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-1H-pyrrolo[2,3-b]pyridines and 5-benzyl-5H-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 AuCl3. 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, AuCl3 cycloisomerization

Introduction
The 1H-pyrrolo[2,3-b]pyridine (or 7-azaindole) nucleus is present in only a few natural products1 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. 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\textit{H}-pyrrolo[2,3-\textit{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 and the ability to inhibit the activity of a mitogen-activated protein kinase (p38 MAP) and a Janus kinase (JAK3), some other derivatives can inhibit cyclin-dependent kinases (CDKs) and glycogen synthase kinase 3 (GSK-3), thereby exerting antiproliferative effects. 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. 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). Recently, a family of pyrrolo[2,3-b]pyrazine derivatives was also studied as CFTR (cystic fibrosis transmembrane conductance regulators) activators. As a consequence, several approaches for the synthesis of pyrrolo[2,3-b]pyrazines have been developed although more general and selective methods to prepare polysubstituted 4,7-diazaindoles would still be welcome.

![Figure 1. Active and natural compounds with a 7-aza- or 4,7-diazaindole skeleton.](image)

As a continuation of our studies on the utility of pyridinium \textit{N}-heteroarylamidines 1 (Scheme 1) as suitable scaffolds to obtain 2-aminoazines compounds that, in addition to other uses, have recently been tested in experimental models of human African trypanosomiasis, we became interested in developing a synthetic route to pyrrolo[2,3-b]pyridines and pyrrolo[2,3-b]pyrazines starting from the corresponding \textit{N}-pyridin-2-yl or pyrazin-2-yl pyridinium amidine (1\textit{a}, 1\textit{b}, Scheme 1). Pyridinium \textit{N}-heteroarylamidines 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.](image)

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 AuCl₃-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 1b24,27 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 K₂CO₃ (10 equiv), and Pd(PPh₃)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 °C 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).

\[
\begin{align*}
\text{Scheme 2. Preparation of } & N\text{-benzyl-3-alkynyl-5-arylpyrazin-2-yl amines 5 from aminides 3.} \\
\end{align*}
\]

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 was also obtained with 11d in an inseparable mixture (13:11d ≈ 4:6 by NMR spectroscopy) (Figure 2).

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

<table>
<thead>
<tr>
<th>Ar (^a)</th>
<th>Compound</th>
<th>Yield (%) (^b)</th>
<th>Compound</th>
<th>Yield (%) (^b)</th>
</tr>
</thead>
</table>
| \[
\begin{align*}
\text{Ar: } & (3\text{-bromo-5-arylpyrazin-2-yl}) \\
\end{align*}
\]| 9a | 71 | 10a | 71 |
| \[
\begin{align*}
\text{Ar: } & (3\text{-bromo-4-methoxyphenyl}) \\
\end{align*}
\]| 9b | 82 | 10b | 63 |
| \[
\begin{align*}
\text{Ar: } & (3\text{-bromo-4-methylphenyl}) \\
\end{align*}
\]| 9c | 62 | 10c | 75 |
| \[
\begin{align*}
\text{Ar: } & (3\text{-bromo-5-phenyl}) \\
\end{align*}
\]| 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

<table>
<thead>
<tr>
<th>Compound</th>
<th>Ar$^a$</th>
<th>Ar$^a$</th>
<th>Yield (%)$^b$</th>
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<tr>
<td>5d</td>
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<tr>
<td>5e</td>
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<td>49</td>
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<tr>
<td>5f</td>
<td><img src="11" alt="Structure" /></td>
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</tbody>
</table>

$^a$ 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 (‘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 °C. 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.\textsuperscript{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\textsuperscript{45-47} to prepare highly functionalized indole derivatives,\textsuperscript{45,47} 2-substituted 7-azaindoles,\textsuperscript{45} pyrrolocoumarin and pyrroloquinolone derivatives.\textsuperscript{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).

\[ \text{Scheme 3. Synthesis of 7-aza- and 4,7-diazaindoles 6 and 7 from alkynylamines 4 and 5.} \]

\[ \text{Scheme 4. Mechanistic interpretation for the AuCl}_3\text{-catalyzed cycloisomerization.} \]
When AuCl$_3$ (3 mol %) was added to a solution of the $N$-benzyl-3-alkynyl-5-arylpurazin(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**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Ar$^a$</th>
<th>Ar$^a$</th>
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<tr>
<td>6b</td>
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<td>7a</td>
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<td><img src="image" alt="Structure 7b" /></td>
<td><img src="image" alt="Structure 7b" /></td>
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<td>48</td>
</tr>
</tbody>
</table>

$^a$Ring numbering employed in NMR analysis. $^b$Yields of isolated pure products.

