Gold catalysis in the synthesis of azaindoles: pyrrolo[2,3-*b*]pyridines and pyrrolo[2,3-*b*]pyrazines

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Dedicated to Professor Rosa María Claramunt on the occasion of her 65th birthday

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Abstract

The synthesis of substituted 1-benzyl-1*H*-pyrrolo[2,3-*b*]pyridines and 5-benzyl-5*H*-pyrrolo-[2,3-*b*]pyrazines has been performed by cycloisomerization of the corresponding *N*-benzyl-3-alkynyl-5-arylpyridin(or pyrazin)-2-yl amines with $AuCl_3$. Alkynylamines have been obtained starting from 3-bromo-5-substituted *N*-(pyridin- or pyrazin-2-yl)pyridinium aminides in a regioselective way.

Keywords: Pyridinium *N*-aminides, pyrrolo[2,3-*b*]pyridines, pyrrolo[2,3-*b*]pyrazines, $AuCl_3$ cycloisomerization

Introduction

The 1*H*-pyrrolo[2,3-*b*]pyridine (or 7-azaindole) nucleus is present in only a few natural products[1] such as variolins – a family of alkaloids isolated from the Antarctic red sponge *Kirckpatrickia varialosa* – which exhibit antitumor and antiviral properties (Figure 1).[2-4] Nevertheless, this class of heterocycles has attracted considerable interest due to their physicochemical and pharmacological properties. In this way, luminescence properties of 7-azaindole derivatives and complexes have been studied and recently reviewed.[5] These compounds have also been examined as models mimicking proton transfer with the assistance of protic solvent molecules in biological processes.[6] Substituted 7-azaindole derivatives have recently been synthesized as kinase modulators.[7-9] In most cases the construction of the pyrrolo[2,3-*b*]pyridine ring is a key step in the synthesis of a more complex molecule. For these and other related reasons, the chemistry of 7-azaindole derivatives has remarkably expanded, allowing the functionalization of

almost all the positions of the nucleus.[10] Even so, the development of general methods for the regioselective synthesis of these compounds continues to be an active area of research.

On the other side, 5*H*-pyrrolo[2,3-*b*]pyrazines (or 4,7-diazaindoles) (Figure 1) have recently gained attention since derivatives of the system exhibit diverse biological activities. In addition to showing antibronchospastic effects[11] and the ability to inhibit the activity of a mitogen-activated protein kinase (p38 MAP)[12] and a Janus kinase (JAK3),[13] some other derivatives can inhibit cyclin-dependent kinases (CDKs) and glycogen synthase kinase 3 (GSK-3), thereby exerting antiproliferative effects.[14-17] Abnormalities and deregulations of CDK activities have been associated with many diseases, including cancer, viral infections, diabetes, ischemia and neurodegenerative disorders such as Alzheimer′s and Parkinson′s diseases.[18] Compounds that inhibit CDKs, mostly related to 4,7-diazaindoles, were named ′aloisines′ on the basis of the first name (Alois) of Dr. Alzheimer (Figure 1).[15] Recently, a family of pyrrolo[2,3-*b*]pyrazine derivatives was also studied as CFTR (cystic fibrosis transmembrane conductance regulators) activators.[19] As a consequence, several approaches for the synthesis of pyrrolo[2,3-*b*]pyrazines have been developed[20-23] although more general and selective methods to prepare polysubtituted 4,7-diazaindoles would still be welcome.

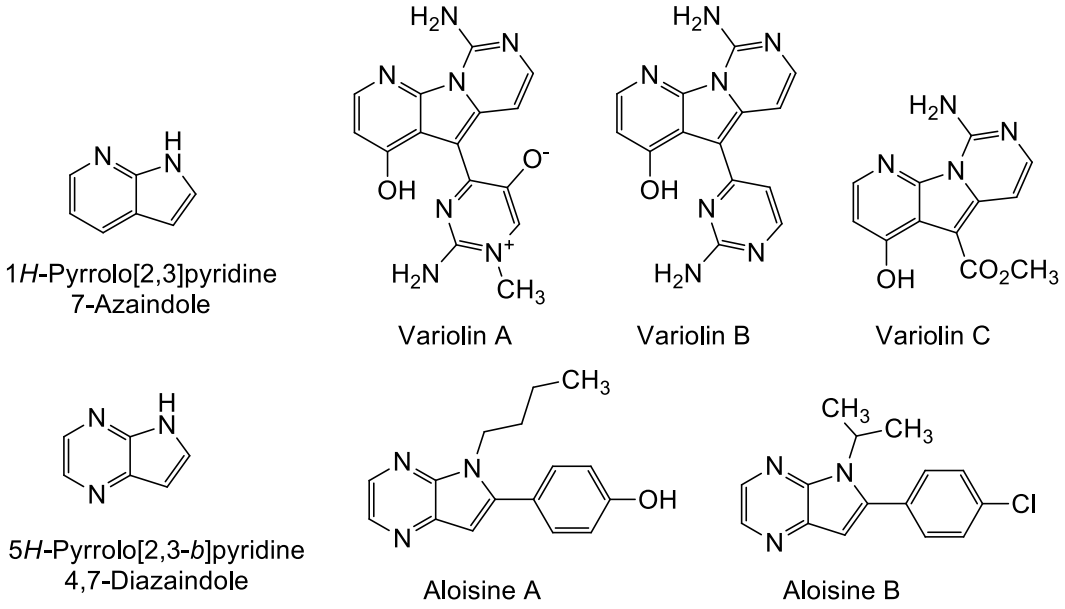
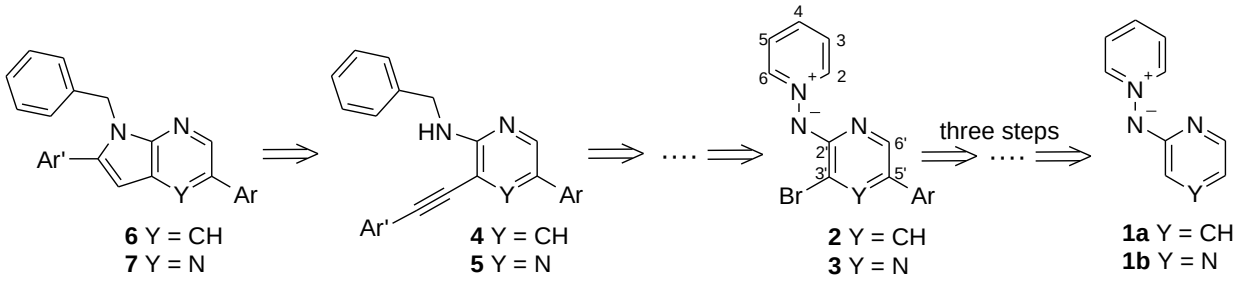


Figure 1. Active and natural compounds with a 7-aza- or 4,7-diazaindole skeleton.

As a continuation of our studies on the utility of pyridinium *N*-heteroarylaminides **1** (Scheme 1) as suitable scaffolds[24-27] to obtain 2-aminoazines,[28-30] compounds that, in addition to other uses, have recently been tested in experimental models of human African trypanosomiasis,[31] we became interested in developing a synthetic route to pyrrolo[2,3-*b*]pyridines and pyrrolo[2,3-*b*]pyrazines starting from the corresponding *N*-pyridin-2-yl or pyrazin-2-yl pyridinium aminide (**1a**, **1b**, Scheme 1). Pyridinium *N*-heteroarylaminides **1** are stable heterocyclic betaines in which

the negative charge is stabilized by both the pyridinium and the azine moieties. An intramolecular hydrogen bridge prevents alkylation of the heterocyclic aminide nitrogen in aprotic solvents.[24] Typical reactions of these aminides are the aromatic electrophilic substitutions that take place in the 3- and 5- positions of the heterocyclic ring.[24,25] Halogenated aminides can be converted by means of Pd coupling processes and reduction of the N–N bond into 3,5-disubstituted 2-aminopyridines and pyrazines **4** and **5**.[28,29] Furthermore, we recently reported the regioselective synthesis of *N*-alkyl-3-alkynyl-5-arylpyridin-2-yl amines **4** through the 3-brominated aminides **2** (Scheme 1).[30]



Scheme 1. Retrosynthetic sequence for compounds **4**, **5**, **6** and **7** from aminides **1.**

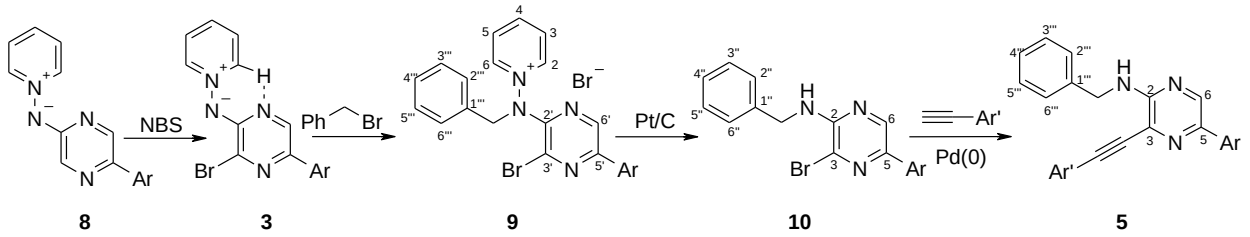
Bearing in mind that conjugated alkynes are valuable intermediates in the synthesis of heterocycles,[32-34] we describe in this paper the results obtained in the synthesis of the *N*-alkyl-3-alkynyl-5-arylpyrazin-2-yl amines **5**, starting from the 3-bromo aminides **3** along with the results of the cyclization of amines **4** and **5** to afford aza- and diazaindoles **6** and **7** (Scheme 1), in an $AuCl_3$-catalyzed processes.

Results and Discussion

The general approach used for the synthesis of *N*-alkyl-3-alkynyl-5-arylpyridin-2-yl amines **5**, azaindoles **6** and diazaindoles **7** is outlined in Scheme 1.

Compounds **3** were obtained starting from the *N*-pyrazin-2-yl pyridinium aminide **1b**[24,27] in a three-step procedure. By using *N*-bromosuccinimide (NBS), derivative **1b** was selectively brominated at the 5-position of the pyrazine nucleus.[25] Such an intermediate was coupled with different boronic acids (1.5 equiv) in the presence of K_2CO_3 (10 equiv), and $Pd(PPh_3)_4$ (5 mol %) in toluene/ethanol (4:1)[28] to afford aminides **8**. Finally, a second bromination at the 3-position,[26] using literature conditions,[29] allowed us to synthesize 3-bromo-5-arylpyrazin-2-yl pyridinium aminides **3** (Scheme 2). When a 1-benzothiophen-3-yl substituent is present, halogenation must be carried out at –50 ºC to avoid the formation of *N*-[5-(2-bromo-1-benzothiophen-3-yl)-3-bromopyrazin-2-yl]pyridinium aminide **3e** by insertion of a second bromine atom at the 2-position of the benzothiophene ring.

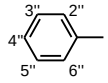
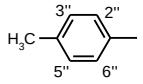
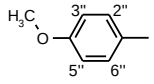
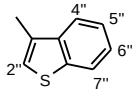
Reaction of 3-bromo-5-aryl *N*-(pyrazin-2-yl)pyridinium aminides **3** with benzyl bromide in anhydrous acetone proceeds to yield the corresponding pyridinium salts **9** by selective alkylation at the exocyclic nitrogen (Scheme 2). Traces of the corresponding aminide **3** and/or benzyl bromide were removed by washing the resulting solid with acetone or ethyl acetate. These salts (**9**) obtained in good yields, were used in the next step without additional purification (see Table 1).



