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Convenient access to *C*-2 or *C*-5 substituted 4-azaindole derivatives

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ABSTRACT

Functionalization at *C*-2 and *C*-5 of *N*-benzenesulfonyl-4-azaindole **1** was performed by lithiation reactions and original palladium-catalyzed chemistry. It led to very useful new substituted 4-azaindole derivatives in fair to high yields.

1. Introduction

Indole is a well-known privileged core in natural products and compounds of pharmaceutical interest. Azaindoles, as indolic bioisosters are thus of prime importance to improve activity, selectivity or bioavailability of drugs.[1,2] For these reasons, access to functionalized azaindoles is a continuous synthetic challenge for organic chemists. A part of our research program is currently dedicated to the design of new antiproliferative compounds containing a 4-azaindole core, thus we were interested in finding simple and flexible methods to easily access 2- and 5-substituted-4-azaindoles type **I** (Fig. 1). It is worth noting that some 5-amino-2-aryl-4-azaindoles have been described as factor VIIa inhibitors,[3] and 2- and/or 5-(di)substituted 4-azaindoles have been cited as adenylate cyclase inhibitors,[4] CFTR modulators[5] or cysteine protease inhibitors.[6]

This paper presents methods for the *C*-2 functionalization of **1** under anionic conditions and *C*-5 arylations and aminations through an original 4-azaindolic triflate under palladium-catalyzed conditions (Fig. 1).

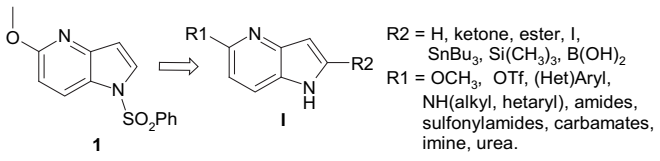


Figure 1. Targeted derivatives I.

2. Results and discussion

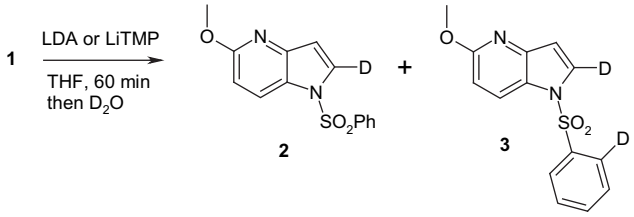
2.1. Functionalization at *C*-2

The most widely studied pathway to 2-substituted-4-azaindoles is the cyclization of 2-alkynyl-3-amino pyridine derivatives using basic conditions[7–11] or gold catalysis.[12]

For our own part, we were more interested in finding a convenient methodology to introduce various types of substituents in *C*-2 from the readily available building block **1**.[13,14]

Commonly used in indole chemistry, the functionalization of *C*-2 through *ortho* directed lithiation appeared as a straightforward method in order to react with different types of electrophiles.[15] Such a strategy has been previously and successfully used in the 5- and 7-azaindole series.[16–18] Considering the 4-aza isomer, we found only one report concerning the preparation of 2-aroyl-4-azaindole derivatives as antimitotic agents.[19] With LDA as lithiating agent, Mahboobi and co-workers reported low to satisfying yields of aroylation through four examples.

As a starting point, we first sought for an optimized lithiation procedure by using LDA or LiTMP in various amounts (Scheme 1, Table 1).



Scheme 1. Lithiation at *C*-2 of 1, for experimental details, see Table 1.

When LDA was used as a base, without additive, a minimal amount of 2.5 equiv was required in order to perform the lithiation

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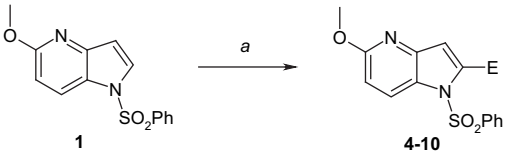
Table 1

Entry	Base	Equiv	T(°C)	1[a] (%)	2[a] (%)	3[a] (%)
1	LDA	1.5	−78	100	—	—
2	LDA	2.5	−78	30	70	—
3	LDA	1.5	−78	10–20	**80–90**	—
	TMEDA	1.4				
4	LiTMP	1.5	−30	32	68	—
5	LiTMP	1.5	−78	10–20	**80–90**	—
6	LDA	3.5	−78	—	70	30
7	LiTMP	3.5	−78	—	70	30

[a] Estimated by ^{1}H NMR after quenching with D_2O.

in an estimated 70% yield. Above 3.0 equiv, a double lithiation occurred and **3** was identified as a by-product after D_2O quenching. Best conditions were obtained with a mixture of LDA (1.5 equiv) and lithium chelator TMEDA (1.4 equiv) at −78 °C for 1 h (entry 3). In such conditions, monoanion was selectively formed in an estimated 80–90% yield. LiTMP proved to be a suitable base as well, as far as the lithiation is conducted at −78 °C with 1.5 or 2.5 equiv (Entry 5).

With these best conditions, we evaluated the reactivity of **1** toward different types of electrophiles (Scheme 2). First, in order to choose between both lithiation procedures (LDA/TMEDA or LiTMP), we performed the functionalization at *C*-2 with representative electrophilic partners (Table 2, Entries 1–6) ,i.e., an acylchloride, an aldehyde and iodine.



Scheme 2. Reagents and conditions. (a) (i) LDA/TMEDA (1.5/1.4 equiv) or LiTMP (1.5 equiv), THF, −78 °C, 1 h. (ii) E^+ (2.0 equiv), THF, −78 °C, 3 h then rt, 18 h. (iii) aqueous saturated NH_4Cl solution.

Table 2
Reactivity of the 2-lithiated derivative

Entry	Method[a]	E^+	E	Product	Yield[b] (%)
1	A	PhCOCl	PhCO	**4**	57
2	B	PhCOCl	PhCO	**4**	51
3	A	4-Br-C_6H_4CHO	4-Br-C_6H_4CHOH	**5**	90
4	B	4-Br-C_6H_4CHO	4-Br-C_6H_4CHOH	**5**	76
5	A	I_2	I	**6**	74
6	B	I_2	I	**6**	63
7	A	$ClCO_2CH_3$	CO_2CH_3	**7**	62
8	A	$(CH_3)_3SiCl$	$Si(CH_3)_3$	**8**	85
9	A	$ClSnBu_3$	$SnBu_3$	**9**	83
10	A	$B(OCH_3)_3$	$B(OH)_2$	**10**	95

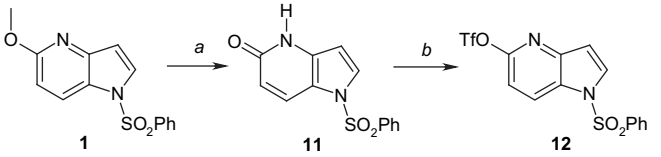
[a] Method A: LDA/TMEDA (1.5 /1.4 equiv), THF, −78 °C, 1 h then E^+; Method B: LiTMP (1.5 equiv), THF, −78 °C, 1 h, then E^+.
[b] Isolated yield.

Yields obtained with LDA/TMEDA as a base are better or slightly better than with LiTMP (compare entries 1, 3, 5 with, respectively, entries 2, 4, 6), plus a commercial solution of LDA (2 M in THF/heptane/ethylbenzene) can be used, which renders the cryogenic procedure more convenient.

Various electrophiles were next engaged in order to obtain representative *C*-2 functionalized 4-azaindoles. Reactions with benzoyl chloride and methylchloroformate are less efficient than bromobenzaldehyde as electrophiles (entries 1, 3, and 7). Silylation, stannylation or boronylation (entries 8–10) are carried out efficiently, with comparable yields. Interestingly, the new compounds **6**, **9**, and **10** are also suitable as building blocks for palladium cross-couplings.

2.2. Functionalization at *C*-5

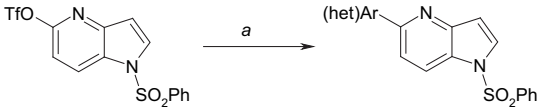
The next step of our study was to replace the methoxyl group at *C*-5 of **1** by an aromatic or an amino functionality. *N*-benzenesulfonyl-5-methoxy-4-azaindole **1** could be converted into the triflate **12** after two steps (Scheme 3).



Scheme 3. Reagents and conditions. (a) NaI (1.6 equiv), TMSCl (1.6 equiv), CH_3CN, reflux, 3.5 h, 88%, (b) Tf_2O (1.1 equiv), DIPEA (1.3 equiv), CH_2Cl_2, 0 °C, 25 min, 99%.

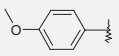
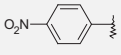
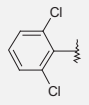
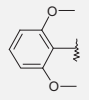
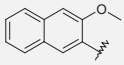
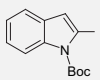
Removal of the methyl ether group was achieved after 3 h with in situ prepared TMSI (1.6 equiv) in a 88% yield, the use of classical Lewis acid conditions ($AlCl_3$) was efficient as well (83% yield) but longer (12 h).[20] Reaction of the resulting pyridinone with triflic anhydride led quantitatively to derivative triflate **12**. Then, compound **12** was used as starting material to introduce *C*–*C* (Suzuki type couplings) or *C*–*N* (Buchwald type couplings) bonds at *C*-5.

Suzuki type couplings were performed from **12** by using only 1% of $Pd(PPh_3)_4$ and a solution of aqueous potassium carbonate (3.0 equiv) in a refluxing mixture of toluene and ethanol (2/1) with various (het)aryl boronic acids (Scheme 4, Table 3).



Scheme 4. Reagents and conditions. (*a*) (Het)ArB$(OH)_2$ (1.5 equiv), $Pd(PPh_3)_4$ (1.0 mol %), aq K_2CO_3 1 M (3.0 equiv), Toluene/EtOH (2/1), reflux.

Table 3
Suzuki cross-coupling reactions from **12**

Entry	(Het)Ar	Reaction time (h)	Product	Yield[a] (%)
1		2	**13**	95
2		2	**14**	70
3		2	**15**	97
4		2	**16**	78
5		1.5	**17**	91
6		5	**18**	17
7		2.5	**19**	88
8		4	**20**	92
9		6	**21**	69

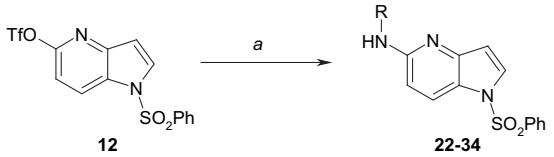
[a] Isolated yields.

Whatever the nature of the boronic derivative (aromatic or heteroaromatic) or the substitution of the ring, reactions proceeded smoothly within a few hours in good to excellent yields. Except for the dichlorophenyl derivative **18** (entry 6), after 5 h, the reaction did not evolve any more.

It should be noted that potassium *N*-Bocindole trifluoroborate[21] led successfully to **21** in a good 69% yield.

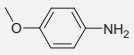
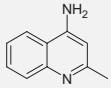
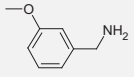
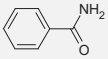
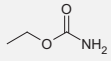
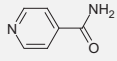
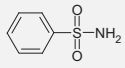
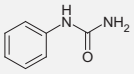
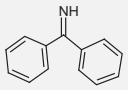
The next issue of this work was the amination at *C*-5 position of triflate **12**. First assays showed that a direct SN_{Ar} was inefficient. We then turned our attention to the Buchwald–Hartwig palladium-catalyzed cross-coupling, which has become a common method to perform aminations in heterocyclic chemistry.[22]

For this purpose, we found that Pd_2dba_3 3%/Xantphos 4.5% with cesium carbonate in refluxing toluene were the best experimental conditions. Various amines (aliphatic, aromatic, cyclic or acyclic), and amides, as well as a urea, a carbamate and a sulfonamide derivative were chosen to increase diversity in position *C*-5 and assess the scope and limitations of the strategy (Scheme 5, Table 4).