**Conclusions**

A regioselective synthesis of $N$-alkyl-3-alkynyl-5-arylpurazin-2-yl-amines 5 has been developed by applying the previously established methodology for the synthesis of the related $N$-alkyl-3-alkynyl-5-arylpurazin-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 spectrometer 2000 spectrophotometer. ¹H and ¹³C 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 F₂₅₄, 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 amine (1 mmol), ¹H NMR (300 MHz, CD₃OD): δ 8.85 (2H, dd, J 7.0 and 1.3 Hz, H₂(6)), 8.12 (1H, tt, J 7.7 and 1.3 Hz, H₄), 8.06 (1H, d, J 1.5 Hz, H₆), 7.95 (1H, d, J 1.5 Hz, H₃), 7.87 (2H, dd, J 7.7 and 7.0 Hz, H₃(5)), 7.77 (2H, ap dd, J 8.5 and 1.3 Hz, H₂(6′)), 7.41 (2H, ap dd, J 8.5 and 7.4 Hz, H₃(5′)), 7.29 (1H, tt, J 7.4 and 1.3 Hz, H₄). **N-(5-Phenylpyrazin-2-yl)pyridinium amide** (8a). ² Yellow solid (230 mg, 93%, dichloromethane/diethyl ether), mp 170–172 °C; ¹H NMR (300 MHz, CD₃OD): δ 8.84 (2H, dd, J 7.0 and 1.3 Hz, H₂(6)), 8.12 (1H, tt, J 7.7 and 1.3 Hz, H₄), 8.06 (1H, d, J 1.5 Hz, H₆), 7.95 (1H, d, J 1.5 Hz, H₃), 7.87 (2H, dd, J 7.7 and 7.0 Hz, H₃(5)), 7.77 (2H, ap dd, J 8.5 and 1.3 Hz, H₂(6′)), 7.41 (2H, ap dd, J 8.5 and 7.4 Hz, H₃(5′)), 7.29 (1H, tt, J 7.4 and 1.3 Hz, H₄). **N-(5-(4-Methylphenyl)pyrazin-2-yl)pyridinium amide** (8b). ² Orange solid (223 mg, 85%, ethyl acetate), mp 143–145 °C; δ 8.84 (2H, dd, J 7.0 and 1.1 Hz, H₂(6)), 8.10 (1H, tt, J 7.7 and 1.1 Hz, H₄), 8.02 (1H, d, J 1.4 Hz, H₆), 7.91 (1H, d, J 1.4 Hz, H₃), 7.86 (2H, dd, J 7.7 and
7.0 Hz, H3(5)), 7.62 (2H, d, J 8.2 Hz, H2(6′)), 7.19 (2H, d, J 8.2 Hz, H3(5′)), 2.34 (3H, s, CH3).

**N-[5-(4-Methoxyphenyl)pyrazin-2-yl]pyridinium aminide (8c)**. Orange solid (247 mg, 89% ethanol), mp 144–146 °C; 1H NMR (300 MHz, CD2OD): δ 8.85 (2H, dd, J 7.0 and 1.3 Hz, H2(6)), 8.11 (1H, tt, J 7.7 and 1.3 Hz, H4), 7.90 (1H, dd, J 1.6 Hz, H3′), 7.88 (2H, dd, J 7.6 and 7.0 Hz, H3(5)), 7.68 (2H, d, J 8.8 Hz, H2′(6′)), 6.95 (2H, d, J 8.8 Hz, H3′(5′)), 3.83 (3H, s, CH3).