Scheme 2. Preparation of *N*-benzyl-3-alkynyl-5-arylpyrazin-2-yl amines **5** from aminides **3.**

The reduction step breaking the N-N bond was achieved using formic acid/triethylamine and platinum on charcoal (5%) in acetonitrile. Under these conditions amines **10** were obtained as the main product (52–75%, see Table 1) but some debromination was observed and the corresponding *N*-benzyl-*N*-(5-arylpyrazin-2-yl)amines **11** were detected (Figure 2). In addition, when chromatographic purification was performed to separate the amines **10**, in the reduction of salt **9a** the *N*-benzyl-*N*-(3-bromopyrazin-2-yl)amine **12** was detected in trace amounts, and, in the case of **9d**, a small amount of 3-bromo-5-(4-methoxyphenyl)pyrazin-2-yl amine **13**[35] was also obtained with **11d**[36] in an inseparable mixture (**13:11d** ≈ 4:6 by NMR spectroscopy) (Figure 2).

Table 1. Yields for compounds **9** and **10**

Ar [a]	Compound	Yield (%) [b]	Compound	Yield (%) [b]
	**9a**	71	**10a**	71
	**9b**	82	**10b**	63
	**9c**	62	**10c**	75
	**9d**	82	**10d**	52

[a] Ring numbering employed in NMR analysis. [b] Yields of isolated pure products.

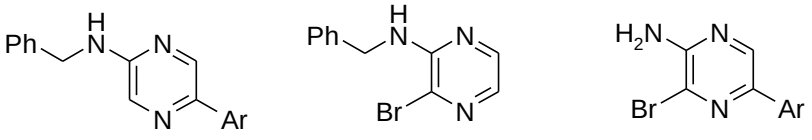
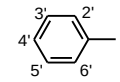
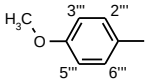
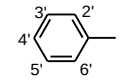
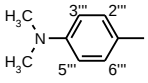
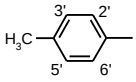
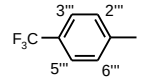
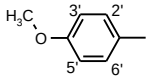
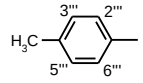
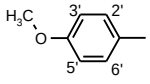
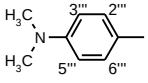
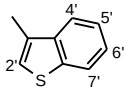
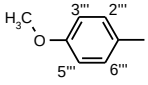


Figure 2. Amines obtained as secondary products in the reduction step.

The last step in the synthesis of *N*-benzyl-3-alkynyl-5-arylpyrazin-2-yl amines **5** was a copper-free Sonogashira coupling between aminopyrazines **10** and the corresponding terminal acetylene. This process was carried out with $PdCl_2(PPh_3)_2$ as the catalyst, using an excess of DABCO (1,4-diazabicyclo[2.2.2]octane) as base and water as solvent with MW irradiation performed at 120 °C for 20 min. The yields obtained for compounds **5** are given in Table 2.

Table 2. Yields for compounds **5**

Compound	Ar [a]	Ar′[a]	Yield (%) [b]
5a			66
5b			73
5c			61
5d			79
5e			49
5f			66

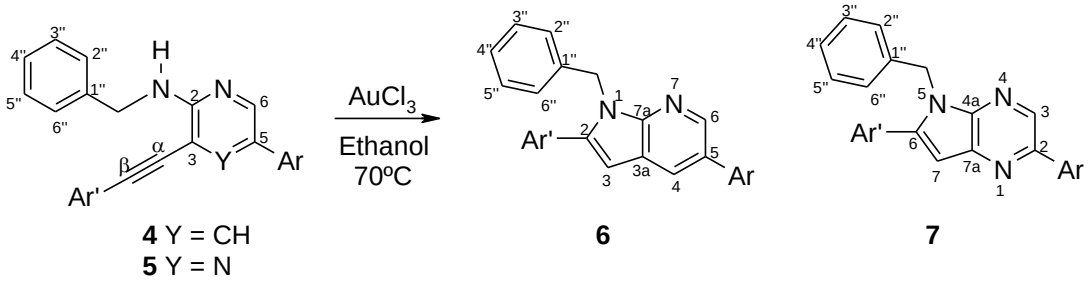
[a] Ring numbering employed in NMR analysis. [b] Yields of isolated pure products.

Several methods have been developed to prepare 7-azaindoles from 3-alkynyl-2-aminopyridines.[37-44] Many of them include the use of base[37-39] and, despite they give rise to *N*-unsubstituted compounds, we have tried to accomplish the synthesis of **6a** by treating the *N*-benzyl-*N*-[3-(4-methylphenyl)ethynyl-5-phenyl]pyridine-2-ylamine with potassium *tert*-butoxide (^{t}BuOK) using *N*-methylpyrrolidone (NMP) as solvent.[38] No reaction was observed after stirring for 24 h at room temperature and the same result was obtained heating the mixture at 80 ºC. Metal catalysts and metal complexes have also been reported to favor this intramolecular cyclization step.[40-42,45-47] Even though, again, the use of these derivatives mainly produces 7-aza-

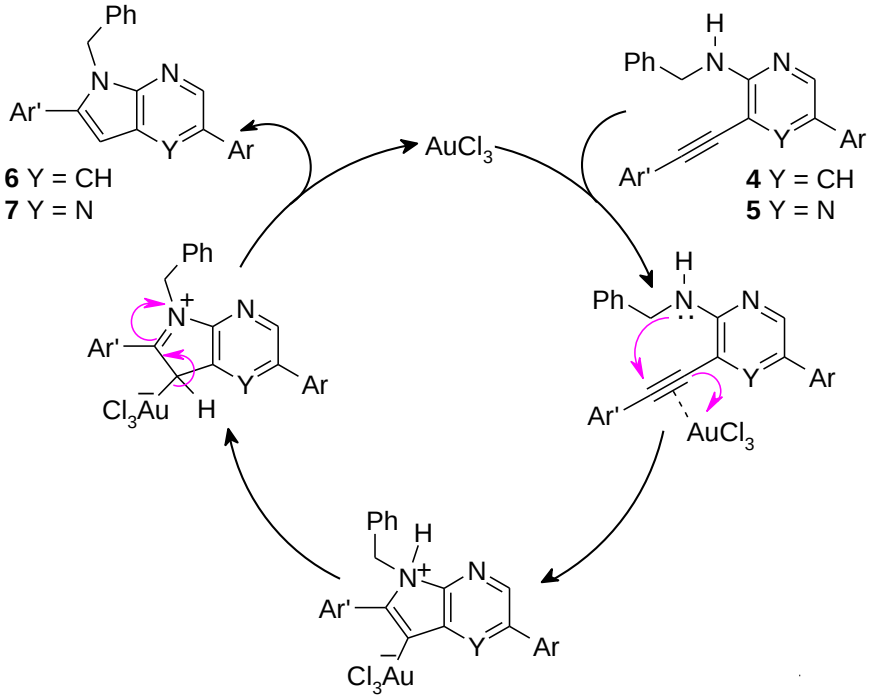
indoles without substituents at the N- position, we decided to attempt the cyclization of alkynylamines using a gold catalyst.

From an environmental point of view, gold catalysts have many valuable features and they have now become a well-established method of choice for many chemical transformations.[48,49] Thanks to gold-based catalysts, various organic transformations have become accessible under mild conditions and give both high yields and chemoselectivity. In recent years intramolecular carboaminations catalyzed by $AuCl_3$ have been developed[45-47] to prepare highly functionalized indole derivatives,[45,47] 2-substituted 7-azaindoles,[45] pyrrolocoumarin and pyrroloquinolone derivatives.[46]

The synthesis of *N*-benzyl pyrrolo[2,3-*b*]pyridines **6** and pyrrolo[2,3-*b*]pyrazines **7** was suitably achieved from the corresponding alkynylamines **4** and **5** which, in the presence of $AuCl_3$ undergo a cycloisomerization process (Scheme 3).



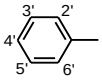
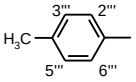
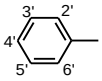
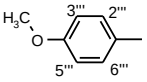
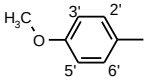
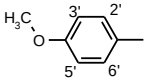
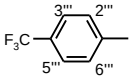
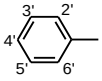
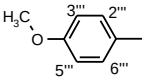
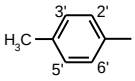
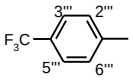
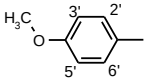
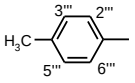
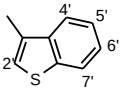
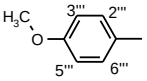
Scheme 3. Synthesis of 7-aza- and 4,7-diazaindoles **6** and **7** from alkynylamines **4** and **5.**



Scheme 4. Mechanistic interpretation for the $AuCl_3$-catalyzed cycloisomerization.

When $AuCl_3$ (3 mol %) was added to a solution of the *N*-benzyl-3-alkynyl-5-arylpyridin(or pyrazin)-2-yl amines **4**, **5** in ethanol and the mixture was stirred at 70 °C, a *5-endo-dig* cyclization took place and the corresponding trisubstituted 7-azaindoles **6** or 4,7-diazaindoles **7** were obtained, after purification, in moderate yields (Table 3). Alkynylamines bearing an electron-releasing dimethylamino group, as **5b** and **5e**, yielded a complex reaction mixture in which the corresponding pyrrolopyrazine was not detected. A tentative mechanism for the cycloisomerization process is given in the Scheme 4.

Table 3. Yields for compounds **6** and **7**

Compound	Ar[a]	Ar′[a]	Yield (%)[b]
6a			44
6b			43
6c			65
6d			46
7a			44
7b			49
7c			59
7d			48

[a] Ring numbering employed in NMR analysis. [b] Yields of isolated pure products.

Conclusions

A regioselective synthesis of *N*-alkyl-3-alkynyl-5-arylpyrazin-2-yl-amines **5** has been developed by applying the previously established methodology for the synthesis of the related *N*-alkyl-3-alkynyl-5-arylpyridin-2-yl-amines **4**. The products **5** were obtained from 2-aminopyrazines **10**, treated with the corresponding aryl-acetylene, through a Sonogashira coupling process. Finally, treatment of the corresponding alkynylamines **4** and **5,** in ethanol at 70 °C and in the presence of $AuCl_3$ produced a cycloisomerization process generating moderate yields of the 1,2,5-

trisubstituted pyrrolo[2,3-*b*]pyridines **6** and 2,5,6-trisubstituted pyrrolo[2,3-*b*]pyrazines **7.** The same approach is presently being studied with different related azaindoles.

Experimental Section

General. Melting points were determined in open capillary tubes on a Stuart Scientific SMP3 melting point apparatus. IR spectra were obtained on a Perkin-Elmer FTIR spectrum 2000 spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on Varian Gemini 200, Varian Unity 300/500 MHz or Varian Mercury VX-300 systems at room temperature. Chemical shifts are given in ppm (δ) downfield from TMS. Coupling constants (*J*) are in Hertz (Hz) and signals are described as follows: s, singlet; d, doublet; t, triplet; q, quadruplet; h, heptuplet; m, multiplet; br, broad; ap, apparent. Low resolution mass spectra (MS) were recorded on a Hewlett-Packard 5988A (70eV) spectrometer using Electronic Impact (EI) or Atmospheric Pressure Chemical Ionization (APCI) and high resolution analysis (TOF) was performed on an Agilent 6210 time-of-flight LC/MS. All reagents were obtained from commercial sources and were used without further purification. TLC analyses were performed on silica gel (Kieselgel 60 F_{254}, Macherey-Nagel) and spots were visualized under UV light. Column chromatography was carried out on silica gel 60 (40–63 μm, Merck) columns, using the eluent reported in each case. Microwave experiments were performed using a Biotage Initiator and a Biotage 5 mL vial. This is a single mode operating system, working at 2.45 GHz, with a programmable power level from 0 to 400 W. Stirring was performed at 400 rpm with the magnetic stirrer included in the apparatus.

