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Palladium-Catalyzed Synthesis of 2,3-Disubstituted 5-Azaindoles via Heteroannulation Reaction and of 2-Substituted 5-Azaindoles through Domino Sila-Sonogashira/5-Endo Cyclization

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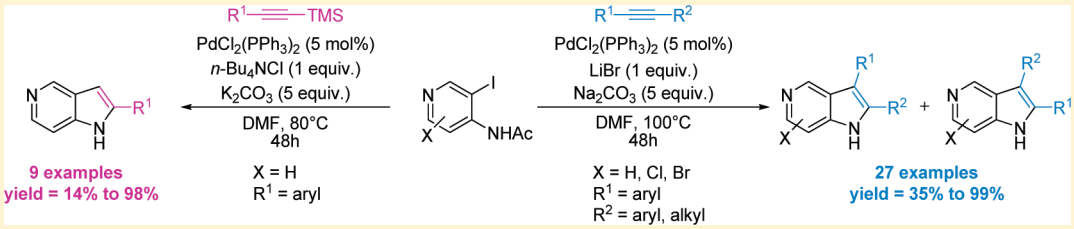
Supporting Information



ABSTRACT: A general and efficient procedure for the synthesis of 2,3-disubstituted 5-azaindoles through the palladium-catalyzed heteroannulation of 4-acetamido-3-iodopyridines and diaryl-, dialkyl-, or arylalkylalkynes is described along with a study of the reaction regioselectivity. The preparation of 2-monosubstituted 5-azaindoles via sila-Sonogashira/5-endo cyclization is also reported. These methods allowed us to prepare 36 diversely substituted 5-azaindoles in good yields.

INTRODUCTION

Aromatics and heteroaromatics rings are present in many natural and/or biologically active compounds, and their efficient construction represents a recurrent challenge. For the synthesis of indoles, many strategies have been developed,[1] including the Madelung reaction,[2] the Fischer synthesis,[3] the Leimgruber−Batcho reaction,[4] the Hemetsberger−Knittel reaction,[5] and the Bartoli reaction.[6] These historical methods, although fairly efficient, suffer from the difficult preparation of the reaction partners and, more importantly, from a lack of flexibility and versatility. Some of these drawbacks could be overcome through the use of palladium catalysis,[7] which over the past two decades has dramatically changed the retrosynthetic analysis of heterocycles.[8] Notably, the palladium catalyzed heteroannulation reaction reported by Larock allows the straightforward preparation of a broad range of 3- or 2,3-disubstituted indole skeletons from easily accessible starting materials.[9] In the course of our ongoing research project aiming at the evaluation of polysubstituted 5-azaindoles as kinase inhibitors, we turned our attention to the preparation of these scaffolds through Larock heteroannulation reaction. Gronowitz and co-workers were the first to apply such strategy for the preparation of a 5-azaindole, which was obtained in a modest yield of 40% (Scheme 1, conditions a).[10] A few years later, Ujjainwalla and co-workers somewhat improved the reaction conditions to access 5-, 6-, or 7-azaindoles.[11,12] Although good yields were obtained for 6 and 7 isomers, in the specific case of 5-azaindoles, only three examples were reported with yields ranging from 22% ($R^1 = R^2 =$ Ph) to 78% ($R^1 = R^2 =$ *n*-Pr) (Scheme 1, conditions b).

Therefore, applying methods of indole synthesis to prepare azaindoles and particularly 5-azaindoles is not trivial.[13−15] Theoretical studies have been realized to explain the particular properties of azaindoles.[16] It seems that the electron-deficient nature of the pyridine ring and, in the case of 5-azaindoles, the *para* relationship between the two nitrogen atoms are responsible of their uncommon behavior. On the other hand, 5-azaindoles possess interesting biological properties and can be found as key skeletons of anthelmintic agents,[17] thrombin inhibitors,[18] coagulation factors inhibitors,[19,20] kinase inhibitors,[21−23] 5-HT_6 receptor ligands,[24] HIV-1 inhibitors,[25] and CB_2 agonists.[26] In this context, a straightforward access to 5-azaindoles is crucial and led us to study in detail the Larock heteroannulation reaction leading to those attractive compounds.

Accordingly, we recently reported the high yield preparation of 2,3-diaryl-5-azaindoles starting from 4-acetamido-3-iodopyridines and diarylalkynes.[27] We wish to report herein a full study of the heteroannulation approach to diversely substituted 5-azaindoles investigating the use of diaryl-, dialkyl-, and alkylarylacetylenes associated with a study of the reaction regioselectivity. The reaction with silylated alkynes leading to the serendipitous preparation of 2-aryl-5-azaindoles is also reported.

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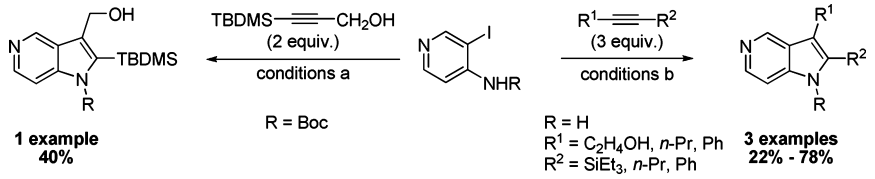
Scheme 1. Literature Examples of 5-Azaindole Synthesis by Larock Heteroannulation

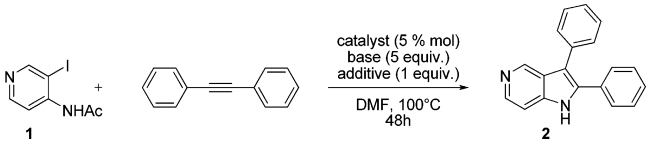


Conditions : a) $Pd(OAc)_2$ (5 mol%), KOAc (5quiv.), n-Bu_4NCl (1 equiv.), DMF, 90°C - 100°C
b) $Pd(dppf)Cl_2$ (5 mol%), Na_2CO_3 (2 equiv.), LiCl (1 equiv.), DMF, 100°C

RESULT AND DISCUSSION

The heteroannulation reaction with diarylalkynes was initially studied starting from 4-acetamido-3-iodopyridine **1** and diphenylacetylene (5 equiv) in DMF at 100 °C during 48 h. Using $Pd(OAc)_2$ (5 mol %) as palladium source, several bases (5 equiv) and additives (1 equiv) were investigated (Table 1).

Table 1. Optimization of the Heteroannulation Reaction between 4-Acetamido-3-iodopyridine 1 and Diphenylacetylene



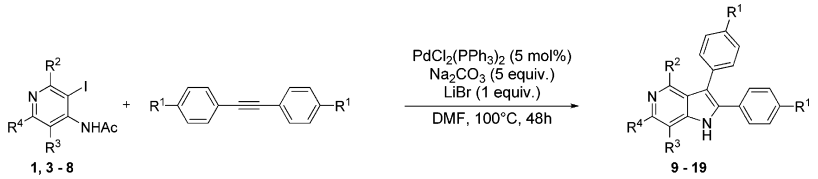
entry	base	additive	catalyst	alkyne (equiv)	**2** (%)
1	K_2CO_3	*n*-Bu_4NCl	$Pd(OAc)_2$	5	0[a]
2	K_2CO_3	LiCl	$Pd(OAc)_2$	5	0[a]
3	KOAc	*n*-Bu_4NCl	$Pd(OAc)_2$	5	24[b]
4	KOAc	LiCl	$Pd(OAc)_2$	5	28[b]
5	NaOAc	LiCl	$Pd(OAc)_2$	5	30[b]
6	Na_2CO_3	*n*-Bu_4NCl	$Pd(OAc)_2$	5	52[b]
7	Na_2CO_3	LiCl	$Pd(OAc)_2$	5	58[b]
8	Na_2CO_3	LiBr	$Pd(OAc)_2$	5	89[b]
9	Na_2CO_3	LiI	$Pd(OAc)_2$	5	83[b]
10	Na_2CO_3	LiBr	$PdCl_2(PPh_3)_2$	3	95

[a]Only starting material was recovered. [b]Uncomplete conversion.

LiCl or *n*-Bu_4NCl did not allow the desired annulation reaction with potassium carbonate as base (Table 1, entries 1 and 2), whereas the desired 5-azaindole **2** was isolated in low yield with potassium and sodium acetate (Table 1, entries 3–5). A significant improvement was observed when sodium carbonate was used as base, since **2** was obtained in 52% employing *n*-Bu_4NCl. Substituting this additive with LiCl, LiBr, or LiI further enhanced reactivity, allowing the isolation of **2** in 58%, 89%, and 83% yield, respectively (Table 1, entries 7, 8, and 9).[28] Finally, the use of $PdCl_2(PPh_3)_2$ as palladium source allowed us to decrease the amount of diphenylacetylene (3 equiv) while obtaining a nearly quantitative yield of the desired 5-azaindole **2** (Table 1, entry 10).

With these optimized reaction conditions in hand, we pursued our studies by the evaluation of the reaction between halogenated acetamidopyridines[29] and/or substituted diarylalkynes. Starting from 4-acetamido-2-chloro-3-iodopyridine **3** and diphenylacetylene, the 5-azaindole **9** was obtained in 80% yield (Table 2, entry 1). Similarly, good yields were obtained from 5- and 6-chloro isomers **4** and **5** (Table 2, entry 2 and 3), thus demonstrating the tolerance of a chlorine atom on every available position of the pyridine ring, and offering the possibility to further functionalize the obtained chloro-5-azaindoles **10** and **11** through cross coupling reactions. In the same way, the 5-bromo isomer **6** allowed the formation of bromo-5-azaindole **12** in good yield (Table 2, entry 4). However, the presence of a bromine atom in position 6 resulted in a significant decrease of efficiency, affording **13** in 60% yield (Table 2, entry 5), and an uncomplete reaction conversion was

Table 2. Heteroannulation Reaction between 4-Acetamido-3-iodopyridine 1 and 3 to 8 and Symmetrical Diarylacetylenes



entry	substrate	R^1	R^2	R^3	R^4	product	yield (%)
1	**3**	H	Cl	H	H	**9**	80
2	**4**	H	H	Cl	H	**10**	99
3	**5**	H	H	H	Cl	**11**	79
4	**6**	H	H	Br	H	**12**	79
5	**7**	H	H	H	Br	**13**	60
6	**8**	H	Br	H	H	**14**	42[a]
7	**1**	Cl	H	H	H	**15**	76
8	**1**	OMe	H	H	H	**16**	85
9	**1**	NO_2	H	H	H	**17**	*b*
10	**3**	OMe	Cl	H	H	**18**	46
11	**5**	OMe	H	H	Cl	**19**	66

[a]Uncomplete conversion. [b]Only starting material was recovered.