**N-[5-(1-benzothiophen-3-yl)pyrazin-2-yl]pyridinium aminide (8d)**. Dark orange solid (259 mg, 85%, ethyl acetate/ethanol), mp 126–128 °C; IR (KBr) νmax (cm−1): 3026, 1574, 1521, 1490, 1470, 1386, 1150, 1022, 1010, 725; 1H NMR (300 MHz, CD2OD): δ 8.90 (2H, dd, J 6.9 and 1.3 Hz, H2(6)), 8.22 (1H, dd, J 5.8 and 2.1 Hz, H4′), 8.17 (1H, tt, J 7.7 and 1.3 Hz, H4), 8.02 (2H, s ap., H3′ and H6′), 7.92 (3H, m, H3(5) and H7′), 7.68 (1H, s, H2′), 7.42 (2H, m, H5′ and H6′); 13C NMR (75 MHz, CD2OD): δ 160.7 (C2′), 144.9 (C2(6)), 142.1 (C7a′), 140.6 (C6′), 139.1 (C4), 138.9 (C3a′ or C5′ or C3′), 136.5 (C3a′ or C5′ or C3′), 136.3 (C3′), 135.5 (C3a′ or C5′ or C3′), 128.7 (C3(5)), 125.5, 125.3, 124.6, 123.9 and 123.7 (C6′, C4′, C5′, C7′ and C2′). MS (EI, m/z): 304 (100, M+), 227 (11), 225 (51), 198 (37), 170 (13); HRMS (ESI-TOF, CH3OH): Calcd for C17H12N4S: [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-arylpypyrazin-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 dichloromethane (8 mL) at room 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)**. Red solid (294 mg, 90% ethyl acetate), mp 68–70 °C; 1H NMR (300 MHz, CD2OD): δ 8.74 (2H, dd, J 6.9 and 1.3 Hz, H2(6)), 8.20 (1H, tt, J 7.7 and 1.3 Hz, H4), 8.02 (1H, s, H6), 7.91 (2H, dd, J 7.7 and 6.9 Hz, H3(5)), 7.68 (2H, d, J 8.8 Hz, H2′(6′)), 6.96 (2H, d, J 8.8 Hz, H3′(5′)), 3.83 (3H, s, CH3).

**N-(3-Bromo-5-(4-methylphenyl)pyrazin-2-yl)pyridinium aminide (3b)**. Orange solid (310 mg, 91% ethyl acetate), mp 179–180 °C; 1H NMR (300 MHz, acetone-d6): δ 8.85 (2H, dd, J 7.0 and 1.3 Hz, H2(6)), 8.10 (1H, tt, J 7.7 and 1.3 Hz, H4), 8.04 (1H, s, H6), 7.89 (2H, dd, J 7.7 and 7.0 Hz, H3(5)), 7.70 (2H, d, J 8.2 Hz, H2′(6′)), 7.15 (2H, d, J 8.2 Hz, H3′(5′)), 2.29 (3H, s, CH3).

**N-(3-Bromo-5-(4-methoxyphenyl)pyrazin-2-yl)pyridinium aminide (3c)**. Red solid (328 mg, 92% ethyl acetate/diethyl ether), mp 58–60 °C; 1H NMR (300 MHz, acetone-d6): δ 8.75 (2H, dd, J 6.9 and 1.3 Hz, H2(6)), 8.22 (1H, tt, J 7.7 and 1.3 Hz, H4), 8.03 (1H, s, H6), 7.93 (2H, dd, J 7.7 and 6.9 Hz, H3(5)), 7.79 (2H, d, J 8.9 Hz, H2′(6′)), 6.96 (2H, d, J 8.9 Hz, H3′(5′)), 3.84 (3H, s, CH3).

**N-[5-(1-benzothiophen-3-yl)-3-bromopyrazin-2-yl]pyridinium aminide (3d)**. Dark orange solid (methanol, 214 mg, 56%), mp > 251 °C (dec.); IR (KBr) νmax (cm−1): 3056, 1515, 1463,
N-[5-(2-Bromo-1-benzo thiophen-3-yl)]-3-bromopyrazin-2-yl]pyridinium aminide (3e).

Orange solid (methanol, 89 mg, 19%), mp 204–206 ºC; IR (KBr) νmax (cm⁻¹): 1479, 1463, 1420, 1153, 1056, 753; ¹H NMR (500 MHz, (CD₃)₂CO): δ 8.90 (2H, dd, J 7.0 and 1.2 Hz, H2(6)), 8.22 (1H, tt, J 7.6 and 1.2 Hz, H4), 7.99 (2H, dd, J 7.6 and 7.0 Hz, H3(5)), 7.93 (1H, m, H4″ or H7″), 7.91 (1H, s, H6′), 7.90 (1H, m, H7″ or H4′″), 7.41 (2H, m, H5″ and H6″); ¹³C NMR (125 MHz, (CD₃)₂CO data from gHSQC and gHMBC experiments): δ 156.9 (C2′), 143.6 (C2(6)), 141.2 (C6′), 139.3 and 138.9 (C7a′ and C3a″), 138.2 (C5′ or C3′), 137.8 (C4), 131.0 (C3″ or C5′), 127.2 (C3(5)), 125.0 and 124.9 (C5″ and C6″), 123.6 and 121.2 (C4″ and C7″) (C3′ and C2″ are not observed). MS (EI, m/z): 464/462/460 (50/100/53, M⁺), 385 (50), 383 (61), 302 (45), 225 (39); HRMS (ESI-TOF, CH₃OH): Calcd for C₁₇H₁₇BrN₃S: [M + H]⁺ 460.9066; Found 460.9027.