***N*-(5-Arylpyrazin-2-yl)pyridinium aminides (8). General procedure.** *N*-(5-Bromopyrazin-2-yl)pyridinium aminide (1 mmol),[25] the corresponding boronic acid (1.5 mmol) and K_2CO_3 (10 mmol) were dissolved in a toluene/ethanol mixture (4:1, 10 mL). $Pd(PPh_3)_4$ (5 mmol %) was added and the mixture was stirred under argon and heated under reflux. The course of the reaction was followed by TLC. Once the starting material had been consumed, the system was allowed to reach room temperature; the mixture was filtered through Celite and washed with acetonitrile until colour was no longer observed in the filtrate. The combined filtrates were evaporated to dryness. The crude product was purified by flash chromatography on a silica gel column, with ethanol as the eluent.

***N*-(5-Phenylpyrazin-2-yl)pyridinium aminide (8a).**[28] Yellow solid (230 mg, 93%, dichloromethane/diethyl ether), mp 170–172 ºC; ^{1}H NMR (300 MHz, CD_3OD): δ 8.85 (2H, dd, *J* 7.0 and 1.3 Hz, *H*2(6)), 8.12 (1H, tt, *J* 7.7 and 1.3 Hz, *H*4), 8.06 (1H, d, *J* 1.5 Hz, *H*6′), 7.95 (1H, d, *J* 1.5 Hz, *H*3′), 7.87 (2H, dd, *J* 7.7 and 7.0 Hz, *H*3(5)), 7.77 (2H, ap dd, *J* 8.5 and 1.3 Hz, *H*2″(6″)), 7.41 (2H, ap dd, *J* 8.5 and 7.4 Hz, *H*3″(5″)), 7.29 (1H, tt, *J* 7.4 and 1.3 Hz, *H*4″).

***N*-[5-(4-Methylphenyl)pyrazin-2-yl]pyridinium aminide (8b).**[28] Orange solid (223 mg, 85%, ethyl acetate), mp 143–145 ºC; δ 8.84 (2H, dd, *J* 7.0 and 1.1 Hz, *H*2(6)), 8.10 (1H, tt, *J* 7.7 and 1.1 Hz, *H*4), 8.02 (1H, d, *J* 1.4 Hz, *H*6′), 7.91 (1H, d, *J* 1.4 Hz, *H*3′), 7.86 (2H, dd, *J* 7.7 and

7.0 Hz, *H*3(5)), 7.62 (2H, d, *J* 8.2 Hz, *H*2″(6″)), 7.19 (2H, d, *J* 8.2 Hz, *H*3″(5″)), 2.34 (3H, s, C*H*$_3$).

***N*-[5-(4-Methoxyphenyl)pyrazin-2-yl]pyridinium aminide (8c).**[28] Orange solid (247 mg, 89% ethanol), mp 144–146 ºC; ^{1}H NMR (300 MHz, CD_3OD): δ 8.85 (2H, dd, *J* 7.0 and 1.3 Hz, *H*2(6)), 8.11 (1H, tt, *J* 7.7 and 1.3 Hz, *H*4), 7.90 (1H, d, *J* 1.6 Hz, *H*3′), 7.88 (2H, dd, *J* 7.6 and 7.0 Hz, *H*3(5)), 7.68 (2H, d, *J* 8.8 Hz, *H*2″(6″)), 6.95 (2H, d, *J* 8.8 Hz, *H*3″(5″)), 3.83 (3H, s, C*H*$_3$).

***N*-[5-(1-benzothiophen-3-yl)pyrazin-2-yl]pyridinium aminide (8d).** Dark orange solid (259 mg, 85%, ethyl acetate/ethanol), mp 126–128 ºC; IR (KBr) ν_{max} (cm^{-1}): 3026, 1574, 1521, 1490, 1470, 1386, 1150, 1022, 1010, 725; ^{1}H NMR (300 MHz, CD_3OD): δ 8.90 (2H, dd, *J* 6.9 and 1.3 Hz, *H*2(6)), 8.22 (1H, dd, *J* 5.8 and 2.1 Hz, *H*4″), 8.17 (1H, tt, *J* 7.7 and 1.3 Hz, *H*4), 8.02 (2H, s ap., *H*3′ and *H*6′), 7.92 (3H, m, *H*3(5) and *H*7″), 7.68 (1H, s, *H*2″), 7.42 (2H, m, *H*5″ and *H*6″); ^{13}C NMR (75 MHz, CD_3OD): δ 160.7 (*C*2′), 144.9 (*C*2(6)), 142.1 (*C*7a″), 140.6 (*C*6′), 139.1 (*C*4), 138.9 (*C*3a″ or *C*5′ or *C*3″), 136.5 (*C*3a″ or *C*5′ or *C*3″), 136.3 (*C*3′), 135.5 (*C*3a″ or *C*5′ or *C*3″), 128.7 (*C*3(5)), 125.5, 125.3, 124.6, 123.9 and 123.7 (*C*6″, *C*4″, *C*5″, *C*7″ and *C*2″). MS (EI, *m*/*z*): 304 (100, $M^{+\bullet}$), 227 (11), 225 (51), 198 (37), 170 (13); HRMS (ESI-TOF, CH_3OH): Calcd for $C_{17}H_{12}N_4S$: $[M + H]^+$ 305.0855; Found 305.0852.

***N*-(5-Aryl-3-bromopyrazin-2-yl)pyridinium aminides (3). General procedure.** To a stirred solution of *N*-(5-arylpyrazin-2-yl)pyridinium aminide **8** (1 mmol) in dichloromethane (8 mL) at room temperature (–50 °C in the case of compound **8d**), a solution of NBS (1.1 mmol) in the same solvent (15 mL) was added dropwise. The reaction mixture was stirred at the same temperature until the starting material had been consumed (TLC analysis). The solvent was evaporated and the residue was purified by flash chromatography on silica gel using ethanol as eluent and then crystallized from a suitable solvent and identified.

***N*-(3-Bromo-5-phenylpyrazin-2-yl)pyridinium aminide (3a).**[26] Red solid (294 mg, 90% ethyl acetate), mp 68–70 ºC; ^{1}H NMR (300 MHz, CD_3OD): δ 8.74 (2H, dd, *J* 6.9 and 1.3 Hz, *H*2(6)), 8.20 (1H, tt, *J* 7.7 and 1.3 Hz, *H*4), 8.02 (1H, s, *H*6′), 7.91 (2H, dd, *J* 7.7 and 6.9 Hz, *H*3(5)), 7.68 (2H, d, *J* 8.8 Hz, *H*2″(6″)), 6.96 (2H, d, *J* 8.8 Hz, *H*3″(5″)), 3.83 (3H, s, C*H*$_3$).

***N*-[3-Bromo-5-(4-methylphenyl)pyrazin-2-yl]pyridinium aminide (3b).**[26] Orange solid (310 mg, 91% ethyl acetate), mp 179–180 ºC; ^{1}H NMR (300 MHz, acetone-d_6): δ 8.85 (2H, dd, *J* 7.0 and 1.3 Hz, *H*2(6)), 8.10 (1H, tt, *J* 7.7 and 1.3 Hz, *H*4), 8.04 (1H, s, *H*6′), 7.89 (2H, dd, *J* 7.7 and 7.0 Hz, *H*3(5)), 7.70 (2H, d, *J* 8.2 Hz, *H*2″(6″)), 7.15 (2H, d, *J* 8.2 Hz, *H*3″(5″)), 2.29 (3H, s, C*H*$_3$).

***N*-[3-Bromo-5-(4-methoxyphenyl)pyrazin-2-yl]pyridinium aminide (3c).**[26] Red solid (328 mg, 92% ethyl acetate/diethyl ether), mp 58–60 ºC; ^{1}H NMR (300 MHz, acetone-d_6): δ 8.75 (2H, dd, *J* 6.9 and 1.3 Hz, *H*2(6)), 8.22 (1H, tt, *J* 7.7 and 1.3 Hz, *H*4), 8.03 (1H, s, *H*6′), 7.93 (2H, dd, *J* 7.7 and 6.9 Hz, *H*3(5)), 7.79 (2H, d, *J* 8.9 Hz, *H*2″(6″)), 6.96 (2H, d, *J* 8.9 Hz, *H*3″(5″)), 3.84 (3H, s, C*H*$_3$).

***N*-[5-(1-benzothiophen-3-yl)-3-bromopyrazin-2-yl]pyridinium aminide (3d).** Dark orange solid (methanol, 214 mg, 56%), mp > 251 ºC (dec.); IR (KBr) ν_{max} (cm^{-1}): 3056, 1515, 1463,

1457, 1434, 1165, 1074, 762; ^{1}H NMR (500 MHz, $(CD_3)_2CO$): δ 8.90 (2H, dd, *J* 6.9 and 1.3 Hz, *H*2(6)), 8.54 (1H, ddd, *J* 7.9, 1.4 and 0.7 Hz, *H*4″), 8.16 (1H, tt, *J* 7.7 and 1.3 Hz, *H*4), 8.08 (1H, s, *H*6′), 7.98 (1H, ddd, *J* 8.0, 1.2 and 0.9 Hz, *H*7″), 7.97 (2H, dd, *J* 7.7 and 6.9 Hz, *H*3(5)), 7.77 (1H, s, *H*2″), 7.48 (1H, ddd, *J* 8.0, 7.9 and 1.3 Hz, *H*5″), 7.42 (1H, ddd, *J* 8.0, 7.9 and 1.3 Hz, *H*6″); ^{13}C NMR (125 MHz, $(CD_3)_2CO$ data from gHSQC and gHMBC experiments): δ 156.8 (*C*2′), 143.1 (*C*2(6)), 140.7 (*C*7a″), 138.1 (*C*6′), 137.7 (*C*3a″), 136.7 (*C*4), 134.2 and 133.7 (*C*5′ and *C*3″), 126.9 (*C*3(5)), 124.4 (*C*6″), 124.3 (*C*4″), 124.2 (*C*5″), 122.6 (*C*7″), 121.4 (*C*2″) (*C*3′ is not observed). MS (EI, *m*/*z*): 384/382 (16/15, $M^{+\bullet}$), 305 (100), 226 (33), 199 (43); HRMS (ESI-TOF, CH_3OH): Calcd for $C_{17}H_{12}{}^{79}BrN_4S$: $[M + H]^+$ 382.9962; Found 382.9954.

***N*-[5-(2-Bromo-1-benzothiophen-3-yl)-3-bromopyrazin-2-yl]pyridinium aminide (3e).** Orange solid (methanol, 89 mg, 19%), mp 204–206 ºC; IR (KBr) ν_{max} (cm^{-1}): 1479, 1463, 1420, 1153, 1056, 753; ^{1}H NMR (500 MHz, $(CD_3)_2CO$): δ 8.90 (2H, dd, *J* 7.0 and 1.2 Hz, *H*2(6)), 8.22 (1H, tt, *J* 7.6 and 1.2 Hz, *H*4), 7.99 (2H, dd, *J* 7.6 and 7.0 Hz, *H*3(5)), 7.93 (1H, m, *H*4″ or *H*7″), 7.91 (1H, s, *H*6′), 7.90 (1H, m, *H*7″ or *H*4″), 7.41 (2H, m, *H*5″ and *H*6″); ^{13}C NMR (125 MHz, $(CD_3)_2CO$ data from gHSQC and gHMBC experiments): δ 156.9 (*C*2′), 143.6 (*C*2(6)), 141.2 (*C*6′), 139.3 and 138.9 (*C*7a″ and *C*3a″), 138.2 (*C*5′ or *C*3″), 137.8 (*C*4), 131.0 (*C*3″ or *C*5′), 127.2 (*C*3(5)), 125.0 and 124.9 (*C*5″ and *C*6″), 123.6 and 121.2 (*C*4″ and *C*7″) (*C*3′ and *C*2″ are not observed). MS (EI, *m*/*z*): 464/462/460 (50/100/53, $M^{+\bullet}$), 385 (50), 383 (61), 302 (45), 225 (39); HRMS (ESI-TOF, CH_3OH): Calcd for $C_{17}H_{12}{}^{79}Br_2N_4S$: $[M + H]^+$ 460.9066; Found 460.9027.