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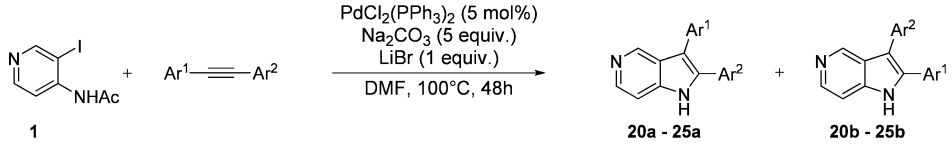
Table 3. Heteroannulation Reaction between 4-Acetamido-3-iodopyridine 1 and Unsymmetrical Diarylacetylenes



entry	Ar^1	Ar^2	products	**a**/**b** ratio[a]	yield (%)
1	Ph	4-CH_2OMe-Ph	**20a**/**20b**	50/50	77
2	Ph	4-Cl-Ph	**21a**/**21b**	50/50	89
3	Ph	4-MeO-Ph	**22a**/**22b**	50/50	87
4	Ph	4-NO_2-Ph	**23a**/**23b**		*b*
5	Ph	4-pyridyl	**24a**/**24b**	50/50	60
6	Ph	2-pyridyl	**25a**/**25b**	100/0	14 (35)[c]

[a]Determined by ^{1}H NMR spectroscopy of the crude mixture. [b]Degradation of the reaction mixture. [c]Based on recovery of starting material.

observed with a bromine atom in position 2. Indeed, **14** was isolated in a modest yield (Table 2, entry 6, 42%), possibly arising from unfavorable steric strains. If the low yield observed in the reaction of 4-acetamido-2-bromopyridines could be attributed to steric hindrance, the general observation of a lower yield with a bromine than with a chlorine could be explained by a better chemoselectivity of the latter during the palladium(0) oxidative addition.

We then evaluated the influence of electron-donating or electron-withdrawing groups in positions 4 and 4′ of the diarylalkyne partner. With aromatic rings bearing a chlorine atom or a methoxy moiety, the reaction of 4-acetamido-3-iodopyridine **1** promoted the formation of the desired products **15** and **16** in good yields of 76% and 85%, respectively (Table 2, entries 7 and 8). However, with a strongly electron-withdrawing substituent, like a nitro group, only starting material was recovered (Table 2, entry 9), probably because electron-poor alkyne difficultly coordinates to the palladium complex and therefore the catalytic cycle cannot be fully achieved. Finally, we combined the use of 2- and 6-chlorinated acetamidopyridines **3** and **5** with the electron-rich 1,2-bis(4-methoxyphenyl)alkyne and could obtain the corresponding azaindoles **18** and **19** with 46% and 66% yield, respectively (Table 2, entries 10 and 11).

The next step was to evaluate the reactivity of unsymmetrical diarylalkynes exhibiting different electronic properties at aryl substituents. To the best of our knowledge, the regioselectivity of this heteroannulation process based on a difference of electronic properties of the two alkyne's substituents was never reported. The reaction was thus realized with alkynes bearing a phenyl group and an electron-rich or electron-poor aromatic ring. When the *para* substituent is a methoxymethyl, a chlorine, or a methoxy, the desired 5-azaindoles **20**, **21**, and **22** were obtained with good yields of 77%, 89%, and 87%, respectively (Table 3, entries 1, 2, and 3). However, similarly to the corresponding symmetrical alkynes, a nitro group hampered the formation of the desired product (Table 3, entry 4). The reaction was also evaluated with a pyridine as the second aromatic ring of the alkyne. With a 4-pyridyl ring, the desired 5-azaindole **24** was formed in 60% yield (Table 3, entry 5), whereas with a 2-pyridyl ring, the product **25** was obtained in a poor yield of 14% (35% based on the recovery of starting material, Table 3, entry 6).

This study proved the regioselectivity of the reaction to be independent of electronic effects as most of the alkynes gave equimolar mixtures of 5-azaindole regioisomers. In the case of 2-(phenylethynyl)pyridine, only one regioisomer was isolated, but the low yield obtained does not allow to clearly rationalize this result.

We next tested the scope of the reaction with dialkylalkynes and arylalkylalkynes. Keeping the same conditions, the reaction proved to be compatible with dialkylalkynes since the use of 4-octyne and 1,4-dimethoxybut-2-yne led to the corresponding 5-azaindoles **26** and **27** in a yield of 63% in both cases (Table 4, entries 1 and 2). Various alkynes bearing a phenyl moiety and an alkyl group were then used. The propynylbenzene promoted the formation of both regioisomers **28a**/**28b** in a 50/50 ratio with a yield of 83% (Table 4, entry 3).

With a little more hindered alkyl group like a *n*-butyl, a slight preference for the regioisomer possessing the alkyl moiety in position 2 appeared (Table 4, entry 4). These two last results showed again the particular behavior of the 5-azaindole core, since a total regioselectivity in favor of the 3-alkyl isomer was described by Larock et al. with similar alkynes in the indole series,[9] and in the 7-azaindole serie by Yum et al.,[12g] whereas the latter recently showed a poor regioselectivity in the context of the preparation of 6-azaindoles.[12i] We then pursued this study of the regioselectivity of annulations with more hindered alkyl substituents. With a methoxymethyl, an isobutyl or an isopropyl group an identical ratio of 60/40 was reached in good yields (Table 4, entries 5−7).With the same efficiency, the regioselectivity could be further improved with a cyclohexyl or a cyclopropyl, reaching a 2-alkyl/3-alkyl ratio of 65/35 and 70/30 respectively (Table 4, entries 8 and 9). Finally, a total regioselectivity was obtained when highly hindered *tert*-butyl phenylacetylene was used, but in this case, the reaction conversion was uncomplete and led to the isolation of 66% of **35a**.

The regioselectivity of the reaction being total when the alkyne bears a phenyl and a *tert*-butyl group, we next envisioned the use of silylalkynes. According to the literature[9] and our present results, the regioselectivity should be total, placing the silyl group in position 2 of the 5-azaindole and the phenyl group in position 3. After protodesilylation, an access to monosubstituted 3-aryl-5-azaindole could therefore be obtained.

Unexpectedly, under our optimized reaction conditions, 4-acetamido-3-iodopyridine **1** and 1-phenyl-2-trimethylsilylacetylene led only to alkyne **37** resulting from TMS deprotection and subsequent Sonogashira coupling (Table 5, entry 1). Changing the additive from LiBr to *n*-Bu_4NCl promoted the formation of the Sonogashira product **37** together with the unanticipated 2-phenyl-5-azaindole **38** (Table 5, entry 2). Considering that the deprotection of the silyl group might be

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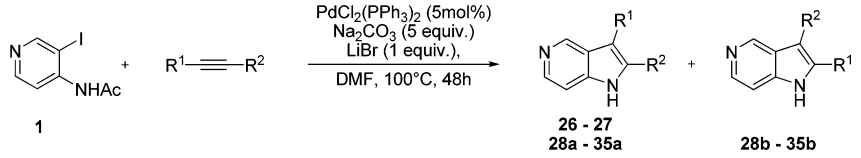
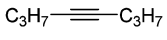
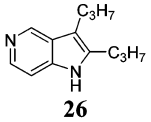
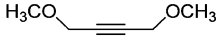
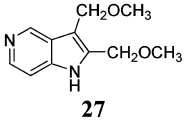
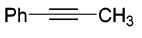
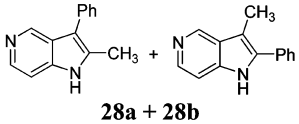
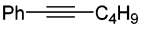
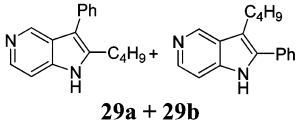
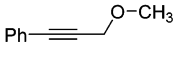
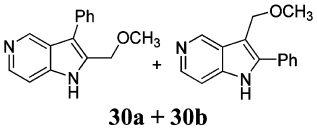
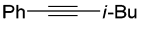
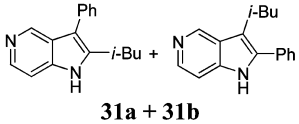
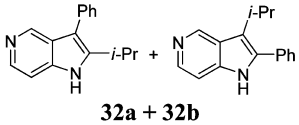
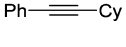
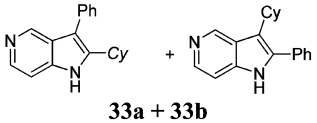
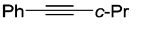
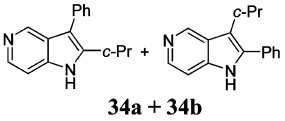
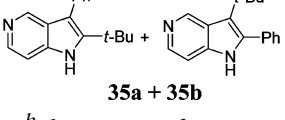
Table 4. Heteroannulation Reaction between 4-Acetamido-3-iodopyridine 1 and Dialkyl- and Arylalkylacetylenes



entry	alkyne	5-azaindole	a/b ratio[a,b]	yield (%)
1		 **26**	-	63
2		 **27**	-	63
3		 **28a + 28b**	50/50	83
4		 **29a + 29b**	55/45	81
5		 **30a + 30b**	60/40	77
6		 **31a + 31b**	60/40	92
7		 **32a + 32b**	60/40	83
8		 **33a + 33b**	65 /35	94
9		 **34a + 34b**	70/30	76
10		 **35a + 35b**	100/0	66 (73)[c]

[a]Determined by ^{1}H NMR spectroscopy of the crude mixture. [b]The structure of major isomer was determined by HMBC, HMQC, or NOESY NMR experiments. [c]Based on recovery of starting material.

responsible of these undesirable processes, more hindered and less labile silyl groups were tested. Accordingly, the reaction was conducted with the 1-phenyl-2-triethylsilylacetylene and LiBr as additive, and allowed the formation of the desired 2-silyl-3-phenyl 5-azaindole **36**, albeit in a low yield of 20% (Table 5, entry 3). Unfortunately, when *n*-Bu_4NCl was used as additive, no formation of the desired product was observed, and instead, 13% of the Sonogashira product **37** with 40% of the

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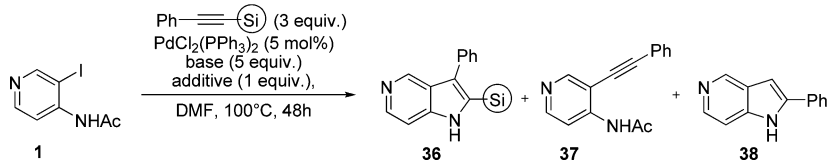
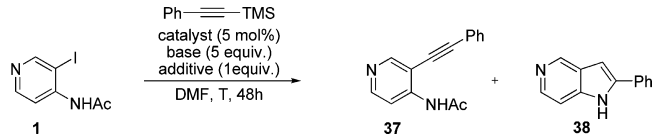
Table 5. Reaction between 4-Acetamido-3-iodopyridine 1 and Various Silylated Phenylacetylenes



entry	Si group	base	additive	catalyst	**36** (%)	**37** (%)	**38** (%)
1	TMS	Na_2CO_3	LiBr	$PdCl_2(PPh_3)_2$		65	
2	TMS	Na_2CO_3	*n*-Bu_4NCl	$PdCl_2(PPh_3)_2$		32	32
3	TES	Na_2CO_3	LiBr	$PdCl_2(PPh_3)_2$	20		
4	TES	Na_2CO_3	*n*-Bu_4NCl	$PdCl_2(PPh_3)_2$		13	40
5	TIPS[a]	Na_2CO_3	LiBr	$PdCl_2(PPh_3)_2$			
6	TBDMS[a]	Na_2CO_3	LiBr	$PdCl_2(PPh_3)_2$			

[a]Degradation of the reaction mixture.