Reaction of 3-bromo-5-substituted pyridinium aminides 3 with benzyl bromide. General procedure. The appropriate am inode 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 aminode 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 aminode 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) νmax (cm⁻¹): 3059, 1615, 1474, 1425, 1341, 1276, 1172, 780, 755, 696; ¹H NMR (300 MHz, CD₃OD): δ 9.31 (2H, dd, J 6.7 and 1.4 Hz, H2(6)), 9.08 (1H, s, H6′), 8.70 (1H, tt, J 7.8 and 1.4 Hz, H4), 8.17 (2H, dd, J 7.8 and 6.7 Hz, H3(5)), 8.14 (2H, dd, J 7.6 and 2.1 Hz, H2′′(6″)), 7.55 (5H, m, H3′′(5′′), H4′′ and H3′′′(5′′′)), 7.37 (3H, m, H2′′′(6″′) and H4″′), 5.32 (2H, s, CH₂); ¹³C NMR (75 MHz, CD₃OD): δ 151.9 (C2′), 149.2 (C5′), 147.6 (C4), 147.0 (C2(6)), 137.7 (C6′), 134.3 and 133.8 (C1′′ and C3′), 132.8 (C1″), 130.6 (C4″ or C4′′), 129.4, 129.0, 129.0, 128.8 and
127.7 (C3(5), C3′(5″), C2″(6″), C3″(5″) and C4″ or C4″), 126.9 (C2″(6″)), 60.1 (CH2). 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, CH3OH): Calcd for C22H1879BrN4: [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 °C; IR (KBr) vmax (cm⁻¹): 3411, 3107, 3029, 2963, 2926, 1613, 1497, 1473, 1430, 1408, 1337, 1264, 1172, 1093, 1077, 1018, 823, 800, 674, 620; 1H NMR (300 MHz, CD2OD): δ 9.29 (2H, dd, J 6.9 and 1.3 Hz, H2(6)), 9.05 (1H, s, H6′), 8.69 (1H, tt, J 7.9 and 1.3 Hz, H4), 8.15 (2H, dd, J 7.9 and 6.9 Hz, H3(5)), 8.04 (2H, d, J 8.2 Hz, H2″(6″)), 7.51 (2H, m, H3″(5″)), 7.40 (2H, d, J 8.2 Hz, H3″(5″)), 7.37 (3H, m, H2″″(6″″) and H4″″), 5.29 (2H, s, CH2), 2.19 (3H, s, CH3); 13C NMR (75 MHz, CD2OD): δ 153.6 (C2′), 150.2 (C5′), 148.9 (C4′), 148.3 (C2(6)), 142.8 (C4′′), 138.8 (C6′), 135.8 (C1″′), 134.2 (C3′), 132.4 (C1″), 131.0, 130.7, 130.3, 130.2 and 130.0 (C3(5), C3″(5″), C2″″(6″″) and C4″″), 128.2 (C2″(6″)), 61.5 (CH2), 21.4 (CH3). 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, CH3OH): Calcd for C23H2679BrN4: [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 °C; IR (KBr) vmax (cm⁻¹): 3445, 3106, 2989, 2940, 1614, 1604, 1519, 1470, 1434, 1343, 1257, 1180, 1014, 856, 715, 676; 1H NMR (300 MHz, CD2OD): δ 9.29 (2H, dd, J 6.9 and 1.3 Hz, H2(6)), 9.02 (1H, s, H6′), 8.68 (1H, tt, J 7.9 and 1.3 Hz, H4), 8.15 (2H, dd, J 7.9 and 6.9 Hz, H3(5)), 8.11 (2H, d, J 9.1 Hz, H2″(6″)), 7.51 (2H, m, H3″(5″)), 7.51 (2H, m, H3″(5″)), 7.37 (3H, m, H2″″(6″″) and H4″″), 7.12 (2H, d, J 9.1 Hz, H3″(5″)), 5.27 (2H, s, CH2), 3.91 (3H, s, CH3); 13C NMR (75 MHz, CD2OD): δ 163.6 (C4″), 153.4 (C2′), 149.6 (C5′), 148.8 (C4′), 148.2 (C2(6)), 138.4 (C6′), 135.9 (C1″′), 134.2 (C3′), 130.7, 130.2, 130.1, 130.0 and 129.9 (C3(5), C2″″(6″″), C3″″(5″″) and C4″″), 127.4 (C1″), 115.7 (C3″(5″)), 61.5 (CH2), 56.0 (CH3). MS (EI, m/z): 449/447 (< 2, M – Br), 369 (9), 368 (5), 367 (8), 281 (16), 277 (15), 277 (20), 276 (100), 266 (16), 264 (16), 262 (13), 261 (70), 233 (32), 91 (28), 78 (12); HRMS (ESI-TOF, CH3OH): Calcd for C23H2479BrN4O: [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 °C; IR (KBr) vmax (cm⁻¹): 3422, 3110, 3064, 3043, 3020, 2963, 1615, 1514, 1470, 1434, 1408, 1310, 1167, 1150, 1073, 1060, 1027, 1008, 968, 919, 768, 730, 668; 1H NMR (300 MHz, CD32CO): δ 9.64 (2H, dd, J 6.6 and 1.6 Hz, H2(6)), 9.23 (1H, s, H6′), 8.86 (1H, tt, J 7.9 and 1.6 Hz, H4), 8.70 (1H, dd, J 6.4 and 1.6 Hz, H4″), 8.69 (1H, s, H2″), 8.35 (2H, dd, J 7.9 and 6.6 Hz, H3(5)), 8.09 (1H, dd, J 6.4 and 1.6 Hz, H7″), 7.65 (2H, m, H3″(5″)), 7.52 (2H, m, H5″ and H6″), 7.35 (3H, m, H2″″(6″″) and H4″″), 5.52 (2H, s, CH2); 13C NMR (75 MHz, CD32CO): δ 152.0 (C2′), 150.0 (C5′), 148.9 (C4′), 148.2 (C2(6)), 142.5 (C7a′), 140.6 (C6′), 137.2 (C3a′), 134.9 and 134.2 (C1″′ and C3′), 131.8 (C4″′), 131.0 (C3″′), 130.6, 130.0 and 129.8...
(C3(5), C2′′(6′′) and C3′′(5′′)), 126.2, 126.1, 125.0, 123.8 and 122.9 (C6′′, C4′′, C5′′, C7′′ and C2′′), 60.7 (CH3). 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, CH3OH): Calcd for C19H15BrN3S: [M – Br – C3H5N]+ 394.0008; Found 394.0041.

