3-(2-fluoro-benzenesulfonyl)-1*H*-pyrrolo[2,3-*b*]pyridine (0.206 g, 0.473 mmol) in 1,2-dichloroethane (7 mL). The reaction mixture was refluxed under nitrogen for 40 min. A second portion of α-chloroethylchloroformate (1.3 mL, 1.2 mmol) was added, and the mixture was refluxed for 2 h. After concentrating, adding methylene chloride and concentrating, ethanol (7 mL) was added. The reaction mixture was refluxed under nitrogen for 1.5 h. The mixture was concentrated. The residue was partitioned in chloroform and aqueous sodium bicarbonate. The organic phase was purified by flash chromatography using 5–10% methanol in methylene chloride and 0.1% ammonium hydroxide/10% methanol in methylene chloride. Concentrating and drying in vacuo at ambient temperature for 1.5 h yielded 3-(2-fluoro-benzenesulfonyl)-1-pyrrolidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine as a light yellow semi-solid (46.7 mg, 28.7%). Ethanol and ethereal hydrogen chloride were added. Concentrating and drying in vacuo at 78 °C for 11 h gave the hydrochloride as a cream solid (48.9 mg, 24.7%); mass spectrum (+EI, $[M+H]^+$) *m/z* 346. ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.32–9.43 (br, 1H), 9.15–9.25 (br, 1H), 8.69 (s, 1H), 8.40–8.41 (m, 1H), 8.05–8.16 (m, 2H), 7.62–7.73 (m, 1H), 7.38–7.42 (m, 1H), 7.30–7.36 (m, 2H), 5.55–5.64 (m, 1H), 3.60–3.75 (m, 2H), 3.50–3.58 (m, 1H), 3.27–3.36 (m, 1H), 2.48–2.55 (m, 1H), 2.30–2.40 ppm (m, 1H). HRMS ($C_{17}H_{16}FN_3O_2S$), calcd $[M+H]^+$ 346.1025, found $[M+H]^+$ 346.1032.

5.3.2. 3-(3-Fluoro-benzenesulfonyl)-1-pyrrolidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine (3b)

5.3.2.1. Step 1. 1-(1-Benzyl-pyrrolidin-3-yl)-3-(3-fluoro-benzenesulfonyl)-1*H*-pyrrolo[2,3-*b*]pyridine was prepared from 1-(1-benzyl-pyrrolidin-3-yl)-1*H*-pyrrolo-[2,3-*b*]pyridine (1.7 g, 6.1 mmol), 3-fluorobenzenesulfonyl chloride (0.80 mL, 6.0 mmol) and silver trifluoromethanesulfonate (2.7 g, 11 mmol) in nitrobenzene as described in Step 1 for compound **3t** to give a yellow semi-solid (0.100 g. 3.86%)

5.3.2.2. Step 2. α-Chloroethylchloroformate (0.1 mL, 0.9 mmol) was added to a solution of 1-(1-benzyl-pyrrolidin-3-yl)-3-(3-fluoro-benzenesulfonyl)-1*H*-pyrrolo[2,3-*b*]pyridine (99.6 mg, 0.229 mmol) in 1,2-dichloroethane (5 mL). The reaction mixture was refluxed under nitrogen for 3.5 h. After concentrating, adding methylene chloride, and concentrating ethanol (5 mL) was added. The reaction mixture was refluxed under nitrogen for 1.5 h. The mixture was concentrated, and the residue was partitioned in chloroform and aqueous sodium bicarbonate. The organic phase was washed with brine, dried with anhydrous magnesium sulfate, filtered, and concentrated. The residue was purified by flash chromatography using 10% methanol in 1,2-dichloroethane and 10% methanol in chloroform and 0.1% ammonium hydroxide/10% methanol in chloroform. Concentrating and drying in in vacuo at 68 °C for 25 min yielded 3-(3-fluoro-benzenesulfonyl)-1-pyrrolidin-3-yl-1*H*-pyrrolo [2,3-*b*]pyridine as an orange foam (21.9 mg, 27.8%). Ethanol and ethereal hydrogen chloride were added. Concentrating and drying in vacuo at 78 °C for 11 h gave the hydrochloride as a light brown solid (20.3 mg, 21.2%); mass spectrum (+EI, $[M+H]^+$) *m/z* 346. ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.19–9.33 (m, br, 2H), 8.66 (s, 1H), 8.41(dd, 1H, *J* = 4.76 Hz and 1.59 Hz), 8.24 (dd, 1H, *J* = 7.93 Hz and 1.58 Hz), 7.79–7.86 (m, 2H), 7.59–7.65 (m, 1H), 7.45–7.50 (m, 1H), 7.33–7.36 (m, 1H), 5.51–5.58 (m, 1H), 3.62-3.72 (m, 2H), 3.49–3.57 (m, 1H), 2.33–2.56 ppm (m, 3H). HRMS ($C_{17}H_{16}FN_3O_2S$), calcd $[M+H]^+$ 346.1025, found $[M+H]^+$ 346.1013.

5.3.3. 3-(4-Fluoro-benzenesulfonyl)-1-pyrrolidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine (3c)

5.3.3.1. Step 1. 1-(1-Benzyl-pyrrolidin-3-yl)-3-(4-fluoro-benzenesulfonyl)-1*H*-pyrrolo[2,3-*b*]pyridine was prepared from 1-(1-benzyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (1.7 g, 6.1 mmol), silver trifluoromethanesulfonate (3.0 g, 12 mmol), and 4-fluorobenzenesulfonyl chloride (1.34 g, 6.89 mmol) in nitrobenzene as described in Step 1 for compound **3t**. Purification furnished a dark yellow gum (0.667 g, 24.7%); mass spectrum (+EI, $[M+H]^+$) *m/z* 436. ^{1}H NMR (500 *MHz*, DMSO-d_6): δ 8.47 (s, 1H), 8.35–8.37 (m, 1H), 8.15–8.17 (d and d, 1H, *J* = 1.34 Hz and 1.46 Hz), 8.03–8.07 (m, 2H), 7.32–7.41 (m, 2H), 7.26–7.31 (m, 5H), 7.20–7.23 (m, 1H), 5.39–5.43 (m, 1H), 3.66 (dd, 2H, *J* = 25.62 Hz and 13.05 Hz), 3.02–3.07 (m, 1H), 2.68–2.78 (m, 2H), 2.01–2.06 ppm (m, 1H).

5.3.3.2. Step 2. α-Chloroethylchloroformate (0.35 mL, 3.2 mmol) was added to a solution of 1-(1-benzyl-pyrrolidin-3-yl)-3-(4-fluoro-benzenesulfonyl)-1*H*-pyrrolo[2,3-*b*]pyridine (0.557 g, 1.28 mmol) in 1,2-dichloroethane (10 mL). The reaction mixture was refluxed under nitrogen for 1 h. A second portion of α-chloroethylchloroformate (0.35 mL, 3.2 mmol) was added, and the mixture was refluxed for two more hours. The solvent was evaporated, and methylene chloride was added and evaporated. Ethanol (10 mL) was then added to the residue, and it was refluxed under nitrogen for 1 h. The reaction mixture was concentrated and partitioned in chloroform and saturated aqueous sodium bicarbonate. The organic phase was washed with water and brine. It was dried with anhydrous magnesium sulfate, filtered, and concentrated. The residue was purified by flash chromatography using 5–10% methanol in methylene chloride and 1.0% ammonium hydroxide/10% methanol in methylene chloride. After concentrating and drying, 3-(4-fluoro-benzenesulfonyl)-1-pyrrolidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine was obtained as a cream foam (0.187 g, 42.3%). It was dissolved in chloroform, and ethereal hydrogen chloride was added. The mixture was concentrated and dried in vacuo for 12 h at 85 °C to yield to hydrochloride as a cream solid (0.191 g, 35.7%): mp 189–190 °C (dec); mass spectrum (+EI, $[M+H]^+$) *m/z* 346. ^{1}H NMR (500 *MHz*, DMSO-d_6): δ 9.23–9.33 (s, br, 2H), 8.64 (s, 1H), 8.41 (dd, 1H, *J* = 4.76 Hz and 1.47 Hz), 8.19–8.21 (d and d, 1H, *J* = 1.59 Hz and 1.47 Hz), 8.02–8.08 (m, 2H), 7.32–7.42 (m, 3H), 5.51–5.58 (m, 1H), 3.60-3.72 (m, 2H), 3.50–3.56 (m, 1H), 3.29-3.35 (m, 1H), 2.48–2.54 (m, 1H), 2.34–2.41 ppm (m, 1H). Anal. ($C_{17}H_{16}FN_3O_2S$·HCl·0.1H_2O) C, H, N.

5.3.4. 3-(3-Chloro-benzenesulfonyl)-1-pyrrolidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine (3d)

5.3.4.1. Step 1. 1-(1-Benzyl-pyrrolidin-3-yl)-3-(3-chloro-benzenesulfonyl)-1*H*-pyrrolo[2,3-*b*]pyridine was prepared from 1-(1-benzyl-pyrrolidin-3-yl)-1*H*-pyrrolo-[2,3-*b*]pyridine (1.7 g, 6.1 mmol), 3-chloro-benzenesulfonyl chloride (0.84 mL, 6.0 mmol), and silver trifluoromethanesulfonate (2.8 g, 11 mmol) in nitrobenzene as described in Step 1 for compound **3t** to give 1-(1-benzyl-pyrrolidin-3-yl)-3-(3-chloro-benzenesulfonyl)-1*H*-pyrrolo[2,3-*b*]pyridine as a light yellow semi-solid (76.1 mg. 2.82%). To a solution of this material (75.2 mg, 0.166 mmol) in 1,2-dichloroethane (5 mL) was added α-chloroethylchloroformate (0.1 mL, 0.9 mmol). The reaction mixture was refluxed under nitrogen for 2 h. After concentrating, adding methylene chloride, and concentrating, ethanol (5 mL) was added. The reaction mixture was refluxed under nitrogen for 1 h. The mixture was concentrated. Water was added to the residue, and it was basified with solid sodium bicarbonate. It was extracted with chloroform and concentrated. The residue was purified by flash chromatography using 10% methanol in chloroform and 0.1% ammonium hydroxide/10% methanol in chloroform. Concentrating and drying in vacuo at 58 °C for 20 min yielded 3-(3-chloro-benzenesulfonyl)-1-pyrrolidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine as a cream semi-solid (38.2 mg, 63.5%). It was dissolved in ethanol, and ethereal hydrogen chloride was added. Concentrating and drying in vacuo at 78 °C for 12 h gave the hydrochloride as an off-white solid (38.8 mg, 53.7%); mass spectrum (+EI, $[M+H]^+$) *m*/*z* 362. ^{1}H NMR (500 *MHz*, DMSO-d_6): δ 9.17–9.38 (br, 2H), 8.67 (s, 1H), 8.40–8.42 (m, 1H), 8.24 (dd, 1H, *J* = 8.05 Hz and 1.58 Hz), 7.96–7.99 (m, 2H), 7.67–7.70 (m, 1H), 7.59 (t, 1H, *J* = 7.93 Hz), 7.34–7.37 (m, 1H), 5.51–5.58 (m, 1H), 3.62–3.72 (m, 2H), 3.51–3.56 (m, 1H), 2.34–2.56 ppm (m, 3H). Anal. ($C_{17}H_{16}ClN_3O_2S$·1.0 HCl·1.2H_2O) C, H, N.

5.3.5. 3-(4-Chloro-benzenesulfonyl)-1-pyrrolidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine (3e)

5.3.5.1. Step 1. 1-(1-Benzyl-pyrrolidin-3-yl)-3-(4-chloro-benzenesulfonyl)-1*H*-pyrrolo[2,3-*b*]pyridine was prepared from 1-(1-benzyl-pyrrolidin-3-yl)-1*H*-pyrrolo-[2,3-*b*]pyridine (1.16 g, 4.18 mmol), 4-chloro-benzenesulfonyl chloride (0.891 g, 4.22 mmol), and silver trifluoromethanesulfonate (2.14 g, 8.33 mmol) as described in Step 1 for compound **3t** to give a yellow gum (0.130 g. 6.88%); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.51 (s, 1H), 8.39 (dd, 1H, *J* = 4.64 Hz and 1.39 Hz), 8.17–8.19 (d and d, 1H, *J* = 1.39 Hz and 1.50 Hz), 7.99–8.02 (m, 2H), 7.63–7.65 (m, 2H), 7.22–7.33 (m, 6H), 5.41–5.45 (m, 1H), 3.62–3.72 (m, 2H), 3.04–3.08 (m, 1H), 2.69–2.80 (m, 2H), 2.39–2.45 (m, 2H), 2.03–2.10 ppm (m, 1H).

5.3.5.2. Step 2. α-Chloroethylchloroformate (0.12 mL, 1.1 mmol) was added to a solution of 1-(1-benzyl-pyrrolidin-3-yl)-3-(4-chloro-benzenesulfonyl)-1*H*-pyrrolo-[2,3-*b*]pyridine (0.205 g, 0.454 mmol) in 1,2-dichloroethane (8 mL). The reaction mixture was refluxed under nitrogen for 2 h. A second portion of α-chloroethylchloroformate (0.12 mL, 1.1 mmol) was added, and the mixture was refluxed for one more hour. After concentrating, adding methylene chloride, and concentrating, ethanol (7 mL) was added. The reaction mixture was refluxed under nitrogen for 2.5 h and concentrated. The residue was partitioned in chloroform and aqueous sodium bicarbonate. The organic phase was purified by flash chromatography using 5–10% methanol in methylene chloride and 0.1% ammonium hydroxide/10% methanol in methylene chloride and 5–7.5% methanol in 1,2-dichloroethane. Concentrating and drying in vacuo at 78 °C for 4 h yielded 3-(4-chloro-benzenesulfonyl)-1-pyrrolidin-3-yl-1*H*-pyrrolo[2, 3-*b*]pyridine as a light orange foam (58.9 mg, 35.9%). It was dissolved in chloroform, and ethereal hydrogen chloride was added. Concentrating and drying in vacuo at 85 °C for 12 h gave the hydrochloride as a light buff solid (55.7 mg, 28.3%): mp 188–190 °C (dec); mass spectrum (+EI, $[M+H]^+$) *m*/*z* 362. ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.12–9.30 (br, 2H), 8.64 (s, 1H), 8.41 (dd, 1H, *J* = 4.76 Hz and 1.46 Hz), 8.19–8.21 (m, 1H), 7.97–8.00 (m, 2H), 7.60–7.64 (m, 2H), 7.33–7.36 (m, 1H), 5.51–5.58 (m, 1H), 3.61–3.71 (m, 2H), 3.50–3.57 (m, 1H), 2.28–2.54 ppm (m*, 3H). Anal. ($C_{17}H_{16}ClN_3O_2S$·2.0HCl) C, H, N.