Scheme 5. Reagents and conditions. (*a*) R–NH_2 (1.2 equiv), Pd_2dba_3 (0.03 equiv), Xantphos (0.045 equiv), Cs_2CO_3 (1.5 equiv), toluene, reflux.

Table 4
Buchwald–Hartwig cross-coupling reactions from **12**

Entry	R-NH_2	Reaction time (h)	Product	Yield[a] (%)
1		1	**22**	98
2		3	**23**	91
3		2.5	**24**	80
4		7	**25**	23
5		7	**26**	25
6		3	**27**	94
7		1.5	**28**	99
8		6.5	**29**	79
9		2.5	**30**	72
10		24	**31**	55[b]
11		24	**32**	0
12		1	**33**	77
13		5.5	**34**	66

[a] Isolated yield.
[b] Dioxane was used in place of toluene, the mixture was stirred at 80 °C.

Nearly quantitative yields are obtained with (Het)aromatic primary amines (entries 1, 2) and sole a secondary aliphatic cyclic amine gave a satisfactory yield (entries 3–5). Indeed, if morpholine was a good substrate, we found that primary aliphatic or benzylic amines gave poor yields of cross-coupled products. In such cases, increasing the quantity of amines (up to 4.0 equiv), lowering the reaction temperature (to 80 °C), changing the solvent to dioxane or the palladium source (to $Pd(OAc)_2$), always resulted in multi spots TLC and low yields.

Despite a poor stability on column chromatography, products **33** and **34** resulting from the coupling of phenylurea and benzophenone imine, respectively, were obtained in good yields.

Benzamide or acetamide gave the desired compounds **27** and **28** in very high yields; piperidin-2-one and carbamic acid ethyl ester gave satisfactory results (entries 6–9).

A 37% yield was obtained from isonicotinamide in toluene. Shifting the solvent for dioxane resulted in a slightly better yield (55%, entry 10). Besides, all assays with acidic phenylsulfonylamide failed (entry 11). Fortunately, phenylurea and benzhydrylidenamine gave good yields (entries 12, 13).

3. Summary

In conclusion, we achieved a regioselective *C*-2 lithiation of *N*-benzenesulfonyl-5-methoxy-4-azaindole **1** using LDA/TMEDA at low temperature. Then, various sets of electrophiles could be reacted in moderate to high yields. Independently, a wide variety of (het)aryl boronic acids have been successfully cross-coupled in position 5 of the key triflated derivative **12**. Through Buchwald–Hartwig type couplings, amino functionalities could also been introduced α to the pyridinic nitrogen, generally in good yields. With these two methodologies, we focus our efforts toward the design and synthesis of more complex azaindolic structures for biological evaluation.

4. Experimental details

4.1. General

All reagents were purchased from Sigma–Aldrich, Acros Organics and Alfa Aesar. We used distilled DIPA, TMP and TMEDA. LDA 2 M in THF/heptane/ethylbenzene and *n*-BuLi 1.6 M in hexane were purchased from Sigma–Aldrich. Melting points are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance DP×250 spectrometer (^{1}H, 250.19 MHz; ^{13}C, 62.89 MHz) or a Bruker Avance II 400 spectrometer (^{1}H, 400 MHz; ^{13}C, 100 MHz) using tetramethylsilane as the internal standard. Chemical shifts are reported in parts per million (ppm, δ units). Coupling constants are reported in Hertz (Hz). Splitting patterns are designated as s: singlet, bs: broad singlet, d: doublet, dd: doublet of doublets, t: triplet, ddd: doublet of doublets of doublets, q: quadruplet, quint: quintuplet, and m: multiplet. IR absorption spectra were recorded on a Nicolet iS10 smart iTR apparatus and values were reported in cm^{-1}. MS (Mass Spectra) were recorded on Perkin–Elmer SCIEX API 300 using ion spray methodology. High-resolution mass spectra (HRMS) were recorded with a TOF spectrometer in the electrospray ionization (ESI) mode or with a Finnigan MAT 95 XL spectrometer in the chemical ionization (Ci) mode at the Regional Center of Physical Measurement, Blaise Pascal University. Column chromatography was carried out using silica gel 60 (spherical, neutral, 40–63 μM, Merck). Thinlayer chromatography was carried out on Merck silica gel 60 F_{254} precoated plates. Visualization was made with UV light.

*4.1.1. 1-Benzenesulfonyl-5-methoxy-1H-pyrrolo[3,2–b] pyridine (**1**)*[23]. A solution of 5-methoxy-1*H*-pyrrolo[3,2–*b*]pyridine[13,14] (3.0 g, 20.3 mmol) in dry dichloromethane (50 mL) was cooled to

0 °C under an atmosphere of argon. Sodium hydroxide (2.43 g, 60.8 mmol) and benzyltriethylammonium chloride (91 mg, 0.40 mmol) were added successively. The mixture was stirred at 0 °C for 10 min, followed by the slow addition of benzenesulfonyl chloride (3.2 mL, 25.3 mmol). After 15 min stirring at 0 °C then 2 h 30 min at rt, the mixture was poured into H_2O (40 mL) and extracted with CH_2Cl_2 (3×40 mL). The combined organic layers were dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure. The crude product was purified by flash chromatography (petroleum ether/EtOAc 7/3) to afford **1** as a white solid (5.7 g, 98%). Mp 128 °C; R_f (petroleum ether/EtOAc 7/3) 0.49; IR (ATR diamond, ν, cm^{-1}) 1580, 1477, 1399, 1256, 1131, 723; ^1H NMR (250 MHz, $CDCl_3$) δ 3.94 (s, 3H, CH_3), 6.70 (d, 1H, H-6, $J_{6,7}$=8.7 Hz), 6.72 (d, 1H, H-3, $J_{3,2}$=3.9 Hz), 7.44 (dd, 2H, 2×CH_{Ar}, J=J'=7.8 Hz), 7.55 (dd, 1H, CH_{Ar}, J=J'=7.8 Hz), 7.66 (d, 1H, H-2, $J_{2,3}$=3.9 Hz), 7.83 (d, 2H, 2×CH_{Ar}, J=7.8 Hz), 8.15 (d, 1H, H-7, $J_{7,6}$=8.7 Hz); ^{13}C NMR (100.61 MHz, $CDCl_3$) δ 53.4 (CH_3), 107.8 (C-6), 109.7 (C-3), 123.9 (C-7+Cq), 126.5 (2×CH_{Ar}), 128.3 (C-2), 129.2 (2×CH_{Ar}), 133.9 (CH_{Ar}), 137.8 (Cq), 145.7 (Cq), 161.9 (Cq); MS (IS) m/z 289.0 $[M+H]^+$.

4.2. General procedures for the preparation of the 2-lithiated derivative from 1

4.2.1. Method A. A mixture of *N*,*N*,*N*′,*N*′-tetramethyl ethylenediamine (0.14 mL, 0.97 mmol) and **1** (200 mg, 0.69 mmol) in dry THF (7 mL) was cooled to −78 °C under an atmosphere of argon. After 20 min stirring at −78 °C, a commercial solution of LDA (2 M in THF/heptane/ethylbenzene, 0.52 mL, 1.03 mmol) was added slowly. The mixture was stirred at −78 °C for 60 min, followed by addition of a solution of the electrophile (1.38 mmol, 2.0 equiv) in dry THF (2 mL). The mixture was stirred at −78 °C for at least 3 h before being warmed to room temperature overnight. The reaction mixture was quenched with a saturated solution of NH_4Cl (10 mL) and extracted with EtOAc (3×15 mL). The combined organic layers were dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure. The crude product was purified by flash chromatography.

4.2.2. Method B. 2,2,6,6-Tetramethylpiperidine (0.19 mL, 1.10 mmol, 1.6 equiv) in dry THF (5 mL) was cooled to −78 °C under an atmosphere of argon then treated with a solution of *n*-BuLi (1.6 M in hexane, 0.65 mL, 1.03 mmol). The mixture was stirred at −78 °C for 20 min, then a solution of **1** (200 mg, 0.69 mmol) in dry THF (7 mL) was added dropwise. The mixture was stirred at −78 °C for 60 min, followed by the slow addition of a solution of the electrophile (1.38 mmol) in dry THF (2 mL). The mixture was stirred at −78 °C for at least 3 h before being warmed to room temperature overnight. The reaction mixture was quenched with a saturated solution of NH_4Cl (10 mL) and extracted with EtOAc (3×15 mL). The combined organic layers were dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure. The crude product was purified by flash chromatography.

*4.2.3. (1-Benzenesulfonyl-5-methoxy-1H-pyrrolo[3,2–b] pyridin-2-yl)-phenyl-methanone (**4**).* The reactions were carried out as described in general procedures A and B using benzoyl chloride as the electrophile (0.16 mL, 1.38 mmol). Purification by flash chromatography (petroleum ether/EtOAc 9/1) yielded **4** as a yellow solid (139 mg, 5, method B or 155 mg, 57%, method A). Mp 184 °C; R_f (petroleum ether/EtOAc 7/3) 0.51; IR (ATR diamond, ν, cm^{-1}) 1660, 1403, 1241, 1182, 723; ^1H NMR (250 MHz, $CDCl_3$) δ 3.96 (s, 3H, CH_3), 6.85 (d, 1H, H-6, $J_{6,7}$=8.0 Hz), 6.96 (s, 1H, H-3), 7.48–7.54 (m, 4H, 4×H_{Ar}), 7.60–7.65 (m, 2H, 2×H_{Ar}), 7.97 (d, 2H, 2×H_{Ar}, J=8.0 Hz), 8.04 (d, 2H, 2×H_{Ar}, J=8.0 Hz), 8.33 (d, 1H, H-7, $J_{7,6}$=8.0 Hz); ^{13}C NMR (100.61 MHz, $CDCl_3$) δ 53.7 (CH_3), 110.6 (C-6), 116.4 (C-3), 125.8 (C-7), 127.4 (Cq), 127.5 (2×CH_{Ar}), 128.6 (2×CH_{Ar}), 129.1 (2×CH_{Ar}), 130.1 (2×CH_{Ar}), 133.8 (CH_{Ar}), 134.2 (CH_{Ar}), 137.1 (Cq), 138.2 (Cq), 139.2 (Cq), 143.4 (Cq), 162.6 (Cq), 187.2 (Cq); HRMS (TOF ES^+) m/z calculated for $C_{21}H_{17}N_2O_4S$ (MH^+) 393.0909; found 393.0918.