Table 6. Tandem Sila-Sonogashira/5-Endo-Cyclization between 4-Acetamido-3-iodopyridine 1 and 1-Phenyl-2-trimethylsilylacetylene



entry	base	additive	catalyst	alkyne (equiv)	*T* (°C)	**37** (%)	**38** (%)
1	NaOAc	*n*-Bu_4NCl	$PdCl_2(PPh_3)_2$	3	100	61	
2	KOAc	*n*-Bu_4NCl	$PdCl_2(PPh_3)_2$	3	100	58	15
3	$NaHCO_3$	*n*-Bu_4NCl	$PdCl_2(PPh_3)_2$	3	100	22	45
4	Cs_2CO_3	*n*-Bu_4NCl	$PdCl_2(PPh_3)_2$	3	100		36
5	$KHCO_3$	*n*-Bu_4NCl	$PdCl_2(PPh_3)_2$	3	100		51
6	K_2CO_3	*n*-Bu_4NCl	$PdCl_2(PPh_3)_2$	3	100		67
7	K_2CO_3	*n*-Bu_4NBr	$PdCl_2(PPh_3)_2$	3	100		63
8	K_2CO_3	*n*-Bu_4NI	$PdCl_2(PPh_3)_2$	3	100		55
9	K_2CO_3	*n*-Bu_4NCl	$Pd(OAc)_2$	3	100		58
10	K_2CO_3	*n*-Bu_4NCl	$PdCl_2(PhCN)_2$	3	100		64
11	K_2CO_3	*n*-Bu_4NCl	$Pd(dppf)Cl_2$	3	100		65
12	K_2CO_3	*n*-Bu_4NCl	$PdCl_2(PPh_3)_2$	5	100		77
13	K_2CO_3	*n*-Bu_4NCl	$PdCl_2(PPh_3)_2$	5	90		85
14	K_2CO_3	*n*-Bu_4NCl	$PdCl_2(PPh_3)_2$	5	80		98

cyclization product **38** were isolated (Table 5, entry 4). On the other hand, the use of very bulky triisopropylsilyl and *tert*-butyldimethylsilyl alkynes resulted mostly in the degradation of the reaction mixture (Table 5, entries 5 and 6).

Although an efficient access to 3-substituted 5-azaindoles could not be obtained from the use of silylalkynes, we decided to take advantage of the serendipitous preparation of 2-substituted 5-azaindole **38**. It is reasonable to consider that its formation resulted from the copper free one pot sila-Sonogashira[30]/5-endo cyclization domino reaction. Such Sonogashira/cyclization approach has already found some success in the preparation of indoles,[7] but has been much less studied in the specific case of 5-azaindoles synthesis. To the best of our knowledge, this strategy has only been reported once by Xu et al. and has been applied to the one pot preparation of only three 5-azaindoles with yields ranging from 44% to 65%.[31] Notably, the same authors obtained much better yields via a sequential approach. In this context, we decided to reinvestigated and optimize this domino strategy for the efficient and versatile synthesis of a broader range of 2-substituted 5-azaindoles.

We thus started to optimize the reaction conditions using the commercially available 1-phenyl-2-trimethylsilylacetylene. As aforementioned, the reaction conditions that we developed for the heteroannulation using *n*-Bu_4NCl as additive led to the formation of 32% of the Sonogashira product **37** and 32% of the desired 5-azaindole **38** (Table 5, entry 2). Various bases were subsequently tested using this additive. Sodium acetate promoted the exclusive formation of the Sonogashira product **37** in 61% yield (Table 6, entry 1), whereas potassium acetate and sodium bicarbonate led to a mixture of the Sonogashira product **37** and the 5-azaindole **38** (Table 6, entries 2 and 3). Pleasingly, when cesium carbonate, potassium bicarbonate, and potassium carbonate were used, the 2-subtituted 5-azaindoles **38** was the only product obtained in a yield of 36%, 51%, and 67%, respectively (Table 6, entries 4, 5, and 6). Keeping potassium carbonate as base, we modified the counterion of the additive to bromide and iodide without improving the yield of the reaction (Table 6, entries 7 and 8). We thus turned our attention to the catalyst but when $Pd(OAc)_2$, $PdCl_2(PhCN)_2$, or $Pd(dppf)Cl_2$ was used the yield remained below 67% (Table 6, entries 9, 10, and 11). The yield reached 77% when the reaction was conducted with 5 equivalents of the alkyne (Table 6, entry 12), but finally a major improvement was obtained when the reaction temperature was decreased. Indeed, at 90 and 80 °C **38** the desired 5-azaindole was formed in

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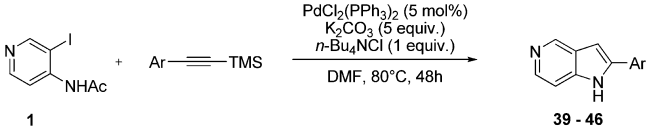
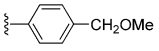
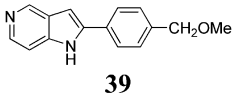
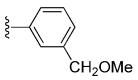
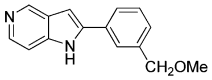
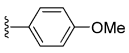
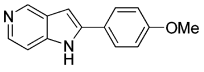
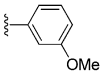
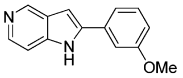
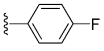
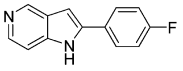
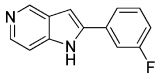
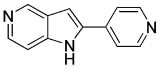
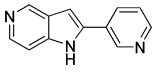
respectively 85% and 98% (Table 6, entries 13 and 14). Notably, below 80 °C, the reaction led to a mixture of the Sonogashira product **37** and the cyclization product **38**.

With these conditions in hand, the scope of the reaction was next explored changing the nature of the aromatic ring of the alkyne. We could demonstrate that the reaction tolerates electron-donating and electron-attracting groups on the aromatic ring.

Indeed, methoxymethyl, methoxy, and fluorine substituents in either *para* or *meta* position relative to the triple bond allowed the preparation of 2-aryl-5 azaindoles **39**-**44** in good to excellent yields ranging from 63% to 95% (Table 7, entries 1 to 6). Lower yields were obtained from 4-pyridyl- and 3-pyridyl-trimethylsilylacetylenes partially due to purification issues because of the high polarity of final compounds (Table 7, entries 7 and 8).

Table 7. Synthesis of 2-Substituted 5-Azaindoles by the Tandem Sila-Sonogashira/5-Endo-Cyclization Process



entry	aryl	5-azaindole	yield (%)
1		 **39**	73
2		 **40**	95
3		 **41**	66
4		 **42**	67
5		 **43**	79
6		 **44**	63
7		 **45**	14
8		 **46**	25

CONCLUSION

In this paper, we reported the palladium catalyzed synthesis of diversely substituted 5-azaindoles from 4-acetamido-3-iodopyridines. 2,3-Disubstituted 5-azaindoles were prepared via heteroannulation reaction with diaryl-, dialkyl-, and arylalkylalkynes in good yields. The use of unsymmetrical alkynes allowed us to evaluate the regioselectivity of the reaction depending on electronic and steric effects. An unexpected sila-Sonogashira/5-endocyclization process led to the preparation of 2-monosubstituted 5-azaindoles. Both methods permitted the synthesis of a large scope of 5-azaindoles possessing various substituents on both the pyridine and the pyrrole ring. A biological evaluation of all the compounds described herein as kinase inhibitors is currently under investigation.

EXPERIMENTAL SECTION

General Methods. All reactions were conducted in flame-dried or oven-dried glassware under dry argon atmosphere unless otherwise indicated. All other commercial reagents and solvents were used as received without additional purification. Reactions were followed with TLC (0.25 mm silica gel 60-F plates). Visualization was accomplished with UV light. Flash chromatography was carried out on silica gel 320−400 mesh. ^{1}H NMR spectra were recorded at 300 MHz. ^{13}C NMR spectra were recorded at 75 MHz with complete proton decoupling. Chemical shifts are reported in ppm relative to the residual solvent peak ($CDCl_3$, DMSO-d_6 or MeOD-d_4) as the internal reference, coupling constants are given in Hertz. Multiplicities are reported as follows: s = singlet, d = doublet, t = triplet, sx = sextuplet, st = septuplet, m = multiplet, s br = broad singlet. IR spectra were taken with FT-IR. Melting points were determined on a Kofler bench and were uncorrected. HRMS were collected using a Bruker maXis (Ultra High Resolution TOF) analyzer.

4-Amino-3-iodopyridine I and 4-Amino-3,5-diiodopyridine II. General procedure C for iodination reaction: A solution of potassium iodide (1.06 g, 6.38 mmol) and iodine (1.00 g, 3.94 mmol) in water (4.20 mL) was added dropwise to a solution of 4-aminopyridine (0.50 g, 5.32 mmol) and sodium carbonate (0.33 g, 3.14 mmol) in water (1.90 mL) at reflux temperature. Upon complete addition, the mixture was stirred for 16 h at reflux then cooled to room temperature and extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with saturated sodium thiosulfate solution (3 × 15 mL), dried over $MgSO_4$, filtered, and concentrated under vacuum. The different products were separated by chromatography (silica gel, EtOAc/cyclohexane 40:60 to 100:0) to give **I** (0.40 g, 34% yield) previously described[19] and **II** (0.16 g, 6% yield) as white solids. **II**. Mp: 103−105 °C. R_f = 0.57 (EtOAc). ^{1}H NMR ($CDCl_3$, 300 MHz), δ (ppm): 8.43 (s, 2H), 5.14 (s br, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz), δ (ppm): 156.4 (2C), 151.7 (2C), 80.3. IR (NaCl, thin film), ν (cm^{-1}): 3279, 3159, 1606, 1470, 1254, 1030, 722. LRMS (ESI^+): m/z = 346.9 ($[M + H]^+$, 100), 301.3 (28). HRMS (ESI^+): calcd for $C_5H_5N_2I_2$ $[M + H]^+$ 346.8542, found 346.8538.