5.3.6. 3-(3-Bromo-benzenesulfonyl)-1-pyrrolidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine (3f)

5.3.6.1. Step 1. 1-(1-Benzyl-pyrrolidin-3-yl)-3-(3-bromo-benzenesulfonyl)-1*H*-pyrrolo[2,3-*b*]pyridine was prepared from 1-(1-benzyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (1.7 g, 6.1 mmol), 3-bromobenzenesulfonyl chloride (0.86 mL, 6.0 mmol), and silver trifluoromethanesulfonate (2.9 g, 11 mmol) in nitrobenzene as described in Step 1 for compound **3t**. Purification using flash chromatography using 100% methylene chloride and 100% ethyl acetate and by HPLC using a gradient of (methylene chloride and methanol) in hexane/TEA yielded 1-(1-benzyl-pyrrolidin-3-yl)-3-(3-bromo-benzenesulfonyl)-1*H*-pyrrolo[2,3-*b*]pyridine (0.110 g. 3.7%) as a yellow semi-solid. To this material (0.109 g, 0.220 mmol) in 1,2-dichloroethane (5 mL) was added α-chloroethylchloroformate (0.12 mL, 1.1 mmol). The reaction mixture was refluxed under nitrogen for 50 min. A second portion of α-chloroethyl-chloroformate (0.1 mL, 0.9 mmol) was added, and this mixture was refluxed for 30 min. After concentrating, adding methylene chloride, and evaporating, ethanol (5 mL) was added. The reaction mixture was refluxed under nitrogen for 55 min. The mixture was concentrated. The residue was purified by flash chromatography using 0.1% ammonium hydroxide/10% methanol in methylene chloride and 10% methanol in methylene chloride. Concentrating and drying in vacuo at ambient temperature for 70 min yielded 3-(3-bromo-benzenesulfonyl)-1-pyrrolidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine as a beige gum (67.5 mg, 75.5%). It was dissolved in chloroform, and ethereal hydrogen chloride was added. Concentrating and drying in vacuo at 85 °C for 12 h gave the hydrochloride as a beige solid (69.2 mg, 65.9%): mp 173–175 °C (dec); mass spectrum (+EI, $[M+H]^+$) *m*/*z* 406. ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.24–9.35 (br, m, 2H), 8.68 (s, 1H), 8.42 (dd, 1H, *J* = 4.76 Hz and 1.46 Hz), 8.24 (dd, 1H, *J* = 8.05 Hz

and 1.46 Hz), 8.10 (t, 1H, J = 1.83 Hz), 8.00–8.02 (m, 1H), 7.80–7.83 (m, 1H), 7.50–7.54 (m, 1H), 7.36 (dd, 1H, J = 8.05 Hz and 4.76 Hz), 5.50–5.57 (m, 1H), 3.64–3.72 (m, 2H), 3.50–3.56 (m, 1H), 2.47–2.56 (m, 1H), 2.34–2.43 ppm (m, 2H). Anal. ($C_{17}H_{16}BrN_3O_2S$·1.5 HCl) C, H, N.

5.3.7. 3-(4-Bromo-benzenesulfonyl)-1-pyrrolidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine (3g)

5.3.7.1. Step 1. 1-(1-Benzyl-pyrrolidin-3-yl)-3-(4-bromo-benzenesulfonyl)-1*H*-pyrrolo[2,3-*b*]pyridine was prepared from 1-(1-benzyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (1.7 g, 6.1 mmol), 4-bromobenzenesulfonyl chloride (1.5 g, 5.9 mmol), and silver trifluoromethanesulfonate (2.9 g, 11 mmol) in nitrobenzene as described in Step 1 for compound **3t**. The compound was obtained as a yellow semi-solid (0.172 g. 5.9%); mass spectrum (+EI, $[M+H]^+$) m/z 496. ^{1}H NMR (500 *MHz*, DMSO-d_6): δ 8.48 (s, 1H), 8.36–8.37 (m, 1H), 8.15 (dd, 1H, J = 8.06 Hz and 1.59 Hz), 7.89–7.92 (m, 2H), 7.74–7.77 (m, 2H), 7.26–7.30 (m, 5H), 7.19–7.23 (m, 1H), 5.40–5.43 (m, 1H), 3.66 (dd, 2H, J = 25.01 Hz and 13.06 Hz), 3.02–3.06 (m, 1H), 2.68–2.78 (m, 2H), 2.01–2.06 ppm (m, 1H).

5.3.7.2. Step 2. α-Chloroethylchloroformate (0.17 mL, 1.6 mmol) was added to a solution of 1-(1-benzyl-pyrrolidin-3-yl)-3-(4-bromo-benzenesulfonyl)-1*H*-pyrrolo[2,3-*b*]pyridine (0.155 g, 0.312 mmol) in 1,2-dichloroethane (6 mL). The reaction mixture was refluxed under nitrogen for 45 min. A second portion of α-chloroethylchloroformate (0.1 mL, 0.9 mmol) and a few mL of ethanol were added, and the mixture was refluxed for 45 min. After concentrating, adding methylene chloride, and concentrating, the residue was partitioned in chloroform and aqueous sodium bicarbonate. The organic phase was mostly concentrated and purified by flash chromatography using 10% methanol in methylene chloride. Concentrating and drying in vacuo at 55 °C for 30 min yielded 3-(4-bromo-benzenesulfonyl)-1-pyrrolidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine as a buff semi-solid (53.0 mg, 41.7%). It was dissolved in chloroform, and ethereal hydrogen chloride was added. Concentrating and drying in vacuo at 85 °C for 12 h gave the hydrochloride as a buff semi-solid (54.8 mg, 36.5%); mass spectrum (+EI, $[M+H]^+$) m/z 406. ^{1}H NMR (500 *MHz*, DMSO-d_6): δ 9.20–9.32 (br, m, 2H), 8.64 (s, 1H), 8.41 (dd, 1H, J = 4.76 and 1.46 Hz), 8.18–8.21 (d and d, 1H, J = 1.59 Hz and 1.47 Hz), 7.89–7.92 (m, 2H), 7.75–7.78 (m, 2H), 7.33–7.36 (m, 1H), 5.51–5.58 (m, 1H), 3.60–3.71 (m, 2H), 3.50–3.56 (m, 1H), 3.29–3.35 (m, 1H), 2.28–2.56 ppm (m, 2H). Anal. ($C_{17}H_{16}BrN_3O_2S$·1.4 HCl) C, H, N.

5.3.8. 1-Pyrrolidin-3-yl-3-(3-trifluoromethyl-benzenesulfonyl)-1*H*-pyrrolo[2,3-*b*]pyridine (3h)

5.3.8.1. Step 1. 1-(1-Benzyl-pyrrolidin-3-yl)-3-(3-trifluoromethyl-benzenesulfonyl)-1*H*-pyrrolo[2,3-*b*]pyridine was prepared from 1-(1-benzyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (1.7 g, 6.1 mmol), 3-trifluoromethylbenzenesulfonyl chloride (0.96 mL, 6.0 mmol), and silver trifluoromethanesulfonate (2.7 g, 11 mmol) in nitrobenzene as described in Step 1 for compound **3t** to give 1-(1-benzyl-pyrrolidin-3-yl)-3-(3-trifluoromethyl-benzenesulfonyl)-1*H*-pyrrolo[2,3-*b*]pyridine as a yellow gum (53.3 mg, 1.84%) which was dissolved in 1,2-dichloroethane (5 mL) and to the resulting solution was added α-chloroethylchloroformate (0.1 mL, 0.9 mmol). The reaction mixture was refluxed under nitrogen for 2 h. After concentrating, adding methylene chloride, and concentrating ethanol (5 mL) was added. The reaction mixture was refluxed under nitrogen for 2 h. The mixture was concentrated and partitioned in chloroform and aqueous sodium bicarbonate. The organic phase was purified by flash chromatography using 7.5–10% methanol in methylene chloride. Concentrating and drying in vacuo at ambient temperature for 70 min yielded 1-pyrrolidin-3-yl-3-(3-trifluoromethyl-benzenesulfonyl)-1*H*-pyrrolo[2,3-*b*]pyridine as a light beige semi-solid (28.4 mg, 65.4%). Ethanol and ethereal hydrogen chloride were added. Concentrating and drying in vacuo at 78 °C for 11 h gave the hydrochloride as a white solid (29.3 mg, 56.9%); mass spectrum (+EI, $[M+H]^+$) m/z 396. ^{1}H NMR (500 *MHz*, DMSO-d_6): δ 9.18–9.32 (br, 2H), 8.73 (s, 1H), 8.41–8.42 (m, 1H), 8.24–8.33 (m, 3H), 8.01 (d, 1H, J = 7.93 Hz), 7.80–7.83 (m, 1H), 7.35–7.38 (m, 1H), 5.50–5.57 (m, 1H), 3.62–3.72 (m, 2H), 3.49–3.56 (m, 1H), 2.48–2.56 (m, 1H), 2.34–2.43 ppm (m, 1H). Anal. ($C_{18}H_{16}F_3N_3O_2S$·1.5HCl·0.5H_2O) C, H, N.

5.3.9. 3-Benzenesulfonyl-1-(1-methyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (3i). A thick suspension of 1-(1-methyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (0.930 g, 4.62 mmol), benzenesulfonyl chloride (0.71 mL, 5.5 mmol), and silver trifluoromethanesulfonate (2.33 g, 9.07 mmol) in nitrobenzene (4.6 mL) was vigorously stirred at 125 °C for 9.5 h. After cooling to ambient temperature, saturated aqueous potassium carbonate and ethyl acetate were added to the reaction mixture, and it was stirred for several min. The layers were separated, and the aqueous layer was further extracted with ethyl acetate. The organic phase was washed with brine, dried with anhydrous magnesium sulfate, filtered, and concentrated. The residue was purified by flash chromatography using 100% ethyl acetate and by HPLC using (8:2 methylene chloride/methanol/0.1% TEA) in hexane/0.1% TEA. Concentrating and drying in vacuo at 80 °C for 20 min yielded 3-benzenesulfonyl-1-(1-methyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine as a pale yellow gum (0.622 g, 39.4%). A small amount (about 100 mg) was dissolved in ethyl acetate, and ethereal hydrogen chloride was added. Concentrating and drying in vacuo at 78 °C for 11 h yielded the hydrochloride as a cream foam (121 mg); mass spectrum (+EI, $[M+H]^+$) m/z 342. ^{1}H NMR (500 MHz, DMSO-d_6): δ 10.57–10.93 (m, 1H), 8.69–8.71 (m, 1H), 8.40–8.41 (m, 1H), 8.20 (d, 1H, J = 8.05 Hz), 7.97–7.99 (m, 2H), 7.53–7.62 (m, 3H), 7.32–7.36 (m, 1H), 5.55–5.75 (m, 1H), 3.81–4.04 (m, 2H), 3.46–3.68 (m, 2H), 2.87–2.90 (m, 3H), 2.28–2.75 ppm (m, 2H). Anal. ($C_{18}H_{19}N_3O_2S$·1.0 HCl·1.4H_2O) C, H, N.

5.3.10. 3-(2-Fluoro-benzenesulfonyl)-1-(1-methyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (3j). A thick suspension of 1-(1-methyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (1.24 g, 6.16 mmol), 2-fluorobenzenesulfonyl chloride (0.99 mL, 7.5 mmol), and silver trifluoromethanesulfonate (3.19 g, 12.4 mmol) in nitrobenzene

(6.2 mL) was vigorously stirred at 125 °C for 9.5 h. After cooling to ambient temperature, saturated aqueous potassium carbonate and ethyl acetate were added to the reaction mixture, and it was stirred for several min. The layers were separated, and the aqueous layer was further extracted with ethyl acetate. The organic phase was washed with brine, dried with anhydrous magnesium sulfate, filtered, and concentrated. The residue was purified by flash chromatography using 100% ethyl acetate and by HPLC using a gradient of (methylene chloride/methanol) in hexane with 0.1% TEA. Concentrating and drying in vacuo at 80 °C for 20 min yielded 3-(2-fluoro-benzenesulfonyl)-1-(1-methyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine as a pale yellow gum (0.483 g, 21.9%). It was dissolved in ethyl acetate, and ethereal hydrogen chloride was added. The precipitate was filtered and dried in vacuo at 78 °C for 14 h to yield the hydrochloride as an off-white solid (0.335 g, 12.6%): mp 177–180 °C (dec); mass spectrum (+EI, $[M+H]^+$) *m/z* 360. ^{1}H NMR (500 *MHz*, DMSO-d_6): δ 10.35–10.85 (m, 1H), 8.73 (s, br, 1H), 8.42 (dd, 1H, J = 4.76 Hz and 1.59 Hz), 8.05–8.15 (m, 2H), 7.65–7.71 (m, 1H), 7.31–7.44 (m, 3H), 5.58–5.78 (m, 1H), 3.48–4.02 (m, 3H), 2.90 (s, br, 3H), 2.27–2.75 ppm (m, 1H). Anal. ($C_{18}H_{18}FN_3O_2S$·1.0 HCl·1.2H_2O) C, H, N.

5.3.11. 3-(3-Fluoro-benzenesulfonyl)-1-(1-methyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (3k). A thick suspension of 1-(1-methyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (1.01 g, 5.02 mmol), 3-fluorobenzenesulfonyl chloride hydrochloride (0.80 mL, 6.0 mmol), and silver trifluoromethanesulfonate (2.60 g, 10.1 mmol) in nitrobenzene (5.0 mL) was vigorously stirred at 125 °C for 14.5 h. After cooling to ambient temperature, saturated aqueous potassium carbonate and ethyl acetate were added to the reaction mixture, and it was stirred for several min. The layers were separated, and the aqueous layer was further extracted with ethyl acetate. The organic phase was washed with brine, dried with anhydrous magnesium sulfate, filtered, and concentrated. The residue was purified by flash chromatography using 100% ethyl acetate and by HPLC using (8:2, methylene chloride/methanol/0.1% TEA) in hexane/0.1% TEA. Concentrating and drying in vacuo at 80 °C for 20 min yielded 3-(3-fluoro-benzenesulfonyl)-1-(1-methyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine as a pale yellow gum (0.337 g, 18.7%). It was dissolved in ethyl acetate, and ethereal hydrogen chloride was added. The precipitate was filtered, rinsed with ether, and dried in vacuo at 78 °C for 14 h to yield the hydrochloride as a white solid (0.241 g, 11.1%): mp 135 °C (dec); mass spectrum (+EI, $[M+H]^+$) *m/z* 360. ^{1}H NMR (500 *MHz*, DMSO-d_6): δ 10.52–10.82 (m, 1H), 8.73 (s, 1H), 8.42 (dd, 1H, J = 4.76 Hz and 1.47 Hz), 8.23–8.25 (d and d, 1H, J = 1.46 Hz and 1.58 Hz), 7.78–7.85 (m, 2H), 7.59–7.64 (m, 1H), 7.45–7.50 (m, 1H), 7.33–7.37 (m, 1H), 5.55–5.72 (m, 1H), 3.49–4.02 (m, 3H), 2.89 (s, br, 3H), 2.28–2.75 ppm (m, 2H). Anal. ($C_{18}H_{18}FN_3O_2S$·1.0 HCl·1.1H_2O) C, H, N.