*4.2.4. (1-Benzenesulfonyl-5-methoxy-1H-pyrrolo[3,2–b]pyridin-2-yl)-(4-bromo-phenyl)-methanol (**5**).* The reactions were carried out as described in general procedures A and B using 4-bromo-benzaldehyde (257 mg, 1.38 mmol) as the electrophile. Purification by flash chromatography (petroleum ether/EtOAc 7/3) yielded **5** as a colorless oil (250 mg, 76%, procedure B or 296 mg, 90%, procedure A). R_f (petroleum ether/EtOAc 7/3) 0.36; IR (ATR diamond, ν, cm^{-1}) 3250, 1586, 1480, 1162, 724; ^1H NMR (250 MHz, $CDCl_3$) δ 3.73 (d, 1H, OH, J=3.0 Hz), 3.89 (s, 3H, CH_3), 6.32–6.33 (m, 2H, H-3+CH_{Ar}), 6.68 (d, 1H, H-6, $J_{6,7}$=9.0 Hz), 7.22 (d, 2H, 2×H_{Ar}, J=8.5 Hz), 7.36–7.44 (m, 4H, 4×H_{Ar}), 7.55 (dd, 1H, H_{Ar}, J=J'=7.5 Hz), 7.65 (d, 2H, 2×H_{Ar}, J=7.5 Hz), 8.24 (d, 1H, H-7, $J_{7,6}$=9.0 Hz); ^{13}C NMR (100.61 MHz, $CDCl_3$) δ 53.5 (CH_3), 68.5 (CHOH), 108.3 (C-6), 112.4 (C-3), 121.9 (Cq), 125.3 (C-7), 126.1 (2×CH_{Ar}), 126.4 (Cq), 128.7 (2×CH_{Ar}), 129.3 (2×CH_{Ar}), 131.4 (2×CH_{Ar}), 134.1 (CH_{Ar}), 138.1 (Cq), 139.4 (Cq), 143.9 (Cq), 145.6 (Cq), 162.2 (Cq); HRMS (TOF ES^+) m/z calculated for $C_{21}H_{18}BrN_2O_4S$ (MH^+) 473.0171; found 473.0164.

*4.2.5. 1-Benzenesulfonyl-2-iodo-5-methoxy-1H-pyrrolo [3,2–b]pyridine (**6**).* The reactions were carried out as described in general procedures A and B using iodine as the electrophile (353 mg, 1.38 mmol). Purification by flash chromatography (petroleum ether/EtOAc 9/1) yielded **6** as a yellow solid (181 mg, 63%, procedure B or 212 mg, 74%, procedure A). Mp 142 °C; R_f (petroleum ether/EtOAc 7/3) 0.54; IR (ATR diamond, ν, cm^{-1}) 1574, 1452, 1395, 1373, 1024, 809, 723; ^1H NMR (250 MHz, $CDCl_3$) δ 3.94 (s, 3H, CH_3), 6.68 (d, 1H, H-6, $J_{6,7}$=7.5 Hz), 7.04 (s, 1H, H-3), 7.46 (dd, 2H, 2×H_{Ar}, J=J'=7.5 Hz), 7.59 (dd, 1H, H_{Ar}, J=J'=7.5 Hz), 7.86 (d, 2H, 2×H_{Ar}, J=7.5 Hz), 8.40 (d, 1H, H-7, $J_{7,6}$=7.5 Hz); ^{13}C NMR (100.61 MHz, $CDCl_3$) δ 53.6 (CH_3), 78.3 (Cq), 108.0 (C-6), 124.5 (C-3), 125.7 (C-7), 127.2 (2×CH_{Ar}), 128.2 (Cq), 129.2 (2×CH_{Ar}), 134.3 (CH_{Ar}), 137.8 (Cq), 146.2 (Cq), 162.0 (Cq); HRMS (TOF ES^+) m/z calculated for $C_{14}H_{12}IN_2O_3S$ (MH^+) 414.9613; found 414.9626.

*4.2.6. 1-Benzenesulfonyl-5-methoxy-1H-pyrrolo[3,2–b]pyri dine-2-carboxylic acid methyl ester (**7**).* The reaction was carried out as described in general procedure A using methylchloroformate (0.107 mL, 1.38 mmol) as the electrophile. Purification by flash chromatography (petroleum ether/EtOAc 9/1) yielded **7** as a colorless solid (150 mg, 62%); MP 156 °C; R_f (petroleum ether/EtOAc 8/2) 0.46; IR (ATR diamond, ν, cm^{-1}) 2942, 2361, 1730, 1535, 1354, 1166, 1123, 725; ^1H NMR (250 MHz, $CDCl_3$) δ 3.92 (s, 3H, CH_3), 3.96 (s, 3H, CH_3), 6.83 (d, 1H, H-6, $J_{6,7}$=9.0 Hz), 7.20 (s, 1H, H-3), 7.50 (dd, 2H, 2×H_{Ar}, J=J'=7.5 Hz), 7.61 (dd, 1H, H_{Ar}, J=J'=7.5 Hz), 7.99 (d, 2H, 2×H_{Ar}, J=7.5 Hz), 8.34 (d, 1H, H-7, $J_{7,6}$=9.0 Hz); ^{13}C NMR (100.61 MHz, $CDCl_3$) δ 52.8 (CH_3), 53.6 (CH_3), 110.8 (C-6), 116.7 (C-3), 126.0 (C-7), 127.2 (2×CH_{Ar}), 128.1 (Cq), 129.0 (2×CH_{Ar}), 132.6 (Cq), 134.0 (CH_{Ar}), 138.5 (Cq), 142.7 (Cq), 161.0 (Cq), 162.4 (Cq); HRMS (TOF ES^+) m/z calculated for $C_{16}H_{15}N_2O_5S$ (MH^+) 347.0702; found 347.0704.

*4.2.7. 1-Benzenesulfonyl-5-methoxy-2-trimethylsilanyl-1H-pyrrolo[3,2–b]pyridine (**8**).* The reaction was carried out as described in general procedure A using trimethylsilyl chloride (0.175 mL, 1.38 mmol) as the electrophile. Purification by flash chromatography (petroleum ether/EtOAc 9/1) yielded **8** as a colorless solid (212 mg, 85%). Mp 126 °C; R_f (petroleum ether/EtOAc 8/2) 0.56; IR (ATR diamond, ν, cm^{-1}) 2950, 1588, 1402, 1260, 1162, 1030, 845, 723; ^1H NMR (250 MHz, $CDCl_3$) δ 0.44 (s, 9H, 3×CH_3), 3.92 (s, 3H, CH_3), 6.62 (d, 1H, H-6, $J_{6,7}$=9.0 Hz), 7.04 (s, 1H, H-3), 7.36 (dd, 2H, 2×H_{Ar}, J=J'=7.5 Hz), 7.49 (dd, 1H, H_{Ar}, J=J'=7.5 Hz), 7.60 (d, 2H, 2×H_{Ar}, J=7.5 Hz), 8.05 (d, 1H, H-7, $J_{7,6}$=9.0 Hz); ^{13}C NMR (100.61 MHz, $CDCl_3$) δ 0.3 (3×CH_3), 53.5 (CH_3), 108.2 (C-6), 121.9 (C-3), 124.6 (C-7), 126.0 (2×CH_{Ar}), 128.0 (Cq), 129.1 (2×CH_{Ar}), 133.6

(CH_{Ar}), 139.1 (Cq), 145.8 (2×Cq), 162.0 (Cq); HRMS (TOF ES$^+$) *m*/*z* calculated for $C_{17}H_{21}N_2O_3SSi$ (MH^+) 361.1042; found 361.1061.

*4.2.8. 1-Benzenesulfonyl-5-methoxy-2-tributylstannanyl-1H-pyrrolo[3,2–b]pyridine (**9**).* The reaction was carried out as described in general procedure A using tributyltin chloride (0.4 mL, 1.38 mmol) as the electrophile. Purification by flash chromatography (petroleum ether/EtOAc 9/1) yielded **9** as a colorless oil (332 mg, 83%). R_f (petroleum ether/EtOAc 8/2) 0.73; IR (ATR diamond, ν, cm^{-1}) 2954, 2913, 2843, 1587, 1361, 1258, 1398, 1160, 815, 724; ^1H NMR (250 MHz, $CDCl_3$) δ 0.437 (t, 9H, 3×CH_3, J=7.5 Hz), 1.15–1.41 (m, 12H, 6×CH_2), 1.50–1.60 (m, 6H, 3×CH_2), 3.95 (s, 3H, CH_3), 6.57 (d, 1H, H-6, $J_{6,7}$=9.0 Hz), 6,92 (s, 1H, H-3), 7.39 (dd, 2H, 2×H_{Ar}, J=J'=7.5 Hz), 7.51 (dd, 1H, H_{Ar}, J=J'=7.5 Hz), 7.59 (d, 2H, 2×H_{Ar}, J=7.5 Hz), 7.99 (d, 1H, H-7, $J_{7,6}$=9.0 Hz); ^{13}C NMR (100.61 MHz, $CDCl_3$) δ 11.8 (3×CH_3), 13.6 (3×CH_2), 27.3 (3×CH_2), 28.9 (3×CH_2), 53.4 (CH_3), 106.9 (C-6), 120.8 (C-3), 123.9 (C-7), 126.0 (2×CH_{Ar}), 127.7 (Cq), 129.1 (2×CH_{Ar}), 133.5 (CH_{Ar}), 139.2 (Cq), 147.0 (Cq), 147.1 (Cq), 161.8 (Cq); HRMS (TOF ES$^+$) *m*/*z* calculated for (MH^+) $C_{26}H_{39}N_2O_3SSn$: 519.1702; found 519.1700.

*4.2.9. 1-Benzenesulfonyl-5-methoxy-1H-pyrrolo[3,2–b]pyri dine-2-boronic acid (**10**).* The reaction was carried out as described in general procedure A using trimethyl borate (0.155 mL, 1.38 mmol) as the electrophile. Product **10** was obtained after evaporation of the organic phase, and did not need further purification (219 mg, 95%). Mp 176 °C; R_f (EtOAc) 0.0; IR (ATR diamond, ν, cm^{-1}) 3101, 2921, 2357, 1736, 1637, 1347, 1139, 951, 725; ^1H NMR (250 MHz, DMSO-d_6) δ 3.87 (s, 3H, CH_3), 6.53 (s, 1H, H-3), 6.68 (d, 1H, H-6, $J_{6,7}$=9.0 Hz), 7.50 (dd, 2H, 2×H_{Ar}, J=J'=7.5 Hz), 7.60 (dd, 1H, H_{Ar}, J=J'=7.5 Hz), 8.02 (d, 2H, 2×H_{Ar}, J=7.5 Hz), 8.04 (d, 1H, H-7, $J_{7,6}$=9.0 Hz); ^{13}C NMR (100.61 MHz, DMSO-d_6) δ 53.8 (CH_3), 104.1 (C-6), 112.9 (C-3), 125.8 (C-7), 126.1 (Cq), 126.7 (2×CH_{Ar}), 129.0 (2×CH_{Ar}), 133.5 (CH_{Ar}), 138.9 (2×Cq), 144.9 (Cq), 160.1 (Cq); HRMS (TOF ES$^+$) *m*/*z* calculated for $C_{14}H_{14}BN_2O_5S$ (MH^+) 333.0716; found 333.0703.

4.3. General procedures for the functionalization at *C*-5

4.3.1. Method C: Suzuki–Miyaura cross-coupling reactions. A solution of trifluoromethanesulfonic acid 1-benzenesulfonyl-1*H*-pyrrolo[3,2-*b*]pyridin-5-yl ester (**12**) (100 mg, 0.25 mmol), boronic acid (0.37 mmol) and an aqueous solution of K_2CO_3 1 M (0.74 mL, 0.74 mmol) in a mixture of toluene (5 mL) and EtOH (3 mL) was degassed by argon bubbling for 30 min. $Pd(PPh_3)_4$ (3.0 mg, 0.0025 mmol) was added and the mixture was immediately plunged in a pre-heated oil bath and refluxed for the indicated time. The solvents were removed under reduced pressure followed by the addition of H_2O (3 mL). The crude material was extracted with EtOAc (3×5 mL). The combined organic layers were washed with brine (5 mL) then dried over $MgSO_4$ and filtered. The solvents were removed under reduced pressure and the residue was purified by flash chromatography.