4-Amino-2-chloro-3-iodopyridine III, 4-Amino-2-chloro-5-iodopyridine IV, and 4-Amino-2-chloro-3,5-diiodopyridine V. General procedure D for iodination reaction: 4-amino-2-chloropyridine (10.20 g, 79.34 mmol) was dissolved in 200 mL of a buffer solution of potassium acetate (pH = 5.5, c = 0.5 mol·L^{-1}). Iodine chloride (14.00 g, 86.22 mmol) was added and the solution was stirred for 4 days at 75 °C. The mixture was neutralized (pH 7−8) with a saturated solution of sodium carbonate and a saturated solution of sodium thiosulfate was added (200 mL). After extraction with EtOAc (3 × 450 mL), the combined organic layers were concentrated under vacuum. The purification of the residue by chromatography (silica gel, EtOAc/cyclohexane 10:90 to 40:60) afforded 9.08 g (45% yield) of **III**, 6.05 g (30% yield) of **IV** and 3.32 g (11% yield) of **V** as white solids. **III**. Mp: 123−125 °C. R_f = 0.50 (EtOAc). ^{1}H NMR ($CDCl_3$, 300 MHz), δ (ppm): 7.84 (d, 1H, J = 5.5 Hz), 6.44 (d, 1H, J = 5.5 Hz), 5.05 (s br, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz), δ (ppm): 155.9, 155.6, 148.2, 107.5, 82.7. IR (NaCl, thin film), ν (cm^{-1}): 3451, 3287, 3156, 1630, 1580, 1379, 1275, 823. LRMS (ESI^+): m/z = 255.0 ($[M + H]^+$, 100), 257.0 (32). HRMS (ESI^+): calcd for $C_5H_5N_2ClI$ $[M + H]^+$ 254.9186, found 254.9175. **IV**. Mp: 131−133 °C. R_f = 0.67 (EtOAc). ^{1}H NMR ($CDCl_3$, 300 MHz), δ (ppm): 8.32 (s, 1H), 6.62 (s, 1H), 4.80 (b.s, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz), δ (ppm): 156.3, 154.3, 152.0, 108.1, 80.6. IR (NaCl, thin film), ν (cm^{-1}): 3446, 3302, 3174, 1616, 1573, 1097. LRMS (ESI^+): m/z = 255.0 ($[M + H]^+$, 100), 257.0

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(32). HRMS (ESI^+): calcd for $C_5H_3N_2ClI$ $[M + H]^+$ 254.9186, found 254.9181. **V**. Mp: 161−162 °C. R_f = 0.50 (EtOAc/cyclohexane 4/6). ^1H NMR ($CDCl_3$, 300 MHz), δ (ppm): 8.23 (s, 1H), 5.41 (s br, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz), δ (ppm): 155.7, 154.7, 154.6, 81.3, 77.4. IR (NaCl, thin film), ν (cm^{-1}): 3445, 3295, 1604, 1542, 1366, 1023. LRMS (ESI^+): m/z = 380.8 ($[M + H]^+$, 100), 382.8 (32). HRMS (ESI^+): calcd for $C_5H_4N_2ClI_2$ $[M + H]^+$ 380.8153, found 380.8168.

4-Amino-2-bromo-3-iodopyridine VI, 4-Amino-2-bromo-5-iodopyridine VII, and 4-Amino-2-bromo-3,5-diiodopyridine VIII. Compounds **VI**−**VII** were prepared following the general procedure C with 5.03 g (29.07 mmol) of 4-amino-2-bromopyridine. The different products were separated by chromatography (silica gel, EtOAc/cyclohexane 5:95 to 50:50) to give starting material (2.32 g, 46% yield), **VI** (2.06 g, 24% yield), **VII** (1.51 g, 17% yield), and **VIII** (0.37 g, 5% yield) as white solids. **VI**. Mp: 142−144 °C. R_f = 0.25 (EtOAc/cyclohexane 4/6). ^1H NMR ($CDCl_3$, 300 MHz), δ (ppm): 7.88 (d, 1H, J = 5.4 Hz), 6.47 (d, 1H, J = 5.4 Hz), 4.90 (s br, 2H). ^{13}C NMR (MeOD, 75 MHz), δ (ppm): 159.1, 149.8, 148.6, 108.5, 86.0. IR (NaCl, thin film), ν(cm^{-1}): 3492, 3389, 1725, 1616, 1372, 1046, 733, 711. LRMS (ESI^+): m/z = 300.8 ($[M + H]^+$, 100), 298.8 (97). HRMS (ESI^+): calcd for $C_5H_5N_2BrI$ $[M + H]^+$ 298.8681, found 298.8692. **VII**. Mp: 141−143 °C. R_f = 0.44 (EtOAc/cyclohexane 4/6). ^1H NMR ($CDCl_3$, 300 MHz), δ (ppm): 8.31 (s, 1H), 6.78 (s, 1H), 4.71 (s br, 2H). ^{13}C NMR (MeOD, 75 MHz), δ (ppm): 157.9, 157.1, 142.2, 112.2, 80.5. IR (NaCl, thin film), ν (cm^{-1}): 3391, 1574, 1090, 745, 731, 706. LRMS (ESI^+): m/z = 300.9 ($[M + H]^+$, 100), 298.9 (97). HRMS (ESI^+): calcd for $C_5H_5N_2BrI$ $[M + H]^+$ 298.8681, found 298.8683. **VIII**. Mp: 142−144 °C. R_f = 0.50 (EtOAc/cyclohexane 4/6). ^1H NMR ($CDCl_3$, 300 MHz), δ (ppm): 8.23 (s, 1H), 5.42 (s br, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz), δ (ppm): 154.9, 154.3, 149.3, 85.6, 78.1. IR (NaCl, thin film), ν (cm^{-1}): 3477, 3372, 1737, 1608, 1254, 752, 714. LRMS (ESI^+): m/z = 422.6 ($[M - H]^-$, 36), 424.6 (26). HRMS (ESI^+): calcd for $C_5H_4N_2BrI_2$ $[M + H]^+$ 424.7647, found 424.7658.

4-Amino-3-chloro-5-iodopyridine IX. Compound **IX** was prepared following the general procedure C with 2.04 g (15.85 mmol) of 4-amino-3-chloropyridine, 9.50 g (57.00 mmol) of potassium iodide and 8.97 g (35.40 mmol) of iodine. The mixture was stirred for 120 h at reflux and then cooled to room temperature and extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with saturated sodium thiosulfate solution (3 × 15 mL), dried over $MgSO_4$, filtered, and concentrated under vacuum. The different products were separated by chromatography (silica gel, EtOAc/cyclohexane 20:80 to 100:0) to give 267 mg (13% yield) of starting material and 1.99 g (49% yield) of **IX** as white solids. **IX**. Mp: 126−128 °C. R_f = 0.39 (EtOAc/cyclohexane 4/6). ^1H NMR ($CDCl_3$, 300 MHz), δ (ppm): 8.44 (s, 1H), 8.18 (s, 1H), 5.06 (s br, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz), δ (ppm): 155.1, 149.1, 148.2, 115.5, 81.2. IR (NaCl, thin film), ν (cm^{-1}): 3490, 3387, 1738, 1612, 1262, 1245, 752, 745. LRMS (ESI^+): m/z = 254.9 ($[M + H]^+$, 100), 256.9 (32). HRMS (ESI^+): calcd for $C_5H_5N_2ClI$ $[M + H]^+$ 254.9186, found 254.9198.

4-Amino-3-bromo-5-iodopyridine X. Compound **X** was prepared following the general procedure C with 5.11 g (29.52 mmol) of 4-amino-3-bromopyridine. The purification of the residue by chromatography (silica gel, EtOAc/cyclohexane 50:50 to 100:0) afforded 2.90 g (57% yield) of starting material and 2.80 g (32% yield) of **X** as white solids. **X**. Mp: 132−134 °C. R_f = 0.42 (EtOAc/cyclohexane 4/6). ^1H NMR ($CDCl_3$, 300 MHz), δ (ppm): 8.45 (s, 1H), 8.28 (s, 1H), 5.11 (s br, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz), δ (ppm): 155.6, 150.1, 149.8, 105.3, 81.1. IR (NaCl, thin film), ν (cm^{-1}): 3485, 3383, 1738, 1612, 1254, 1245, 736, 704. LRMS (ESI^+): m/z = 296.8 ($[M - H]^-$, 100), 298.8 (97). HRMS (ESI^-): calcd for $C_5H_3N_2BrI$ $[M - H]^-$ 296.8524, found 296.8522.

3-Phenyl-2-(pyridin-4-yl)-1*H*-pyrrolo[3,2-*c*]pyridine 24a and 2-Phenyl-3-(pyridin-4-yl)-1*H*-pyrrolo[3,2-*c*]pyridine 24b. General procedure A for the heteroannulation reaction: Under argon atmosphere, 4-acetamido-3-iodopyridine **1** (226 mg, 0.863 mmol) was dissolved in 4.3 mL of anhydrous DMF, along with $PdCl_2(PPh_3)_2$ (30 mg, 0.043 mmol), LiBr (74 mg, 0.863 mmol), and Na_2CO_3 (450 mg, 4.25 mmol). Then, 4-(phenylethynyl)pyridine (463, 2.598 mmol) was added. The reaction mixture was warmed to 100 °C and stirred at this temperature for 48 h. After this time, it was cooled to rt and concentrated. Two milliliters of water were then added, and the aqueous layer was extracted with EtOAc (3 × 7 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under vacuum. The purification of the residue by chromatography (silica gel, cyclohexane/EtOAc/MeOH 70:30:0 to 0:90:10) gave **24a** (71.0 mg, 30%) and **24b** (70.0 mg, 30% yield) as yellow solids. **24a**. Mp > 260 °C. R_f = 0.15 (EtOAc/MeOH 9/1). ^1H NMR (DMSO, 300 MHz), δ (ppm): 12.27 (s br, 1H), 8.76 (s, 1H), 8.56 (d, J = 5.1 Hz, 2H), 8.29 (s br, 1H), 7.52−7.36 (m, 8H). ^{13}C NMR (DMSO, 75 MHz), δ (ppm): 149.6 (2C), 142.2, 141.3, 139.4, 138.5, 132.9, 131.5, 129.4 (2C), 128.7 (2C), 126.9, 124.5, 121.9 (2C), 115.1, 106.6. IR (CH_2Cl_2), ν (cm^{-1}): 3442, 3047, 2964, 2928, 1601, 763, 751, 698, 609. LRMS (ES^+): m/z = 272.1 ($[M + H]^+$, 100). HRMS (ESI^+): calcd for $C_{18}H_{14}N_3$ $[M + H]^+$ 272.1188, found 272.1192. **24b**. Mp: 249−251 °C. R_f = 0.10 (EtOAc/MeOH 9/1). ^1H NMR (DMSO, 300 MHz), δ (ppm): 12.29 (s br, 1H), 8.92 (s, 1H), 8.55 (d, J = 4.5 Hz, 2H), 8.29 (s br, 1H), 7.52−7.40 (m, 6H), 7.37 (d, J = 4.5 Hz, 2H). ^{13}C NMR (DMSO, 75 MHz), δ (ppm): 149.9 (2C), 142.0, 141.7, 141.2, 139.6, 136.9, 131.0, 129.7, 128.8 (4C), 124.2 (2C), 122.2, 109.7, 106.9. IR (CH_2Cl_2), ν (cm^{-1}): 3442, 3047, 2964, 2928, 1601, 763, 751, 698, 609. LRMS (ESI^+): m/z = 272.1 ($[M + H]^+$, 100). HRMS (ESI^+): calcd for $C_{18}H_{14}N_3$ $[M + H]^+$ 272.1188, found 272.1192.