5.3.12. 3-(4-Fluoro-benzenesulfonyl)-1-(1-methyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (3l). A thick suspension of 1-(1-methyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (0.837 g, 4.16 mmol), 4-fluorobenzenesulfonyl chloride (0.905 g, 4.65 mmol), and silver trifluoromethanesulfonate (2.29 g, 8.91 mmol) in nitrobenzene (4.2 mL) was vigorously stirred at 125 °C for 14.5 h. After cooling to ambient temperature, saturated aqueous potassium carbonate and chloroform were added to the reaction mixture, and it was stirred for several min. The layers were separated, and the aqueous layer was further extracted with chloroform. The organic phase was washed with brine, dried with anhydrous magnesium sulfate, filtered, and concentrated. The residue was purified by flash chromatography using 100% ethyl acetate. Concentrating and drying in vacuo at 80 °C for 20 min yielded 3-(4-fluoro-benzenesulfonyl)-1-(1-methyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine as a yellow gum (0.622 g, 41.5%). It was dissolved in ether, and ethereal hydrochloride was added. Filtering and drying in vacuo for 12 h at 72 °C gave the hydrochloride as a light yellow solid (0.615 g, 34.2%): mp 150 °C (dec); mass spectrum (+EI, $[M+H]^+$) *m/z* 360. ^{1}H NMR (500 MHz, DMSO-d_6): δ 10.68–10.99 (m, 1H), 8.70–8.73 (m, 1H), 8.40–8.42 (m, 1H), 8.20 (d, 1H, J = 7.81 Hz), 8.04–8.08 (m, 2H), 7.33–7.41 (m, 3H), 5.55–5.73 (m, 1H), 3.83–4.04 (m, 2H), 3.59–3.69 (m, 1H), 3.46–3.56 (m, 1H), 3.16–3.36 (m, 1H), 2.88–2.90 (m, 3H), 2.28–2.75 ppm (m, 2H). Anal. ($C_{18}H_{18}FN_3O_2S$·1.0 HCl·0.25H_2O) C, H, N.

5.3.13. 3-(2-Chloro-benzenesulfonyl)-1-(1-methyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (3m). A thick suspension of 1-(1-methyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (0.889 g, 4.41 mmol), 2-chlorobenzenesulfonyl chloride (0.72 mL, 5.3 mmol), and silver trifluoromethanesulfonate (2.32 g, 9.03 mmol) in nitrobenzene (4.4 mL) was vigorously stirred at 125 °C for 9.5 h. After cooling to ambient temperature, saturated aqueous potassium carbonate and ethyl acetate were added to the reaction mixture, and it was stirred for several min. The layers were separated, and the aqueous layer was further extracted with ethyl acetate. The organic phase was washed with brine, dried with anhydrous magnesium sulfate, filtered, and concentrated. The residue was purified by flash chromatography using 100% ethyl acetate and 10% methanol in ethyl acetate. Concentrating and drying in vacuo at 80 °C for 40 min yielded 3-(2-chloro-benzenesulfonyl)-1-(1-methyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine as a yellow foam (0.610 g, 36.7%). A small amount was dissolved in ethyl acetate, and ethereal hydrochloride was added. The mixture was concentrated and dried in vacuo at 76 °C for 12 h to yield the hydrochloride as a pale yellow solid (120 mg): mp 135 °C; mass spectrum (+EI, $[M+H]^+$) *m/z* 376. ^{1}H NMR (500 *MHz*, DMSO-d_6): δ 10.44–10.70 (m, 1H), 8.83 (d, 1H, J = 9.88 Hz), 8.39–8.41 (d and d, 1H, J = 1.58 Hz and 1.47 Hz), 8.31–8.33 (d and d, 1H, J = 1.83 and 1.95 Hz), 8.01–8.05 (m, 1H), 7.54–7.65 (m, 3H), 7.28–7.32 (m, 1H), 5.61–5.82 (m, 1H), 3.82–4.08 (m, 2H), 3.61–3.74 (m, 1H), 3.50–3.60 (m, 1H), 2.88–2.96 (m, 3H), 2.28–2.78 ppm (m, 2H). Anal. ($C_{18}H_{18}ClN_3O_2S$·1.5 HCl·0.5H_2O) C, H, N.

5.3.14. 3-(3-Chloro-benzenesulfonyl)-1-(1-methyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (3n). A thick suspension of 1-(1-methyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-

b]pyridine (0.754 g, 3.75 mmol), 3-chlorobenzenesulfonyl chloride (0.63 mL, 4.5 mmol), and silver trifluoromethanesulfonate (2.02 g, 7.86 mmol) in nitrobenzene (3.8 mL) was vigorously stirred at 125 °C for 14.5 h. After cooling to ambient temperature, saturated aqueous sodium bicarbonate and ethyl acetate were added to the reaction mixture, and it was stirred for several minutes. The layers were separated, and the aqueous layer was further extracted with ethyl acetate. The organic phase was washed with brine, dried with anhydrous magnesium sulfate, filtered, and concentrated. The residue was purified by flash chromatography using 100% ethyl acetate. Concentrating and drying in vacuo at 80 °C for 20 min yielded 3-(3-chloro-benzenesulfonyl)-1-(1-methyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine as a light yellow foam (0.529 g, 37.5%). It was dissolved in ethyl acetate, and ethereal hydrogen chloride was added. The precipitate was filtered and rinsed with ethyl acetate and ether. It was then dried in vacuo at 75 °C for 14 h to yield the hydrochloride as a cream-colored solid (0.429 g, 25.5%): mp 147–150 °C (dec); mass spectrum (+EI, $[M+H]^+$) *m/z* 376. ^{1}H NMR (500 *MHz*, DMSO-d_6): δ 10.70–11.10 (m, 1H), 8.73–8.78 (m, 1H), 8.41–8.43 (m, 1H), 8.24 (d, 1H, J = 8.24 Hz), 7.96–7.99 (m, 2H), 7.69 (d, 1H, J = 7.57 Hz), 7.57–7.61 (m, 1H), 7.35–7.38 (m, 1H), 5.53–5.76 (m, 1H), 3.93–4.05 (m, 1H), 3.17–3.84 (m, 3H), 2.87–2.91 (m, 3H), 2.28–2.76 ppm (m, 2H). HRMS ($C_{20}H_{18}ClN_4O_2S$), calcd $[M+H]^+$ 376.0886, found $[M+H]^+$ 376.0890.

5.3.15. 3-(4-Chloro-benzenesulfonyl)-1-(1-methyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (3o). A thick suspension of 1-(1-methyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (1.10 g, 5.47 mmol), 4-chlorobenzenesulfonyl chloride (1.27 g, 6.02 mmol), and silver trifluoromethanesulfonate (2.89 g, 11.2 mmol) in nitrobenzene (5 mL) was vigorously stirred at 125 °C for 17 h. After cooling to ambient temperature, saturated aqueous sodium bicarbonate and ethyl acetate were added to the reaction mixture, and it was stirred for several min. The layers were separated, and the aqueous layer was further extracted with ethyl acetate. The organic phase was washed with brine, dried with anhydrous magnesium sulfate, filtered, and concentrated. The residue was purified by flash chromatography using 100% ethyl acetate. After concentration, it was recrystallized from ethyl acetate and dried in vacuo at 75 °C for 5 h. 3-(4-Chloro-benzenesulfonyl)-1-(1-methyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine was obtained as an off-white solid (0.333 g, 16.2%): mp 136–138 °C; mass spectrum (+EI, $[M+H]^+$) *m/z* 376. ^{1}H NMR (500 *MHz*, DMSO-d_6): δ 8.43 (s, 1H), 8.37–8.39 (m, 1H), 8.14 (dd, 1H, J = 8.05 Hz and 1.59 Hz), 7.98–8.01 (m, 2H), 7.58–7.62 (m, 2H), 7.28–7.31 (m, 1H), 5.39–5.45 (m, 1H), 2.99–3.04 (m, 1H), 2.86–2.89 (m, 1H), 2.62 (dd, 1H, J = 10.13 Hz and 6.59 Hz), 2.31 (s, 3H), 1.92–2.00 ppm (m, 1H). Anal. ($C_{18}H_{18}ClN_3O_2S$·1.5 HCl·0.5H_2O) C, H, N.

5.3.16. 3-(3-Bromo-benzenesulfonyl)-1-(1-methyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (3p). The title compound was prepared from 1-(1-methyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (0.993 g, 4.93 mmol), 3-bromobenzenesulfonyl chloride (0.85 mL, 5.9 mmol), and silver trifluoromethanesulfonate (2.53 g, 9.85 mmol) in nitrobenzene (4.9 mL) as described for compound **3o**. Following work-up, the residue was purified by flash chromatography using 100% ethyl acetate and by HPLC (Luna CN column) using (8:2, methylene chloride/methanol/TEA) in hexane/TEA. Concentrating and drying in vacuo yielded a yellow gum (0.258 g, 12.5%). About 78 mg was dissolved in ethyl acetate, and ethereal hydrogen chloride was added. Concentrating and drying in vacuo furnished the hydrochloride salt as an off-white solid (76.2 mg): mp 145 °C (dec); mass spectrum (+EI, $[M+H]^+$) *m/z* 420. ^{1}H NMR (500 MHz, DMSO-d_6): δ 10.45–10.85 (m, 1H), 8.73 (s, 1H), 8.41–8.43 (m, 1H), 8.24 (dd, 1H, J = 8.06 Hz and 1.47 Hz), 8.10 (t, 1H, J = 1.83 Hz), 8.00–8.02 (m, 1H), 7.80–7.83 (m, 1H), 7.50–7.54 (m, 1H), 7.35–7.38 (m, 1H), 5.51–5.74 (m, 1H), 3.47–4.02 (m, 3H), 2.89 (s, br, 3H), 2.34–2.75 ppm (m, 1H). Anal. ($C_{18}H_{18}BrN_3O_2S$·1.5HCl·1.0H_2O) C, H, N.

5.3.17. 3-Benzenesulfonyl-1-(1-ethyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (3q). A thick suspension of 1-(1-ethyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (1.30 g, 6.04 mmol), benzenesulfonyl chloride (0.92 mL, 7.3 mmol), and silver trifluoromethanesulfonate (3.22 g, 12.5 mmol) in nitrobenzene (6.0 mL) was vigorously stirred at 125 °C for 16.5 h. After cooling to ambient temperature, saturated aqueous potassium carbonate and ethyl acetate were added to the reaction mixture, and it was stirred for several minutes. The layers were separated, and the aqueous layer was further extracted with ethyl acetate. The organic phase was washed with brine, dried with anhydrous magnesium sulfate, filtered, and concentrated. The residue was purified by flash chromatography using 100% ethyl acetate. Concentrating and drying in vacuo at 80 °C for 20 min gave 3-benzenesulfonyl-1-(1-ethyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine as a light yellow semi-solid (0.888 g, 41.3%). It was dissolved in ethyl acetate, and ethereal hydrogen chloride was added. The precipitate was filtered, rinsed with ethyl acetate, and dried in vacuo at 74 °C for 14 h. The hydrochloride was obtained as a light buff solid (0.670 g, 25.9%): mp 152–155 °C (dec); Mass spectrum (+EI, $[M+H]^+$) *m/z* 356. ^{1}H NMR (500 MHz, DMSO-d_6): δ 10.75–11.15 (m, 1H), 8.69–8.77 (s and s, 1H), 8.41 (dd, 1H, J = 4.76 Hz and 1.34 Hz), 8.19–8.22 (m, 1H), 7.97–8.01 (m, 2H), 7.53–7.61 (m, 3H), 7.32–7.36 (m, 1H), 5.52–5.78 (m, 1H), 3.87–4.04 (m, 1H), 3.48–3.86 (m, 2H), 3.18–3.30 (m, 3H), 2.48–2.73 (m, 1H), 2.28–2.42 (m, 1H), 1.22–1.26 ppm (m, 3H). Anal. ($C_{19}H_{21}N_3O_2S$) C, N. H, calcd 4.95; found: 4.54.

5.3.18. 1-(1-Ethyl-pyrrolidin-3-yl)-3-(3-fluoro-benzenesulfonyl)-1*H*-pyrrolo[2,3-*b*]pyridine (3r). A thick suspension of 1-(1-ethyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (0.890 g, 4.13 mmol), 3-fluorobenzenesulfonyl chloride (0.62 mL, 4.7 mmol), and silver trifluoromethanesulfonate (2.35 g, 9.15 mmol) in nitrobenzene (4.1 mL) was vigorously stirred at 125 °C for 18 h. After cooling to ambient temperature, saturated aqueous sodium bicarbonate and ethyl acetate were added to the reaction mixture, and it was stirred for several min. The layers were separated,

and the aqueous layer was further extracted with ethyl acetate. The organic phase was washed with brine, dried with anhydrous magnesium sulfate, filtered, and concentrated. The residue was purified by flash chromatography using 100% ethyl acetate. Concentrating and drying in vacuo at 80 °C for 30 min gave 1-(1-ethyl-pyrrolidin-3-yl)-3-(3-fluoro-benzenesulfonyl)-1*H*-pyrrolo[2,3-*b*]pyridine as a yellow semi-solid (0.474 g, 30.8%). It was dissolved in ethyl acetate, and ethereal hydrogen chloride was added. The precipitate was filtered, rinsed with ether, and dried in vacuo at 75 °C for 15.5 h. The hydrochloride was obtained as a white solid (0.405 g, 22.0%): mp 200–202 °C (dec); mass spectrum (+EI, $[M+H]^+$) *m/z* 374. ^{1}H NMR (500 MHz, DMSO-d_6): δ 10.75–11.15 (m, 1H), 8.72–8.81 (s and s, 1H), 8.42 (dd, 1H, J = 4.64 Hz and 1.35 Hz), 8.23–8.25 (d and d, 1H, J = 1.34 Hz and 1.47 Hz), 7.79–7.87 (m, 2H), 7.59–7.64 (m, 1H), 7.45–7.50 (m, 1H), 7.33–7.37 (m, 1H), 5.52–5.78 (m, 1H), 3.89–4.06 (m, 1H), 3.79–3.88 (m, 1H), 3.47–3.58 (m, 1H), 3.16–3.31 (m, 3H), 2.32–2.74 (m, 2H), 1.22–1.26 ppm (m, 3H). Anal. ($C_{19}H_{20}FN_3O_2S$·2.5 HCl) C, H, N.