4.3.2. Method D: Buchwald cross-coupling reactions. A solution of **12** (100 mg, 0.25 mmol), amine (0.29 mmol), Cs_2CO_3 (120 mg, 0.37 mmol) and Xantphos (6.4 mg, 0.045 equiv) in toluene (7 mL) was degassed by argon bubbling for 30 min. Pd_2dba_3 (7.0 mg, 0.00738 mmol) was added and the mixture was immediately plunged in a pre-heated oil bath and refluxed for the indicated time. The mixture was cooled to room temperature and toluene was removed under reduced. The residue was purified by flash chromatography.

*4.3.3. 1-Benzenesulfonyl-1,4-dihydro-pyrrolo[3,2–b]pyri dine-5-one (**11**).*[23] To a solution of **1** (1.00 g, 3.47 mmol) in CH_3CN (40 mL) at 0 °C, was added sodium iodide (832 mg, 5.55 mmol) and trimethylsilyl chloride (0.70 mL, 5.55 mmol). The mixture was refluxed for 3.5 h then cooled to 0 °C. The reaction was stopped by addition of MeOH (40 mL). The solvents were removed under vacuum and the residue was purified by flash chromatography (CH_2Cl_2/MeOH 95/5) to afford **11** as a brown solid (838 mg, 88%). Mp 223 °C; R_f (EtOAc) 0.16; IR (ATR diamond, ν, cm^{-1}) 3653, 1654, 1148, 723; ^1H NMR (250 MHz, $CDCl_3$) δ 6.48 (d, 1H, H-6, $J_{6,7}$=8.0 Hz), 6.49 (d, 1H, H-3, $J_{3,2}$=4.0 Hz), 7.48–7.52 (m, 3H, H-2, 2×H_{Ar}), 7.61 (dd, 1H, H_{Ar}, J=J'=8.0 Hz), 7.84 (d, 2H, 2×H_{Ar}, J=8.0 Hz), 8.11 (d, 1H, H-7, $J_{7,6}$=8.0 Hz), 13.56 (bs, 1H, NH); ^{13}C NMR (100.61 MHz, $CDCl_3$) δ 103.2 (CH_{Ar}), 115.7 (CH_{Ar}), 118.6 (Cq), 126.7 (2×CH_{Ar}), 127.6 (C-2), 128.8 (C-7), 129.6 (2×CH_{Ar}), 134.4 (CH_{Ar}), 135.7 (Cq), 137.8 (Cq), 164.6 (Cq); MS (IS) *m*/*z* 275.0 $[M+H]^+$.

*4.3.4. Trifluoro-methanesulfonic acid 1-benzenesulfonyl-1H-pyrrolo[3,2–b]pyridin-5-yl ester (**12**).* A solution of **11** (1.80 g, 6.56 mmol) in CH_2Cl_2 (40 mL) was cooled to 0 °C. Diisopropylethyl amine (1.5 mL, 8.53 mmol) was added and the mixture was stirred at 0 °C for 10 min. Triflic anhydride (1.2 mL, 7.22 mmol) was added dropwise then the reaction was stirred at 0 °C for 25 min. The reaction was stopped by addition of a saturated aqueous solution of $NaHCO_3$ (30 mL). The crude material was extracted with CH_2Cl_2 (3×40 mL). The combined organic layers were washed with brine (40 mL) then dried over $MgSO_4$ and filtered. The solvents were removed under reduced pressure and the residue was purified by flash chromatography (petroleum ether/EtOAc 8/2) to yield **12** as a yellow oil (3.00 g, 99%). R_f (petroleum ether/EtOAc 7/3) 0.56; IR (ATR diamond, ν, cm^{-1}) 1603, 1562, 1404, 1384, 1211, 1128, 867, 724; ^1H NMR (250 MHz, $CDCl_3$) δ 6.86 (d, 1H, H-3, $J_{3,2}$=4.0 Hz), 7.12 (d, 1H, H-6, $J_{6,7}$=9.0 Hz), 7.51 (dd, 2H, 2×H_{Ar}, J=J'=7.5 Hz), 7.63 (dd, 1H, H_{Ar}, J=J'=7.5 Hz), 7.88–7.92 (m, 3H, 2×H_{Ar}, H-2), 8.43 (d, 1H, H-7, $J_{7,6}$=9.0 Hz); ^{13}C NMR (100.61 MHz, $CDCl_3$) δ 109.5 (C-3), 110.4 (C-6), 118.6 (q, CF_3, J=1280 Hz), 125.0 (C-7), 126.8 (2×CH_{Ar}), 127.8 (Cq), 129.7 (2×CH_{Ar}), 131.5 (C-2), 134.8 (CH_{Ar}), 137.5 (Cq), 146.7 (Cq), 152.4 (Cq); HRMS (TOF ES$^+$) *m*/*z* calculated for $C_{14}H_{10}F_3N_2O_5S_2$ (MH^+) 406.9983; found 406.9972.

*4.3.5. 1-Benzenesulfonyl-5-(4-methoxy-phenyl)-1H-pyrrolo [3,2–b]pyridine (**13**).* The reaction was carried out as described in general procedure C using the 4-methoxyphenylboronic acid (56 mg, 0.37 mmol). The mixture was refluxed for 2 h. The residue was purified by flash chromatography (petroleum ether/EtOAc 8/2) to afford **13** as a brown oil (85 mg, 95%). R_f (petroleum ether/EtOAc 7/3) 0.27; IR (ATR diamond, ν, cm^{-1}) 2954, 1587, 1403, 1365, 1248, 1128, 815, 724; ^1H NMR (250 MHz, $CDCl_3$) δ 3.84 (s, 3H, CH_3), 6.91 (d, 1H, H-3, $J_{3,2}$=3.7 Hz), 6.98 (d, 2H, 2×H_{Ar}, J=9.0 Hz), 7.45 (dd, 2H, 2×H_{Ar}, J=J'=7.5 Hz), 7.55 (dd, 1H, H_{Ar}, J=J'=7.5 Hz), 7.62 (d, 1H, H-6, $J_{6,7}$=8.8 Hz), 7.77 (d, 1H, H-2, $J_{2,3}$=3.7 Hz), 7.88 (d, 2H, 2×H_{Ar}, J=7.5 Hz), 7.93 (d, 2H, 2×H_{Ar}, J=9.0 Hz), 8.28 (d, 1H, H-7, $J_{7,6}$=8.8 Hz); ^{13}C NMR (100.61 MHz, $CDCl_3$) δ 55.3 (CH_3), 110.7 (C-3), 114.1 (2×CH_{Ar}), 116.2 (C-6), 121.4 (C-7), 126.7 (2×CH_{Ar}), 127.1 (Cq), 128.3 (2×CH_{Ar}), 129.4 (2×CH_{Ar}), 129.6 (C-2), 132.1 (Cq), 134.2 (CH_{Ar}), 137.9 (Cq), 148.8 (Cq), 154.4 (Cq), 160.3 (Cq); HRMS (TOF ES$^+$) *m*/*z* calculated for $C_{20}H_{17}N_2O_3S$ (MH^+) 365.0960; found 365.0968.

*4.3.6. 1-Benzenesulfonyl-5-(2-methoxy-phenyl)-1H-pyrrolo[3,2–b]pyridine (**14**).* The reaction was carried out as described in general procedure C using the 2-methoxyphenylboronic acid (56 mg, 0.37 mmol). The mixture was refluxed for 2 h. The residue was purified by flash chromatography (petroleum ether/EtOAc 7/3) to afford **14** as a white solid (62.5 mg, 70%). Mp 134 °C; R_f (petroleum ether/EtOAc 6/4) 0.37; IR (ATR diamond, ν, cm^{-1}) 3146, 3060, 2925, 2852, 1375, 1128, 733; ^1H NMR (250 MHz, $CDCl_3$) δ 3.83 (s, 3H, CH_3), 6.93 (d, 1H, H-3, $J_{3,2}$=4.0 Hz), 7.0 (d, 1H, H_{Ar}, J=7.6 Hz), 7.07 (dd, 1H, H_{Ar}, J=J'=7.6 Hz), 7.36 (ddd, 1H, J=J'=7.5 Hz, J''=2.0 Hz), 7.47 (dd, 2H, 2×H_{Ar}, J=J'=7.6 Hz), 7.56 (dd, 1H, H_{Ar}, J=J'=7.6 Hz), 7.71 (dd, 1H, H_{Ar}, J=7.6 Hz, J'=2.0 Hz), 7.75 (d, 1H, H-6, $J_{6,7}$=8.8 Hz), 7.79 (d, 1H,

H-2, $J_{2,3}$=4.0 Hz), 7.92 (d, 2H, 2×H_{Ar}, J=7.6 Hz), 8.28 (d, 1H, H-7, $J_{7,6}$=8.8 Hz); ^{13}C NMR (100.61 MHz, $CDCl_3$) δ 55.5 (CH_3), 110.6 (C-3), 111.3 (CH_{Ar}), 120.2 (C-7), 121.0 (C-6+CH_{Ar}), 126.7 (2×CH_{Ar}), 127.0 (Cq), 129.1 (C-2), 129.2 (Cq), 129.4 (2×CH_{Ar}), 129.8 (CH_{Ar}), 131.2 (CH_{Ar}), 134.1 (CH_{Ar}), 138.0 (Cq), 148.5 (Cq), 153.2 (Cq), 156.7 (Cq); HRMS (TOF ES$^+$) m/z calculated for $C_{20}H_{17}N_2O_3S$ (MH^+) 365.0960; found 365.0971.

*4.3.7. 1-Benzenesulfonyl-5-pyridin-4-yl-1H-pyrrolo[3,2–b]pyridine (**15**).* The reaction was carried out as described in general procedure C using the 4-pyridineboronic acid (48 mg, 0.37 mmol). The mixture was refluxed for 2 h. The residue was purified by flash chromatography (CH_2Cl_2/MeOH 98/2) to afford **15** as a yellow solid (80 mg, 97%). Mp 145 °C; R_f (CH_2Cl_2/MeOH 9/1) 0.43; IR (ATR diamond, ν, cm^{-1}) 3113, 1597, 1372, 1170, 1136, 752, 722; ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.95 (d, 1H, H-3, $J_{3,2}$=4.0 Hz), 7.48 (dd, 2H, 2×H_{Ar}, J=J'=7.5 Hz), 7.59 (dd, 1H, H_{Ar}, J=J'=7.5 Hz), 7.76 (d, 1H, H-6, $J_{6,7}$=8.8 Hz), 7.86 (d, 1H, H-2, $J_{2,3}$=4.0 Hz), 7.89–7.92 (m, 4H, 4×H_{py}), 8.38 (d, 1H, H-7, $J_{7,6}$=8.8 Hz), 8.71 (d, 2H, 2×H_{Ar}, J=6.3 Hz) ; ^{13}C NMR (100.61 MHz, $CDCl_3$) δ 110.5 (CH-3), 116.8 (C-6), 121.3 (2×CH_{Ar}), 121.5 (C-7), 126.8 (2×CH_{Ar}), 128.2 (Cq), 129.6 (2×CH_{Ar}), 130.5 (C-2), 134.4 (CH_{Ar}), 137.8 (Cq), 146.5 (Cq), 149.2 (Cq), 150.4 (2×CH_{Ar}), 151.5 (Cq); HRMS (TOF ES$^+$) m/z calculated for $C_{18}H_{14}N_3O_2S$ (MH^+) 336.0807; found 336.0824.