Reaction of 3-bromo-5-substituted pyridinium aminides 3 with benzyl bromide. General procedure. The appropriate aminide **3** (1 mmol) was dissolved in anhydrous acetone (11 mL) in a dry round-bottomed flask. The corresponding benzyl bromide (3.5 mmol) was added and the mixture was stirred at room temperature under argon until the starting aminide was no longer detected by TLC. Once the reaction was complete, the solid was filtered off and washed well with cold ethyl acetate. The salt **9a** is soluble in acetone and, in this case, once the solvent had been eliminated *in vacuo*, the residue was dissolved in a small amount of DMF and poured over ethyl acetate. The resulting suspension was filtered and the solid was washed with ethyl acetate (3 × 5 mL) to remove excess benzyl bromide. Alkylation of aminide **3d**, which is not totally soluble in acetone, was performed in dry DMF and the salt **9d** was isolated by removing the solvent and treating the residue with ethyl acetate in an ultrasonic bath. The salts **9** were used in the next step without further purification.

1-[*N*-Benzyl-*N*-(3-bromo-5-phenylpyrazin-2-yl)amino]pyridinium bromide (9a). After nine days the title compound was obtained as a beige solid (354 mg, 71%), mp 125–127 ºC; IR (KBr) ν_{max} (cm^{-1}): 3059, 1615, 1474, 1425, 1341, 1276, 1172, 780, 755, 696; ^{1}H NMR (300 MHz, CD_3OD): δ 9.31 (2H, dd, *J* 6.7 and 1.4 Hz, *H*2(6)), 9.08 (1H, s, *H*6′), 8.70 (1H, tt, *J* 7.8 and 1.4 Hz, *H*4), 8.17 (2H, dd, *J* 7.8 and 6.7 Hz, *H*3(5)), 8.14 (2H, dd, *J* 7.6 and 2.1 Hz, *H*2″(6″)), 7.55 (5H, m, *H*3″(5″), *H*4″ and *H*3‴(5‴)), 7.37 (3H, m, *H*2‴(6‴) and *H*4‴), 5.32 (2H, s, CH_2); ^{13}C NMR (75 MHz, CD_3OD): δ 151.9 (*C*2′), 149.2 (*C*5′), 147.6 (*C*4), 147.0 (*C*2(6)), 137.7 (*C*6′), 134.3 and 133.8 (*C*1‴ and *C*3′), 132.8 (C1″), 130.6 (*C*4″ or *C*4‴), 129.4, 129.0, 129.0, 128.8 and

127.7 (*C*3(5), *C*3″(5″), *C*2‴(6‴), *C*3‴(5‴) and *C*4‴ or *C*4″), 126.9 (*C*2″(6″)), 60.1 (*C*H$_2$). MS (EI, *m*/*z*): 419/417 (< 2, M − Br$^-$), 341 (24), 340 (48), 339 (100), 338 (66), 337 (97), 330 (24), 329 (33), 328 (61), 327 (53), 326 (90), 249 (16), 248 (18), 247 (18), 91 (36), 81 (41); HRMS (ESI-TOF, CH$_3$OH): Calcd for $C_{22}H_{18}{}^{79}BrN_4$: [M − Br]$^+$ 417.0709; Found 417.0852.

1-[*N*-Benzyl-*N*-[3-bromo-5-(4-methylphenyl)pyrazin-2-yl]amino]pyridinium bromide (9b). After twelve days the title compound was obtained as a white solid (420 mg, 82%), mp 141–143 ºC; IR (KBr) ν_{max} (cm^{-1}): 3411, 3107, 3029, 2963, 2926, 1613, 1497, 1473, 1430, 1408, 1337, 1264, 1172, 1093, 1077, 1018, 823, 800, 674, 620; ^{1}H NMR (300 MHz, CD$_3$OD): δ 9.29 (2H, dd, *J* 6.9 and 1.3 Hz, *H*2(6)), 9.05 (1H, s, *H*6′), 8.69 (1H, tt, *J* 7.9 and 1.3 Hz, *H*4), 8.15 (2H, dd, *J* 7.9 and 6.9 Hz, *H*3(5)), 8.04 (2H, d, *J* 8.2 Hz, *H*2″(6″)), 7.51 (2H, m, *H*3‴(5‴)), 7.40 (2H, d, *J* 8.2 Hz, *H*3″(5″)), 7.37 (3H, m, *H*2‴(6‴) and *H*4‴), 5.29 (2H, s, C*H*$_2$), 2.19 (3H, s, *C*H$_3$); ^{13}C NMR (75 MHz, CD$_3$OD): δ 153.6 (*C*2′), 150.2 (*C*5′), 148.9 (*C*4), 148.3 (*C*2(6)), 142.8 (*C*4″), 138.8 (*C*6′), 135.8 (*C*1‴), 134.2 (*C*3′), 132.4 (*C*1″), 131.0, 130.7, 130.3, 130.2 and 130.0 (*C*3(5), *C*3″(5″), *C*2‴(6‴), *C*3‴(5‴) and *C*4‴), 128.2 (*C*2″(6″)), 61.5 (*C*H$_2$), 21.4 (*C*H$_3$). MS (EI, *m*/*z*): 433/431 (< 2, M − Br$^-$), 354 (19), 353 (83), 352 (43), 351 (77), 250 (80), 248 (81), 169 (29), 116 (58), 115 (47), 91 (100), 79 (51); HRMS (ESI-TOF, CH$_3$OH): Calcd for $C_{23}H_{20}{}^{79}BrN_4$: [M − Br]$^+$ 431.0871; Found 431.0879.

1-[*N*-Benzyl-*N*-[3-bromo-5-(4-methoxyphenyl)pyrazin-2-yl]amino]pyridinium bromide (9c). After eleven days the title compound was obtained as a white solid (328 mg, 62%), mp 130–132 ºC; IR (KBr) ν_{max} (cm^{-1}): 3445, 3106, 2989, 2940, 1614, 1604, 1519, 1470, 1434, 1343, 1257, 1180, 1014, 856, 715, 676; ^{1}H NMR (300 MHz, CD$_3$OD): δ 9.29 (2H, dd, *J* 6.9 and 1.3 Hz, *H*2(6)), 9.02 (1H, s, *H*6′), 8.68 (1H, tt, *J* 7.9 and 1.3 Hz, *H*4), 8.15 (2H, dd, *J* 7.9 and 6.9 Hz, *H*3(5)), 8.11 (2H, d, *J* 9.1 Hz, *H*2″(6″)), 7.51 (2H, m, *H*3‴(5‴)), 7.51 (2H, m, *H*3″(5″)), 7.37 (3H, m, *H*2‴(6‴) and *H*4‴), 7.12 (2H, d, *J* 9.1 Hz, *H*3″(5″)), 5.27 (2H, s, C*H*$_2$), 3.91 (3H, s, C*H*$_3$); ^{13}C NMR (75 MHz, CD$_3$OD): δ 163.6 (*C*4″), 153.4 (*C*2′), 149.6 (*C*5′), 148.8 (*C*4), 148.2 (*C*2(6)), 138.4 (*C*6′), 135.9 (*C*1‴), 134.2 (*C*3′), 130.7, 130.2, 130.1, 130.0 and 129.9 (*C*3(5), *C*2″(6″), *C*2‴(6‴), *C*3‴(5‴) and *C*4‴), 127.4 (*C*1″), 115.7 (*C*3″(5″)), 61.5 (*C*H$_2$), 56.0 (*C*H$_3$). MS (EI, *m*/*z*): 449/447 (< 2, M − Br$^-$), 369 (9), 368 (5), 367 (8), 281 (16), 279 (15), 277 (20), 276 (100), 266 (16), 264 (16), 262 (13), 261 (70), 233 (32), 91 (28), 78 (12); HRMS (ESI-TOF, CH$_3$OH): Calcd for $C_{23}H_{20}{}^{79}BrN_4O$: [M − Br]$^+$ 447.0817; Found 447.0804.

1-[*N*-Benzyl-*N*-[3-bromo-5-(1-benzothiophen-3-yl)pyrazin-2-yl]amino]pyridinium bromide (9d). After five days the title compound was obtained as a beige solid (454 mg, 82%), mp 163–165 ºC; IR (KBr) ν_{max} (cm^{-1}): 3422, 3110, 3064, 3043, 3020, 2963, 1615, 1551, 1514, 1470, 1434, 1408, 1310, 1167, 1150, 1073, 1060, 1027, 1008, 968, 919, 768, 730, 668; ^{1}H NMR (300 MHz, CD$_3$OD): δ 9.64 (2H, dd, *J* 6.6 and 1.6 Hz, *H*2(6)), 9.23 (1H, s, *H*6′), 8.86 (1H, tt, *J* 7.9 and 1.6 Hz, *H*4), 8.70 (1H, dd, *J* 6.4 and 1.6 Hz, *H*4″), 8.69 (1H, s, *H*2″), 8.35 (2H, dd, *J* 7.9 and 6.6 Hz, *H*3(5)), 8.09 (1H, dd, *J* 6.4 and 1.6 Hz, *H*7″), 7.65 (2H, m, *H*3‴(5‴)), 7.52 (2H, m, *H*5″ and *H*6″), 7.35 (3H, m, *H*2‴(6‴) and *H*4‴), 5.52 (2H, s, C*H*$_2$); ^{13}C NMR (75 MHz, (CD$_3$)$_2$CO): δ 152.0 (*C*2′), 150.0 (*C*5′), 148.9 (*C*4), 148.2 (*C*2(6)), 142.5 (*C*7a″), 140.6 (*C*6′), 137.2 (*C*3a″), 134.9 and 134.2 (*C*1‴ and *C*3′), 131.8 (*C*4‴), 131.0 (*C*3″), 130.6, 130.0 and 129.8

(*C*3(5), *C*2‴(6‴) and *C*3‴(5‴), 126.2, 126.1, 125.0, 123.8 and 122.9 (*C*6″, *C*4″, *C*5″, *C*7″ and *C*2″), 60.7 (*C*H$_2$). MS (EI, *m*/*z*): 475/473 (< 2, M − Br$^-$), 396 (28), 395 (100), 394 (39), 393 (85), 292 (69), 290 (67), 211 (24), 184 (41), 172 (25), 159 (21), 158 (67), 157 (15), 140 (72), 106 (22), 91 (46); HRMS (ESI-TOF, CH$_3$OH): Calcd for $C_{19}H_{15}{}^{79}BrN_3S$: [M – Br – C_5H_5N]$^+$ 394.0008; Found 394.0041.