5.3.19. 3-(3-Chloro-benzenesulfonyl)-1-(1-ethyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (3s). A thick suspension of 1-(1-ethyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (0.879 g, 4.08 mmol), 3-chlorobenzenesulfonyl chloride (0.69 mL, 4.9 mmol), and silver trifluoromethanesulfonate (2.11 g, 8.21 mmol) in nitrobenzene (4.1 mL) was vigorously stirred at 125 °C for 16 h. After cooling to ambient temperature, saturated aqueous sodium bicarbonate and ethyl acetate were added to the reaction mixture, and it was stirred for several min. The layers were separated, and the aqueous layer was further extracted with ethyl acetate. The organic phase was washed with brine, dried with anhydrous magnesium sulfate, filtered, and concentrated. The residue was purified by flash chromatography using 100% ethyl acetate. Concentrating and drying in vacuo at 80 °C for 25 min gave 3-(3-chloro-benzenesulfonyl)-1-(1-ethyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine as a yellow foam (0.540 g, 34.0%). It was dissolved in ethyl acetate, and ethereal hydrogen chloride was added. The precipitate was filtered, rinsed with ethyl acetate and dried in vacuo at 75 °C for 12.5 h. The hydrochloride was obtained as a cream solid (0.491 g, 27.0%): mp 166–168 °C (dec); Mass spectrum (+EI, $[M+H]^+$) *m/z* 390. ^{1}H NMR (500 MHz, DMSO-d_6): δ 11.00–11.40 (m, 1H), 8.73–8.86 (s and s, 1H), 8.41–8.43 (m, 1H), 8.22–8.25 (d and d, 1H, J = 1.34 Hz and 1.46 Hz) 7.95–8.00 (m, 2H), 7.67–7.70 (m, 1H), 7.56–7.61 (m, 1H), 7.34–7.37 (m, 1H), 5.53–5.78 (m, 1H), 3.87–4.05 (m, 1H), 3.48–3.82 (m, 2H), 3.19–3.28 (m, 3H), 2.33–2.73 (m, 2H), 1.22–1.26 ppm (m, 3H). Anal. ($C_{19}H_{20}ClN_3O_2S$·2.0HCl·0.75H_2O) C, H, N.

5.3.20. 3-(5-Chloro-thiophene-2-sulfonyl)-1-pyrrolidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine (3t)

5.3.20.1. Step 1. A suspension of 1-(1-benzyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (1.1 g, 4.0 mmol), 5-chloro-thiophene-2-sulfonyl chloride (0.9 g, 4 mmol) and silver trifluoromethanesulfonate (2.4 g, 9.3 mmol) in nitrobenzene (2.1 mL) was stirred at 140 °C under nitrogen for 17.5 h. After cooling to ambient temperature, the reaction mixture was diluted with ethyl acetate, and filtered. The filtrate was washed with aqueous potassium carbonate and brine. The organic phase was dried with anhydrous magnesium sulfate, filtered, and concentrated. The residue was purified by flash chromatography twice using 100% methylene chloride, and 100% ethyl acetate and by HPLC using 2–15% (8:2 methylene chloride/methanol/TEA) in hexane/TEA. Concentrating and drying in vacuo at 62 °C for 35 min yielded 1-(1-benzyl-pyrrolidin-3-yl)-3-(5-chloro-thiophene-2-sulfonyl)-1*H*-pyrrolo[2,3-*b*]pyridine as a dark yellow gum (0.357 g, 19.8%); Mass spectrum (+EI, $[M+H]^+$) *m/z* 458. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.48 (s, 1H), 8.39–8.41 (m, 1H), 8.17–8.19 (d and d, 1H, J = 1.46 Hz and 1.59 Hz), 7.73 (d, 1H, J = 4.15 Hz), 7.16–7.34 (m, 7H), 5.40–5.46 (m, 1H), 3.70 (d, 1H, J = 13.17 Hz), 3.62 (d, 1H, J = 13.05 Hz), 3.04–3.09 (m, 1H), 2.77 (dd, 1H, J = 9.89 Hz and 2.69 Hz), 2.67–2.71 (m, 1H), 2.37–2.43 (m, 2H), 2.01–2.08 ppm (m, 1H).

5.3.20.2. Step 2. α-Chloroethylchloroformate (0.2 mL, 2 mmol) was added to a solution of 1-(1-benzyl-pyrrolidin-3-yl)-3-(5-chloro-thiophene-2-sulfonyl)-1*H*-pyrrolo[2,3-*b*]pyridine (0.295 g, 0.644 mmol) in 1,2-dichloroethane (6 mL). The reaction mixture was refluxed under nitrogen for 4.5 h. After concentrating, adding methylene chloride and concentrating, ethanol (5 mL) was added. The reaction mixture was refluxed under nitrogen for 1.5 h. The mixture was concentrated. Aqueous sodium bicarbonate was added, and the mixture was extracted with chloroform. The organic phase was concentrated and was purified by flash chromatography using 10% methanol in chloroform and 0.1% ammonium hydroxide/10% methanol in chloroform. Concentrating and drying in vacuo at 60 °C for 1 h, 40 min yielded 3-(5-chloro-thiophene-2-sulfonyl)-1-pyrrolidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine as a light brown gum (112 mg, 47.3%). Ethanol and ethereal hydrogen chloride were added. Concentrating and drying in vacuo at 80 °C for 12 h gave the hydrochloride as a beige solid (124 mg, 43.7%); mass spectrum (+EI, $[M+H]^+$) *m/z* 368. ^{1}H NMR (500 *MHz*, DMSO-d_6): δ 9.33–9.44 (br, 1H), 9.19–9.31 (br, 1H), 8.66 (s, 1H), 8.44 (dd, 1H, J = 4.64 and 1.47 Hz), 8.22–8.24 (d and d, 1H, J = 1.59 and 1.47 Hz), 7.74 (d, 1H, J = 4.15 Hz), 7.38 (dd, 1H, J = 8.06 and 4.76 Hz), 7.22 (d, 1H, J = 4.15 Hz), 5.53–5.61 (m, 1H), 3.61–3.70 (m, 2H), 3.28–3.34 (m, 1H), 2.34–2.54 ppm (m, 3H). Anal. ($C_{15}H_{14}ClN_3O_2S_2$·1.5HCl) C, H, N.

5.3.21. 8-(1-Pyrrolidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine-3-sulfonyl)-quinoline (3u)

5.3.21.1. Step 1. 8-[1-(1-Benzyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine-3-sulfonyl]-quinoline was prepared from 1-(1-benzyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (1.7 g, 6.1 mmol), quinoline-8-sulfonyl chloride (1.36 g, 6.0 mmol), and silver trifluoromethanesulfonate (2.44 g, 9.50 mmol) in nitrobenzene as described in Step 1 for compound **3t** to give a yellow semi-solid (0.108 g. 3.86%); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.78–8.80 (m, 1H), 8.75 (s, 1H), 8.62–8.65 (m, 1H), 8.42–8.44 (m, 1H), 8.25–8.31 (m, 3H), 7.78–7.82 (m,

1H), 7.55–7.58 (m, 1H), 7.23–7.36 (m, 6H), 5.43–5.45 (m, 1H), 3.67–3.76 (d and d, 2H, $J = 12.64$ Hz and 13.22 Hz), 3.09–3.18 (m, 1H), 2.80–2.83 (m, 1H), 2.70–2.74 (m, 1H), 1.89–1.97 ppm (m, 1H).

5.3.21.2. Step 2. α-Chloroethylchloroformate (0.1 mL, 0.9 mmol) was added to a solution of 8-[1-(1-benzyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine-3-sulfonyl]-quinoline (0.107 g, 0.228 mmol) in 1,2-dichloroethane (5 mL). The reaction mixture was refluxed under nitrogen for 2 h, 45 min. A second portion of α-chloroethylchloroformate (0.1 mL, 0.9 mmol) was added, and the mixture was refluxed for 45 min. After concentrating, adding methylene chloride, and concentrating, ethanol (5 mL) was added. The reaction mixture was refluxed under nitrogen for 45 min. The mixture was concentrated. Water and solid sodium bicarbonate were added to the residue, and it was extracted with chloroform and concentrated. The residue was purified by flash chromatography using 10% methanol in chloroform and 0.1% ammonium hydroxide/10% methanol in chloroform. Concentrating and drying in vacuo at 58 °C for 20 min yielded 8-(1-pyrrolidin-3-yl-1*H*-pyrrolo-[2,3-*b*]pyridine-3-sulfonyl)-quinoline as a brown-orange gum (32.7 mg, 37.8%). Methanol, ethanol, and ethereal hydrogen chloride were added. Concentrating and drying in vacuo at 78 °C for 12 h gave the hydrochloride as a light brown semi-solid (32.4 mg, 29.2%); mass spectrum (+EI, $[M+H]^+$) *m/z* 379. ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.20–9.37 (br, m, 2H), 8.95–8.98 (m, 1H), 8.83 (s, 1H), 8.60–8.63 (m, 1H), 8.42–8.46 (m, 1H), 8.31–8.33 (m, 2H), 8.25–8.29 (m, 1H), 7.75–7.82 (m, 1H), 7.57–7.62 (m, 1H), 7.28–7.32 (m, 1H), 5.56–5.63 (m, 1H), 3.65–3.74 (m, 1H), 3.50–3.62 (m, 2H), 3.26–3.36 (m, 1H), 2.27–2.37 ppm (m, 1H). HRMS ($C_{20}H_{18}N_4O_2S$), calcd $[M+H]^+$ 379.1236, found $[M+H]^+$ 379.1228.

5.3.22. 3-(6-Chloro-imidazo[2,1-*b*]thiazole-5-sulfonyl)-1-pyrrolidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine (3v)

5.3.22.1. Step 1. 1-(1-Benzyl-pyrrolidin-3-yl)-3-(6-chloro-imidazo[2,1-*b*]thiazole-5-sulfonyl)-1*H*-pyrrolo[2,3-*b*]pyridine was prepared from 1-(1-benzyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (1.1 g, 4.0 mmol), 6-chloro-imidazo[2,1-*b*]thiazole-5-sulfonyl chloride (1.03 g, 4.01 mmol), and silver trifluoromethanesulfonate (2.9 g, 11 mmol) in nitrobenzene as described in Step 1 for compound **3t** to give a yellow foam (0.140 g, 7.0%); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.65 (s, 1H), 8.37 (dd, 1H, $J = 4.64$ Hz and 1.51 Hz), 8.26 (d, 1H, $J = 4.41$ Hz), 8.18 (dd, 1H, $J = 8.00$ Hz and 1.51 Hz), 7.59–7.61 (m, 1H), 7.19–7.32 (m, 6H), 5.40–5.43 (m, 1H), 3.65 (dd, 2H, $J = 30.02$ Hz and 12.99 Hz), 3.04–3.08 (m, 1H), 2.77–2.80 (m, 1H), 2.69–2.73 (m, 1H), 2.01–2.08 ppm (m, 1H).

5.3.22.2. Step 2. α-Chloroethylchloroformate (0.1 mL, 0.9 mmol) was added to a solution of 1-(1-benzyl-pyrrolidin-3-yl)-3-(6-chloro-imidazo[2,1-*b*]thiazole-5-sulfonyl)-1*H*-pyrrolo[2,3-*b*]pyridine (0.131 g, 0.263 mmol) in 1, 2-dichloroethane (5 mL). The reaction mixture was refluxed under nitrogen for 4.5 h. After concentrating, adding methylene chloride, and concentrating, ethanol (5 mL) was added. The reaction mixture was refluxed under nitrogen for 1 h. The mixture was concentrated, and the residue was partitioned in chloroform and aqueous sodium bicarbonate. The organic phase was concentrated and purified by flash chromatography using 7.5–10% methanol in chloroform. Concentrating and drying in vacuo at 70 °C for 20 min yielded 3-(6-chloro-imidazo[2,1-*b*]thiazole-5-sulfonyl)-1-pyrrolidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine as a light yellow semi-solid (61.6 mg, 57.6%). Ethanol and ethereal hydrogen chloride were added. Concentrating and drying in vacuo at 78 °C for 11 h gave the hydrochloride as a yellow semi-solid (58.2 mg, 46.2%); mass spectrum (+EI, $[M+H]^+$) *m/z* 408. ^{1}H NMR (500 *MHz*, DMSO-d_6): δ 9.28–9.34 (br, 2H), 8.86 (s, 1H), 8.42 (dd, 1H, $J = 4.64$ Hz and 1.59 Hz), 8.28 (d, 1H, $J = 4.52$ Hz), 8.24 (dd, 1H, $J = 8.06$ Hz and 1.59 Hz), 7.63 (d, 1H, $J = 4.51$ Hz), 7.36–7.39 (m, 1H), 5.51–5.58 (m, 1H), 3.59–3.75 (m, 2H), 3.29–3.56 (m*, 2H), 2.48–2.56 (m, 1H), 2.32–2.42 ppm (m, 1H). HRMS ($C_{16}H_{14}ClN_5O_2S_2$), calcd $[M+H]^+$ 408.0355, found $[M+H]^+$ 408.0349.

5.3.23. 3-(6-Chloro-imidazo[2,1-*b*]thiazole-5-sulfonyl)-1-(1-methyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (3w).