*4.3.8. 1-Benzenesulfonyl-5-pyridin-3-yl-1H-pyrrolo[3,2–b] pyridine (**16**).* The reaction was carried out as described in general procedure C using the 3-pyridineboronic acid (48 mg, 0.37 mmol). The mixture was refluxed for 2 h. The residue was purified by flash chromatography (CH_2Cl_2/MeOH 98/2) to afford **16** as a yellow solid (64.4 mg, 78%). Mp 145 °C; R_f (CH_2Cl_2/MeOH 9/1) 0.50; IR (ATR diamond, ν, cm^{-1}) 3146, 3105, 2357, 1573, 1407, 1168, 723; ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.93 (d, 1H, H-3, $J_{3,2}$=3.6 Hz), 7.37 (dd, 1H, H_{py}, J=8.0 Hz, J'=4.8 Hz), 7.45 (dd, 2H, 2×H_{Ar}, J=J'=7.6 Hz), 7.55 (dd, 1H, H_{Ar}, J=7.6 Hz), 7.69 (d, 1H, H-6, $J_{6,7}$=8.8 Hz), 7.85 (d, 1H, H-2, $J_{2,3}$=3.6 Hz), 7.91 (d, 2H, 2×H_{Ar}, J=7.6 Hz), 8.31 (dd, 1H, H_{py}, J=8.0 Hz, J'=2.0 Hz), 8.36 (d, 1H, H-7, $J_{7,6}$=8.8 Hz), 8.63 (dd, 1H, H_{py}, J=4.8 Hz, J'=2.0 Hz), 9.22 (dd, 1H, H_{py}, J=J'=2.0 Hz); ^{13}C NMR (100.61 MHz, $CDCl_3$) δ 110.3 (C-3), 116.4 (C-6), 121.4 (C-7), 123.3 (CH_{Ar}), 126.5 (2×CH_{Ar}), 127.4 (Cq), 129.3 (2×CH_{Ar}), 130.0 (C-2), 134.1 (CH_{Ar}), 134.2 (CH_{Ar}), 134.7 (Cq), 137.5 (Cq), 148.1 (CH_{Ar}), 148.9 (Cq), 149.4 (CH_{Ar}), 151.4 (Cq); HRMS (TOF ES$^+$) m/z calculated for $C_{18}H_{14}N_3O_2S$ (MH^+) 336.0807; found 336.0802.

*4.3.9. 1-Benzenesulfonyl-5-(4-nitrophenyl)-1H-pyrrolo[3, 2–b]pyridine (**17**).* The reaction was carried out as described in general procedure C using the 4-nitrophenylboronic acid (62 mg, 0.37 mmol). The mixture was refluxed for 1.5 h. The residue was purified by flash chromatography (petroleum ether/EtOAc 7/3) to afford **17** as a yellow solid (85 mg, 91%). Mp 196 °C; R_f (petroleum ether/EtOAc 8/2) 0.27; IR (ATR diamond, ν, cm^{-1}) 3138, 2929, 2353, 1512, 1345, 1133, 751; ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.94 (d, 1H, H-3, $J_{3,2}$=3.7 Hz), 7.48 (dd, 2H, 2×H_{Ar}, J=J'=7.5 Hz), 7.59 (dd, 1H, H_{Ar}, J=J'=7.5 Hz), 7.75 (d, 1H, H-6, $J_{6,7}$=8.8 Hz), 7.86 (d, 1H, H-2, $J_{2,3}$=3.7 Hz), 7.91 (d, 2H, 2×H_{Ar}, J=7.5 Hz), 8.16 (d, 2H, 2×H_{Ar}, J=8.8 Hz), 8, 29 (d, 2H, 2×H_{Ar}, J=8.8 Hz), 8.37 (d, 1H, H-7, $J_{7,6}$=8.8 Hz); ^{13}C NMR (100.61 MHz, $CDCl_3$) δ 110.5 (C-3), 117.1 (C-6), 121.5 (C-7), 123.9 (2×CH_{Ar}), 126.7 (2×CH_{Ar}), 127.8 (2×CH_{Ar}), 127.9 (Cq), 129.6 (2×CH_{Ar}), 130.6 (C-2), 134.4 (CH_{Ar}), 137.7 (Cq), 145.4 (Cq), 147.9 (Cq), 149.2 (Cq), 151.6 (Cq); HRMS (TOF ES$^+$) m/z calculated for $C_{19}H_{14}N_3O_4S$ (MH^+) 380.0705; found 380.0689.

*4.3.10. 1-Benzenesulfonyl-5-(2,6-dichloro-phenyl)-1H-pyrro lo[3,2–b]pyridine (**18**).* The reaction was carried out as described in general procedure C using the 2,6-dichlorophenylboronic acid (70 mg, 0.37 mmol). The mixture was refluxed for 5 h. The residue was purified by flash chromatography (petroleum ether/EtOAc 7/3) to afford **18** as a white solid (17 mg, 17%). Mp 158 °C; R_f (petroleum ether/EtOAc 7/3) 0.38; IR (ATR diamond, ν, cm^{-1}) 3101, 1585, 1565, 1434, 1373, 1142, 782, 724; ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.93 (d, 1H, H-3, $J_{3,2}$=3.8 Hz), 7.24–7.307 (m, 2H, 2×CH_{Ar}), 7.39–7.42 (m, 2H, 2×H_{Ar}), 7.52 (dd, 2H, 2×H_{Ar}, J=J'=7.5 Hz), 7.63 (dd, 1H, H_{Ar}, J=J'=7.5 Hz), 7.86 (d, 1H, H-2, $J_{2,3}$=3.8 Hz), 7.96 (d, 2H, 2×H_{Ar}, J=7.5 Hz), 8.38 (d, 1H, H-7, $J_{7,6}$=9.0 Hz) ; ^{13}C NMR (100.61 MHz, $CDCl_3$) δ 110.4 (C-3), 120.6 (C-6), 121.1 (C-7), 126.9 (2×CH_{Ar}), 127.5 (Cq), 128.1 (2×CH_{Ar}), 129.6 (2×CH_{Ar}), 129.8 (CH_{Ar}), 129.9 (C-2), 134.4 (CH_{Ar}), 134.9 (2×Cq), 138.0 (Cq), 138.4 (Cq), 148.4 (Cq), 152.0 (Cq); HRMS (TOF ES$^+$) m/z calculated for $C_{19}H_{13}Cl_2N_2O_2S$ (MH^+) 403.0075; found 403.0096.

*4.3.11. 1-Benzenesulfonyl-5-(2,6-dimethoxy-phenyl)-1H-pyrrolo[3,2–b]pyridine (**19**).* The reaction was carried out as described in general procedure C using the 2,6-dimethoxyphenylboronic acid (67 mg, 0.37 mmol). The mixture was refluxed for 2.5 h. The residue was purified by flash chromatography (petroleum ether/EtOAc 3/7) to afford **19** as a white solid (85 mg, 88%). Mp 174 °C; R_f (petroleum ether/EtOAc 3/7) 0.43; IR (ATR diamond, ν, cm^{-1}) 3105, 2950, 2921, 2839, 1585, 1365, 1247, 1108, 726; ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.66 (s, 6H, 2×CH_3), 6.63 (d, 2H, 2×H_{Ar}, J=8.4 Hz), 6.91 (d, 1H, H-3, $J_{3,2}$=3.8 Hz), 7.27 (d, 1H, H-6, $J_{6,7}$=8.4 Hz), 7.30 (dd, 1H, H_{Ar}, J=J'=7.5 Hz), 7.46 (dd, 2H, 2×H_{Ar}, J=J'=7.5 Hz), 7.55 (dd, 1H, H_{Ar}, J=J'=7.5 Hz), 7.77 (d, 1H, H-2, $J_{2,3}$=3.8 Hz), 7.93 (d, 2H, 2×H_{Ar}, J=7.5 Hz), 8.28 (d, 1H, H-7, $J_{7,6}$=8.4 Hz) ; ^{13}C NMR (100.61 MHz, $CDCl_3$) δ 55.8 (2×CH_3), 104.0 (2×CH_{Ar}), 110.5 (C-3), 118.7 (Cq), 120.4 (C-7), 121.9 (C-6), 126.8 (2×CH_{Ar}), 126.9 (Cq), 128.6 (C-2), 129.4 (2×CH_{Ar}), 129.6 (CH_{Ar}), 134.1 (CH_{Ar}), 138.1 (Cq), 148.3 (Cq), 151.1 (Cq), 158.0 (2×Cq); HRMS (TOF ES$^+$) m/z calculated for $C_{21}H_{19}N_2O_4S$ (MH^+) 395.1066; found 395.1061.

*4.3.12. 1-Benzenesulfonyl-5-(1-methoxy-naphthalen-2-yl)-1H-pyrrolo[3,2–b]pyridine (**20**).* The reaction was carried out as described in general procedure C using the 1-methoxynaphthalene-2-boronic acid (75 mg, 0.37 mmol). The mixture was refluxed for 4 h. The residue was purified by flash chromatography (petroleum ether/EtOAc 7/3) to afford **20** as a white solid (94 mg, 92%). Mp 173 °C; R_f (petroleum ether/EtOAc 7/3) 0.35; IR (ATR diamond, ν, cm^{-1}) 3142, 2938, 2827, 1368, 1167, 1126, 737, 723; ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.96 (s, 3H, CH_3), 6.98 (d, 1H, H-3, $J_{3,2}$=3.6 Hz), 7.25 (s, 1H, H_{Ar}), 7.35 (dd, 1H, H_{Ar}, J=J'=8.0 Hz), 7.46 (dd, 1H, H_{Ar}, J=J'=8.0 Hz), 7.50 (dd, 2H, 2×H_{Ar}, J=J'=7.5 Hz), 7.60 (dd, 1H, H_{Ar}, J=J'=7.5 Hz), 7.75–7.83 (m, 4H, 4×H_{Ar}), 7.93 (d, 2H, 2×H_{Ar}, J=7.5 Hz), 8.14 (s, 1H, H_{Ar}), 8.31 (d, 1H, H-7, $J_{7,6}$=8.4 Hz); ^{13}C NMR (100.61 MHz, $CDCl_3$) δ 55.6 (CH_3), 106.1 (CH_{Ar}), 110.7 (C-3), 120.4 (C-7), 121.3 (CH_{Ar}), 124.0 (CH_{Ar}), 126.3 (CH_{Ar}), 126.8 (CH_{Ar}), 126.9 (2×CH_{Ar}), 127.3 (Cq), 128.3 (CH_{Ar}), 128.8 (Cq), 129.3 (CH_{Ar}), 129.5 (2×CH_{Ar}), 130.8 (Cq), 131.2 (CH_{Ar}), 134.2 (CH_{Ar}), 134.5 (Cq), 138.1 (Cq), 148.6 (Cq), 153.1 (Cq), 155.1 (Cq); HRMS (TOF ES$^+$) m/z calculated for $C_{24}H_{19}N_2O_3S$ (MH^+) 415.1116; found 415.1126.