***N*-Benzyl-*N*-(3-bromo-5-arylpyrazin-2-yl)amines (10). General procedure.** Platinum on charcoal (5%) (130 mg) was suspended in a stirred solution of the corresponding pyridinium salts (0.6 mmol) in CH$_3$CN (9 mL) and the mixture was cooled in an ice bath. Formic acid (98%, 2.6 mL) in CH$_3$CN (4.5 mL) and then triethylamine (6.2 mL) in the same solvent (9 mL) were added dropwise. The reaction mixture was stirred at the temperature and for the time indicated in each case. The resulting suspension was filtered through Celite. The filtrate was evaporated, made basic with saturated aqueous potassium carbonate and extracted with ethyl acetate (3 × 25 mL). The combined organic phases were dried over MgSO$_4$, filtered and evaporated to dryness. The residue was purified by flash chromatography (hexane/ethyl acetate, 7:3) and identified. The corresponding debrominated derivatives **11** were also isolated in low yield.

***N*-Benzyl-*N*-(3-bromo-5-phenylpyrazin-2-yl)amine (10a).** This compound was obtained, after the reaction mixture was heated under reflux for four hours, as an orange solid (144 mg, 71%), mp 62–64 ºC; IR (KBr) ν_{max} (cm^{-1}): 3463, 3432, 3025, 2928, 1636, 1582, 1531, 1453, 1349, 1170, 1106, 1033, 1020, 773, 739, 697; ^{1}H NMR (300 MHz, CDCl$_3$): δ 8.42 (1H, s, *H*6), 7.82 (2H, br. d, *J* 8.4 Hz, *H*2′(6′)), 7.37 (8H, m, *H*3′(5′), *H*4′, *H*2″(6″), *H*3″(5″) and *H*4″), 5.60 (1H, br. t, *J* 5.6 Hz, N*H*), 4.69 (2H, d, *J* 5.6 Hz, C*H*$_2$); ^{13}C NMR (75 MHz, CDCl$_3$): δ 150.4 (*C*2), 141.4 (*C*5), 138.3 (*C*1″), 137.4 (*C*6), 135.7 (*C*1′), 128.8 and 128.7 (*C*3′(5′) and *C*3″(5″)), 128.2 (*C*4′), 127.6 and 127.5 (*C*2″(6″) and *C*4″), 127.1 (*C*3), 125.5 (*C*2′(6′)), 45.7 (*C*H$_2$). MS (EI, *m*/*z*): 341/339 (70/70, M$^{+\bullet}$), 338 (20), 260 (33), 258 (25), 116 (19), 106 (100), 91 (91), 65 (25); HRMS (ESI-TOF, CH$_3$OH): Calcd for $C_{17}H_{15}{}^{79}BrN_3$: [M + H]$^+$ 340.0444; Found 340.0428.

***N*-Benzyl-*N*-(5-phenylpyrazin-2-yl)amine (11a).**[50] Orange solid (36 mg, 23%), mp 77–79 ºC; IR (KBr) ν_{max} (cm^{-1}): 3469, 3225, 3031, 2869, 1589, 1561, 1460, 1447, 1361, 1166, 1026, 1007, 753, 694; ^{1}H NMR (300 MHz, CDCl$_3$): δ 8.42 (1H, d, *J* 1.8 Hz, *H*6), 7.96 (1H, d, *J* 1.8 Hz, *H*3), 7.84 (2H, dd, *J* 8.3 and 1.3 Hz, *H*2′(6′)), 7.35 (8H, m, *H*3′(5′), *H*4′, *H*2″(6″), *H*3″(5″) and *H*4″), 5.10 (1H, br. t, *J* 5.8 Hz, N*H*), 4.59 (2H, d, *J* 5.8 Hz, C*H*$_2$); ^{13}C NMR (75 MHz, CDCl$_3$): δ 153.1 (*C*2), 141.7 (*C*5), 139.0 (*C*6), 138.4 and 137.1 (*C*1″ and *C*1′), 130.9 (*C*3), 128.7 (two overlapped signals *C*3″(5″) and *C*3′(5′)), 127.9 (*C*4′), 127.5 (two overlapped signals *C*2″(6″) and *C*4″), 125.4 *C*2′(6′), 45.7 (*C*H$_2$). MS (EI, *m*/*z*): 261 (100, M$^{+\bullet}$), 260 (36), 184 (15), 157 (17), 116 (14), 106 (90), 91 (64), 65 (18); HRMS (ESI-TOF, CH$_3$OH): Calcd for $C_{17}H_{16}N_3$: [M + H]$^+$ 262.1339; Found 262.1341.

***N*-Benzyl-*N*-(3-bromopyrazin-2-yl)amine (12).** Orange solid (9 mg, 6%), mp 84–86 ºC; IR (KBr) ν_{max} (cm^{-1}): 3414, 3237, 1573, 1356, 1091, 1009, 748, 699; ^{1}H NMR (300 MHz, CDCl$_3$): δ 8.07 (1H, d, *J* 1.7 Hz, *H*6), 7.65 (1H, d, *J* 1.7 Hz, *H*5), 7.32 (5H, m, *H*2′(6′), *H*3′(5′) and *H*4′), 4.99 (1H, m, N*H*), 4.51 (2H, d, *J* 5.6 Hz, C*H*$_2$); ^{13}C NMR (75 MHz, CDCl$_3$): δ 153.3 (*C*2), 144.1 (*C*6), 137.9 (*C*1′), 131.0 (*C*5), 128.8 (*C*3′(5′)), 127.7 (*C*4′), 127.5 *C*2′(6′), 125.9 (*C*3), 45.8 (*C*H$_2$).

MS (EI, *m*/*z*): 265/263 (29/30, $M^{+\bullet}$), 184 (26), 106 (70), 91 (100), 65 (22); HRMS (ESI-TOF, CH_3OH): Calcd for $C_{11}H_{11}{}^{79}BrN_3$: $[M + H]^+$ 264.0131; Found 264.0126.

***N*-Benzyl-*N*-[3-bromo-5-(4-methylphenyl)pyrazin-2-yl]amine (10b).** This compound was obtained, after the reaction mixture was heated under reflux for three hours, as a yellow oil (152 mg, 63%); IR (NaCl) ν_{max} (cm^{-1}): 3473, 3319, 3030, 2963, 2922, 1607, 1581, 1503, 1462, 1261, 1091, 1032, 819, 800; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.31 (1H, s, *H*6), 7.65 (2H, d, *J* 8.6 Hz, *H*2′(6′)), 7.24 (5H, m, *H*2″(6″), *H*3″(5″) and *H*4″), 7.14 (2H, br. d, *J* 7.9 Hz, *H*3′(5′)), 5.42 (1H, br. t, *J* 5.6 Hz, N*H*), 4.59 (2H, d, *J* 5.6 Hz, CH_2), 2.28 (3H,s, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 150.0 (*C*2), 141.4 (*C*5), 138.3 and 138.1 (*C*4′ and *C*1″), 137.0 (*C*6), 132.9 (*C*1′), 129.5 and 128.7 (*C*3′(5′) and *C*3″(5″)), 127.5 and 127.4 (*C*4″ and *C*2″(6″)), 126.9 (*C*3), 125.3 (*C*2′(6′)), 45.7 (*C*H_2), 21.2 (*C*H_3). MS (EI, *m*/*z*): 355/353 (8/8, $M^{+\bullet}$), 265/263 (97/100), 262 (12), 185 (10), 184 (40), 157 (23), 130 (34), 115 (11), 106 (14), 103 (12), 91 (14); HRMS (ESI-TOF, CH_3OH): Calcd for $C_{18}H_{17}{}^{79}BrN_3$: $[M + H]^+$ 354.0600; Found 354.0601.

***N*-Benzyl-*N*-[5-(4-methylphenyl)pyrazin-2-yl]amine (11b).** Yellow oil (21 mg, 11%); IR (KBr) ν_{max} (cm^{-1}): 3417, 3222, 2963, 2917, 2849, 1589, 1570, 1262, 1097, 1020, 801, 741, 700; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.35 (1H, d, *J* 1.3 Hz, *H*6), 8.11 (1H, d, *J* 1.3 Hz, *H*3), 7.71 (2H, d, *J* 8.2 Hz, *H*2′(6′)), 7.33 (5H, m, *H*2″(6″), *H*3″(5″) and *H*4″), 7.24 (2H, br. d, *J* 7.9 Hz, *H*3′(5′)), 6.09 (1H, m, N*H*), 4.62 (2H, br. s, CH_2), 2.37 (3H, s, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 151.1 (*C*2), 141.5 (*C*5), 138.5 (*C*6), 137.4, 134.7 and 133.0 (*C*1″, *C*1′ and *C*4′), 131.9 (*C*3), 129.7 and 128.9 (*C*3′(5′) and *C*3″(5″)), 127.8 (*C*4″), 127.4 (*C*2″(6″)), 125.4 (*C*2′(6′), 46.0 (*C*H_2), 21.3 (*C*H_3). MS (EI, *m*/*z*): 275 (82, $M^{+\bullet}$), 274 (77), 263 (15), 185 (100), 184 (23), 158 (36), 157 (28), 130 (34), 119 (19), 106 (83); HRMS (ESI-TOF, CH_3OH): Calcd for $C_{18}H_{18}N_3$: $[M + H]^+$ 276.1495; Found 276.1495.

***N*-Benzyl-*N*-[3-bromo-5-(4-methoxyphenyl)]pyrazin-2-yl amine (10c).** This compound was obtained, after the reaction mixture was stirred at room temperature for two hours, as a white solid (166 mg, 75%) mp 94–96 ºC; IR (KBr) ν_{max} (cm^{-1}): 3412, 2840, 1607, 1576, 1559, 1540, 1507, 1248, 1171, 1117, 1026, 829, 797, 709, 693; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.35 (1H, s, *H*6), 7.77 (2H, d, *J* 8.7 Hz, *H*2′(6′)), 7.34 (5H, m, *H*2″(6″), *H*3″(5″) and *H*4″), 6.95 (2H, d, *J* 8.7 Hz, *H*3′(5′)), 5.53 (1H, m, N*H*), 4.68 (2H, d, *J* 5.6 Hz, CH_2), 3.83 (3H, s, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.9 (*C*4′), 149.8 (*C*2), 141.5 (*C*5), 138.3 (*C*1″), 136.5 (*C*6), 128.8 (*C*3″(5″)), 128.4 (*C*1′), 127.6 (*C*2″(6″)), 127.6 (*C*4″), 127.0 (*C*3), 126.8 (*C*2′(6′)), 114.2 (*C*3′(5′)), 55.3 (*C*H_3), 45.7 (*C*H_2). MS (EI, *m*/*z*): 371/369 (52/53, $M^{+\bullet}$), 290 (20), 288 (16), 281 (18), 279 (19), 266 (28), 264 (24), 199 (30), 146 (29), 107 (25), 106 (100), 91 (76); HRMS (ESI-TOF, CH_3OH): Calcd for $C_{18}H_{16}{}^{79}BrN_3O$: $[M + H]^+$ 370.055; Found 370.0544.