A thick suspension of 1-(1-methyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (1.02 g, 5.07 mmol), 6-chloro-imidazo[2,1-*b*]thiazole-5-sulfonyl chloride (1.56 g, 6.08 mmol), and silver trifluoromethanesulfonate (2.66 g, 10.4 mmol) in nitrobenzene (5.1 mL) was vigorously stirred at 125 °C for 14.5 h. After cooling to ambient temperature, saturated aqueous potassium carbonate and ethyl acetate were added to the reaction mixture, and it was stirred for several minutes. The layers were separated, and the aqueous layer was further extracted with ethyl acetate. The organic phase was washed with brine, dried with anhydrous magnesium sulfate, filtered, and concentrated. The residue was purified by flash chromatography using 100% ethyl acetate and 10% methanol in ethyl acetate and by HPLC using (8:2, methylene chloride/methanol/TEA) in hexane/TEA. Concentrating and drying in vacuo at 80 °C for 20 min yielded 3-(6-chloro-imidazo[2,1-*b*]thiazole-5-sulfonyl)-1-(1-methyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine as a light yellow solid (0.143 g, 6.68%). It was dissolved in chloroform, and ethereal hydrogen chloride was added. Concentrating and drying in vacuo at 78 °C for 13 h yielded the hydrochloride as a pale yellow solid (0.163 g): MP: 158–160 °C (dec); mass spectrum (+EI, $[M+H]^+$) *m/z* 422. ^{1}H NMR (500 MHz, DMSO-d_6): δ 10.65–10.80 (m, 1H), 8.88–8.97 (m, 1H), 8.42 (dd, 1H, $J = 4.76$ Hz and 1.59 Hz), 8.21–8.29 (m, 2H), 7.61–7.64 (d and d, 1H, $J = 4.39$ Hz and 4.52 Hz), 7.35–7.39 (m, 1H), 5.54–5.73 (m, 1H), 3.82–4.09 (m, 2H), 3.48–3.72 (m, 2H), 2.90 (dd, 3H, $J = 12.20$ Hz and 4.88 Hz), 2.28–2.77 ppm (m, 2H). Anal. ($C_{17}H_{16}ClN_5O_2S_2$) C, H, N.

5.3.24. 3-(6-Chloro-imidazo[2,1-*b*]thiazole-5-sulfonyl)-1-(1-ethyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (3x).

A thick suspension of 1-(1-ethyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (1.03 g, 4.78 mmol), 6-chloroimidazo[2,1-*b*]thiazole-5-sulfonyl chloride (1.35 g, 5.26 mmol), and silver trifluoromethanesulfonate

(2.52 g, 9.81 mmol) in nitrobenzene (4.7 mL) was vigorously stirred at 125 °C for 18 h. After cooling to ambient temperature, saturated aqueous potassium carbonate and ethyl acetate were added to the reaction mixture, and it was stirred for several min. The layers were separated, and the aqueous layer was further extracted with ethyl acetate. The organic phase was washed with brine, dried with anhydrous magnesium sulfate, filtered, and concentrated. The residue was purified by flash chromatography using 100% ethyl acetate. Concentrating and drying in vacuo at 80 °C for 30 min gave 3-(6-chloroimidazo[2,1-*b*]thiazole-5-sulfonyl)-1-(1-ethyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine as a light buff foam (0.704 g, 33.8%). Ethyl acetate, ethanol, chloroform, and ethereal hydrogen chloride were added. The mixture was concentrated and recrystallized from isopropanol. It was then dried in vacuo at 72 °C for 12 h. The hydrochloride was obtained as a cream solid (0.360 g, 13.8%): mp 160 °C (dec); mass spectrum (+EI, $[M+H]^+$) *m/z* 436. ^{1}H NMR (500 MHz, DMSO-d_6): δ 11.00–11.10 (m, 1H), 8.88–9.09 (s and s, 1H), 8.42–8.43 (m, 1H), 8.21–8.34 (m, 2H), 7.60–7.65 (d and d, 1H, J = 4.51 Hz and 4.39 Hz), 7.35–7.39 (m, 1H), 5.52–5.76 (m, 1H), 3.808–4.02 (m, 2H), 3.48–3.74 (m, 2H), 3.17–3.25 (m, 2H), 2.36–2.70 (m, 2H), 1.21–1.26 ppm (m, 3H). Anal. ($C_{18}H_{18}ClN_5O_2S_2$·1.5HCl·0.5H_2O) C, H calcd 3.82, found, 3.18. N, calcd 16.60, found, 16.19.

5.3.25. 3-(Phenylsulfonyl)sulfonyl]-1-piperidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine, hydrochloride (4a). The title compound was prepared from 1-(1-ethylpiperidin-3-yl)-3-(phenylsulfonyl)-1*H*-pyrrolo[2,3-*b*]pyridine in substantially the same manner, as described for compound **4n**. The product was obtained as a light brown solid, hydrochloride salt. Mass spectrum (ES, $[M+H]^+$) *m/z* 342. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.59 (s, 1H), 8.38 (dd, 1H, J = 4.76 and 1.46 Hz), 8.17 (dd, 1H, J = 8.05 and 1.58 Hz), 7.97 (d, 2H, J = 6.83 Hz), 7.56 (m, 3H), 7.42 (dd, 1H, J = 8.05 and 7.93 Hz), 4.92 (m, 1H), 3.45 (m, 1H), 3.15 (m, 1H), 3.05 (m, 1H), 2.66 (m, 1H), 2.10 (m, 1H), 2.00 (m, 1H), 1.80 (m, 1H), and 1.65 ppm (m, 1H). Anal. ($C_{18}H_{19}N_3O_2S$·0.7HCl·0.2Dioxane) C, H, N.

5.3.26. 1-(1-Ethylpiperidin-3-yl)-3-(phenylsulfonyl)-1*H*-pyrrolo[2,3-*b*]pyridine, hydrochloride (4b). The title compound was prepared from 1-(1-ethylpiperidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine and 4-bromobenzenesulfonyl chloride in substantially the same manner, as described for compound **4p**. The product was obtained as a light brown solid, hydrochloride salt, mp 147–148 °C. Mass spectrum (ES, $[M+H]^+$) *m/z* 370. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.24 (s, 1H), 8.56 (s, 1H), 8.42 (d, 1H, J = 3.42 Hz), 8.21 (d, 1H, J = 6.71 Hz), 7.98 (d, 1H, J = 6.85 Hz), 7.58 (m, 2H), 7.34 (dd, 1H, J = 7.81 and 4.64 Hz), 5.22 (m, 1H), 3.71 (m, 1H), 3.51 (m, 1H), 3.12 (m, 2H), 2.88 (m, 1H), 2.17 (m, 1H), 2.07 (m, 1H), 1.90 (m, 1H), and 1.21 ppm (t, 3H, J = 7.72 Hz). Anal. ($C_{20}H_{23}N_3O_2S$·2.2HCl) C, H, N.

5.3.27. 3-[(2-Chlorophenyl)sulfonyl]-1-piperidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine, hydrochloride (4c)

5.3.27.1. Step 1. 1-(1-Ethylpiperidin-3-yl)-3-[(2-chlorophenyl)sulfonyl]-1*H*-pyrrolo[2,3-*b*]pyridine, hydrochloride was prepared from 1-(1-ethylpiperidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine and 2-chlorobenzenesulfonyl chloride in substantially the same manner, as described for compound **4p**. The product was obtained as a light yellow solid, hydrochloride salt, mp 152–153 °C. Mass spectrum (ES, $[M+H]^+$) *m/z* 404. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.51 (s, 1H), 8.71 (s, 1H), 8.41 (d, 1H, J = 4.04 Hz), 8.34 (d, 1H, J = 7.83 Hz), 8.01 (d, 1H, J = 7.68 Hz), 7.61 (m, 3H), 7.30 (dd, 1H, J = 7.93 and 4.63 Hz), 5.27 (m, 1H), 3.68 (m, 1H), 3.53 (m, 2H), 3.12 (m, 2H), 2.88 (m, 1H), 2.15 (m, 1H), 2.06 (m, 3H), and 1.21 ppm (t, 3H, J = 7.32 Hz). Anal. ($C_{20}H_{22}ClN_3O_2S$·2.0HCl·0.2Et_2O) C, H, N.

5.3.27.2. Step 2. 1-(1-ethylpiperidin-3-yl)-3-[(2-chlorophenyl)sulfonyl]-1*H*-pyrrolo[2,3-*b*]pyridine was converted to the title compound in substantially the same manner, as described for the preparation of compound **4n**. The product was obtained as a light brown solid, hydrochloride salt, mp 129–130 °C. Mass spectrum (ES, $[M+H]^+$) *m/z* 376. ^{1}H NMR (400 *MHz*, DMSO-d_6) δ 9.40 (m, 1H), 9.11 (m, 1H), 8.75 (s, 1H), 8.64 (m, 2H), 8.00 (d, 1H, J = 7.81 Hz), 7.55 (m, 3H), 5.20 (m, 1H), 3.52 (m, 3H), 2.84 (m, 1H), 2.20 (m, 1H), 2.00 (m, 2H), and 1.85 ppm (m, 1H).

Anal. ($C_{18}H_{18}ClN_3O_2S$·2.8HCl·0.05Et_2O) C, H, N.

5.3.28. 3-[(3-Chlorophenyl)sulfonyl]-1-piperidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine, hydrochloride (4d)

5.3.28.1. Step 1. 1-(1-Ethylpiperidin-3-yl)-3-[(3-chlorophenyl)sulfonyl]-1*H*-pyrrolo[2,3-*b*]pyridine was prepared from 1-(1-ethylpiperidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine and 3-chlorobenzenesulfonyl chloride in substantially the same manner, as described for compound **4p**. The product was obtained as a light brown solid, hydrochloride salt, mp 115 °C (dec). Mass spectrum (ES, $[M+H]^+$) *m/z* 404. ^{1}H NMR (400 *MHz*, DMSO-d_6) δ 10.03 (s, 1H), 8.60 (s, 1H), 8.43 (dd, 1H, J = 4.64 and 1.47 Hz), 8.25 (dd, 1H, J = 7.93 and 1.47 Hz), 7.98 (m, 2H), 7.70 (d, 1H, J = 8.59 Hz), 7.60 (dd, 1H, J = 7.80 and 7.93 Hz), 7.37 (dd, 1H, J = 8.05 and 4.75 Hz), 5.21 (m, 1H), 3.70 (m, 1H), 3.53 (m, 2H), 3.12 (m, 2H), 2.88 (m, 1H), 2.15 (m, 1H), 2.06 (m, 3H), and 1.21 ppm (t, 3H, J = 7.3 Hz).

5.3.28.2. Step 2. 1-(1-Ethylpiperidin-3-yl)-3-[(3-chlorophenyl)sulfonyl]-1*H*-pyrrolo[2,3-*b*]pyridine was converted to the title compound in substantially the same manner, as described for compound **4n**. The product was obtained as a white solid, hydrochloride salt, mp 181–182 °C. Mass spectrum (ES, $[M+H]^+$) *m/z* 376. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.15 (m, 1H), 8.93 (m, 1H), 8.64 (s, 1H), 8.42 (d, 1H, J = 4.76 Hz), 8.24 (d, 1H, J = 8.05 Hz), 7.97 (m, 2H), 7.68 (d, 1H, J = 8.29 Hz), J = 7.60 (dd, 1H, J = 7.80 and 7.06 Hz), J = 7.35 (dd, 1H, J = 7.81 and 4.76 Hz), 5.13 (m, 1H), 3.50 (m, 1H), 3.45 (m, 1H), 3.32 (m, 1H), 2.85 (m, 1H), 2.18 (m, 1H), 2.10 (m, 1H), 1.95 (m, 1H), and 1.82 ppm (m, 1H). Anal. ($C_{18}H_{18}ClN_3O_2S$·1.5 HCl) C, H, N.

5.3.29. 3-[(4-Chlorophenyl)sulfonyl]-1-piperidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine, hydrochloride (4e). The title compound was prepared from 1-(1-ethylpiperidin-3-yl)-3-

[(4-chlorophenyl)sulfonyl]-1*H*-pyrrolo[2,3-*b*]pyridine in substantially the same manner, as described for compound **4n**. The product was obtained as a white solid, hydrochloride salt, mp 166–167 °C. Mass spectrum (ES, $[M+H]^+$) *m/z* 376. ^{1}H NMR (400 *MHz*, DMSO-d_6) δ 9.15 (m, 1H), 8.85 (m, 1H), 8.61 (s, 1H), 8.41 (dd, 1H, J = 4.64 and 1.47 Hz), 8.20 (dd, 1H, J = 8.05 and 1.47 Hz), 7.98 (d, 2H, J = 8.67 Hz), 7.63 (d, 2H, J = 8.76 Hz), 7.35 (dd, 1H, J = 8.06 and 4.63 Hz), 5.13 (m, 1H), 3.48 (m, 2H), 3.31 (m, 1H), 2.85 (m, 1H), 2.17 (m, 1H), 2.06 (m, 1H), 1.90 (m, 1H), and 1.82 ppm (m, 1H). Anal. ($C_{18}H_{18}ClN_3O_2S$·2.5 HCl) C, H, N.

5.3.30. 3-[(4-Chlorophenyl)sulfonyl]-1-(1-methylpiperidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine, hydrochloride (4f). The title compound was prepared from 3-[(4-chlorophenyl)sulfonyl]-1-piperidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine and formaldehyde in substantially the same manner, as described for compound **4o**. The product was obtained as a yellow solid, hydrochloride salt, mp 176–176 °C. Mass spectrum (ES, $[M+H]^+$) *m/z* 390. ^{1}H NMR (400 *MHz*, DMSO-d_6) δ 10.48 (s, 1H), 8.56 (s, 1H), 8.42 (d, 1H, J = 4.64 Hz), 8.22 (dd, 1H, J = 8.05 and 1.58 Hz), 7.98 (d, 1H, J = 8.54 Hz), 7.63 (d, 1H, J = 8.54 Hz), 7.35 (dd, 1H, J = 7.93 and 4.75 Hz), 5.25 (m, 1H), 3.60 (m, 1H), 3.45 (m, 2H), 2.90 (m, 1H), 2.79 (s, 3H), 2.05 ppm (m, 3H). Anal. ($C_{19}H_{20}ClN_3O_2S$·2.0HCl·0.15-H_2O) C, H, N.

5.3.31. 1-(1-Ethylpiperidin-3-yl)-3-[(4-chlorophenyl)sulfonyl]-1*H*-pyrrolo[2,3-*b*]pyridine, hydrochloride (4g). The title compound was prepared from 1-(1-ethylpiperidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine and 4-chlorobenzenesulfonyl chloride in substantially the same manner, as described for compound **4p**. The product was obtained as a light brown solid, hydrochloride salt, mp 142-143 °C. Mass spectrum (ES, $[M+H]^+$) *m/z* 404. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.05 (s, 1H), 8.57 (s, 1H), 8.43 (dd, 1H, J = 4.75 and 1.46 Hz), 8.21 (dd, 1H, J = 7.93 and 1.47 Hz), 7.98 (dd, 2H, J = 8.66 and 1.95 Hz), 7.64 (dd, 2H, J = 8.79 and 1.96 Hz), 7.36 (dd, 1H, J = 7.93 and 4.75 Hz), 5.22 (m, 1H), 3.68 (m, 1H), 3.50 (m, 2H), 3.12 (m, 2H), 2.88 (m, 1H), 2.15 (m, 1H), 2.06 (m, 2H), 1.90 (m, 1H), and 1.21 ppm (t, 3H, J = 6.65). Anal. ($C_{20}H_{22}ClN_3O_2S$·2.0HCl·0.1H_2O) C, H, N.