**N-Benzyl-N-(3-bromo-5-arylpurazin-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 CH3CN (9 mL) and the mixture was cooled in an ice bath. Formic acid (98%, 2.6 mL) in CH3CN (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, 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 MgSO4, 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-phenylpurazin-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 °C; IR (KBr) νmax (cm−1): 3463, 3432, 3025, 2928, 1636, 1582, 1531, 1453, 1349, 1170, 1106, 1033, 1020, 773, 739, 697; 1H NMR (300 MHz, CDCl3): δ 8.42 (1H, s, H6), 7.82 (2H, br. d, J 8.4 Hz, H2′(6′)), 7.37 (8H, m, H3′(5′), H4′, H2′′(6′′), H3′′(5′′) and H4′′), 5.60 (1H, br. t, J 5.6 Hz, NH), 4.69 (2H, d, J 5.6 Hz, CH2); 13C NMR (75 MHz, CDCl3): δ 150.4 (C2), 141.4 (C5), 138.3 (C1′), 137.4 (C6), 135.7 (C1′), 128.8 and 128.7 (C3′(5′) and C3′′(5′′)), 128.2 (C4′), 127.6 and 127.5 (C2′′(6′′) and C4′′), 127.1 (C3), 125.5 (C2′(6′)) 45.7 (CH2). MS (EI, m/z): 341/339 (70/70, M+), 338 (20), 260 (33), 258 (25), 116 (19), 106 (100), 91 (91), 65 (25); HRMS (ESI-TOF, CH3OH): Calcd for C17H15BrN3: [M + H]+ 340.0444; Found 340.0428.