*4.3.13. 2-(1-Benzenesulfonyl-1H-pyrrolo[3,2–b]pyridin-5-yl)-indole-1-carboxylic acid tert-butyl ester (**21**).* The reaction was carried out as described in general procedure C using the *N*-(*tert*-butoxycarbonyl)-indole-2-trifluoro borate[21] (119 mg, 0.37 mmol). The mixture was refluxed for 6 h. The residue was purified by flash chromatography (petroleum ether/EtOAc 7/3) to afford **21** as a colorless oil (81 mg, 69%). R_f (petroleum ether/EtOAc 7/3) 0.42; IR (ATR diamond, ν, cm^{-1}) 2974, 2353, 1730, 1327, 1127, 728; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.1 (s, 9H, 3×CH_3), 6.75 (s, 1H, H_{ind}), 6.89 (d, 1H, H-3, $J_{3,2}$=4.0 Hz), 7.24 (dd, 1H, H_{ind}, J=J'=8.4 Hz), 7.34 (dd, 1H, H_{ind}, J=J'=8.4 Hz), 7.45–7.49 (m, 3H, H-6+2×H_{Ar}), 7.55–7.59 (m, 2H, 2×H_{Ar}), 7.84 (d, 1H, H-2, $J_{2,3}$=4.0 Hz), 7.90 (d, 2H, 2×H_{Ar}, J=7.5 Hz), 8.19 (d, 1H, H_{ind}, J=8.4 Hz), 8.31 (d, 1H, H-7, $J_{7,6}$=8.8 Hz); ^{13}C NMR (100.61 MHz, $CDCl_3$) δ 27.3 (3×CH_3), 83.1 (Cq), 110.4 (C-3), 111.0

(CH_{Ar}), 115.0 (CH_{Ar}), 119.3 (C-6), 120.7 (C-7), 120.8 (CH_{Ar}), 122.9 (CH_{Ar}), 124.9 (CH_{Ar}), 126.7 (2×CH_{Ar}), 127.1 (Cq), 128.8 (Cq), 129.5 (2×CH_{Ar}), 130.1 (C-2), 134.2 (CH_{Ar}), 137.7 (Cq), 137.8 (Cq), 139.0 (Cq), 148.1 (Cq), 149.9 (Cq), 150.1 (Cq); HRMS (TOF ES$^+$) *m/z* calculated for $C_{26}H_{24}N_3O_4S$ (MH^+) 474.1488; found 474.1473.

*4.3.14. (1-Benzenesulfonyl-1H-pyrrolo[3,2–b]pyridin-5-yl)-(4-methoxy-phenyl)-amine (**22**).* The reaction was carried out as described in general procedure D using the 4-methoxy-phenylamine (36 mg, 0.295 mmol). The mixture was refluxed for 1 h. The residue was purified by flash chromatography (petroleum ether/EtOAc 5/5) to afford **22** as brown oil (91.4 mg, 98%). R_f (petroleum ether/EtOAc 5/5) 0.45; IR (ATR diamond, ν, cm^{-1}) 3179, 3105, 3007, 2933, 2835, 1591, 1509, 1409, 1168, 1120, 723; ^1H NMR (250 MHz, $CDCl_3$) δ 3.78 (s, 3H, CH_3), 6.57 (d, 1H, H-3, $J_{3,2}$=4.0 Hz), 6.62 (d, 1H, H-6, $J_{6,7}$=9.0 Hz), 6.87 (d, 2H, 2×H_{Ar}, J=8.8 Hz), 7.26 (d, 2H, 2×H_{Ar}, J=8.8 Hz), 7.41 (dd, 2H, 2×H_{Ar}, J=J'=7.5 Hz), 7.52 (dd, 1H, H_{Ar}, J=J'=7.5 Hz), 7.59 (d, 1H, H-2, $J_{2,3}$=4.0 Hz), 7.80 (d, 2H, 2×H_{Ar}, J=7.5 Hz), 8.02 (d, 1H, H-7, $J_{7,6}$=9.0 Hz); ^{13}C NMR (100.61 MHz, $CDCl_3$) δ 55.4 (CH_3), 105.3 (C-6), 109.9 (C-3), 114.5 (2×CH_{Ar}), 122.9 (Cq), 123.2 (C-7), 123.7 (2×CH_{Ar}), 126.6 (2×CH_{Ar}), 128.6 (C-2), 129.2 (2×CH_{Ar}), 133.5 (Cq), 133.9 (CH_{Ar}), 137.9 (Cq), 147.3 (Cq), 155.1 (Cq), 156.1 (Cq); HRMS (TOF ES$^+$) *m/z* calculated for $C_{20}H_{18}N_3O_3S$ 380.1069 (MH^+); found 380.1077.

*4.3.15. (1-Benzenesulfonyl-1H-pyrrolo[3,2–b]pyridin-5-yl)-(2-methyl-quinolin-4-yl)-amine (**23**).* The reaction was carried out as described in general procedure D using the 2-methyl-quinolin-4-ylamine (47 mg, 0.295 mmol). The mixture was refluxed for 3 h. The residue was purified by flash chromatography (CH_2Cl_2/MeOH 95/5) to afford **23** as a light brown solid (93 mg, 91%). Mp 123 °C; R_f (CH_2Cl_2/MeOH 9/1) 0.39; IR (ATR diamond, ν, cm^{-1}) 3166, 1569, 1365, 1165, 1136, 754, 722; ^1H NMR (250 MHz, $CDCl_3$) δ 2.65 (s, 3H, CH_3), 6.75 (d, 1H, H-3, $J_{3,2}$=4.0 Hz), 7.12 (d, 1H, H-6, $J_{6,7}$=9.0 Hz), 7.38 (dd, 1H, H_{Ar}, J=J'=8.0 Hz), 7.46 (dd, 2H, 2×H_{Ar}, J=J'=7.5 Hz), 7.57 (dd, 1H, H_{Ar}, J=J'=7.5 Hz), 7.61 (dd, 1H, H_{Ar}, J=J'=8.0 Hz), 7.74 (d, 1H, H-2, $J_{2,3}$=4.0 Hz), 7.83 (s, 1H, H_{Ar}), 7.87 (d, 2H, 2×H_{Ar}, J=7.5 Hz), 7.94 (d, 1H, H_{Ar}, J=8.0 Hz), 7.97 (d, 1H, H_{Ar}, J=8.0 Hz), 8.22 (d, 1H, H-7, $J_{7,6}$=9.0 Hz); ^{13}C NMR (100.61 MHz, $CDCl_3$) δ 25.7 (CH_3), 106.2 (CH_{Ar}), 109.4 (C-6), 109.9 (C-3), 118.9 (Cq), 119.8 (CH_{Ar}), 123.3 (C-7), 124.4 (Cq), 125.0 (CH_{Ar}), 126.7 (2×CH_{Ar}), 129.1 (C-2), 129.4 (CH_{Ar}), 129.5 (3×CH_{Ar}), 134.2 (CH_{Ar}), 137.9 (Cq), 144.4 (Cq), 147.3 (Cq), 148.5 (Cq), 151.6 (Cq), 159.6 (Cq); HRMS (TOF ES$^+$) *m/z* calculated for $C_{23}H_{19}N_4O_2S$ (MH^+) 415.1229; found 415.1223.

*4.3.16. 1-Benzenesulfonyl-5-morpholin-4-yl-1H-pyrrolo [3,2–b]pyridine (**24**).* The reaction was carried out as described in general procedure D using the morpholine (0.026 mL, 0.295 mmol). The mixture was refluxed for 2.5 h. The residue was purified by flash chromatography (petroleum ether/EtOAc 6/4) to afford **24** as a light brown solid (68 mg, 80%). Mp 130 °C; R_f (petroleum ether/EtOAc 5/5) 0.43; IR (ATR diamond, ν, cm^{-1}) 3093, 2856, 1574, 1362, 1247, 1168, 724; ^1H NMR (250 MHz, $CDCl_3$) δ 3.50 (t, 4H, 2×CH_2, J=4.8 Hz), 3.82 (t, 4H, 2×CH_2, J=4.8 Hz), 6.64 (d, 1H, H-3, $J_{3,2}$=3.6 Hz), 6.66 (d, 1H, H-6, $J_{6,7}$=9.0 Hz), 7.43 (dd, 2H, 2×H_{Ar}, J=J'=7.6 Hz), 7.53 (dd, 1H, H_{Ar}, J=J'=7.6 Hz), 7.62 (d, 1H, H-2, $J_{2,3}$=3.6 Hz), 7.81 (d, 2H, 2×H_{Ar}, J=J'=7.6 Hz), 8.10 (d, 1H, H-7, $J_{7,6}$=9.0 Hz); ^{13}C NMR (100.61 MHz, $CDCl_3$) δ 46.3 (2×CH_2), 66.8 (2×CH_2), 104.6 (C-6), 110.2 (C-3), 122.7 (Cq), 123.1 (C-7), 126.6 (2×CH_{Ar}), 128.8 (C-2), 129.3 (2×CH_{Ar}), 133.9 (CH_{Ar}), 138.0 (Cq), 147.4 (Cq), 157.8 (Cq); HRMS (TOF ES$^+$) *m/z* calculated for $C_{17}H_{18}N_3O_3S$ (MH^+) 344.1057; found 344.1069.

*4.3.17. (1-Benzenesulfonyl-1H-pyrrolo[3,2–b]pyridin-5-yl)-nonyl-amine (**25**).* The reaction was carried out as described in general procedure D using the nonylamine (0.054 mL, 0.295 mmol). The mixture was refluxed for 7 h. The residue was purified by flash chromatography (petroleum ether/EtOAc 8/2) to afford **25** as brown oil (20 mg, 23%). R_f (petroleum ether/EtOAc 7/3) 0.43; IR (ATR diamond, ν, cm^{-1}) 2924, 2856, 1593, 1370, 1168, 1131, 723; ^1H NMR (250 MHz, $CDCl_3$) δ 0.87 (t, 3H, CH_3, J=7.2 Hz), 1.26–1.38 (m, 12H, 6×CH_2), 1.60 (quint, 2H, CH_2, J=7.2 Hz), 3.28 (q, 2H, CH_2, J=7.2 Hz), 4.44 (t, 1H, NH, J=7.2 Hz), 6.36 (d, 1H, H-6, $J_{6,7}$=9.0 Hz), 6.58 (d, 1H, H-3, $J_{3,2}$=3.6 Hz), 7.43 (dd, 2H, 2×H_{Ar}, J=J'=7.5 Hz), 7.53 (dd, 1H, H_{Ar}, J=J'=7.5 Hz), 7.56 (d, 1H, H-2, $J_{2,3}$=3.6 Hz), 7.80 (d, 2H, 2×H_{Ar}, J=7.5 Hz), 8.01 (d, 1H, H-7, $J_{7,6}$=9.0 Hz); ^{13}C NMR (100.61 MHz, $CDCl_3$) δ 14.1 (CH_3), 22.6 (CH_2), 27.0 (CH_2), 29.2 (CH_2), 29.4 (CH_2), 29.5 (CH_2), 29.6 (CH_2), 31.8 (CH_2), 42.5 (CH_2), 104.7 (C-6), 110.0 (C-3), 122.2 (Cq), 123.3 (C-7), 126.6 (2×CH_{Ar}), 128.3 (C-2), 129.2 (2×CH_{Ar}), 133.8 (CH_{Ar}), 138.1 (Cq), 147.5 (Cq), 157.0 (Cq); HRMS (TOF ES$^+$) *m/z* calculated for $C_{22}H_{30}N_3O_2S$ (MH^+) 400.2059; found 400.2073.