***N*-Benzyl-*N*-[3-bromo-5-(1-benzothiophen-3-yl)pyrazin-2-yl]amine (10d).** This compound was obtained, after the reaction mixture was stirred at room temperature for two hours, as a white solid (124 mg, 52%); mp 72–74 ºC; IR (NaCl) ν_{max} (cm^{-1}): 3419, 3029, 2924, 2853, 1577, 1531, 1497, 1095, 1061, 1044, 963, 759, 773; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.40 (1H, s, *H*6), 8.35 (1H, dd, *J* 7.4 and 1.5 Hz, *H*4′), 7.88 (1H, dd, *J* 7.4 and 1.5 Hz, *H*7′), 7.63 (1H, s, *H*2′), 7.39 (7H, m, *H*5′, *H*6′, *H*2″(6″), *H*3″(5″) and *H*4″), 5.66 (1H, br. t, *J* 5.4 Hz, N*H*), 4.72 (2H, d, *J* 5.4

Hz, C*H*$_2$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 150.2 (*C*2), 140.7 (*C*5), 139.1 (*C*6), 138.4 and 138.2 (*C*3′ and *C*1″), 136.8 (*C*7a′), 132.3 (*C*3a′), 128.7 (*C*3″(5″)), 127.6 (two overlapped signals *C*2″(6″) and *C*4″), 126.5 (*C*3), 124.7, 124.6 and 124.5 (*C*6′, *C*5′ and *C*4′), 123.6 and 122.7 (*C*7′ and *C*2′), 45.6 (*C*H$_2$). MS (EI, *m*/*z*): 397/395 (55/58, $M^{+\bullet}$), 316 (18), 173 (17), 106 (100), 91 (56); HRMS (ESI-TOF, CH_3OH): Calcd for $C_{19}H_{15}{}^{79}BrN_3S$: $[M + H]^+$ 396.0165; Found 396.0190.

***N*-Benzyl-*N*-[5-(1-benzothiophen-3-yl)pyrazin-2-yl]amine (11d).** Yellow oil (53 mg, 28%); IR (NaCl) ν_{max} (cm^{-1}): 3415, 2923, 1589, 1538, 1495, 1022, 760, 733; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.42 (1H, d, *J* 1.7 Hz, *H*6), 8.32 (1H, dd, *J* 6.6 and 1.4 Hz, *H*4′), 8.02 (1H, d, *J* 1.7 Hz, *H*3), 7.88 (1H, dd, *J* 6.6 and 1.4 Hz, *H*7′), 7.63 (1H, s, *H*2′), 7.37 (7H, m, *H*5′, *H*6′, *H*2″(6″), *H*3″(5″) and *H*4″), 5.08 (1H, br. t, *J* 5.6 Hz, N*H*), 4.61 (2H, d, *J* 5.6 Hz, C*H*$_2$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 152.9 (*C*2), 140.7 (two overlapped signals *C*6 and *C*5), 139.3, 138.4 and 137.2 (*C*3′, *C*7a′ and *C*1″), 133.9 (*C*3a′), 130.8 (*C*3), 128.8 (*C*3″(5″)), 127.6 (two overlapped signals *C*2″(6″) and *C*4″), 124.5 (two overlapped signals *C*5′ and *C*6′), 123.8 and 123.7 (*C*2′ and *C*4′), 122.7 (*C*7′), 45.7 (*C*H$_2$). MS (EI, *m*/*z*): 317 (100, $M^{+\bullet}$), 307 (27), 305 (26), 214 (22), 199 (25), 172 (42), 106 (82), 91 (23); HRMS (ESI-TOF, CH_3OH): Calcd for $C_{19}H_{16}N_3S$: $[M + H]^+$ 318.1059; Found 318.1075.

***N*-Benzyl-*N*-(5-aryl-3-ethynyl)pyrazin-2-yl amines (5). General procedure.** The corresponding *N*-benzyl-*N*-(3-bromo-5-arylpyrazin-2-yl) amine **10** (0.2 mmol), DABCO (0.08 g, 0.72 mmol), $PdCl_2(PPh_3)_2$ (10 mol %), water (1 mL) and the corresponding acetylene (0.4 mmol) were placed in a Biotage Initiator system. The reaction mixture was stirred and irradiated with MW at 120 ºC for 20 min. The solvent was removed under vacuum and the product was purified by chromatography on silica gel, using hexane/ethyl acetate (8:2) as eluent.

***N*-Benzyl-*N*-[3-(4-methoxyphenyl)ethynyl-5-phenyl-]pyrazin-2-yl amine (5a).** Yellow solid (51 mg, 66%) mp 116–118 ºC; IR (KBr) ν_{max} (cm^{-1}): 3427, 2923, 2204, 1603, 1571, 1530, 1492, 1456, 1292, 1254, 1188, 1169, 1020, 826, 763, 735, 693; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.44 (1H, s, *H*6), 7.88 (2H, br. d, *J* 8.5 Hz, *H*2′(6′)), 7.49 (2H, d, *J* 8.8 Hz, *H*2‴(6‴)), 7.37 (8H, m, *H*3′(5′), *H*4′, *H*2″(6″), *H*3″(5″) and *H*4″), 6.87 (2H, d, *J* 8.8 Hz, *H*3‴(5‴)), 5.76 (1H, br. t, *J* 5.6 Hz, N*H*), 4.76 (2H, d, *J* 5.6 Hz, C*H*$_2$), 3.82 (3H, s, C*H*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.5 (*C*4‴), 153.2 (*C*2), 141.4 (*C*5), 138.8 (*C*1″), 138.0 (*C*6), 136.9 (*C*1′), 133.6 (*C*2‴(6‴)), 128.7 (two overlapped signals *C*3′(5′) and *C*3″(5″)), 128.0 (*C*4′), 127.4 and 127.3 (*C*2″(6″) and *C*4″), 125.7 (*C*2′(6′)), 125.1 (*C*3), 114.2 (*C*3‴(5‴)), 113.5 (*C*1‴), 96.8 (C_β≡), 83.2 (C_α≡), 55.3 (*C*H$_3$), 45.2 (*C*H$_2$). MS (EI, *m*/*z*): 391 (54, $M^{+\bullet}$), 390 (21), 315 (26), 314 (100), 299 (10), 284 (22), 271 (14), 116 (21), 91 (28); HRMS (ESI-TOF, CH_3OH): Calcd for $C_{26}H_{22}N_3O$: $[M + H]^+$ 392.1757; Found 392.1772.

***N*-Benzyl-*N*-[3-(4-dimethylaminophenyl)ethynyl-5-phenyl]pyrazin-2-yl amine (5b).** Orange oil (59 mg, 73%); IR (NaCl) ν_{max} (cm^{-1}): 3418, 3031, 2923, 2852, 2188, 1606, 1525, 1361, 1177, 1129, 1028, 818, 763, 734, 696; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.40 (1H, s, *H*6), 7.89 (2H, dd, *J* 8.5 and 1.4 Hz, *H*2′(6′)), 7.38 (10H, m, *H*3′(5′), *H*4′, *H*2″(6″), *H*3″(5″), *H*4″ and *H*2‴(6‴)), 6.62 (2H, d, *J* 9.1 Hz, *H*3‴(5‴)), 5.78 (1H, br. t, *J* 5.7 Hz, N*H*), 4.75 (2H, d, *J* 5.7 Hz, C*H*$_2$), 2.99 (3H, s, C*H*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 153.2 (*C*2), 150.7 (*C*4‴), 141.2 (*C*5), 139.0 (*C*1″),

137.6 (*C*6), 137.1 (*C*1′), 133.2 (*C*2″′(6″′)), 128.7 (two overlapped signals *C*3′(5′) and *C*3″(5″)), 127.8 (*C*4′), 127.4 and 127.3 (*C*2″(6″) and *C*4″), 127.0 (*C*3), 125.7 (*C*2′(6′)), 111.6 (*C*3″′(5″′)), 110.6 (*C*1″′), 98.6 (C_β≡), 82.8 (C_α≡), 45.1 (*C*H_2), 40.1 (*C*H_3). MS (EI, *m*/*z*): 404 (100, $M^{+\bullet}$), 327 (13), 314 (27), 313 (66), 298 (10), 297 (25); HRMS (ESI-TOF, CH_3OH): Calcd for $C_{27}H_{25}N_4$: $[M + H]^+$ 405.2074; Found 405.2077.

***N*-Benzyl-*N*-[3-(4-trifluoromethylphenyl)ethynyl-5-(4-methylphenyl)]pyrazin-2-yl amine (5c).** Orange oil (54 mg, 61%); IR (NaCl) ν_{max} (cm^{-1}): 3426, 3030, 2922, 1615, 1568, 1532, 1501, 1323, 1170, 1127, 1066, 1017, 910, 841, 822, 734, 699; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.54 (1H, s, *H*6), 7.84 (2H, d, *J* 8.2 Hz, *H*2′(6′)), 7.69 (4H, m, *H*2″′(6″′) and *H*3″′(5″′)), 7.42 (5H, m, *H*2″(6″), *H*3″(5″) and *H*4″), 7.30 (2H, br. d, *J* 7.9 Hz, *H*3′(5′)), 5.71 (1H, br. t, *J* 5.6 Hz, N*H*), 4.82 (2H, d, *J* 5.6 Hz, CH_2), 2.44 (3H, s, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 153.3 (*C*2), 141.9 (*C*5), 138.8 (*C*6), 138.7 and 138.2 (*C*1″ and *C*4′), 133.8 (*C*1′), 132.2 (*C*2″′(6″′)), 131.3 (*C*1″′), 130.3 (c, $^2J_{C–F}$ = 33.7 Hz, *C*4″′), 129.5 (*C*3′(5′)), 128.7 (*C*3″(5″)), 127.5 (*C*4″), 127.4 (*C*2″(6″)), 125.7 (*C*2′(6′)), 125.4 (c, $^3J_{C–F}$ = 3.9 Hz, *C*3″′(5″′)), 123.7 (c, $^1J_{C–F}$ = 272.4 Hz, *C*F_3), 123.5 (*C*3), 94.5 (C_β≡), 86.5 (C_α≡), 45.2 (*C*H_2), 21.3 (*C*H_3). MS (EI, *m*/*z*): 443 (64, $M^{+\bullet}$), 442 (26), 367 (17), 366 (69), 299 (27), 298 (100), 147 (37), 130 (39), 115 (26), 103 (21), 91 (42); HRMS (ESI-TOF, CH_3OH): Calcd for $C_{27}H_{21}F_3N_3$: $[M + H]^+$ 444.1682; Found 444.1675.

***N*-Benzyl-*N*-[3-(4-methylphenyl)ethynyl-5-(4-methoxyphenyl)]pyrazin-2-yl amine (5d).** Dark yellow oil (64 mg, 79%); IR (NaCl) ν_{max} (cm^{-1}): 3420, 2917, 2849, 2200, 1609, 1569, 1559, 1506, 1498, 1248, 1173, 1030, 833, 816, 731, 698; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.39 (1H, s, *H*6), 7.82 (2H, d, *J* 8.7 Hz, *H*2′(6′)), 7.44 (2H, d, *J* 8.2 Hz, *H*2″′ (6″′)), 7.24 (5H, m, *H*2″(6″), *H*3″(5″) and *H*4″), 7.16 (2H, d, *J* 8.2 Hz, *H*3″(5″)), 6.96 (2H, d, *J* 8.7 Hz, *H*3′(5′)), 5.70 (1H, m, N*H*), 4.75 (2H, d, *J* 5.9 Hz, CH_2), 3.83 (3H, s, OCH_3), 2.36 (3H, s, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.7 (*C*4′), 153.0 (*C*2), 141.5 (*C*5), 139.8 (*C*4″′), 138.9 (*C*1″), 137.7 (*C*6), 131.9 (*C*2″′(6″′)), 129.6 (*C*1′), 129.3 (*C*3″′(5″′)), 128.7 (*C*3″(5″)), 127.4 (two overlapped signals *C*4″ and (*C*2″(6″)), 127.0 (*C*2′(6′)), 124.6 (*C*3), 118.5 (*C*1″′), 114.1 (*C*3′(5′)), 96.7 (C_β≡), 83.8 (C_α≡), 55.3 (OCH_3), 45.2 (*C*H_2), 21.6 (*C*H_3). MS (EI, *m*/*z*): 405 (50, $M^{+\bullet}$), 404 (16), 329 (24), 328 (100), 314 (44), 285 (18), 163 (23), 147 (15), 146 (46); HRMS (ESI-TOF, CH_3OH): Calcd for $C_{27}H_{23}N_3O$: $[M + H]^+$ 406.1914; Found 406.1879.