**N-Benzyl-N-(5-phenylpurazin-2-yl)amine (11a).** Orange solid (36 mg, 23%), mp 77–79 °C; IR (KBr) νmax (cm−1): 3469, 3225, 3031, 2869, 1636, 1582, 1453, 1349, 1170, 1106, 1033, 1020, 773, 739, 697; 1H NMR (300 MHz, CDCl3): δ 8.42 (1H, d, J 1.8 Hz, H6), 7.96 (1H, d, J 1.8 Hz, H3), 7.84 (2H, dd, J 8.3 and 1.3 Hz, H2′(6′)), 7.35 (8H, m, H3′(5′), H4′, H2′′(6′′), H3′′(5′′) and H4′′), 5.10 (1H, br. t, J 5.8 Hz, NH), 4.59 (2H, d, J 5.8 Hz, CH2); 13C NMR (75 MHz, CDCl3): δ 153.1 (C2), 141.7 (C5), 139.0 (C6), 138.4 and 137.1 (C1′ and C1′), 130.9 (C3), 128.7 (two overlapped signals C3′(5′) and C3′(5′)), 127.9 (C4′), 127.5 (two overlapped signals C2′(6′) and C4′), 125.4 C2′(6′), 45.7 (CH2). MS (EI, m/z): 261 (100, M+), 260 (36), 184 (15), 157 (17), 116 (14), 106 (90), 91 (64), 65 (18); HRMS (ESI-TOF, CH3OH): Calcd for C17H16N3: [M + H]+ 262.1339; Found 262.1341.

**N-Benzyl-N-(3-bromopyrazin-2-yl)amine (12).** Orange solid (9 mg, 6%), mp 84–86 °C; IR (KBr) νmax (cm−1): 3414, 3237, 1573, 1356, 1091, 1009, 748, 699; 1H NMR (300 MHz, CDCl3): δ 8.07 (1H, d, J 1.7 Hz, H6), 7.65 (1H, d, J 1.7 Hz, H5), 7.32 (5H, m, H2′(6′), H3′(5′) and H4′), 4.99 (1H, m, NH), 4.51 (2H, d, J 5.6 Hz, CH2); 13C NMR (75 MHz, CDCl3): δ 153.3 (C2), 144.1 (C6), 137.9 (C1′), 131.0 (C5), 128.8 (C3′(5′)), 127.7 (C4′), 127.5 C2′(6′), 125.9 (C3), 45.8 (CH2).
N-Benzyl-N-[3-bromo-5-(4-methylenephenoxy)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) \( \nu_{\text{max}} \) (cm\(^{-1}\)): 3473, 3319, 3030, 2963, 2922, 1607, 1581, 1503, 1462, 1261, 1091, 1032, 819, 800; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \( \delta \) 8.35 (1H, d, \( J = 1.3 \text{ Hz}, H_6 \)), 8.11 (1H, d, \( J = 1.3 \text{ Hz}, H_3 \)), 7.71 (2H, d, \( J = 8.2 \text{ Hz}, H_2'(6') \)), 7.33 (5H, m, \( H_2''(6'') \)), 6.09 (1H, m, \( H_7 \)), 4.62 (2H, br. s, \( H_2 \)), 2.37 (3H, s, \( CH_3 \)); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \( \delta \) 151.1 (C2), 141.5 (C5), 138.5 (C6), 137.4, 134.7 and 133.0 (C1\(^\prime\), C1\(^\prime\) and C4\(^\prime\)), 131.9 (C3), 129.7 and 128.9 (C3\(^\prime\) and C3\(^\prime\)\(^\prime\)), 127.8 (C4\(^\prime\)), 127.4 (C2\(^\prime\)'(6'')), 125.4 (C2\(^\prime\)'(6)), 46.0 (CH\(_2\)), 21.3 (CH\(_3\)). MS (EI, \( m/z \)): 275 (82, M\(^+\)), 274 (77), 263 (15), 185 (100), 184 (23), 158 (36), 157 (28), 130 (34), 119 (19), 106 (83); HRMS (ESI-TOF, CH\(_3\)OH): Calcd for C\(_{18}\)H\(_{17}\)BrN\(_3\): [M + H\(^+\)] 354.0600; Found 354.0601.