*4.3.18. (1-Benzenesulfonyl-1H-pyrrolo[3,2-b]pyridin-5-yl)-(3-methoxy-benzyl)-amine (**26**).* The reaction was carried out as described in general procedure D using the 3-methoxy-benzylamine (0.040 mL, 0.295 mmol). The mixture was refluxed for 7 h. The residue was purified by flash chromatography (petroleum ether/EtOAc 7/3) to afford **26** as brown oil (24 mg, 25%). R_f (petroleum ether/EtOAc 6/4) 0.39; IR (ATR diamond, ν, cm^{-1}) 3428, 2954, 1588, 1367, 1167, 1130, 723; ^1H NMR (250 MHz, $CDCl_3$) δ 3.84 (s, 3H, CH_3), 4.52 (d, 2H, CH_2, J=6.0 Hz), 4.97 (t, 1H, NH, J=6.0 Hz), 6.38 (d, 1H, H-6, $J_{6,7}$=9.0 Hz), 6.60 (d, 1H, H-3, $J_{3,2}$=3.6 Hz), 6.86–6.90 (m, 2H, 2×H_{Ar}), 7.23 (dd, 1H, H_{Ar}, J=9.0 Hz, J'=1.6 Hz), 7.31 (dd, 1H, H_{Ar}, J=9.0 Hz, J'=1.6 Hz), 7.42 (dd, 2H, 2×H_{Ar}, J=J'=7.5 Hz), 7.53 (dd, 1H, H_{Ar}, J=J'=7.5 Hz), 7.56 (d, 1H, H-2, $J_{2,3}$=3.6 Hz), 7.80 (d, 2H, 2×H_{Ar}, J=7.5 Hz), 7.98 (d, 1H, H-7, $J_{7,6}$=9.0 Hz); ^{13}C NMR (100.61 MHz, $CDCl_3$) δ 42.0 (CH_3), 55.3 (CH_2), 105.1 (C-6), 110.0 (CH_{Ar}), 110.2 (C-3), 120.5 (CH_{Ar}), 122.3 (Cq), 123.2 (C-7), 126.6 (2×CH_{Ar}), 127.1 (Cq), 128.2 (C-2), 128.5 (CH_{Ar}), 129.1 (CH_{Ar}), 129.2 (2×CH_{Ar}), 133.8 (CH_{Ar}), 138.1 (Cq), 147.4 (Cq), 156.9 (Cq), 157.5 (Cq); HRMS (TOF ES$^+$) *m/z* calculated for $C_{21}H_{20}N_3O_3S$ (MH^+) 394.1219; found 394.1225.

*4.3.19. N-(1-Benzenesulfonyl-1H-pyrrolo[3,2-b]pyridin-5-yl)-benzamide (**27**).* The reaction was carried out as described in general procedure D using the benzamide (36 mg, 0.295 mmol). The mixture was refluxed for 3 h. The residue was purified by flash chromatography (petroleum ether/EtOAc 6/4) to afford **27** as a light brown solid (87 mg, 94%). Mp 134 °C; R_f (petroleum ether/EtOAc 6/4) 0.39; IR (ATR diamond, ν, cm^{-1}) 3134, 3105, 1661, 1533, 1406, 1349, 1287, 1168, 1131, 723, 686; ^1H NMR (250 MHz, $CDCl_3$) δ 6.61 (d, 1H, H-3, $J_{3,2}$=3.6 Hz), 7.42–7.59 (m, 6H, 6×H_{Ar}), 7.74 (d, 1H, H-2, $J_{2,3}$=3.6 Hz), 7.86–7.92 (m, 4H, 4×H_{Ar}), 8.33 (d, 1H, H-7, $J_{7,6}$=9.0 Hz), 8.44 (d, 1H, H-6, $J_{6,7}$=9.0 Hz), 8.92 (d, 1H, NH, J=7.2 Hz); ^{13}C NMR (100.61 MHz, $CDCl_3$) δ 109.2 (C-3), 110.7 (C-6), 123.2 (C-7), 125.9 (Cq), 126.7 (2×CH_{Ar}), 127.2 (2×CH_{Ar}), 128.7 (2×CH_{Ar}), 129.4 (2×CH_{Ar}), 129.9 (C-2), 132.2 (CH_{Ar}), 134.2 (CH_{Ar}), 134.2 (Cq), 137.7 (Cq), 146.6 (Cq), 148.9 (Cq), 165.7 (Cq); HRMS (TOF ES$^+$) *m/z* calculated for $C_{20}H_{16}N_3O_3S$ (MH^+) 378.0912; found 378.0912.

*4.3.20. N-(1-Benzenesulfonyl-1H-pyrrolo[3,2–b]pyridin-5-yl)-acetamide (**28**).* The reaction was carried out as described in general procedure D using the acetamide (14 mg, 0.295 mmol). The mixture was refluxed for 1.5 h. The residue was purified by flash chromatography (petroleum ether/EtOAc 4/6) to afford **28** as a colorless oil (78 mg, 99%); R_f (CH_2Cl_2/MeOH 98/2) 0.3; IR (ATR diamond, ν, cm^{-1}) 3412, 3277, 3097, 1674, 1532, 1405, 1376, 1129, 726; ^1H NMR (250 MHz, $CDCl_3$) δ 2.14 (s, 3H, CH_3), 6.63 (d, 1H, H-3, $J_{3,2}$=3.8 Hz), 7.43 (dd, 2H, 2×H_{Ar}, J=J'=7.5 Hz), 7.54 (dd, 1H, H_{Ar}, J=J'=7.5 Hz), 7.74 (d, 1H, H-2, $J_{2,3}$=3.8 Hz), 7.84 (d, 2H, 2×H_{Ar}, J=J'=7.5 Hz), 8.22–8.28 (m, 2H, H-6, H-7), 8.77 (bs, 1H, NH); ^{13}C NMR (100.61 MHz, $CDCl_3$) δ 24.6 (CH_3), 108.8 (C-6), 110.6 (C-3), 123.6 (C-7), 125.7 (Cq), 126.7 (2×CH_{Ar}), 129.5 (2×CH_{Ar}), 130.0 (C-2), 134.3 (CH_{Ar}), 137.7 (Cq), 145.7

(Cq), 148.7 (Cq), 168.8 (Cq); HRMS (TOF ES$^+$) m/z calculated for $C_{15}H_{14}N_3O_3S$ (MH^+) 316.0756; found 316.0765.

*4.3.21. 1-(1-Benzenesulfonyl-1H-pyrrolo[3,2–b]pyridin-5-yl)-piperidin-2-one (**29**).* The reaction was carried out as described in general procedure D using the piperidin-2-one (29 mg, 0.295 mmol). The mixture was refluxed for 6.5 h. The residue was purified by flash chromatography (petroleum ether/EtOAc 2/8) to afford **29** as brown oil (69 mg, 79%). R_f (EtOAc) 0.30; IR (ATR diamond, ν, cm^{-1}) 3105, 2954, 2864, 1651, 1401, 1373, 1167, 1127, 728; ^1H NMR (250 MHz, $CDCl_3$) δ 1.91–1.96 (m, 4H, 2×CH_2), 2.59 (t, 2H, CH_2, J=6.4 Hz), 3.91 (t, 2H, CH_2, J=6.4 Hz), 6.79 (d, 1H, H-3, $J_{3,2}$=4.0 Hz), 7.47 (dd, 2H, 2×H_{Ar}, J=J'=7.6 Hz), 7.57 (dd, 1H, H_{Ar}, J=7.6 Hz), 7.60 (d, 1H, H-6, $J_{6,7}$=9.2 Hz), 7.77 (d, 1H, H-2, $J_{2,3}$=4.0 Hz), 7.88 (d, 2H, 2×CH, J=7.6 Hz), 8.25 (d, 1H, H-7, $J_{7,6}$=9.2 Hz); ^{13}C NMR (100.61 MHz, $CDCl_3$) δ 21.0 (CH_2), 23.1 (CH_2), 33.3 (CH_2), 48.6 (CH_2), 109.8 (C-3), 117.1 (C-6), 121.9 (C-7), 126.1 (Cq), 126.7 (2×CH_{Ar}), 129.3 (C-2), 129.5 (2×CH_{Ar}), 134.2 (CH_{Ar}), 137.8 (Cq), 146.9 (Cq), 151.9 (Cq), 170.9 (Cq); HRMS (TOF ES$^+$) HRMS (TOF ES$^+$) m/z calculated for $C_{18}H_{18}N_3O_3S$ (MH^+) 356.1069; found 356.1063.

*4.3.22. (1-Benzenesulfonyl-1H-pyrrolo[3,2–b]pyridin-5-yl)-carbamic acid ethyl ester (**30**).* The reaction was carried out as described in general procedure D using the ethyl carbamate (26 mg, 0.295 mmol). The mixture was refluxed for 2.5 h. The residue was purified by flash chromatography (petroleum ether/EtOAc 6/4) to afford **30** as a white solid (61 mg, 72%). Mp 153 °C; R_f (petroleum ether/EtOAc 5/5) 0.58; IR (ATR diamond, ν, cm^{-1}) 2987, 2361, 1714, 1556, 1373, 1172, 725; ^1H NMR (250 MHz, $CDCl_3$) δ 1.30 (t, 3H, CH_3, J=7.2 Hz), 4.23 (q, 2H, CH_2, J=7.2 Hz), 6.68 (d, 1H, H-3, $J_{3,2}$=3.6 Hz), 7.46 (dd, 2H, 2×H_{Ar}, J=J'=7.6 Hz), 7.57 (dd, 1H, H_{Ar}, J=J'=7.6 Hz), 7.60 (bs, 1H, NH), 7.72 (d, 1H, H-2, $J_{2,3}$=3.6 Hz), 7.85 (d, 2H, 2×H_{Ar}, J=7.6 Hz), 8.0 (d, 1H, H-6, $J_{6,7}$=9.0 Hz), 8.26 (d, 1H, H-7, $J_{7,6}$=9.0 Hz); ^{13}C NMR (100.61 MHz, $CDCl_3$) δ 14.5 (CH_3), 61.5 (CH_2), 108.9 (C-6), 109.5 (C-3), 123.3 (C-7), 125.5 (Cq), 126.7 (2×CH_{Ar}), 129.5 (2×CH_{Ar}), 129.6 (C-2), 134.2 (CH_{Ar}), 137.9 (Cq), 146.7 (Cq), 149.0 (Cq), 153.4(Cq); HRMS (TOF ES$^+$) m/z calculated for $C_{16}H_{16}N_3O_4S$ (MH^+) 346.0862; found 346.0848.