5.3.32. 3-[(3-Fluorophenyl)sulfonyl]-1-(1-isopropylpiperidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine, hydrochloride (4h). The title compound was prepared from 3-[(4-chlorophenyl)sulfonyl]-1-piperidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine and acetone in substantially the same manner, as described for compound **4o**. The product was obtained as a yellow solid, hydrochloride salt, mp 185–186 °C. Mass spectrum (ES, $[M+H]^+$) *m/z* 418. ^{1}H NMR (400 *MHz*, DMSO-d_6) δ 10.36 (s, 1H), 8.64 (s, 1H), 8.43 (d, 1H, J = 3.79 Hz), 8.20 (d, 1H, J = 7.07 Hz), 7.98 (d, 2H, J = 8.42 Hz), 7.64 (d, 2H, J = 8.41 Hz), 7.35 (dd, 1H, J = 7.93 and 4.75 Hz), 5.38 (m, 1H), 3.55 (m, 3H), 3.40 (m, 1H), 2.95 (m, 1H), 2.10 (m, 2H), 2.00 (m, 2H), and 1.25 ppm (m, 6H). Anal. ($C_{21}H_{24}ClN_3O_2$-S·1.7HCl·0.2Et_2O) C, H, N.

5.3.33. 3-{[3-(Trifluoromethyl)phenyl]sulfonyl}-1-piperidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine, hydrochloride (4i)

5.3.33.1. Step 1. 1-(1-Ethylpiperidin-3-yl)-3-{[3-(trifluoromethyl)phenyl]sulfonyl}-1*H*-pyrrolo[2,3-*b*]pyridine, hydrochloride was prepared from 1-(1-ethylpiperidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine and 3-(trifluoromethyl)benzenesulfonyl chloride in substantially the same manner, as described for compound **4p**. The product was obtained as a light brown solid, hydrochloride salt, mp 146–147 °C. Mass spectrum (ES, $[M+H]^+$) *m/z* 438. NMR (400 MHz, DMSO-d_6) δ 10.15 (s, 1H), 8.66 (s, 1H), 8.44 (m, 1H), 8.30 (m, 2H), 8.23 (s, 1H), 8.02 (d, 1H, J = 7.93 Hz), 7.82 (t, 1H, J = 7.81 Hz), 7.39 (m, 1H), 5.22 (m, 1H), 3.70 (m, 1H), 3.51 (m, 1H), 3.12 (m, 2H), 2.88 (m, 1H), 2.17 (m, 1H), 2.07 (m, 1H), 1.91 (m, 1H), and 1.21 ppm (t, 3H, J = 7.32 Hz). Anal. ($C_{21}H_{22}F_3N_3O_2S$·1.3HCl·0.2 H_2O) C, H, N.

5.3.33.2. Step 2. The title compound was prepared from 1-(1-ethylpiperidin-3-yl)-3-{[3-(trifluoromethyl)-phenyl]sulfonyl}- 1*H*-pyrrolo[2,3-*b*]pyridine in substantially the same manner, as described for compound **4n**. The product was obtained as a light brown solid, hydrochloride salt, mp 172–173 °C. Mass spectrum (ES, $[M+H]^+$) *m/z* 410. ^{1}H NMR (400 *MHz*, DMSO-d_6) δ 9.23 (m, 1H), 8.95 (m, 1H), 8.70 (s, 1H), 8.43 (d, 1H, J = 4.75 Hz), 8.24 (m, 3H), 8.01 (d, 1H, J = 7.56 Hz), 7.82 (dd, 1H, J = 7.81 and 7.93 Hz), J = 7.36 (dd, 1H, J = 4.76 and 4.76 Hz), 5.14 (m, 1H), 3.50 (m, 2H), 3.22 (m, 1H), 2.85 (m, 1H), 2.19 (m, 1H), 2.07 (m, 1H), 1.95 (m, 1H), and 1.82 ppm (m, 1H). Anal. ($C_{19}H_{18}F_3N_3O_2$-S·1.5HCl) C, H, N.

5.3.34. 3-{[4-(Trifluoromethyl)phenyl]sulfonyl}-1-piperidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine, hydrochloride (4j)

5.3.34.1. Step 1. 1-(1-Ethylpiperidin-3-yl)-3-{[4-(trifluoromethyl)phenyl]sulfonyl}-1*H*-pyrrolo[2,3-*b*]pyridine, hydrochloride was prepared from 1-(1-ethylpiperidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine and 4-(trifluoromethyl)benzenesulfonyl chloride in substantially the same manner, as described for compound **4p**. The product was obtained as a light brown solid, hydrochloride salt, mp 145–146 °C. Mass spectrum (ES, $[M+H]^+$) *m/z* 438. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.40 (s, 1H), 8.63 (s, 1H), 8.44 (d, 1H, J = 3.42 Hz), 8.20 (m, 3H), 7.94 (d, 2H, J = 8.17 Hz), 7.37 (m, 1H), 5.22 (m, 1H), 3.70 (m, 1H), 3.51 (m, 1H), 3.12 (m, 2H), 2.88 (m, 1H), 2.17 (m, 1H), 2.07 (m, 1H), 1.91 (m, 1H), and 1.21 ppm (t, 3H, J = 7.2 Hz). Anal. ($C_{21}H_{22}F_3N_3O_2S$·2.5 HCl) C, H, N.

5.3.34.2. Step 2. The title compound was prepared from 1-(1-ethylpiperidin-3-yl)-3-{[4-(trifluoromethyl)-phenyl]sulfonyl}-1*H*-pyrrolo[2,3-*b*]pyridine in substantially the same manner, as described for compound **4n**. The product was obtained as a light brown solid, hydrochloride salt, mp 136–137 °C. Mass spectrum (ES, $[M+H]^+$) *m/z* 410. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.33 (m, 1H), 9.06 (m, 1H), 8.67 (s, 1H), 8.41 (d, 1H, J = 3.90 Hz), 8.22 (d, 1H, J = 7.57 Hz), 8.18 (d, 2H, J = 7.93 Hz), 7.93 (d, 2H, J = 8.05 Hz), 7.35 (m,1H), 5.15 (m, 1H), 3.31 (m, 1H), 2.82 (m, 1H), 2.17 (m, 1H), 2.06 (m, 1H), 1.90 (m, 1H), and 1.82 ppm

(m, 1H). Anal. ($C_{19}H_{18}F_3N_3O_2S$·2.6 HCl·0.15Et_2O) C, H, N.

5.3.35. 3-{[3-(Trifluoromethyl)phenyl]sulfonyl}-1-(1- methylpiperidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine, hydrochloride (4k). The title compound was prepared from 3-{[3-(trifluoromethyl)phenyl]sulfonyl}-1-piperidin-3-yl-1*H*-pyrrolo-[2,3-*b*]pyridine and formaldehyde in substantially the same manner, as described for compound **4o**. The product was obtained as a light green solid, hydrochloride salt, mp 127–128 °C. Mass spectrum (ES, $[M+H]^+$) *m*/*z* 424. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.39 (s, 1H), 8.64 (s, 1H), 8.43 (m, 1H), 8.29 (m, 2H), 8.23 (s, 1H), 8.02 (d, 1H, J = 7.56 Hz), 7.82 (t, 1H, J = 8.05), 7.37 (m, 1H), 5.20 (m, 1H), 3.65 (m, 1H), 3.50 (m, 1H), 2.90 (m, 1H), 2.79 (s, 3H), 2.11 (m, 2H), 1.90 ppm (m, 1H). Anal. ($C_{20}H_{20}F_3N_3O_2S$·1.9HCl) C, H, N.

5.3.36. 3-[(3-Bromophenyl)sulfonyl]-1-piperidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine, hydrochloride (4l)

5.3.36.1. Step 1. 1-(1-Ethylpiperidin-3-yl)-3-[(3-bromophenyl)sulfonyl]-1*H*-pyrrolo[2,3-*b*]pyridine, hydrochloride was prepared from 1-(1-ethylpiperidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine and 3-bromobenzenesulfonyl chloride in substantially the same manner, as described for compound **4p**. The product was obtained as a yellow solid, hydrochloride salt, mp >155 °C (dec). Mass spectrum (ES, $[M+H]^+$) *m*/*z* 448. ^{1}H NMR (400 *MHz*, DMSO-d_6) δ 10.14 (s, 1H), 8.72 (s, 1H), 8.38 (m, 2H), 7.99 (dd, 1H, J = 8.01 and 1.46 Hz), 7.74 (d, 1H, J = 8.05 Hz), 7.65 (t, 1H, J = 6.96 Hz), 7.52 (t, 1H, J = 7.81 Hz), 7.29 (m, 1H), 5.25 (m, 1H), 3.52 (m, 2H), 3.12 (m, 2H), 2.88 (m, 1H), 2.19 (m, 1H), 2.06 (m, 2H), 1.92 (m, 1H), and 1.21 ppm (t, 3H, J = 7.19 Hz). Anal. ($C_{20}H_{22}BrN_3O_2S$·1.4HCl) C, H, N.

5.3.36.2. Step 2. The title compound was prepared from 1-(1-ethylpiperidin-3-yl)-3-[(3-bromophenyl)sulfonyl]-1*H*-pyrrolo[2,3-*b*]pyridine in substantially the same manner, as described for compound **4n**. The product was obtained as an off-white solid, hydrochloride salt, mp 184–185 °C. Mass spectrum (ES, $[M+H]^+$) *m*/*z* 420. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.15 (m, 1H), 8.90 (m, 1H), 8.77 (s, 1H), 8.40 (m, 2H), 7.89 (dd, 1H, J = 7.94 and 1.47 Hz), 7.73 (d, 1H, J = 7.81 Hz), 7.65 (t, 1H, J = 7.07), 7.52 (t, 1H, J = 7.68), 7.28 (dd, 1H, J = 8.03 and 4.64 Hz), 5.19 (m, 1H), 3.50 (m, 2H), 3.32 (m, 1H), 2.85 (m, 1H), 2.21 (m, 1H), 2.07 (m, 1H), 1.95 (m, 1H), and 1.82 ppm (m, 1H). Anal. ($C_{18}H_{18}BrN_3O_2S$·1.3HCl·0.1H_2O) C, H, N.

5.3.37. 3-[(2-Fluorophenyl)sulfonyl]-1-piperidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine, hydrochloride (4m). The title compound was prepared from 1-(1-ethylpiperidin-3-yl)-3-[(2-fluorophenyl)sulfonyl]-1*H*-pyrrolo[2,3-*b*]pyridine in substantially the same manner, as described for the preparation of compound **4n**. The product was obtained as a light brown solid, hydrochloride salt, mp 165–166 °C. Mass spectrum (ES, $[M+H]^+$) *m*/*z* 360. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.24 (m, 1H), 8.95 (m, 1H), 8.67 (s, 1H), 8.42 (dd, 1H, J = 4.67 and 1.59 Hz), 8.12 (dd, 1H, J = 8.18 and 1.34 Hz), 8.08 (dd, 1H, J = 7.68 and 1.70 Hz), 7.74 (m, 1H), 7.42 (dd, 1H, J = 8.41 and 7.81 Hz), 7.34 (m, 2H), 5.19 (m, 1H), 3.52 (m, 2H), 2.86 (m, 1H), 2.49 (m, 1H), 2.19 (m, 1H), 2.05 (m, 1H), 1.95 (m, 1H), and 1.82 ppm (m, 1H). Anal. ($C_{18}H_{18}FN_3O_2S$·1.5HCl) C, H, N.

5.3.38. 3-[(3-Fluorophenyl)sulfonyl]-1-piperidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine, hydrochloride (4n). α-Chloroethylchloroformate (0.24 mL, 2.2 mmol) was added to a stirred solution of **4p** (0.167 g, 0.43 mmol) and proton-sponge (0.047 g, 0.22 mmol) in 1,2-dichloroethane (7 mL) under a nitrogen atmosphere at room temperature. The mixture was stirred while heating at 100 °C and monitored by TLC. After no starting material was detected (8 h), the solvents were evaporated in vacuo. The residue was dissolved in 10% water in dioxane (7 mL) and the mixture was stirred at 100 °C for 5 h. The solvents were evaporated in vacuo and the residue was purified by flash column chromatography using 10% methanol in dichloromethane as an eluant to give a semi-solid, 123 mg, (79% yield). The semi-solid was converted to HCl salt using ethereal hydrogen chloride to give an off-white solid, mp 190–191 °C. Mass spectrum (ES, $[M+H]^+$) *m*/*z* 360. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.25 (m, 1H), 8.96 (m, 1H), 8.63 (s, 1H), 8.42 (dd, 1H, J = 4.64 and 1.35 Hz), 8.24 (dd, 1H, J = 8.04 and 1.47 Hz), 7.82 (m, 2H), 7.62 (m, 1H), 7.48 (m, 1H), J = 7.35 (dd, 1H, J = 8.05 and 4.63 Hz), 5.14 (m, 1H), 3.50 (m, 2H), 3.32 (m, 1H), 2.83 (m, 1H), 2.22 (m, 1H), 2.07 (m, 1H), 1.95 (m, 1H), and 1.82 ppm (m, 1H). Anal. ($C_{18}H_{18}FN_3O_2S$·1.3HCl) C, H, N.

5.3.39. 3-[(3-Fluorophenyl)sulfonyl]-1-(1-methylpiperidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine, hydrochloride (4o). Formaldehyde (0.0095 mL, 0.35 mmol) was added dropwise at room temperature to a stirred solution of **4n** (0.033 g, 0.1 mmol) and sodium triacetoxyborohydride (0.09 g, 0.4 mmol) in acetonitrile (2.1 mL) under a nitrogen atmosphere. The reaction mixture was stirred at room temperature for 3 h. then quenched with water and extracted with methylene chloride. The organic layer was separated, washed with water and brine, dried with anhydrous magnesium sulfate, filtered, and solvent evaporation to give a solid, 33 mg, (90% yield). The solid was converted to HCl salt using ethereal hydrogen chloride. The title compound was obtained as a yellow solid, mp 147–148 °C. Mass spectrum (ES, $[M+H]^+$) *m*/*z* 374. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.57 (s, 1H), 8.58 (s, 1H), 8.43 (d, 1H, J = 3.42 Hz), 8.25 (dd, 1H, J = 8.06 and 1.22 Hz), 7.81 (m, 2H), 7.63 (m, 1H), 7.48 (m, 1H), 7.36 (m, 1H), 5.23 (m, 1H), 3.60 (m, 2H), 2.90 (m, 1H), 2.79 (s, 3H), 2.05 ppm (m, 3H). Anal. ($C_{19}H_{20}FN_3O_2S$·1.8HCl·0.1H_2O) C, H, N.