N-Benzyl-N-[5-(4-methoxyphenyloxy)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 °C; IR (NaCl) \( \nu_{\text{max}} \) (cm\(^{-1}\)): 3412, 2840, 1607, 1576, 1559, 1540, 1507, 1248, 1171, 1117, 1026, 829, 797, 709, 693; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \( \delta \) 8.35 (1H, d, \( J = 8.7 \text{ Hz}, H_6 \)), 7.77 (2H, d, \( J = 8.7 \text{ Hz}, H_2'(6') \)), 7.34 (5H, m, \( H_2''(6'') \)), 6.95 (2H, d, \( J = 8.7 \text{ Hz}, H_3'(5') \)), 5.53 (1H, m, \( H_7 \)), 4.68 (2H, d, \( J = 5.6 \text{ Hz}, CH_2 \)), 3.83 (3H, s, \( CH_3 \)); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \( \delta \) 159.9 (C4\(^\prime\)), 149.8 (C2), 141.5 (C5), 138.3 (C1\(^\prime\)), 136.5 (C6), 128.8 (C3\(^\prime\)), 128.4 (C1\(^\prime\)), 127.6 (C2\(^\prime\)'(6'')), 127.6 (C4\(^\prime\)), 127.0 (C3), 126.8 (C2\(^\prime\)'(6)), 114.2 (C3\(^\prime\)), 55.3 (CH\(_3\)), 45.7 (CH\(_2\)). MS (EI, \( m/z \)): 371/369 (52/53, M\(^+\)), 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\(_3\)OH): Calcd for C\(_{18}\)H\(_{16}\)BrN\(_3\): [M + H\(^+\)] 370.0545; Found 370.0544.

N-Benzyl-N-[3-bromo-5-(1-benzo[b]thiophen-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 °C; IR (NaCl) \( \nu_{\text{max}} \) (cm\(^{-1}\)): 3419, 3029, 2924, 2853, 1577, 1531, 1497, 1095, 1061, 1044, 963, 759, 773; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \( \delta \) 8.40 (1H, s, \( H_6 \)), 8.35 (1H, dd, \( J = 7.4 \text{ and } 1.5 \text{ Hz}, H_4' \)), 7.88 (1H, dd, \( J = 7.4 \text{ and } 1.5 \text{ Hz}, H_7' \)), 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, \( J = 5.4 \text{ Hz}, NH_2 \)), 4.72 (2H, d, \( J = 5.4 \text{ Hz}, H_2''(6'') \)).
Hz, CH$_2$); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 150.2 (C2), 140.7 (C5), 139.1 (C6), 138.4 and 138.2 (C3' and C1''), 136.8 (C7a'), 132.3 (C3a'), 128.7 (C3''(5'')), 127.6 (two overlapped signals C2''(6'') and C4''), 126.5 (C3), 124.7, 124.6 and 124.5 (C6', C5' and C4'), 123.6 and 122.7 (C7' and C2'), 45.6 (CH2). MS (EI, m/z): 397/395 (55/58, M$^+$), 316 (18), 173 (17), 106 (100), 91 (56); HRMS (ESI-TOF, CH$_3$OH): Calcd for C$_{10}$H$_{15}$BrN$_3$S: [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) $\nu_{\text{max}}$ (cm$^{-1}$): 3415, 2923, 1589, 1538, 1495, 1022, 760, 733; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.42 (1H, d, J 1.7 Hz, H6), 8.32 (1H, dd, J 6.6 and 1.4 Hz, H4$'$), 8.02 (1H, d, J 1.7 Hz, H3), 7.88 (1H, dd, J 6.6 and 1.4 Hz, H7$'$), 7.63 (1H, s, H2$'$), 7.37 (7H, m, H5', H6', H2''(6''), H3''(5''), and H4''), 5.08 (1H, br. t, J 5.6 Hz, NH), 4.61 (2H, d, J 5.6 Hz, CH$_2$); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 152.9 (C2), 140.7 (two overlapped signals C6 and C5), 139.3, 138.4 and 137.2 (C3', C7a' and C1''), 133.9 (C3a'), 130.8 (C3), 128.8 (C3''(5'')), 127.6 (two overlapped signals C2''(6'') and C4''), 124.5 (two overlapped signals C5' and C6'), 123.8 and 123.7 (C2' and C4'), 122.7 (C7'), 45.7 (CH2). MS (EI, m/z): 317 (100, M$^+$), 307 (27), 305 (26), 214 (22), 199 (25), 172 (42), 106 (82), 91 (23); HRMS (ESI-TOF, CH$_3$OH): Calcd for C$_{19}$H$_{16}$N$_3$S: [M + H]$^+$ 318.1059; Found 318.1075.