***N*-Benzyl-*N*-[3-(4-dimethylaminophenyl)ethynyl-5-(4-methoxyphenyl)]pyrazin-2-yl amine (5e).** Orange oil (43 mg, 49%); IR (NaCl) ν_{max} (cm^{-1}): 3419, 2922, 2854, 2185, 1653, 1607, 1559, 1540, 1522, 1506, 1360, 1249, 1170, 1129, 1030, 946, 816, 729, 699; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.34 (1H, s, *H*6), 7.83 (2H, d, *J* 8.8 Hz, *H*2′(6′)), 7.36 (7H, m, *H*2″′(6″′), *H*2″(6″), *H*3″(5″) and *H*4″), 6.95 (2H, d, *J* 8.8 Hz, *H*3′(5′)), 6.62 (2H, d, *J* 9.0 Hz, *H*3″′(5″′)), 5.73 (1H, br t, *J* 5.6 Hz, N*H*), 4.74 (2H, d, *J* 5.6 Hz, CH_2), 3.83 (3H, s, OCH_3), 2.98 (6H, s, NCH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.3 (*C*4′), 152.6 (*C*2), 150.4 (*C*4″′), 141.0 (*C*5), 138.9 (*C*1″), 136.8 (*C*6), 133.0 (*C*2″′(6″′)), 130.3 (*C*1′), 128.5 (*C*3″(5″)), 127.2, 127.1 and 126.8 (*C*2″(6″), *C*4″ and *C*2′(6′)), 125.4 (*C*3), 113.9 (*C*3′(5′)), 111.5 (*C*3″′(5″′)), 110.4 (*C*1″′), 98.4 (C_β≡), 82.8 (C_α≡), 55.4 (OCH_3), 45.2 (*C*H_2), 40.2 (NCH_3). MS (EI, *m*/*z*): 434 (83, $M^{+\bullet}$), 433 (15), 358 (22), 357 (86), 344

(29), 343 (100), 328 (26), 327 (15), 314 (22), 300 (25), 171 (17), 146 (24), 91 (15); HRMS (ESI-TOF, CH_3OH): Calcd for $C_{28}H_{26}N_4O$: $[M + H]^+$ 435.2179; Found 435.2174.

***N*-Benzyl-*N*-[5-(1-benzothiophen-3-yl)-3-(4-methoxyphenyl)ethynyl]pyrazin-2-yl amine (5f).** Yellow oil (59 mg, 66%); IR (NaCl) ν_{max} (cm^{-1}): 3411, 3071, 3059, 3030, 2970, 2904, 2192, 1646, 1541, 1508, 1475, 1403, 1282, 1093, 1030, 1016, 898, 791, 728, 672; ^1H NMR (300 MHz, $CDCl_3$): δ 8.39 (1H, s, *H*6), 8.32 (1H, dd, *J* 7.9 and 0.9 Hz, *H*4′), 7.88 (1H, dd, *J* 7.9 and 0.9 Hz, *H*7′), 7.67 (1H, s, *H*2′), 7.43 (7H, m, *H*2″(6″), *H*3″(5″), *H*4″ and *H*2‴(6‴)), 6.89 (4H, m, *H*5′, *H*6′ and *H*3‴(5‴)), 5.77 (1H, br. t, *J* 5.6 Hz, N*H*), 4.77 (2H, d, *J* 5.6 Hz, CH_2), 3.82 (3H, s, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.1 (*C*4‴), 152.7 (*C*2), 140.3 (*C*5), 139.5 (*C*6), 138.4, 138.3 and 136.9 (*C*1″, *C*3′ and *C*7a′), 133.2 (*C*2‴(6‴)), 132.5 (*C*3a′), 128.3 (*C*3″(5″)), 127.5 (*C*4″), 127.0 (*C*2″(6″)), 126.8 (*C*3), 124.1, 124.0 and 123.9 (*C*2′, *C*5′ and *C*6′), 123.3 (*C*4′), 122.3 (*C*7′), 113.8 (*C*3‴(5‴)), 113.4 (*C*1‴), 96.4 (C_β≡), 82.7 (C_α≡), 54.9 (*C*H_3), 44.7 (*C*H_2). MS (EI, *m*/*z*): 447 (78, $M^{+\bullet}$), 446 (20), 371 (29), 370 (100), 340 (19), 173 (39); HRMS (ESI-TOF, CH_3OH): Calcd for $C_{28}H_{22}N_3OS$: $[M + H]^+$ 448.1478; Found 448.1474.

Pyrrolo[2,3-*b*]pyridines (6) and pyrrolo[2,3-*b*]pyrazines (7). General procedure. $AuCl_3$ (3 mol%, $1 \cdot 10^{-3}$ g) was added to a solution of the corresponding *N*-benzyl-*N*-(5-aryl-3-ethynyl)pyridine (or pyrazin)-2-yl amines **4**,[30] **5** (0.07 mmol) in ethanol (0.1 mL). The mixture was stirred at 70 °C and the title compounds were obtained after 4 h (compounds **6**) or 24 h (compounds **7**). The solvent was evaporated and the residue was purified by flash chromatography (hexane/ethyl acetate, 8:2).

1-Benzyl-2-(4-methylphenyl)-5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine (6a). Yellow solid (11.5 mg, 44%) mp 125–127 ºC; IR (NaCl) ν_{max} (cm^{-1}): 3029, 2923, 2852, 1601, 1495, 1472, 1447, 1410, 1361, 895, 823, 769, 698; ^1H NMR (500 MHz, $CDCl_3$): δ 8.55 (1H, d, *J* 2.1 Hz, *H*6), 8.09 (1H, d, *J* 2.1 Hz, *H*4), 7.63 (2H, dd, *J* 8.2 and 1.2 Hz, *H*2′(6′)), 7.46 (2H, dd, *J* 8.2 and 7.3 Hz, *H*3′(5′)), 7.35 (1H, tt, *J* 7.3 and 1.2 Hz, *H*4′), 7.29 (2H, d, *J* 8.2 Hz, *H*2‴(6‴)), 7.18 (5H, m, *H*3‴(5‴), *H*3″(5″) and *H*4″), 6.99 (2H, m, *H*2″(6″)), 6.57 (1H, s, *H*3), 5.57 (2H, s, CH_2), 2.38 (3H, s, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 148.8 (*C*7a), 142.8 (*C*2), 142.2 (*C*6), 139.8 (*C*1″), 138.5 and 138.4 (*C*1′ and *C*4‴), 130.2 (*C*5), 130.1 (*C*1‴), 129.3 (*C*2‴(6‴)), 129.1, 129.0 and 128.9 (*C*3‴(5‴), *C*3″(*C*5″) and *C*3′(*C*5′)), 127.4 (*C*2′(6′)), 127.0, 126.9 and 126.5 (*C*4, *C*4′ and *C*4″), 126.5 (*C*2″(6″)), 120.6 (*C*3a), 100.1 (*C*3), 46.1 (*C*H_2), 21.3 (*C*H_3). MS (EI, *m*/*z*): 374 (100, $M^{+\bullet}$), 373 (81), 297 (36), 283 (20), 91 (12); HRMS (ESI-TOF, CH_3OH): Calcd for $C_{27}H_{23}N_2$: $[M + H]^+$ 375.1856; Found 375.1867.

1-Benzyl-2-(4-methoxyphenyl)-5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine (6b). Yellow solid (11.8 mg, 43%) mp 122–124 ºC; IR (NaCl) ν_{max} (cm^{-1}): 3042, 2926, 1607, 1495, 1473, 1409, 1361, 1292, 1250, 1177, 1030, 835, 769, 699; ^1H NMR (300 MHz, $CDCl_3$): δ 8.59 (1H, d, *J* 2.2 Hz, *H*6), 8.13 (1H, d, *J* 2.2 Hz, *H*4), 7.68 (2H, br. d, *J* 7.3 Hz, *H*2′(6′)), 7.51 (2H, br. t, *J* 7.8 Hz, *H*3′(5′)), 7.39 (1H, m, *H*4′), 7.36 (2H, d, *J* 8.8 Hz, *H*2‴(6‴)), 7.25 (3H, m, *H*3″(5″) and *H*4″), 7.04 (2H, br. d, *J* 7.3 Hz, *H*2″(6″)), 6.95 (2H, d, *J* 8.8 Hz, *H*3‴(5‴), 6.58 (1H, s, *H*3), 5.60 (2H, s, CH_2), 3.87 (3H, s, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.8 (*C*4‴), 148.7 (*C*7a), 142.5 (*C*2), 142.1 (*C*6), 139.7 (*C*1″), 138.5 (*C*1′), 130.5 (*C*2‴(6‴)), 130.1 (*C*5), 128.8 and 128.5 (*C*3′(5′) and

*C*3″(*C*5″)), 127.3 (*C*2′(6′)), 127.0, 126.8 and 126.3 (*C*4, *C*4′ and *C*4″), 126.4 (*C*2″(6″)), 124.6 (*C*1‴), 120.6 (*C*3a), 114.0 (*C*3‴(5‴)), 99.8 (*C*3), 55.3 (CH_3), 46.0 (CH_2). MS (EI, *m*/*z*): 390 (100, $M^{+\bullet}$), 389 (61), 314 (11), 313 (35), 299 (10), 283 (11), 256 (10), 255 (11), 91 (12); HRMS (ESI-TOF, CH_3OH): Calcd for $C_{27}H_{23}N_2O$: $[M + H]^+$ 391.1805; Found 391.1826.

1-Benzyl-5-(4-methoxyphenyl)-2-thiophen-3-yl-1*H*-pyrrolo[2,3-*b*]pyridine (6c). Yellow solid (18 mg, 65%) mp 132–134 ºC; IR (KBr) ν_{max} (cm^{-1}): 3102, 3059, 3032, 2963, 1607, 1522, 1474, 1407, 1361, 1293, 1243, 1182, 1028, 833, 757, 695; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.56 (1H, d, *J* 2.3 Hz, *H*6), 8.09 (1H, d, *J* 2.3 Hz, *H*4), 7.60 (2H, d, *J* 8.6 Hz, *H*2′(6′)), 7.40 (1H, dd, *J* 5.0 and 3.0 Hz, *H*5‴), 7.29 (4H, m, *H*3″(5″), *H*4″ and *H*2‴), 7.24 (1H, dd, *J* 5.0 and 1.6 Hz, *H*4‴), 7.09 (2H, m, *H*2″(6″)), 7.06 (2H, d, *J* 8.6 Hz, *H*3′(5′)), 6.69 (1H, s, *H*3), 5.70 (2H, s, CH_2), 3.90 (3H, s, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 158.9 (*C*4′), 148.4 (*C*7a), 142.3 (*C*6), 138.4 (*C*2), 137.3 (*C*1″), 132.6 and 132.2 (*C*1′ and *C*3‴), 130.5 (*C*5), 128.7 and 128.4 (*C*2′(6′) and *C*3″(*C*5″)), 128.2 and 127.1 (*C*4″), 126.1 and 126.0 (*C*2″(6″) and two overlapped carbons signals *C*5‴ and *C*2‴), 123.7 (*C*4‴), 120.3 (*C*3a), 114.4 (*C*3′(5′)), 100.0 (*C*3), 55.4 (CH_3), 46.0 (CH_2). MS (EI, *m*/*z*): 396 (100, $M^{+\bullet}$), 395 (61), 320 (14), 319 (57), 313 (11), 305 (12), 262 (12), 261 (12), 91 (29); HRMS (ESI-TOF, CH_3OH): Calcd for $C_{25}H_{21}N_2OS$: $[M + H]^+$ 397.1369; Found 397.1372.