3-Phenyl-2-(pyridin-2-yl)-1*H*-pyrrolo[3,2-*c*]pyridine 25a. Compound **25a** was prepared following the general procedure A with 225 mg (0.859 mmol) of 4-acetamido-3-iodopyridine **1** and 461 mg (2.576 mmol) of 2-(phenylethynyl)pyridine. Purification of the residue by chromatography (silica gel, cyclohexane/EtOAc/MeOH 70:30:0 to 0:90:10) gave starting material (157 mg, 68% yield) and **25a** (32.6 mg, 14% yield and 35% corrected yield) as a yellow solid. R_f = 0.19 (EtOAc/MeOH 9/1). ^1H NMR (DMSO, 300 MHz), δ (ppm): 12.14 (s br, 1H), 9.18 (s, 1H), 8.67 (d, J = 3.6 Hz, 2H), 8.23 (s br, 1H), 7.66 (t, J = 7.8 Hz, 1H), 7.54−7.41 (m, 5H), 7.27−7.22 (m, 1H), 7.21 (d, J = 8.1 Hz, 1H). ^{13}C NMR (DMSO, 75 MHz), δ (ppm): 154.2, 150.1, 143.8, 141.2, 140.0, 138.0, 136.8, 132.2, 129.4 (2C), 129.3 (3C), 124.9, 124.0, 121.6, 112.8, 107.2. IR (CH_2Cl_2), ν (cm^{-1}): 3443, 2958, 2928, 2856, 2360, 1724, 1465, 1269, 751, 745, 708, 698. LRMS (ESI^+): m/z = 272.1 ($[M + H]^+$, 100). HRMS (ESI^+): calcd for $C_{18}H_{14}N_3$ $[M + H]^+$ 272.1188, found 272.1191.

2,3-Dipropyl-1*H*-pyrrolo[3,2-*c*]pyridine 26. Compound **26** was prepared following the general procedure A with 201 mg (0.767 mmol) of 4-acetamido-3-iodopyridine **1** and 337 μL (2.298 mmol) of 4-octyne. The purification of the crude by chromatography (silica gel, cyclohexane/EtOAc/MeOH 70:30:0 to 0:90:10) gave **26** (97 mg, 63% yield) as a brown oil. R_f = 0.17 (EtOAc/MeOH 9/1). ^1H NMR (DMSO, 300 MHz), δ (ppm): 11.13 (s br, 1H), 8.69 (s, 1H), 8.05 (d br, 1H), 7,21 (d, J = 5.4 Hz, 1H), 2.65 (t, J = 7.5 Hz, 2H), 2.64 (t, J = 7.5 Hz, 2H), 1.64 (sx, J = 7.5 Hz, 2H), 1.58 (sx, J = 7.5 Hz, 2H), 0.89 (t, J = 7.5 Hz, 3H), 0.88 (t, J = 7.5 Hz, 3H). ^{13}C NMR (DMSO, 75 MHz), δ (ppm): 141.3, 139.9, 139.7, 137.8, 126.0, 110.9, 106.8, 28.2, 26.3, 24.9, 23.4, 14.7, 14.6. IR (CH_2Cl_2), ν (cm^{-1}): 3456, 3043, 2963, 2933, 2360, 1618, 1471, 736, 706, 613. LRMS (ESI^+): m/z = 203.2 ($[M + H]^+$, 100). HRMS (ESI^+): calcd for $C_{13}H_{19}N_2$ $[M + H]^+$ 203.1548, found 203.1540.

2,3-Bis(methoxymethyl)-1*H*-pyrrolo[3,2-c]pyridine 27. Compound **27** was prepared following the general procedure A with 249 mg (0.948 mmol) of 4-acetamido-3-iodopyridine **1** and 344 μL (2.854 mmol) of 1,4-dimethoxybut-2-yne. The purification of the residue by chromatography (silica gel, cyclohexane/EtOAc/MeOH 70:30:0 to 0:90:10) gave **27** (124 mg, 63% yield) as a yellow oil. R_f = 0.09 (EtOAc/MeOH 9/1). ^1H NMR (DMSO, 300 MHz), δ (ppm): 11.63 (s br, 1H), 8.84 (s, 1H), 8.16 (d, J = 5.6 Hz, 1H), 7.30 (d, J = 5.6 Hz, 1H), 4.63 (s, 2H), 4.59 (s, 2H), 3.29 (s, 3H), 3.25 (s, 3H). ^{13}C NMR (DMSO, 75 MHz), δ (ppm): 142.5, 140.9, 139.5, 135.5, 124.9, 110.1, 107.0, 64.8, 64.2, 57.9, 57.3. IR (CH_2Cl_2), ν (cm^{-1}): 3447, 3045, 2929, 2825, 2360, 1469, 1088, 751, 737, 725. LRMS (ESI^+): m/z = 207.1 ($[M + H]^+$, 100). HRMS (ESI^+): calcd for $C_{11}H_{15}N_2O_2$ $[M + H]^+$ 207.1137, found 207.1128.

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2-Methyl-3-phenyl-1*H*-pyrrolo[3,2-*c*]pyridine 28a and 3-Methyl-2-phenyl-1*H*-pyrrolo[3,2-*c*]pyridine 28b. Compounds **28a** and **28b** were prepared following the general procedure A with 201 mg (0.767 mmol) of 4-acetamido-3-iodopyridine **1** and 286 μL (2.302 mmol) of propynylbenzene. The purification of the residue by chromatography (silica gel, cyclohexane/EtOAc/MeOH 70:30:0 to 0:90:10) gave a mixture of **28a** and **28b** (132 mg, 83% yield) as a white solid. R_f = 0.17 (EtOAc/MeOH 9/1). **28a**. ^{1}H NMR (DMSO, 300 MHz), δ (ppm): 11.63 (s br, 1H), 8.79 (s, 1H), 8.16 (d, *J* = 5.0 Hz, 1H), 7.5667.37 (m, 5H), 7.33 (d, *J* = 5.0 Hz, 1H), 2.48 (s, 3H). ^{13}C NMR (DMSO, 75 MHz), δ (ppm): 142.7, 141.5, 141.4, 139.6, 134.4, 129.6 (2C), 128.5 (2C), 126.7, 124.8, 112.7, 107.0, 13.1. IR (CH_2Cl_2), ν (cm^{-1}): 3451, 3046, 2974, 2361, 1469, 744, 728, 605. LRMS (ESI$^+$): *m/z* = 209.1 ([M + H]$^+$, 100). HRMS (ESI$^+$): calcd for $C_{14}H_{13}N_2$ [M + H]$^+$: 209.1079, found 209.1071. **28b**. ^{1}H NMR (DMSO, 300 MHz), δ (ppm): 11.63 (s br, 1H), 8.84 (s, 1H), 8.18 (d, *J* = 5.0 Hz, 1H), 7.69 (d, *J* = 7.5 Hz, 2H), 7.56−7.37 (m, 3H), 7.31 (d, *J* = 5.0 Hz, 1H), 2.46 (s, 3H). ^{13}C NMR (DMSO, 75 MHz), δ (ppm): 142.7, 140.9, 140.0, 135.5, 135.2, 133.0, 129.7 (2C), 128.7 (2C), 127.1, 107.4, 107.1, 10.4.

2-Butyl-3-phenyl-1*H*-pyrrolo[3,2-*c*]pyridine 29a and 3-Butyl-2-phenyl-1*H*-pyrrolo[3,2-*c*]pyridine 29b. Compounds **29a** and **29b** were prepared following the general procedure A with 202 mg (0.771 mmol) of 4-acetamido-3-iodopyridine **1** and 363 mg (2.313 mmol) of hex-1-ynylbenzene. The purification of the residue by chromatography (silica gel, cyclohexane/EtOAc/MeOH 70:30:0 to 0:90:10) gave a mixture of **29a** and **29b** (156 mg, 81% yield) as a white solid. R_f = 0.16 (EtOAc/MeOH 9/1). **29a**. ^{1}H NMR (DMSO, 300 MHz), δ (ppm): 11.62 (s br, 1H), 8.74 (s, 1H), 8.17 (s br, 1H), 7.53−7.47 (m, 5H), 7.31 (s br, 1H), 2.82 (t, *J* = 8.1 Hz, 2H), 1.74−1.62 (m, 2H), 1.35−1.24 (m, 2H), 0.84 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (DMSO, 75 MHz), δ (ppm): 140.3, 139.6, 138.9, 137.5, 133.9, 128.7 (2C), 128.4 (2C), 125.7, 123.7, 111.6, 105.9, 30.9, 25.1, 21.6, 13.2. IR (CH_2Cl_2), ν (cm^{-1}): 3450, 3048, 2961, 2932, 1468, 751, 714, 698. LRMS (ESI$^+$): *m/z* = 251.2 ([M + H]$^+$, 100). HRMS (ESI$^+$): calcd for $C_{17}H_{19}N_2$ [M + H]$^+$ 251.1548, found 251.1545. **29b**. ^{1}H NMR (DMSO, 300 MHz), δ (ppm): 11.62 (s br, 1H), 8.86 (s, 1H), 8.17 (s br, 1H), 7.53−7.47 (m, 5H), 7.32 (s br, 1H), 2.88 (t, *J* = 7.5 Hz, 2H), 1.70−1.58 (m, 2H), 1.41−1.27 (m, 2H), 0.87 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (DMSO, 75 MHz), δ (ppm): 141.4, 139.9, 138.9, 134.5, 131.9, 128.5 (2C), 127.6 (2C), 125.7, 123.9, 111.6, 106.0, 32.6, 23.2, 21.2, 13.4.