5.3.40. 1-(1-Ethylpiperidin-3-yl)-3-[(3-fluorophenyl)sulfonyl]-1*H*-pyrrolo[2,3-*b*]pyridine, hydrochloride (4p). A mixture of 1-(1-ethylpiperidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (0.4 g, 1.74 mmol), 3-fluorobenzenesulfonyl chloride (0.381 g, 1.92 mmol), and silver trifluoromethanesulfonate (0.9 g, 3.5 mmol) in nitrobenzene (0.8 mL) was heated at 130 °C for 20 hr in a pressure vessel. The reaction mixture was cooled down and purified by flash column chromatography using 0–7% meth-

anol in methylene chloride as an eluant to give an oil, 242 mg, (36% yield). The product was converted to HCl salt using ethereal hydrogen chloride to give a gray solid, mp 180–181 °C. Mass spectrum (ES, $[M+H]^+$) *m/z* 388. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.17 (s, 1H), 8.59 (s, 1H), 8.43 (dd, 1H, J = 4.63 and 1.34 Hz), 8.25 (dd, 1H, J = 7.97 and 1.34 Hz), 7.82 (m, 2H), 7.63 (m, 1H), 7.48 (m, 1H), 7.36 (m, 1H), 5.22 (m, 1H), 3.71 (m, 1H), 3.45 (m, 2H), 3.13 (q, 2H), 2.88 (m, 1H), 2.15 (m, 1H), 2.09 (m, 2H), 1.91 (m, 1H), and 1.22 ppm (t, 3H, J = 7.26 Hz). Anal. ($C_{20}H_{22}FN_3O_2S$·1.0HCl·0.8-H_2O) C, H, N.

5.3.41. 3-[(3-Fluorophenyl)sulfonyl]-1-(1-isopropylpiperidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine, hydrochloride (4q). The title compound was prepared from 3-[(3-fluorophenyl)sulfonyl]-1-piperidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine and acetone in substantially the same manner, as described for compound **4o**. The product was obtained as a yellow solid, hydrochloride salt, mp 155–156 °C. Mass spectrum (ES, $[M+H]^+$) *m/z* 402. ^{1}H NMR (400 *MHz*, DMSO-d_6) δ 10.28 (s, 1H), 8.66 (s, 1H), 8.43 (d, 1H, J = 4.02 Hz), 8.24 (d, 1H, J = 7.32 Hz), 7.82 (m, 2H), 7.63 (m, 1H), 7.47 (m, 1H), 7.36 (m, 1H), 5.33 (m, 1H), 3.55 (m, 3H), 3.40 (m, 1H), 2.95 (m, 1H), 2.10 (m, 2H), 2.00 (m, 2H), and 1.25 ppm (m, 6H). Anal. ($C_{21}H_{24}FN_3O_2S$·2.0HCl) C, H, N.

5.3.42. 3-[(3-Bromophenyl)sulfonyl]-1-(1-isopropylpiperidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine, hydrochloride (4r). The title compound was prepared from 3-[(3-bromophenyl)sulfonyl]-1-piperidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine and acetone in substantially the same manner, as described for compound **4o**. The product was obtained as a yellow solid, hydrochloride salt, mp 178–179 °C. Mass spectrum (ES, $[M+H]^+$) *m/z* 462. ^{1}H NMR (400 *MHz*, DMSO-d_6) δ 10.15 (s, 1H), 8.82 (s, 1H), 8.39 (m, 2H), 7.98 (d, 1H, J = 7.69 Hz), 7.74 (d, 1H, J = 7.80 Hz), 7.65 (t, 1H, J = 7.56 Hz), 7.52 (t, 1H, J = 7.57 Hz), 7.29 (m, 1H), 5.40 (m, 1H), 3.55 (m, 3H), 3.40 (m, 1H), 2.95 (m, 1H), 2.15 (m, 1H), 2.05 (m, 3H), and 1.27 ppm (m, 6H). Anal. ($C_{21}H_{24}BrN_3O_2S$·2.2HCl) C, H, N.

5.3.43. 3-[(3,5-Dichlorophenyl)sulfonyl]-1-piperidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine, hydrochloride (4s). The title compound was prepared from 1-(1-ethylpiperidin-3-yl)-3-[(3,5-dichlorophenyl)sulfonyl]-1*H*-pyrrolo[2,3-*b*]pyridine in substantially the same manner, as described for compound **4n**. The product was obtained as an off-white solid, hydrochloride salt, mp 171–172 °C. Mass spectrum (ES, $[M+H]^+$) *m/z* 410. ^{1}H NMR (400 *MHz*, DMSO-d_6) δ 9.30 (m, 1H), 9.06 (m, 1H), 8.67 (s, 1H), 8.43 (d, 1H, J = 4.63 Hz), 8.30 (dd, 1H, J = 8.05 and 1.46 Hz), 7.99 (s, 2H), 7.91 (s, 1H), 7.37 (dd, 1H, J = 8.06 and 4.76 Hz), 5.14 (m, 1H), 3.50 (m, 1H), 3.42 (m, 1H), 3.30 (m, 1H), 2.82 (m, 1H), 2.19 (m, 1H), 2.07 (m, 1H), 1.95 (m, 1H), and 1.82 ppm (m, 1H). Anal. ($C_{18}H_{17}Cl_2N_3O_2S$·1.5HCl) C, H, N.

5.3.44. 3-[(3,5-Dichlorophenyl)sulfonyl]-1-(1-methylpiperidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine, hydrochloride (4t). The title compound was prepared from 3-[(3,5-dichlorophenyl)sulfonyl]-1-piperidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine and formaldehyde in substantially the same manner, as described for compound **4o**. The product was obtained as a yellow solid, hydrochloride salt, mp 162–163 °C. Mass spectrum (ES, $[M+H]^+$) *m/z* 424. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.58 (s, 1H), 8.62 (s, 1H), 8.44 (dd, 1H, J = 5.46 and 1.47 Hz), 8.32 (dd, 1H, J = 7.93 and 1.10 Hz), 8.00 (s, 2H), 7.92 (s, 1H), 7.37 (dd, 1H, J = 8.05 and 3.64 Hz), 5.20 (m, 1H), 3.65 (m, 1H), 3.50 (m, 1H), 2.90 (m, 1H), 2.79 (s, 3H), 2.05 ppm (m, 3H). Anal. ($C_{19}H_{19}Cl_2N_3O_2S$·1.6HCl·0.1 H_2O) C, H, N.

5.3.45. 1-(1-Ethylpiperidin-3-yl)-3-[(3,5-dichlorophenyl)-sulfonyl]-1*H*-pyrrolo[2,3-*b*]pyridine, hydrochloride (4u). The title compound was prepared from 1-(1-ethylpiperidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine and 3-(3,5-dichlorophenyl)sulfonyl chloride in substantially the same manner, as described for compound **4p**. The product was obtained as a light brown solid, hydrochloride salt, mp 153–154 °C. Mass spectrum (ES, $[M+H]^+$) *m/z* 438. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.63 (s, 1H), 8.44 (dd, 1H, J = 4.76 and 1.47 Hz), 8.32 (dd, 1H, J = 7.93 and 1.46 Hz), 8.00 (s, 2H), 7.92 (s, 1H), 7.37 (dd, 1H, J = 7.93 and 4.64 Hz), 5.22 (m, 1H), 3.71 (m, 1H), 3.51 (m, 1H), 3.12 (m, 2H), 2.88 (m, 1H), 2.17 (m, 1H), 2.07 (m, 1H), 1.91 (m, 1H), and 1.21 ppm (t, 3H, J = 7.32). Anal. ($C_{20}H_{21}Cl_2N_3O_2S$·2.0HCl) C, H, N.

5.3.46. 3-[(5-Chlorothien-2-yl)sulfonyl]-1-piperidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine, hydrochloride (4v). The title compound was prepared from 1-(1-ethylpiperidin-3-yl)-3-[(5-chlorothien-2-yl)sulfonyl]-1*H*-pyrrolo[2,3-*b*]pyridine in substantially the same manner, as described for compound **4n**. The product was obtained as a light brown solid, hydrochloride salt, mp 175–176 °C. Mass spectrum (ES, $[M+H]^+$) *m/z* 382. ^{1}H NMR (400 *MHz*, DMSO-d_6) δ 9.33 (m, 1H), 9.05 (m, 1H), 8.63 (s, 1H), 8.42 (dd, 1H, J = 4.64 and 1.47 Hz), 8.23 (dd, 1H, J = 8.05 and 1.58 Hz), 7.75 (d, 1H, J = 6.14 Hz), 7.37 (dd, 1H, J = 8.01 and 7.93 Hz), 7.22 (d, 1H, J = 4.15 Hz), 5.16 (m, 1H), 3.48 (m, 2H), 3.40 (m, 1H), 2.85 (m, 1H), 2.19 (m, 1H), 2.06 (m, 1H), 1.95 (m, 1H), and 1.84 ppm (m, 1H). Anal. ($C_{16}H_{16}ClN_3O_2S_2$·1.2HCl) C, H, N.

5.3.47. 3-[(5-Chlorothien-2-yl)sulfonyl]-1-(1-methylpiperidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine, hydrochloride (4w). The title compound was prepared from 3-[(5-chlorothien-2-yl)sulfonyl]-1-piperidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine and formaldehyde in substantially the same manner, as described for compound **4o**. The product was obtained as a yellow solid, hydrochloride salt, mp 165–166 °C. Mass spectrum (ES, $[M+H]^+$) *m/z* 396. ^{1}H NMR (400 *MHz*, DMSO-d_6) δ 10.40 (s, 1H), 8.57 (s, 1H), 8.45 (dd, 1H, J = 4.63 and 1.46 Hz), 8.24 (dd, 1H, J = 7.93 and 1.34 Hz), 7.75 (d, 1H, J = 4.03 Hz), 7.39 (dd, 1H, J = 8.05 and 4.76 Hz), 7.22 (d, 1H, J = 4.15 Hz), 5.20 (m, 1H), 3.65 (m, 1H), 3.50 (m, 1H), 2.90 (m, 1H), 2.79 (s, 3H), 2.18 (m, 1H), 2.05 (m, 1H), 1.90 ppm (m, 1H). Anal. ($C_{17}H_{18}ClN_3O_2S_2$·1.7HCl) C, H, N.

5.3.48. 1-(1-Ethylpiperidin-3-yl)-3-[(5-chlorothien-2-yl)-sulfonyl]-1*H*-pyrrolo[2,3-*b*]pyridine, hydrochloride (4x). The title compound was prepared from 1-(1-ethylpiperi-

din-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine and 3-(5-chlorothien-2-yl)sulfonyl chloride in substantially the same manner, as described for compound **4p**. The product was obtained as a gray solid, hydrochloride salt, mp 166–167 °C. Mass spectrum (ES, $[M+H]^+$) *m/z* 410. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.34 (s, 1H), 8.59 (s, 1H), 8.45 (dd, 1H, J = 4.63 and 1.46 Hz), 8.24 (dd, 1H, J = 8.05 and 1.59 Hz), 7.75 (d, 1H, J = 4.15 Hz), 7.39 (dd, 1H, J = 8.05 and 4.76 Hz), 7.22 (d, 1H, J = 4.15 Hz), 5.25 (m, 1H), 3.68 (m, 1H), 3.51 (m, 1H), 3.12 (m, 2H), 2.88 (m, 1H), 2.17 (m, 1H), 2.07 (m, 1H), 1.94 (m, 1H), and 1.21 ppm (t, 3H, J = 7.02 Hz). Anal. ($C_{18}H_{20}ClN_3O_2S_2 \cdot 1.4HCl \cdot 0.67Et_2O$).

5.3.49. 3-[(6-Chloroimidazo[2,1-*b*][1,3]thiazol-5-yl)sulfonyl]-1-piperidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine, hydrochloride (4y). The title compound was prepared from 3-[(6-chloroimidazo[2,1-*b*][1,3]thiazol-5-yl)sulfonyl]-1-(1-ethylpiperidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine in substantially the same manner, as described for compound **4n**. The product was obtained as an off-white solid, hydrochloride salt, mp 221–222 °C. Mass spectrum (ES, $[M+H]^+$) *m/z* 422. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.05 (m, 1H), 8.82 (s, 1H), 8.42 (d, 1H, J = 4.76 Hz), 8.25 (d, 1H, J = 4.52 Hz), 8.23 (d, 1H, J = 8.06), 7.64 (d, 1H, J = 4.51 Hz), 7.36 (m, 1H), 5.14 (m, 1H), 3.48 (m, 2H), 3.40 (m, 1H), 2.85 (m, 1H), 2.19 (m, 1H), 2.06 (m, 1H), 1.95 (m, 1H), and 1.84 ppm (m, 1H). Anal. ($C_{17}H_{16}ClN_5O_2S_2 \cdot 1.5HCl$) C, H, N.

5.3.50. 3-[(6-Chloroimidazo[2,1-*b*][1,3]thiazol-5-yl)sulfonyl]-1-(1-methylpiperidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine, hydrochloride (4z). The title compound was prepared from 3-[(6-Chloroimidazo[2,1-*b*][1,3]thiazol-5-yl)sulfonyl]-1-piperidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine and formaldehyde in substantially the same manner, as described for compound **4o**. The product was obtained as a yellow solid, hydrochloride salt, mp 190-191 °C. Mass spectrum (ES, $[M+H]^+$) *m/z* 436. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.75 (s, 1H), 8.44 (dd, 1H, J = 4.64 and 1.34 Hz), 8.24 (s, 2H), 7.65 (d, 1H, J = 4.52 Hz), 7.39 (dd, 1H, J = 7.93 and 4.63 Hz), 5.20 (m, 1H), 3.65 (m, 1H), 3.49 (m, 1H), 2.90 (m, 1H), 2.79 (s, 3H), 2.18 (m, 1H), 2.05 (m, 1H), 1.90 ppm (m, 1H). Anal. ($C_{18}H_{18}ClN_5O_2S_2 \cdot 2.0HCl \cdot 0.1H_2O$) C, H, N.