1-Benzyl-5-(4-methoxyphenyl)-2-(4-trifluoromethylphenyl)-1*H*-pyrrolo[2,3-*b*]pyridine (6d). Yellow solid (14.8 mg, 46%) mp 126–128 ºC; IR (KBr) ν_{max} (cm^{-1}): 3045, 2922, 1616, 1521, 1474, 1412, 1365, 1328, 1248, 1166, 1121, 1072, 852, 833, 766, 702; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.56 (1H, d, *J* 2.4 Hz, *H*6), 8.07 (1H, d, *J* 2.4 Hz, *H*4), 7.62 (2H, d, *J* 8.2 Hz, *H*3‴(5‴)), 7.55 (2H, d, *J* 8.6 Hz, *H*2′(6′)), 7.51 (2H, d, *J* 8.2 Hz, *H*2‴ (6‴)), 7.20 (3H, m, *H*3″(5″) and *H*4″), 7.01 (2H, d, *J* 8.6 Hz, *H*3′(5′)), 6.97 (2H, br. dd, *J* 7.3 and 2.0 Hz, *H*2″(6″)), 6.64 (1H, s, *H*3), 5.58 (2H, s, CH_2), 3.86 (3H, s, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.0 (*C*4′), 148.7 (*C*7a), 142.9 (*C*6), 140.8 (*C*2), 138.1 (*C*1″), 135.9 (*C*1′), 132.0 (*C*1‴), 130.3 (*C*5), 130.3 (c, $^2J_{CF}$ = 32.7 Hz, *C*4‴), 129.3, 128.6 and 128.4 (*C*2‴(6‴), *C*2′(6′) and *C*3″(*C*5″)), 127.3 and 126.6 (*C*4 and *C*4″), 126.3 (*C*2″(6″)), 125.5 (c, $^3J_{CF}$ = 3.8 Hz, *C*3‴(*C*5‴)), 124.0 (c, $^1J_{CF}$ = 272 Hz, CF_3), 120.3 (*C*3a), 114.4 (*C*3′(5′)), 101.5 (*C*3), 55.4 (CH_3), 46.2 (CH_2). MS (EI, *m*/*z*): 358 (100, $M^{+\bullet}$), 382 (27), 313 (7), 91 (8); HRMS (ESI-TOF, CH_3OH): Calcd for $C_{28}H_{22}F_3N_2O$: $[M + H]^+$ 459.1679; Found 459.1661.

5-Benzyl-6-(4-methoxyphenyl)-2-phenyl-5*H*-pyrrolo[2,3-*b*]pyrazine (7a). Yellow oil (12 mg, 44%); IR (NaCl) ν_{max} (cm^{-1}): 3062, 3030, 2960, 2925, 2854, 1610, 1495, 1464, 1444, 1418, 1360, 1257, 1210, 1176, 1101, 1028, 935, 864, 835, 800, 695; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.67 (1H, s, *H*3), 8.02 (2H, br. d, *J* 7.2 Hz, *H*2′(6′)), 7.50 (2H, br. t, *J* 7.7 Hz, *H*3′(5′)), 7.36 (3H, m, *H*4′ and *H*2‴(6‴)), 7.20 (3H, m, *H*3″(5″) and *H*4″), 6.99 (2H, m, *H*2″(6″)), 6.94 (2H, d, *J* 9.0 Hz, *H*3‴(5‴)), 6.79 (1H, s, *H*7), 5.54 (2H, s, CH_2), 3.84 (3H, s, CH_3); ^{13}C NMR (50.29 MHz, $CDCl_3$): δ 160.4 (*C*4″), 147.2 (*C*6), 142.1 (*C*2), 137.7, 137.6, 137.1 and 136.1 (*C*4a, *C*7a, *C*1′ and *C*1″), 134.9 (*C*3), 130.6 (*C*2‴(6‴)), 128.9 and 128.6 6 (*C*3′(*C*5′) and (*C*3″(5″)), 127.4 (*C*4′), 127.1 (*C*2′(6′)), 126.8 (*C*4″), 126.4 (*C*2″(6″)), 123.6 (*C*1‴), 114.2 (*C*3″(*C*5″)),100.8 (*C*7), 55.4

(*C*H$_3$), 46.2 (*C*H$_2$). MS (EI, *m*/*z*): 391 (100, M$^{+\bullet}$), 390 (9), 314 (15), 300 (9), 257 (14), 91 (4); HRMS (ESI-TOF, CH$_3$OH): Calcd for $C_{26}H_{21}N_3O$: [M + H]$^+$ 392.1757; Found 392.1757.

5-Benzyl-2-(4-methylphenyl)-6-(4-trifluoromethylphenyl)-5*H*-pyrrolo[2,3-*b*]pyrazine (7b). Yellow solid (15.2 mg, 49%) mp 170–172 ºC; IR (KBr) ν_{max} (cm^{-1}): 3090, 3066, 3032, 2922, 2852, 1618, 1497, 1465, 1452, 1411, 1326, 1207, 1166, 1123, 1068, 1017, 851, 819, 722, 695; ^{1}H NMR (300 MHz, CDCl$_3$): δ 8.77 (1H, s, *H*3), 7.98 (2H, d, *J* 7.9 Hz, *H*2′(6′)), 7.72 (2H, d, *J* 8.4 Hz, *H*3″′(5″′)), 7.60 (2H, d, *J* 8.4 Hz, *H*2″′(6″′)), 7.37 (2H, br. d, *J* 7.9 Hz, *H*3′(5′)), 7.27 (3H, m, *H*3″(5″) and *H*4″), 7.01 (2H, m, *H*2″(6″)), 6.93 (1H, s, *H*7), 5.60 (2H, s, C*H*$_2$), 2.47 (3H, s, C*H*$_3$); ^{13}C NMR (125 MHz, CDCl$_3$): δ 146.1 (*C*2), 142.9 and 142.8 (*C*6 and *C*4a), 139.7 and 139.6 (*C*7a and *C*1″), 137.0 (*C*4′), 136.1 (*C*3), 134.6 (*C*1′), 130.8 (*C*1″′), 129.9 and 129.6 (*C*3′(*C*5′) and (*C*2″′(6″′)), 128.9 (*C*3″(*C*5″)), 127.8 (*C*4″), 127.3 (*C*2′(6′)), 126.4 (*C*2″(6″)), 125.8 (c, $^3J_{CF}$ = 3.7 Hz, *C*3″′(*C*5″′)), 102.1 (*C*7), 46.5 (*C*H$_2$), 21.4 (*C*H$_3$), (*C*F$_3$ and *C*4″ were not clearly identified); ^{19}F NMR (282 MHz, CDCl$_3$): δ –62.7 (C*F*$_3$). MS (EI, *m*/*z*): 443 (100, M$^{+\bullet}$), 442 (54), 366 (13), 352 (28), 298 (14), 91 (26); HRMS (ESI-TOF, CH$_3$OH): Calcd for $C_{27}H_{21}F_3N_3$: [M + H]$^+$ 444.1682; Found 444.1674.

5-Benzyl-2-(4-methoxyphenyl)-6-(4-methylphenyl)-5*H*-pyrrolo[2,3-*b*]pyrazine (7c). White solid (16.9 mg, 59%) mp 144–146 ºC; IR (KBr) ν_{max} (cm^{-1}): 2920, 1609, 1559, 1516, 1461, 1415, 1249, 1213, 1181, 1146, 1033, 839, 808, 728, 696; ^{1}H NMR (300 MHz, CDCl$_3$): δ 8.66 (1H, s, *H*3), 8.02 (2H, d, *J* 8.8 Hz, *H*2′(6′)), 7.37 (2H, d, *J* 8.2 Hz, *H*2″′(6″′)), 7.26 (5H, m, *H*2″(6″), *H*3″(5″) and *H*4″), 7.05 (4H, m, *H*3′(5′) and *H*3″′(5″′)), 6.81 (1H, s, *H*7), 5.57 (2H, s, C*H*$_2$), 3.90 (3H, s, OC*H*$_3$), 2.43 (3H, s, C*H*$_3$); ^{13}C NMR (75 MHz, CDCl$_3$): δ 159.8 (*C*4′), 147.2 and 146.6 (*C*6 and *C*2), 141.4, 139.0 (two overlapped signals) and 137.5 (*C*4a, *C*7a, *C*1″ and *C*4″′), 134.4 (*C*3), 130.7 (*C*1″′), 129.2, 128.9, 128.4 and 128.1 (*C*2′(6′), *C*2″(6″), *C*3″(5″) and *C*3″′(*C*5″′)), 128.4 (*C*4″), 126.3 *C*2″′(6″′), 114.2 (*C*3′(*C*5′)), 101.1 (*C*7), 55.4 (OC*H*$_3$), 46.2 (*C*H$_2$), 21.5 (*C*H$_3$). MS (EI, *m*/*z*): 405 (100, M$^{+\bullet}$), 328 (17), 315 (10), 314 (31), 299 (21), 298 (21), 271 (23), 146 (22), 91 (39); HRMS (ESI-TOF, CH$_3$OH): Calcd for $C_{27}H_{23}F_3N_3O$: [M + H]$^+$ 406.1914; Found 406.1910.

2-(1-Benzothiophen-3-yl)-5-benzyl-6-(4-methoxyphenyl)-5*H*-pyrrolo[2,3-*b*]pyrazine (7d). Yellow solid (15 mg, 48%) mp 131–133 ºC; IR (KBr) ν_{max} (cm^{-1}): 2957, 2924, 2853, 1608, 1492, 1467, 1355, 1257, 1247, 1203, 1174, 1028, 841, 760, 729, 708, 695; ^{1}H NMR (500 MHz, CDCl$_3$): δ 8.63 (1H, s, *H*3), 8.48 (1H, d, *J* 8.0 Hz, *H*4′), 7.92 (1H, d, *J* 7.5 Hz, *H*7′), 7.80 (1H, s, *H*2′), 7.45 (1H, ap. td, *J* 7.1 and 1.1 Hz, *H*5′), 7.39 (3H, m, *H*6′ and *H*2″′(6″′)), 7.24 (3H, m, *H*3″(5″) and *H*4″), 7.03 (2H, br. d, *J* 6.4 Hz, *H*2″(6″)), 6.95 (2H, d, *J* 8.7 Hz, *H*3″′(5″′), 6.80 (1H, s, *H*7), 5.31 (2H, s, C*H*$_2$), 3.84 (3H, s, C*H*$_3$); ^{13}C NMR (125 MHz, CDCl$_3$): δ 160.4 (*C*4″′), 147.0 (*C*6), 144.8 (*C*2), 141.5 (*C*4a), 140.8 (*C*7a′), 139.4 (*C*7a), 137.7 and 137.6 (*C*1″ and *C*3a′), 136.3 (*C*3), 135.1 (*C*3′), 130.6 (*C*2″′(6″′)), 128.7 (*C*3″(*C*5″)), 127.4 (*C*4″), 126.5 (*C*2″(6″)), 125.6 (*C*2′), 124.7 and 124.6 (*C*5′ and *C*6′), 124.0 (*C*4′), 123.7 (*C*1″′), 123.7 (*C*7′), 114.2 (*C*3″′(5″′)), 101.1 (*C*7), 55.4 (*C*H$_3$), 46.1 (*C*H$_2$). MS (EI, *m*/*z*): 447 (100, M$^{+\bullet}$), 356 (33), 313 (26), 172 (22); HRMS (ESI-TOF, CH$_3$OH): Calcd for $C_{28}H_{22}N_3OS$: [M + H]$^+$ 448.1487; Found 448.1478.

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