*4.3.23. N-(1-Benzenesulfonyl-1H-pyrrolo[3,2–b]pyridin-5-yl)-isonicotinamide (**31**).* The reaction was carried out as described in general procedure D using dioxane instead of toluene and the isonicotinamide (60 mg, 0.493 mmol, 2 equiv). The mixture was stirred for 24 h at 80 °C. The residue was purified by flash chromatography (CH_2Cl_2/MeOH 98/2) to afford **31** as a light brown solid (51 mg, 55%). Mp 200 °C; R_f (CH_2Cl_2/MeOH 9/1) 0.54; IR (ATR diamond, ν, cm^{-1}) 3105, 1700, 1542, 1408, 1350, 1288, 1172, 1123, 727; ^1H NMR (250 MHz, $CDCl_3$) δ 6.65 (d, 1H, H-3, $J_{3,2}$=4.0 Hz), 7.48 (dd, 2H, 2×H_{Ar}, J=J'=7.5 Hz), 7.59 (dd, 1H, H_{Ar}, J=J'=7.5 Hz), 7.76 (d, 2H, 2×H_{Ar}, J=6.0 Hz), 7.79 (d, 1H, H-2, $J_{2,3}$=4.0 Hz), 7.89 (d, 2H, 2×H_{Ar}, J=7.5 Hz), 8.35 (d, 1H, H-7, $J_{7,6}$=9.0 Hz), 8.39 (d, 1H, H-6, $J_{6,7}$=9.0 Hz), 8.78 (d, 2H, 2×H_{Ar}, J=6.0 Hz), 9.04 (bs, 1H, NH); ^{13}C NMR (100.61 MHz, $CDCl_3$) δ 109.1 (C-3), 110.8 (C-6), 120.9 (2×CH_{Ar}), 123.3 (C-7), 126.1 (Cq), 126.7 (2×CH_{Ar}), 129.5 (2×CH_{Ar}), 130.2 (C-2), 134.3 (CH_{Ar}), 137.7 (Cq), 141.3 (Cq), 146.6 (Cq), 148.2 (Cq), 150.8 (2×CH_{Ar}), 163.7 (Cq); HRMS (TOF ES$^+$) m/z calculated for $C_{19}H_{15}N_4O_3S$ (MH^+) 379.0865; found 379.0845.

*4.3.24. 1-(1-Benzenesulfonyl-1H-pyrrolo[3,2–b]pyridin-5-yl)-3-phenyl-urea (**33**).* The reaction was carried out as described in general procedure D using the phenyl-urea (40 mg, 0.295 mmol). The mixture was refluxed for 1 h. The residue was purified by flash chromatography (petroleum ether/EtOAc 5/5) to afford **33** as a white solid (74 mg, 77%). Mp 240 °C; R_f (CH_2Cl_2/MeOH 98/2) 0.11; IR (ATR diamond, ν, cm^{-1}) 3215, 3023, 2966, 1690, 1564, 1275, 729, 676; ^1H NMR (250 MHz, DMSO-d_6) δ 6.96 (d, 1H, H-3, $J_{3,2}$=3.6 Hz), 7.03 (dd, 1H, H_{Ar}, J=J'=8.0 Hz), 7.32 (dd, 2H, 2×H_{Ar}, J=J'=8.0 Hz), 7.50 (d, 1H, H-6, $J_{6,7}$=9.0 Hz), 7.56–7.64 (m, 4H, 4×H_{Ar}), 7.73 (dd, 1H, H_{Ar}, J=J'=7.5 Hz), 8.03 (d, 2H, 2×H_{Ar}, J=7.5 Hz), 8.07 (d, 1H, H-2, $J_{2,3}$=3.6 Hz), 8.33 (d, 1H, H-7, $J_{7,6}$=9.0 Hz), 8.74 (bs, 1H, NH), 9.71 (bs, 1H, NH); ^{13}C NMR (100.61 MHz, DMSO-d_6) δ 108.8 (C-6), 109.5 (C-3), 118.8 (2×CH_{Ar}), 122.4 (CH_{Ar}), 123.5 (Cq), 123.6 (C-7), 126.7 (2×CH_{Ar}), 128.8 (2×CH_{Ar}), 129.8 (2×CH_{Ar}), 130.2 (C-2), 134.8 (CH_{Ar}), 136.7 (Cq), 138.9 (Cq), 145.2 (Cq), 150.4 (Cq), 152.0 (Cq); HRMS (TOF ES$^+$) m/z calculated for $C_{20}H_{17}N_4O_3S$ (MH^+) 393.1021; found: 393.1032.

*4.3.25. (1-Benzenesulfonyl-1H-pyrrolo[3,2–b]pyridin-5-yl)-benzhydrylidene-amine (**34**).* The reaction was carried out as described in general procedure D using the benzophenone imine (0.05 mL, 0.295 mmol). The mixture was refluxed for 5.5 h. The residue was purified by flash chromatography (petroleum ether/EtOAc 6/4) to afford **34** as yellow oil (71 mg, 66%). R_f (petroleum ether/EtOAc 7/3) 0.18; IR (ATR diamond, ν, cm^{-1}) 3060, 1736, 1568, 1372, 1127, 725, 685; ^1H NMR (250 MHz, $CDCl_3$) δ 6.50 (d, 1H, H-6, $J_{6,7}$=8.8 Hz), 6.70 (d, 1H, H-3, $J_{3,2}$=3.6 Hz), 7.12–7.19 (m, 4H, 4×H_{Ar}), 7.24 (dd, 1H, H_{Ar}, J=J'=7.2 Hz), 7.37–7.44 (m, 4H, 4×H_{Ar}), 7.47 (dd, 1H, H_{Ar}, J=J'=7.2 Hz), 7.55 (dd, 1H, H_{Ar}, J=J'=7.6 Hz), 7.65 (d, 1H, H-2, $J_{2,3}$=3.6 Hz), 7.76–7.81 (m, 4H, 4×H_{Ar}), 8.01 (d, 1H, H-7, $J_{7,6}$=8.8 Hz); ^{13}C NMR (100.61 MHz, $CDCl_3$) δ 110.5 (C-3), 112.0 (C-6), 122.4 (C-7), 125.0 (Cq), 126.5 (4×CH_{Ar}), 127.8 (CH_{Ar}), 128.0 (C-2), 128.8 (CH_{Ar}), 129.2 (2×CH_{Ar}), 129.3 (4×CH_{Ar}), 129.6 (CH_{Ar}), 131.2 (CH_{Ar}), 134.0 (CH_{Ar}), 136.0 (Cq), 137.8 (Cq), 138.7 (Cq), 147.6 (Cq), 160.7 (Cq), 170.5 (Cq); HRMS (TOF ES$^+$) m/z calculated for $C_{26}H_{20}N_3O_2S$ (MH^+) 438.1276; found 438.1277.

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References and notes

1. Song, J. J.; Reeves, J. T.; Gallou, F.; Tan, Z.; Yee, N. K.; Senanayake, C. H. *Chem. Soc. Rev.* **2007**, *36*, 1120–1132.
2. Popowycz, F.; Mérour, J.-Y.; Joseph, B. *Tetrahedron* **2007**, *63*, 8689–8707.
3. Rai, R.; Kolesnikov, A.; Sprengeler, P. A.; Torkelson, S.; Ton, T.; Katz, B. A.; Yu, C.; Hendrix, J.; Shrader, W. D.; Stephens, R.; Cabuslay, R.; Sanford, E.; Young, W. B. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 2270–2273.
4. Buchmann, B.; Haerter, M.; Cancho-Grande, Y.; Kosemund, D.; Schirok, H.; Nguyen, D.; Fritsch, M. Preparation of azaindoles as inhibitors of soluble adenylate cyclase PCT Int. Appl. WO 2,009,030,725, 2009.
5. Hadida Ruah, S.; Zhou, J.; Miller, M.; Bear, B. Preparation of azaindole derivatives as therapeutic CFTR modulators PCT Int. Appl. WO 2,008,127,399, 2008.
6. Oballa, R.M.; Prasit, P.; Robichaud, J.S.; Isabel, E.; Mendonca, R.V.; Venkatraman, S.; Setti, E.; Wang, D.-X. Preparation of *N*-cyanomethyl amides as cysteine protease inhibitors PCT Int. Appl. WO 2,001,049,288, 2001.
7. Rodriguez, A. L.; Koradin, C.; Dohle, W.; Knochel, P. *Angew. Chem., Int. Ed.* **2000**, *39*, 2488–2490.
8. Harcken, C.; Ward, Y.; Thomson, D.; Riether, D. *Synlett* **2005**, 3121–3125.
9. McLaughlin, M.; Palucki, M.; Davies, I. W. *Org. Lett.* **2006**, *8*, 3307–3310.
10. Majumdar, K. C.; Mondal, S. *Tetrahedron Lett.* **2007**, *48*, 6951–6953.
11. Sun, L.-P.; Wang, J.-X. *Synth. Commun.* **2007**, *37*, 2187–2193.
12. Majumdar, K. C.; Samanta, S.; Chattopadhyay, B. *Tetrahedron Lett.* **2008**, *49*, 7213–7216.
13. Makosza, M.; Danikiewicz, W.; Wojciechowski, K. *Liebigs Ann. Chem.* **1988**, 203–208.
14. Jeanty, M.; Suzenet, F.; Guillaumet, G. *J. Org. Chem.* **2008**, *73*, 7390–7393.
15. (a) Sundberg, R. J.; Russell, H. F. *J. Org. Chem.* **1973**, *38*, 3324–3330; (b) Gharpure, M.; Stoller, A.; Bellamy, F.; Firnau, G.; Snieckus, V. *Synthesis* **1991**, 1079–1082; (c) Collins, M.A.; Tanis, S.P. 2-Lithio- *N*-phenylsulfonylindole, e-EROS Encyclopedia of Reagents for Organic Synthesis, 2001.
16. Dormoy, J.-R.; Heymes, A. *Tetrahedron* **1993**, *49*, 2885–2914.
17. Desarbre, E.; Coudret, S.; Meheust, C.; Mérour, J.-Y. *Tetrahedron* **1997**, *53*, 3637–3648.
18. Lefoix, M.; Daillant, J.-P.; Routier, S.; Mérour, J.-Y.; Gillaizeau, I.; Coudert, G. *Synthesis* **2005**, 3581–3588.
19. Mahboobi, S.; Pongratz, H.; Hufsky, H.; Hockemeyer, J.; Frieser, M.; Lyssenko, A.; Paper, D. H.; Brgermeister, J.; Bhmer, F.-D.; Fiebig, H.-H.; Burger, A. M.; Baasner, S.; Beckers, T. *J. Med. Chem.* **2001**, *44*, 4535–4553.

20. Gesenberg, K.; Deshpande, P. P.; Pullockaran, A.; Xu, F.; Wu, D.; Gao, Q.; Pathirana, C.; Castoro, J.; Soundararajan, N.; Staab, A. *Tetrahedron Lett.* **2007**, *48*, 2675–2677.
21. Kassis, P.; Bénéteau, V.; Mérour, J.-Y.; Routier, S. *Synthesis* **2009**, 2447–2453.
22. (a) Hartwig, J. F. *Angew. Chem., Int. Ed.* **1998**, *37*, 2046–2067; (b) Yin, J.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 6043–6048; (c) Yang, B. H.; Buchwald, S. L. *J. Organomet. Chem.* **1999**, *576*, 125–146; (d) Ahman, J.; Buchwald, S. L. *Tetrahedron Lett.* **1997**, *38*, 6363–6366; (e) Wolfe, J. P.; Buchwald, S. L. *J. Org. Chem.* **1997**, *62*, 1264–1267; (f) Louie, J.; Driver, M. S.; Hamann, B. C.; Hartwig, J. F. *J. Org. Chem.* **1997**, *62*, 1268–1273; (g) Wolfe, J. P.; Tomori, H.; Sadighi, J. P.; Yin, J.; Buchwald, S. L. *J. Org. Chem.* **2000**, *65*, 1158–1174.
23. Larraya, C.; Guillard, J.; Renard, P.; Audinot, V.; Boutin, J. A.; Delagrange, P.; Bennejean, C.; Viaud-Massuard, M. C. *Eur. J. Med. Chem.* **2004**, *39*, 515–526.