5.3.51. 3-[(6-Chloroimidazo[2,1-*b*][1,3]thiazol-5-yl)sulfonyl]-1-(1-ethylpiperidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine, hydrochloride (4aa). The title compound was prepared from 1-(1-ethylpiperidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine and 3-(6-chloroimidazo[2,1-*b*][1,3]thiazol-5-yl)sulfonyl chloride in substantially the same manner, as described for compound **4p**. The product was obtained as a white solid, hydrochloride salt, mp >167 °C (dec). Mass spectrum (ES, $[M+H]^+$) *m/z* 450. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.77 (s, 1H), 8.44 (dd, 1H, J = 4.63 and 1.46 Hz), 8.23 (s, 2H), 7.65 (d, 1H, J = 4.52 Hz), 7.39 (dd, 1H, J = 7.93 and 4.63 Hz), 5.21 (m, 1H), 3.68 (m, 1H), 3.51 (m, 1H), 3.12 (m, 2H), 2.88 (m, 1H), 2.17 (m, 1H), 2.07 (m, 1H), 1.94 (m, 1H), and 1.21 ppm (t, 3H, J = 7.02 Hz). Anal. ($C_{19}H_{20}ClN_5O_2S_2 \cdot 1.5HCl \cdot 0.2H_2O$) C, H, N.

5.3.52. 3-[(6-Chloroimidazo[2,1-*b*][1,3]thiazol-5-yl)sulfonyl]-1-(1-isopropylpiperidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine, hydrochloride (4ab). The title compound was prepared from 3-[(6-chloroimidazo[2,1-*b*][1,3]thiazol-5-yl)sulfonyl]-1-piperidin-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine and acetone in substantially the same manner, as described for compound **4o**. The product was obtained as a yellow solid, hydrochloride salt, mp 176–177 °C. Mass spectrum (ES, $[M+H]^+$) *m/z* 464. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.22 (s, 1H), 8.84 (s, 1H), 8.44 (d, 1H, J = 4.63 Hz), 8.23 (s, 2H), 7.65 (d, 1H, J = 4.39 Hz), 7.36 (dd, 1H, J = 7.93 and 4.63 Hz), 5.35 (m, 1H), 3.55 (m, 4H), 2.95 (m, 1H), 2.10 (m, 4H), and 1.25 ppm (m, 6H). Anal. ($C_{20}H_{22}ClN_5O_2S_2 \cdot 2.0HCl$) C, H, N.

5.3.53. 1-Benzyl-3-chloro-pyrrolidine (6a, R = benzyl). Phosphorus oxychloride (43 mL, 460 mmol) was added to a solution of 1-benzyl-pyrrolidin-3-ol (19.8 g, 112 mmol) in toluene (200 mL). The reaction mixture was refluxed under nitrogen for 2 h. About 150 mL of solvent was evaporated, and the remaining mixture was poured into ice-water. Solid potassium carbonate was added until basic. It was extracted with ethyl acetate and washed with brine. The organic phase was dried with anhydrous magnesium sulfate, filtered, and concentrated. Drying at 80 °C in vacuo for 30 min resulted in 1-benzyl-3-chloro-pyrrolidine as a dark brown oil (18.7 g, 85.4%); ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.20–7.32 (m, 5H), 4.48–4.53 (m, 1H), 3.60 (dd, 2H, J = 20.88 Hz and 13.11 Hz), 2.91 (dd, 1H, J = 10.68 Hz and 6.15 Hz), 2.64–2.73 (m, 2H), 2.32–2.46 (m, 2H), 1.87–1.95 ppm (m, 1H).

5.3.54. Toluene-4-sulfonic acid 1-methyl-pyrrolidin-3-yl ester (6b, R = Me). *p*-Toluenesulfonyl chloride (11.5 g, 60.3 mmol) was added to a solution of 1-methyl-3-pyrrolidinol (6.1 g, 60 mmol) in methylene chloride (60 mL). Triethylamine (8.4 mL, 60 mmol) was then added to the reaction mixture. After stirring at ambient temperature for 5 h, the mixture was purified by flash chromatography using 10% methanol in chloroform. Concentrating and drying in vacuo at 60 °C for 20 min gave toluene-4-sulfonic acid 1-methyl-pyrrolidin-3-yl ester as a golden-yellow syrup (10.1 g, 66.0%); ^{1}H NMR (400 *MHz*, DMSO-d_6): δ 7.76 (dd, 2H, J = 6.61 Hz and 1.74 Hz), 7.46 (d, 2H, J = 8.01 Hz), 4.89–4.94 (m, 1H), 2.59–2.64 (m, 1H), 2.50–2.56 (m, 1H), 2.42–2.46 (m, 1H), 2.40 (s, 3H), 2.15 (s, 3H), 2.00–2.13 (m, 2H), 1.67–1.72 ppm (m, 1H).

5.3.55. Toluene-4-sulfonic acid 1-ethyl-pyrrolidin-3-yl ester (6b, R = Et). Triethylamine (3.1 mL, 22 mmol) was added to a solution of 1-ethyl-3-pyrrolidinol (2.52 g, 21.9 mmol) in methylene chloride (25 mL). *p*-Toluenesulfonyl chloride (4.21 g, 22.1 mmol) was then added to the reaction mixture. After stirring at ambient temperature for 1.5 h, a second portion of triethylamine (3.1 mL, 22 mmol) was added to the reaction mixture, and it was stirred for 1.5 h. The mixture was concentrated, and purified by flash chromatography using 100% ethyl acetate. Concentrating and drying in vacuo at 80 °C for 20 min gave toluene-4-sulfonic acid 1-ethyl-pyrrolidin-3-yl ester as a light brown-yellow oil (4.42 g, 74.9%); mass spectrum (+EI, $[M+H]^+$) *m/z*

360. ^{1}H NMR (400 *MHz*, DMSO-d_6): δ 7.75–7.78 (m, 2H), 7.45–7.47 (m, 2H), 4.89–4.94 (m, 1H), 2.58–2.68 (m, 2H), 2.43–2.45 (m, 1H), 2.40 (s, 3H), 2.32–2.35 (m, 2H), 2.12–2.17 (m, 1H), 2.00–2.07 (m, 1H), 1.64–1.71 (m, 1H), 0.93 ppm (t, 3H, J = 7.19 Hz).

5.3.56. 1-(1-Benzyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (7, R = benzyl). A mixture of 1-benzyl-3-chloro-pyrrolidine (9.2 g, 42 mmol), 7-azaindole (5.44 g, 46.0 mmol), and cesium carbonate (46.0 g, 141 mmol) in DMSO (100 mL) was heated at 80 °C under nitrogen for 16 h. After cooling to ambient temperature, the reaction mixture was poured into excess water. It was then extracted with ethyl acetate and washed with brine. The organic phase was dried with anhydrous magnesium sulfate, filtered, and concentrated. The residue was purified by flash chromatography using 10–25% *tert*-butyl methyl ether in hexane. Concentrating and drying at 80 °C for 35 min yielded 1-(1-benzyl-pyrrolidin-3-yl)-1*H*-pyrrolo-[2,3-*b*]pyridine as a yellow gum (6.9 g, 53%); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.19–8.20 (m, 1H), 7.91–7.93 (m, 1H), 7.70 (d, 1H, J = 3.60 Hz), 7.28–7.35 (m, 4H), 7.19–7.24 (m, 1H), 7.03–7.06 (m, 1H), 6.48 (d, 1H, J = 3.59 Hz), 5.42–5.48 (m, 1H), 3.61-3.69 (m, 2H), 2.94–3.00 (m, 1H), 2.70–2.80 (m, 2H), 2.40–2.45 (m, 2H), 1.90–1.97 ppm (m, 1H).

5.3.57. 1-(1-Methyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (7, R = Me). A suspension of 7-azaindole (0.428 g, 3.62 mmol), toluene-4-sulfonic acid 1-methyl-pyrrolidin-3-yl ester (0.893 g, 3.50 mmol), and cesium carbonate (2.38 g, 7.30 mmol) in DMSO (10 mL) was heated at 80 °C for 17 h. The reaction mixture was then allowed to cool to ambient temperature. It was then diluted with ethyl acetate and poured into excess water. The organic phase was washed with brine, dried with anhydrous magnesium sulfate, filtered, concentrated, and dried in vacuo at 80 °C for 20 min to give 1-(1-methyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine as a light brown gum (0.480 g, 68.1%); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.18 (dd, 1H, J = 4.64 Hz and 1.51 Hz), 7.89-7.91 (m, 1H), 7.63 (d, 1H, J = 3.60 Hz), 7.03 (dd, 1H, J = 7.77 Hz and 4.64 Hz), 6.44 (d, 1H, J = 3.59 Hz), 5.39–5.44 (m, 1H), 2.88–2.93 (m, 1H), 2.70 (d, 2H, J = 5.68 Hz), 2.32–2.43 (m, 2H), 2.28 (s, 3H), 1.86–1.93 ppm (m, 1H).

5.3.58. 1-(1-Ethyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (7, R = Et). A suspension of 7-azaindole (2.50 g, 21.2 mmol), toluene-4-sulfonic acid 1-ethyl-pyrrolidin-3-yl ester (5.6 g, 21 mmol) and cesium carbonate (15.6 g, 47.9 mmol) in DMSO (60 mL) was heated at 80 °C for 16 h. The reaction mixture was then allowed to cool to ambient temperature. It was then poured into excess water and extracted with ethyl acetate. The organic phase was washed with brine, dried with anhydrous magnesium sulfate, filtered, and concentrated. The residue was purified by flash chromatography using 75% ethyl acetate in hexane, 100% ethyl acetate, and 10% methanol in chloroform. It was concentrated and dried in vacuo at 80 °C for 20 min to give 1-(1-ethyl-pyrrolidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine as a dark yellow oil (2.51 g, 55.5%); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.19 (dd, 1H, J = 4.64 Hz and 1.51 Hz), 7.90 (dd, 1H, J = 7.77 Hz and 1.63 Hz), 7.64 (d, 1H, J = 3.59 Hz), 7.01–7.04 (m, 1H), 6.44 (d, 1H, J = 3.59 Hz), 5.38–5.44 (m, 1H), 2.91–2.96 (m, 1H), 2.73 (d, 2H, J = 5.68 Hz), 2.34–2.44 (m, 3H), 1.84–1.93 (m, 1H), 1.02 ppm (t, 3H, J = 7.19 Hz).

5.3.59. 1-(1-Ethylpiperidin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (8, R = Et). A solution of n-butyllithium (2.16 M, titrated, 124 mL) in hexane was added dropwise to a solution of *N*-(1-ethylpiperidin-3-yl)-3-methylpyridin-2-amine (14.54 g, 66.3 mmol) in THF (217 mL) while stirring at 0 °C over a period of 45 min. After the addition completed, the reaction mixture was stirred at 0 °C for 1 h, then warmed up to 20 °C and stirred at this temperature for 45 min. The reaction mixture was then re-cooled to 0 °C and stirred at 0 °C for 5 h. Distilled DMF (40.3 mL, 298 mmol) was added dropwise over a period of 5 min. The mixture was stirred at 20 °C for 3 h. then kept at −5 to 0 °C overnight. The mixture was transferred, over 1 h, into cooled 5.5 M HCl (150 mL) at such a rate that the temperature was maintained at <15 °C. The mixture was then stirred at 20 °C for 0.5 h before basified with 30% aqueous NaOH to pH 12 at <15 °C. The mixture was extracted with methylene chloride. The organic layer was separated and washed with water, aqueous ammonium chloride, water, and brine, and then evaporated to give an oil. This crude oil was purified by flash column chromatography using 10–20% methanol in methylene chloride as an eluant to provide the title compound as an oil, 7.5 g, (49% yield). Mass spectrum (ES, $[M+H]^+$) m/z 230. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.20 (dd, 1H, J = 4.63 and 1.59 Hz), 7.91 (dd, 1H, J = 7.80 and 1.59 Hz), 7.67 (d, 1H, J = 3.57 Hz), 7.03 (dd, 1H, J = 7.81 and 4.64 Hz), 6.43 (d, 1H, J = 3.54 Hz), 4.81 (m, 1H), 2.90 (m, 1H), 2.75 (m, 1H), 2.32 (m, 2H), 2.27 (m, 1H), 2.01 (m, 1H), 1.86 (m, 2H), 1.75 (m, 1H), 1.61 (m, 1H), and 0.96 ppm (t, 3H, J = 7.20 Hz).

5.3.60. *N*-(1-Ethylpiperidin-3-yl)-3-methylpyridin-2-amine (19, R = Et). A mixture of 2-amino-3-picoline (10 g, 88 mmol), 1-ethyl-3-piperidinone hydrate (14.85 g, 88 mmol), *para*-toluenesulfonic acid hydrate (3.2 g), and benzene (600 mL) was heated to reflux (oil bath temperature: 100 °C) overnight in a flask equipped with a Dean Stark Trap (water removal). Solvents were evaporated from reaction mixture to yield an oily residue. This oil was dissolved in methanol (600 mL) and sodium borohydride was added portionwise at room temperature (water bath was used to keep the reaction temperature around room temperature) over a period of 30 min. The reaction mixture was then stirred at room temperature for 2 h then quenched with water and extracted with chloroform. The organic layer was separated and washed with water, aqueous ammonium chloride, and brine. Purification by flash column chromatography using 5–15% methanol in methylene chloride as an eluant provided the title compound as an oil, 3.6 g, (36% yield). Mass spectrum (ES, $[M+H]^+$) m/z 220. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.81 (dd, 1H, J = 6.47 and 1.47 Hz), 7.16 (dd, 1H, J = 6.22 and 1.71 Hz), 7.40 (dd, 1H, J = 7.08 and 7.08 Hz), 5.26 (d, 1H, J = 5.80 Hz), 4.04 (m, 1H), 2.81 (m, 1H), 2.63 (m,

1H), 2.30 (q, 2H), 1.98 (s, 3H), 1.90 (m, 2H), 1.73 (m, 1H), 1.63 (m, 1H), 1.46 (m, 1H), 1.36 (m, 1H), and 0.95 ppm (t, 3H, $J = 7.19$ Hz).

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.bmc.2007.06.024.

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18. Binding assays were run using [3H]-LSD as the radioligand. For conditions, see: Bernotas, R.C.; Lenicek, S.E.; Antane, S.A.; Zhou, P.; Li, Y. WO patent 2003101962.
19. Cyclase assay: HeLa cells transfected with the human 5-HT_6 receptor were washed with Krebs buffer and incubated at 37 °C in Krebs buffer supplemented with 500 μM IBMX for 5 min at 37 °C. Cells were then stimulated with test compound in the concentration range 0.1–10000 nM for an additional 10 min at 37 °C. The assay was terminated with the addition of 0.5 M perchloric and intracellular cAMP levels were determined by radioimmunoassay with the cAMP Scintillation Proximity Assay System (Amersham).
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