2-(Methoxymethyl)-3-phenyl-1*H*-pyrrolo[3,2-*c*]pyridine 30a and 3-(Methoxymethyl)-2-phenyl-1*H*-pyrrolo[3,2-*c*]pyridine 30b. Compounds **30a** and **30b** were prepared following the general procedure A with 223 mg (0.851 mmol) of 4-acetamido-3-iodopyridine **1** and 373 mg (2.553 mmol) of (3-methoxyprop-1-ynyl)benzene. The purification of the residue by chromatography (silica gel, cyclohexane/EtOAc/MeOH 70:30:0 to 0:90:10) gave a mixture of **30a** and **30b** (157 mg, 77% yield) as a white solid. **30a**. R_f = 0.29 (EtOAc/MeOH 9/1). ^{1}H NMR (DMSO, 300 MHz), δ (ppm): 11.91 (s br, 1H), 8.89 (s, 1H), 8.23 (d, *J* = 5.5 Hz, 1H), 7.56−7.43 (m, 4H), 7.38 (d, *J* = 5.5 Hz, 1H), 7.33 (t, *J* = 7.0 Hz, 1H), 4.59 (s, 2H), 3.33 (s, 3H). ^{13}C NMR (DMSO, 75 MHz), δ (ppm): 142.0, 140.7, 139.1, 133.5, 133.2, 129.0 (2C), 128.8 (2C), 126.4, 123.3, 114.3, 106.7, 65.1, 57.7. IR (CH_2Cl_2), ν (cm^{-1}): 3664, 3051, 2981, 1627, 1270, 724, 712, 704. LRMS (ESI$^+$): *m/z* = 239.1 ([M + H]$^+$, 100). HRMS (ESI$^+$): calcd for $C_{15}H_{15}N_2O$ [M + H]$^+$: 239.1184, found 239.1175. **30b**. R_f = 0.21 (EtOAc/MeOH 9/1). ^{1}H NMR (DMSO, 300 MHz), δ (ppm): 11.93 (s br, 1H), 8.97 (s br, 1H), 8.23 (s, 1H), 7.73 (d, *J* = 7.5 Hz, 2H), 7.56 (t, J = 7.5 Hz, 2H), 7.46 (d, *J* = 7.5 Hz, 1H), 7.42 (d, *J* = 4.8 Hz, 1H), 4.65 (s, 2H), 3.35 (s, 3H). ^{13}C NMR (DMSO, 75 MHz), δ (ppm): 141.9, 140.7, 139.1, 137.9, 131.2, 128.9 (2C), 128.3, 128.1 (2C), 125.8, 108.2, 106.5, 64.2, 57.1.

2-Isobutyl-3-phenyl-1*H*-pyrrolo[3,2-*c*]pyridine 31a and 3-Isobutyl-2-phenyl-1*H*-pyrrolo[3,2-*c*]pyridine 31b. Compounds **31a** and **31b** were prepared following the general procedure A with 203 mg (0.775 mmol) of 4-acetamido-3-iodopyridine **1** and 367 mg (2.324 mmol) of (4-methylpent-1-ynyl)benzene. The purification of the residue by chromatography (silica gel, Cyclohexane/EtOAc/MeOH 70:30:0 to 0:90:10) gave a mixture of **31a** and **31b** (176 mg, 92% yield) as a white solid. R_f = 0.31 (EtOAc/MeOH 9/1). **31a**. ^{1}H NMR (DMSO, 300 MHz), δ (ppm): 11.60 (s br, 1H), 8.73 (s, 1H), 8.18 (d br, 1H), 7.61−7.47 (m, 6H), 2.72 (d, *J* = 7.2 Hz, 2H), 2.12−2.01 (m, 1H), 0.82 (d, *J* = 6.0 Hz, 6H). ^{13}C NMR (DMSO, 75 MHz), δ (ppm): 141.2, 140.7, 139.6, 137.4, 134.9, 132.0, 129.6 (2C), 129.2 (2C), 128.2, 113.2, 106.8, 35.3, 28.8, 22.7 (2C). IR (CH_2Cl_2), ν (cm^{-1}): 3451, 3045, 2959, 2869, 1605, 1468, 1172, 770, 751, 670. LRMS (ESI$^+$): *m/z* = 251.1 ([M + H]$^+$, 100). HRMS (ESI$^+$): calcd for $C_{17}H_{18}N_2$ [M + H]$^+$: 251.1548, found 251.1547. **31b**. ^{1}H NMR (DMSO, 300 MHz), δ (ppm): 11.67 (s br, 1H), 8.87 (s, 1H), 8.18 (s br, 1H), 7.61−7.47 (m, 6H), 2.78 (d, *J* = 7.2 Hz, 2H), 2.01−1.88 (m, 1H), 0.84 (d, *J* = 6.3 Hz, 6H). ^{13}C NMR (DMSO, 75 MHz), δ (ppm): 142.6, 140.4, 139.4, 135.9, 133.0, 131.9, 129.2 (2C), 128.6 (2C), 126.5, 111.4, 106.8, 33.4, 30.1, 23.0 (2C).

2-Isopropyl-3-phenyl-1*H*-pyrrolo[3,2-*c*]pyridine 32a and 3-Isopropyl-2-phenyl-1*H*-pyrrolo[3,2-*c*]pyridine 32b. Compounds **32a** and **32b** were prepared following the general procedure A with 202 mg (0.771 mmol) of 4-acetamido-3-iodopyridine **1** and 333 mg (2.313 mmol) of (3-methylbut-1-ynyl)benzene. The purification of the residue by chromatography (silica gel, cyclohexane/EtOAc/MeOH 70:30:0 to 0:90:10) gave a mixture of **32a** and **32b** (150 mg, 83% yield) as a white solid. R_f = 0.18 (EtOAc/MeOH 9/1). **32a**. ^{1}H NMR (DMSO, 300 MHz), δ (ppm): 11.57 (s br, 1H), 8.68 (s, 1H), 8.14 (d, *J* = 5.1 Hz, 1H), 7.55−7.29 (m, 5H), 7.30 (d, *J* = 5.1 Hz, 1H), 3.28 (st, *J* = 7.1 Hz, 1H), 1.31 (d, *J* = 7.1 Hz, 6H). ^{13}C NMR (DMSO, 75 MHz), δ (ppm): 144.2, 141.4, 140.6, 140.0, 133.1, 129.7 (2C), 129.5 (2C), 127.1, 124.6, 111.4, 107.4, 26.1, 23.4 (2C). IR (CH_2Cl_2), ν (cm^{-1}): 3452, 3047, 2967, 2360, 1469, 745, 729, 698. LRMS (ESI$^+$): *m/z* = 237.1 ([M + H]$^+$, 100). HRMS (ESI$^+$): calcd for $C_{16}H_{17}N_2$ [M + H]$^+$ 237.1392, found 237.1381. **32b**. ^{1}H NMR (DMSO, 300 MHz), δ (ppm): 11.52 (s br, 1H), 9.02 (s, 1H), 8.15 (d, *J* = 5.1 Hz, 1H), 7.55−7.29 (m, 5H), 7.33 (d, *J* = 5.1 Hz, 1H), 3.29 (st, *J* = 7.1 Hz, 1H), 1.41 (d, *J* = 7.1 Hz, 6H). ^{13}C NMR (DMSO, 75 MHz), δ (ppm): 143.4, 140.6, 140.4, 135.1, 134.9, 130.1 (2C), 129.7 (2C), 128.9, 124.8, 118.7, 107.7, 26.2, 24.4 (2C).

2-Cyclohexyl-3-phenyl-1*H*-pyrrolo[3,2-*c*]pyridine 33a and 3-Cyclohexyl-2-phenyl-1*H*-pyrrolo[3,2-*c*]pyridine 33b. Compounds **33a** and **33b** were prepared following the general procedure A with 238 mg (0.908 mmol) of 4-acetamido-3-iodopyridine **1** and 501 mg (2.725 mmol) of (cyclohexylethynyl)benzene. The purification of the residue by chromatography (silica gel, cyclohexane/EtOAc/MeOH 70:30:0 to 0:90:10) gave a mixture of **33a** and **33b** (242.3 mg, 94% yield) as a white solid. **33a**. R_f = 0.19 (EtOAc/MeOH 9/1). ^{1}H NMR (DMSO, 300 MHz), δ (ppm): 11.79 (s br, 1H), 8.68 (s, 1H), 8.13 (d br, 1H), 7.52−7.35 (m, 5H), 7.33 (d br, *J* = 3.6 Hz, 1H), 2.97−2.81 (m, 1H), 1.88−1.62 (m, 7H), 1.39−1.24 (m, 3H). ^{13}C NMR (DMSO, 75 MHz), δ (ppm): 142.1, 140.5, 138.8, 138.6, 134.0, 128.9 (2C), 128.4 (2C), 125.8, 123.8, 110.2, 106.0, 35.0, 32.1 (2C), 25.8 (2C), 25.1. IR (CH_2Cl_2), ν (cm^{-1}): 3450, 3049, 2931, 2854, 2360, 1467, 744, 714, 698. LRMS (ESI$^+$): *m/z* = 277.2 ([M + H]$^+$, 100). HRMS (ESI$^+$): calcd for $C_{19}H_{21}N_2$ [M + H]$^+$: 277.1705, found 277.1698. **33b**. R_f = 0.23 (EtOAc/MeOH 9/1). ^{1}H NMR (DMSO, 300 MHz), δ (ppm): 11.79 (s br, 1H), 9.06 (s, 1H), 8.13 (d br, 1H), 7.54−7.38 (m, 5H), 7.33 (d br, 1H), 2.97−2.81 (m, 1H), 2.03−1.92 (m, 2H), 1.83−1.61 (m, 5H), 1.40−1.25 (m, 3H). ^{13}C NMR (DMSO, 75 MHz), δ (ppm): 142.7, 142.1, 139.3, 134.0, 132.1, 128.4 (4C), 127.6, 123.8, 116.6, 106.4, 35.5, 33.0 (2C), 26.3 (2C), 25.2.

2-Cyclopropyl-3-phenyl-1*H*-pyrrolo[3,2-*c*]pyridine 34a and 3-Cyclopropyl-2-phenyl-1*H*-pyrrolo[3,2-*c*]pyridine 34b. Compounds **34a** and **34b** were prepared following the general procedure A with 200 mg (0.763 mmol) of 4-acetamido-3-iodopyridine **1** and 327 mg (2.290 mmol) of (cyclopropylethynyl)benzene. The purification of the residue by chromatography (silica gel, Cyclohexane/EtOAc/MeOH 70:30:0 to 0:90:10) gave a mixture of **34a** and **34b** (136 mg, 76% yield) as a white solid. R_f = 0.25 (EtOAc/MeOH 9/1). **34a**. ^{1}H NMR (DMSO, 300 MHz), δ (ppm): 11.60 (s br, 1H), 8.86 (s, 1H), 8.13 (d, *J* = 5.1 Hz, 1H), 7,82 (d, *J* = 7.5 Hz, 2H), 7,51 (t, *J* = 7.5 Hz, 2H), 7,38 (t, *J* = 7.5 Hz, 1H), 7.29 (d, *J* = 5.1 Hz, 1H), 2.13−2.03 (m,

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1H), 0.95 (d, J = 8.1 Hz, 2H), 0.51 (d, J = 4.8 Hz, 2H). ^{13}C NMR (DMSO, 75 MHz), δ (ppm): 142.4, 140.8, 139.5, 136.8, 132.4, 128.9 (2C), 128.4 (2C), 128.2, 126.4, 113.0, 106.9, 7.5 (2C), 6.9. IR (CH_2Cl_2), ν (cm^{-1}): 3452, 3047, 2961, 2360, 1467, 764, 698, 609. LRMS (ESI$^+$): m/z = 235.1 ([M + H]$^+$, 100). HRMS (ESI$^+$): calcd for $C_{16}H_{15}N_2$ [M + H]$^+$: 235.1235, found 235.1225. **34b**. ^{1}H NMR (DMSO, 300 MHz), δ (ppm): 11.64 (s br, 1H), 8.87 (s, 1H), 8.14 (s, 1H), 7,83 (d, J = 7.5 Hz, 2H), 7,50 (t, J = 7.5 Hz, 2H), 7,40 (t, J = 7.5 Hz, 1H), 7.30 (s, 1H), 2.13−2.03 (m, 1H), 0.95 (d, J = 8.4 Hz, 2H), 0.50 (d, J = 5.4 Hz, 2H). ^{13}C NMR (DMSO, 75 MHz), δ (ppm): 141.4, 139.8, 138.6, 135.9, 131.4, 128.0 (2C), 127.5 (2C), 127.3, 125.5, 112.1, 106.0, 7.8 (2C), 6.0.

2-*tert*-Butyl-3-phenyl-1*H*-pyrrolo[3,2-*c*]pyridine 35a. Compound **35a** was prepared following the general procedure A with 220 mg (0.840 mmol) of 4-acetamido-3-iodopyridine **1** and 398 mg (2.519 mmol) of (3,3-dimethylbut-1-ynyl)benzene. The purification of the residue by chromatography (silica gel, cyclohexane/EtOAc/MeOH 70:30:0 to 0:90:10) gave starting material **1** (31 mg, 14% yield) and **35a** (139 mg, 66% yield and 73% corrected yield) as a white solid. R_f = 0.20 (EtOAc/MeOH 9/1). ^{1}H NMR (DMSO, 300 MHz), δ (ppm): 11.24 (s br, 1H), 8.17 (s, 1H), 8.11 (d br, 1H), 7.44−7.29 (m, 6H), 1.26 (s, 9H). ^{13}C NMR (DMSO, 75 MHz), δ (ppm): 144.8, 141.7, 140.8, 138.6, 136.7, 132.0 (2C), 128.8 (2C), 127.7, 112.1, 110.0, 106.8, 34.2, 31.8 (3C). IR (CH_2Cl_2), ν (cm^{-1}): 3469, 3053, 2967, 2361, 1476, 731, 706. LRMS (ESI$^+$): m/z = 251.2 ([M + H]$^+$, 100). HRMS (ESI$^+$): calcd for $C_{17}H_{19}N_2$ [M + H]$^+$ 251.1548, found 251.1536.

3-Phenyl-2-(triethylsilyl)-1*H*-pyrrolo[3,2-*c*]pyridine 36. Compound **36** was prepared following the general procedure A with 200 mg (0.763 mmol) of 4-acetamido-3-iodopyridine **1** and 495 mg (2.290 mmol) of triethyl(phenylethynyl)silane. The crude product was purified twice by chromatography (silica gel, Cyclohexane/EtOAc/MeOH 70:30:0 to 0:90:10 and toluene/EtOAc 80:20 to 50:50) to give 48 mg (20% yield) of **36** as a white solid. Mp: 180−182 °C (recrystallized from EtOAc). R_f = 0.18 (EtOAc/cyclohexane 5/5). ^{1}H NMR (DMSO, 300 MHz), δ (ppm): 11.25 (s br, 1H), 8.61 (s, 1H), 8.18 (d, J = 5.7 Hz, 1H), 7.47−7.39 (m, 6H), 0.84−0.79 (m, 9H), 0.73−0.68 (m, 6H). ^{13}C NMR (DMSO, 75 MHz), δ (ppm): 141.8, 141.7, 140.5, 135.3, 133.1, 129.9 (2C), 128.2 (2C), 127.0, 126.4, 124.9, 106.6, 7.2 (3C), 3.3 (3C). IR (CH_2Cl_2), ν (cm^{-1}): 3459, 2958, 1369, 1261, 1120, 745, 706. LRMS (ESI$^+$): m/z = 309.2 ([M + H]$^+$, 100). HRMS (ESI$^+$): calcd for $C_{19}H_{25}N_2Si$ [M + H]$^+$ 309.1781, found 309.1782.

***N*-(3-(Phenylethynyl)pyridin-4-yl)acetamide 37.** Compound **37** was prepared following the general procedure A with 152 mg (0.580 mmol) of 4-acetamido-3-iodopyridine **1** and 342 μL (1.740 mmol) of trimethyl(phenylethynyl)silane. The crude product was purified by chromatography (silica gel, Cyclohexane/EtOAc/MeOH 70:30:0 to 0:90:10) to give 89 mg (65% yield) of **37** as a pale brown solid. Mp: 100−102 °C. R_f = 0.52 (EtOAc/cyclohexane 5/5). ^{1}H NMR (DMSO, 300 MHz), δ (ppm): 9.66 (s, 1H), 8.67 (s, 1H), 8.45 (d, J = 5.4 Hz, 1H), 8.06 (d, J = 5.7 Hz, 1H), 7.70−7.67 (m, 2H), 7.48−7.46 (m, 3H), 2.23 (s, 3H). ^{13}C NMR (DMSO, 75 MHz), δ (ppm):169.6, 152.9, 149.5, 145.4, 131.6 (2C), 129.2, 128.6 (2C), 121.9, 114.8, 109.7, 97.5, 82.5, 24.1. IR (CH_2Cl_2), ν (cm^{-1}): 3395, 3050, 1712, 1570, 1503, 1265, 754, 706. LRMS (ESI$^+$): m/z = 237.1 ([M + H]$^+$, 100). HRMS (ESI$^+$): calcd for $C_{15}H_{13}N_2O$ [M + H]$^+$ 237.1020, found 237.1028.

3-Phenyl-1*H*-pyrrolo[3,2-*c*]pyridine 38. General procedure B for the synthesis of 2-substituted 5-azaindoles: Under argon atmosphere, to a solution of 4-acetamido-3-iodopyridine **1** (150 mg, 0.572 mmol), $PdCl_2(PPh_3)_2$ (20 mg, 0.029 mmol), tetrabutylammonium chloride (159 mg, 0.572 mmol), and potassium carbonate (395 mg, 2.860 mmol) in anhydrous DMF was added trimethylsilylacetylene (563 μL, 2.860 mmol). The mixture was stirred at 80 °C for 48 h, then cooled to room temperature and concentrated. Two mL of water were added and the aqueous layer was extracted with EtOAc (3 × 7 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under vacuum. The purification of the residue by chromatography (silica gel, cyclohexane/EtOAc/MeOH 70:30:0 to 0:90:10) gave **38** (109 mg, 98% yield) as a pale brown solid. Mp: 264−266 °C. R_f = 0.12 (EtOAc/MeOH 9/1). ^{1}H NMR (DMSO, 300 MHz), δ (ppm): 11.97 (s br, 1H), 8.81 (s, 1H), 8.17 (d, J = 5.7 Hz, 1H), 7.90 (d, J = 8.1 Hz, 2H), 7.49 (t, J = 7.9 Hz, 2H), 7.39−7.36 (m, 2H), 7.05 (s, 1H). ^{13}C NMR (DMSO, 75 MHz), δ (ppm): 143.0, 140.5, 140.4, 138.9, 131.4, 129.0 (2C), 128.1, 125.8, 125.4 (2C), 106.6, 97.6. IR (CH_2Cl_2), ν (cm^{-1}): 3006, 1271, 1258, 765, 744, 703. LRMS (ESI$^+$): m/z = 195.2 ([M + H]$^+$, 100). HRMS (ESI$^+$): calcd for $C_{13}H_{11}N_2$ [M + H]$^+$ 195.0922, found 195.0927.

2-(4-(Methoxymethyl)phenyl)-1*H*-pyrrolo[3,2-*c*]pyridine 39. Compound **39** was prepared following the general procedure B with 100 mg (0.382 mmol) of 4-acetamido-3-iodopyridine **1** and 415 mg (1.910 mmol) of ((4-(methoxymethyl)phenyl)ethynyl)trimethylsilane. The crude product was purified by chromatography (silica gel, cyclohexane/EtOAc/MeOH 70:30:0 to 0:90:10) to give 66 mg (73% yield) of **39** as a pale brown solid. Mp: 206−208 °C. R_f = 0.34 (EtOAc/MeOH 9/1). ^{1}H NMR (DMSO, 300 MHz), δ (ppm): 11.97 (s br, 1H), 8.81 (s, 1H), 8.17 (s br, 1H), 7.88 (d, J = 7.8 Hz, 2H), 7.43 (d, J = 7.8 Hz, 2H), 7.36 (d, J = 5.1 Hz, 1H), 7.04 (s, 1H), 4.45 (s, 2H), 3.32 (s, 3H). ^{13}C NMR (DMSO, 75 MHz), δ (ppm): 142.9, 140.4, 140.3, 138.7, 138.0, 130.6, 128.1 (2C), 125.9, 125.3 (2C), 106.6, 97.5, 73.2 57.59. IR (CH_2Cl_2), ν (cm^{-1}): 3685, 2928, 1606, 1268, 1261, 1099, 752, 721, 706. LRMS (ESI$^+$): m/z = 239.1 ([M + H]$^+$, 100). HRMS (ESI$^+$): calcd for $C_{15}H_{15}N_2O$ [M + H]$^+$ 239.1179, found 239.1182.

2-(3-(Methoxymethyl)phenyl)-1*H*-pyrrolo[3,2-*c*]pyridine 40. Compound **40** was prepared following the general procedure B with 100 mg (0.382 mmol) of 4-acetamido-3-iodopyridine **1** and 415 mg (1.910 mmol) of ((3-(methoxymethyl)phenyl)ethynyl)trimethylsilane. The crude product was purified by chromatography (silica gel, cyclohexane/EtOAc/MeOH 70:30:0 to 0:90:10) to give 86 mg (95% yield) of **40** as a brown gummy product. R_f = 0.29 (EtOAc/MeOH 9/1). ^{1}H NMR (DMSO, 300 MHz), δ (ppm): 12.01 (s br, 1H), 8.82 (s, 1H), 8.18 (s br, 1H), 7.85 (s, 1H), 7.81 (s, 1H), 7.47 (dd, J = 7.8 Hz and J = 7.5 Hz, 1H), 7.37 (d, J = 5.1 Hz, 1H), 7.30 (d, J = 7.5 Hz, 1H), 7.05 (s, 1H), 4.49 (s, 2H), 3.35 (s, 3H). ^{13}C NMR (DMSO, 75 MHz), δ (ppm): 142.9, 140.4 (2C), 139.2, 138.8, 131.4, 128.9, 127.2, 125.7, 124.6, 124.3, 106.5, 97.7, 73.5, 57.7. IR (CH_2Cl_2), ν (cm^{-1}): 3454, 2928, 1462, 1288, 1262, 1100, 753, 721, 696. LRMS (ESI$^+$): m/z = 239.1 ([M + H]$^+$, 100). HRMS (ESI$^+$): calcd for $C_{15}H_{15}N_2O$ [M + H]$^+$ 239.1179, found 239.1181.

2-(4-Methoxyphenyl)-1*H*-pyrrolo[3,2-*c*]pyridine 41. Compound **41** was prepared following the general procedure B with 120 mg (0.458 mmol) of 4-acetamido-3-iodopyridine **1** and 468 mg (2.290 mmol) of ((4-methoxyphenyl)ethynyl)trimethylsilane. The crude product was purified by chromatography (silica gel, Cyclohexane/EtOAc/MeOH 70:30:0 to 0:90:10) to give 68 mg (66% yield) of **41** as a pale brown solid. Mp: 257−259 °C. R_f = 0.10 (EtOAc/MeOH 9/1). ^{1}H NMR (DMSO, 300 MHz), δ (ppm): 11.88 (s br, 1H), 8.77 (s, 1H), 8.14 (d, J = 5.5 Hz, 1H), 7.83 (d, J = 8.7 Hz, 2H), 7.34 (d, J = 5.5 Hz, 1H), 7.06 (d, J = 8.7 Hz, 2H), 6.90 (s, 1H), 3.81 (s, 3H). ^{13}C NMR (DMSO, 75 MHz), δ (ppm): 159.3, 142.5, 140.2, 140.1, 139.0, 126.8 (2C), 125.9, 124.0, 114.4 (2C), 106.4, 96.1, 55.3. IR (CH_2Cl_2), ν (cm^{-1}): 3451, 2960, 2930, 1605, 1506, 1464, 1291, 1032, 741, 733. LRMS (ESI$^+$): m/z = 225.1 ([M + H]$^+$, 100). HRMS (ESI$^+$): calcd for $C_{14}H_{13}N_2O$ [M + H]$^+$ 225.1022, found 225.1024.

2-(3-Methoxyphenyl)-1*H*-pyrrolo[3,2-*c*]pyridine 42. Compound **42** was prepared following the general procedure B with 120 mg (0.458 mmol) of 4-acetamido-3-iodopyridine **1** and 468 mg (2.290 mmol) of ((4-(methoxymethyl)phenyl)ethynyl)trimethylsilane. The crude product was purified by chromatography (silica gel, Cyclohexane/EtOAc/MeOH 70:30:0 to 0:90:10) to give 69 mg (67% yield) of **42** as a pale brown solid. Mp: 177−179 °C. R_f = 0.20 (EtOAc/MeOH 9/1). ^{1}H NMR (DMSO, 300 MHz), δ (ppm): 11.97 (s br, 1H), 8.81 (s, 1H), 8.17 (d, J = 5.7 Hz, 1H), 7.50−7.47 (m, 2H), 7.42−7.36 (m, 2H), 7.07 (s, 1H), 6.94 (d, J = 7.2 Hz, 1H), 3.85 (s, 3H). ^{13}C NMR (DMSO, 75 MHz), δ (ppm): 159.8, 143.0, 140.5, 140.3, 138.8, 132.7, 130.1, 125.7, 117.8, 113.8, 110.7, 106.6, 97.9, 55.3. IR (CH_2Cl_2), ν (cm^{-1}): 3685, 3054, 1605, 1425, 1267, 1262, 754, 730, 706. LRMS (ESI$^+$): m/z = 225.1 ([M + H]$^+$, 100). HRMS (ESI$^+$): calcd for $C_{14}H_{13}N_2O$ [M + H]$^+$ 225.1022, found 225.1025.

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2-(4-Fluorophenyl)-1*H*-pyrrolo[3,2-c]pyridine 43. Compound **43** was prepared following the general procedure B with 200 mg (0.763 mmol) of 4-acetamido-3-iodopyridine **1** and 735 mg (3.815 mmol) of ((4-fluorophenyl)ethynyl)trimethylsilane. The crude product was purified by chromatography (silica gel, Cyclohexane/EtOAc/MeOH 70:30:0 to 0:90:10) to give 129 mg (79% yield) of **43** as a pale yellow solid. Mp: 237−239 °C. R_f = 0.09 (EtOAc/MeOH 9/1). ^{1}H NMR (DMSO, 300 MHz), δ (ppm): 11.99 (s br, 1H), 8.81 (s, 1H), 8.16 (d, J = 5.4 Hz, 1H), 7.94 (dd, J = 8.7 Hz and $^4J_{HF}$ = 8.7 Hz, 2H), 7.37−7.31 (m, 3H), 7.02 (s, 1H). ^{13}C NMR (DMSO, 75 MHz), δ (ppm): 161.7 (d, $^1J_{CF}$ = 244 Hz, 1C), 142.7, 140.3, 140.2, 137.8, 127.9 (d, $^4J_{CF}$ = 3.2 Hz, 1C), 127.3 (d, $^3J_{CF}$ = 8.3 Hz, 2C), 125.6, 115.8 (d, $^2J_{CF}$ = 21.5 Hz, 2C), 106.4, 97.4. IR (CH_2Cl_2), ν (cm^{-1}): 3686, 2929, 1604, 1502, 1234, 840, 747. LRMS (ESI$^+$): m/z = 213.1 ([M + H]$^+$, 100). HRMS (ESI$^+$): calcd for $C_{13}H_{10}FN_2$ [M + H]$^+$ 213.0823, found 213.0823.

2-(3-Fluorophenyl)-1*H*-pyrrolo[3,2-c]pyridine 44. Compound **44** was prepared following the general procedure B with 200 mg (0.763 mmol) of 4-acetamido-3-iodopyridine **1** and 735 mg (3.815 mmol) of ((3-fluorophenyl)ethynyl)trimethylsilane. The crude product was purified by chromatography (silica gel, Cyclohexane/EtOAc/MeOH 70:30:0 to 0:90:10) to give 102 mg (63% yield) of **44** as a pale yellow solid. mp 228−230 °C. R_f = 0.18 (EtOAc/MeOH 9/1). ^{1}H NMR (DMSO, 300 MHz), δ (ppm): 12.05 (s br, 1H), 8.84 (s, 1H), 8.19 (d, J = 5.4 Hz, 1H), 7.79−7.74 (m, 2H), 7.55−7.52 (m, 1H), 7.39 (d, J = 5.5 Hz, 1H), 7.20−7.16 (m, 2H). ^{13}C NMR (DMSO, 75 MHz), δ (ppm): 162.8 (d, $^1J_{CF}$ = 242 Hz, 1C), 143.3, 140.8, 140.4, 137.5 (d, $^4J_{CF}$ = 2.8 Hz, 1C), 133.8 (d, $^3J_{CF}$ = 8.3 Hz, 1C), 131.1 (d, $^3J_{CF}$ = 8.6 Hz, 1C), 125.5, 121.5, 114.7 (d, $^2J_{CF}$ = 20.9 Hz, 1C), 112.0 (d, $^2J_{CF}$ = 23.0 Hz, 1C), 106.7, 98.8. IR (CH_2Cl_2), ν (cm^{-1}): 3453, 2929, 1613, 1486, 1266, 752, 706. LRMS (ESI$^+$): m/z = 213.1 ([M + H]$^+$, 100). HRMS (ESI$^+$): calcd for $C_{13}H_{10}FN_2$ [M + H]$^+$ 213.0823, found 213.0824.

2-(Pyridin-4-yl)-1H-pyrrolo[3,2-c]pyridine 45. Compound **45** was prepared following the general procedure B with 150 mg (0.572 mmol) of 4-acetamido-3-iodopyridine **1** and 501 mg (2.860 mmol) of 4-((trimethylsilyl)ethynyl)pyridine. The crude product was purified by chromatography (silica gel, Cyclohexane/EtOAc/MeOH 70:30:0 to 0:90:10) to give 16 mg (14% yield) of **45** as a pale yellow solid. mp 183−185 °C. R_f = 0.11 (EtOAc/MeOH 8/2). ^{1}H NMR (DMSO, 300 MHz), δ (ppm): 12.25 (s br, 1H), 8.89 (s, 1H), 8.66 (d, J = 6 Hz, 2H), 8.23 (d, J = 5.1 Hz, 1H), 7.87 (d, J = 6.3 Hz, 1H), 7.43 (d, J = 5.7 Hz, 2H), 7.36 (s, 1H). ^{13}C NMR (DMSO, 75 MHz), δ (ppm): 150.4 (2C), 143.9, 141.4, 140.7, 138.3, 136.0, 125.3, 119.4 (2C), 106.9, 100.8. IR (CH_2Cl_2), ν (cm^{-1}): 3039, 1266, 756, 702. LRMS (ESI$^+$): m/z = 196.1 ([M + H]$^+$, 100). HRMS (ESI$^+$): calcd for $C_{12}H_{10}N_3$ [M + H]$^+$ 196.0869, found 196.0871.

2-(Pyridin-3-yl)-1*H*-pyrrolo[3,2-*c*]pyridine 46. Compound **46** was prepared following the general procedure B with 150 mg (0.572 mmol) of 4-acetamido-3-iodopyridine **1** and 501 mg (2.860 mmol) of 4-((trimethylsilyl)ethynyl)pyridine. The crude product was purified by chromatography (silica gel, cyclohexane/EtOAc/MeOH 70:30:0 to 0:90:10) to give 28 mg (25% yield) of **46** as a pale yellow solid. Mp: 173−175 °C. R_f = 0.10 (EtOAc/MeOH 8/2). ^{1}H NMR (DMSO, 300 MHz), δ (ppm): 12.14 (s br, 1H), 9.15 (s, 1H), 8.86 (s, 1H), 8.55 (d, J = 3.9 Hz, 1H), 8.29−8.20 (m, 2H), 7.52 (dd, J = 4.8 Hz and J = 7.8 Hz, 1H), 7.41 (d, J = 5.4 Hz, 1H), 7.20 (s, 1H). ^{13}C NMR (DMSO, 75 MHz), δ (ppm): 148.8, 146.6, 143.3, 140.8, 140.6, 135.9, 132.5, 127.4, 125.5, 124.0, 106.7, 98.9. IR (CH_2Cl_2), ν (cm^{-1}): 3453, 2928, 1606, 1268, 747, 706. LRMS (ESI$^+$): m/z = 196.1 ([M + H]$^+$, 100). HRMS (ESI$^+$): calcd for $C_{12}H_{10}N_3$ [M + H]$^+$ 196.0869, found 196.0871.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H NMR and ^{13}C NMR spectra of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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