N-Benzyl-N-(5-arylmethoxyphenyl)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 °C 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)ethyl]pyrazin-2-yl amine (5a). Yellow solid (51 mg, 66%) mp 116–118 °C; IR (KBr) $\nu_{\text{max}}$ (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$_3$): $\delta$ 8.44 (1H, s, H6), 7.88 (2H, br. d, J 8.5 Hz, H2'(6'))), 7.49 (2H, d, J 8.8 Hz, H2''(6'')), 7.37 (8H, m, H3'(5''), H4', H2''(6''), H3''(5'') and H4''), 6.87 (2H, d, J 8.8 Hz, H3''(5'')), 5.76 (1H, br. t, J 5.6 Hz, NH), 4.76 (2H, d, J 5.6 Hz, CH$_2$), 3.82 (3H, s, CH$_3$); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 160.5 (C4''), 153.2 (C2), 141.4 (C5), 138.8 (C1''), 138.0 (C6), 136.9 (C1'), 133.6 (C2''(6'')), 128.7 (two overlapped signals C3'(5') and C3''(5'')), 128.0 (C4'), 127.4 and 127.3 (C2''(6'') and C4''), 125.7 (C2'(6')), 125.1 (C3), 114.2 (C3''(5''))), 113.5 (C1'), 96.8 (C$_{10}$=), 83.2 (C$_{10}$=), 55.3 (CH3), 45.2 (CH2). MS (EI, m/z): 391 (54, M$^+$), 390 (21), 315 (26), 314 (100), 299 (10), 284 (22), 271 (14), 116 (21), 91 (28); HRMS (ESI-TOF, CH$_3$OH): Calcd for C$_{26}$H$_{22}$N$_3$O: [M + H]$^+$ 392.1757; Found 392.1772.

N-Benzyl-N-[3-(4-dimethylaminophenyl)ethyl]pyrazin-2-yl amine (5b). Orange oil (59 mg, 73%); IR (NaCl) $\nu_{\text{max}}$ (cm$^{-1}$): 3418, 3031, 2923, 2852, 2188, 1606, 1525, 1361, 1177, 1129, 1028, 818, 763, 734, 696; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.40 (1H, s, H6), 7.89 (2H, dd, J 8.5 and 1.4 Hz, H2'(6'))), 7.38 (10H, m, H3'(5'), H4', H2''(6'), H3''(5'), H4' and H2''(6'')), 6.62 (2H, d, J 9.1 Hz, H3''(5'')), 5.78 (1H, br. t, J 5.7 Hz, NH), 4.75 (2H, d, J 5.7 Hz, CH$_2$), 2.99 (3H, s, CH$_3$); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 153.2 (C2), 150.7 (C4''), 141.2 (C5), 139.0 (C1''),
137.6 (C6), 137.1 (C1′), 133.2 (C2″("6″)), 128.7 (two overlapped signals C3′(5′) and C3″(5″)), 127.8 (C4′), 127.4 and 127.3 (C2″("6″) and C4″), 127.0 (C3), 125.7 (C2′(6′)), 111.6 (C3″(5″)), 110.6 (C1″), 98.6 (C5≡), 82.8 (Cα≡), 45.1 (CH2), 40.1 (CH3). MS (EI, m/z): 404 (100, M⁺), 327 (13), 314 (27), 313 (66), 298 (10), 297 (25); HRMS (ESI-TOF, CH3OH): Calcd for C27H25N4: [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) νmax (cm⁻¹): 3426, 3030, 2922, 1615, 1568, 1532, 1501, 1323, 1170, 1127, 1066, 1017, 910, 841, 822, 734, 699; ¹H NMR (300 MHz, CDCl3): δ 8.54 (1H, s, H6), 7.84 (2H, d, J 8.2 Hz, H2′(6′)), 7.69 (4H, m, H2″("6″) and H3″("5″)), 7.42 (5H, m, H2"("6″), H3"("5″) and H4″), 7.30 (2H, br, d, J 7.9 Hz, H3′(5′)), 5.71 (1H, br, t, J 5.6 Hz, NH), 4.82 (2H, d, J 5.6 Hz, CH2), 2.44 (3H, s, CH3); ¹³C NMR (75 MHz, CDCl3): δ 153.3 (C2), 141.9 (C5), 138.8 (C6), 138.7 and 138.2 (C1′ and C4′), 133.8 (C1′), 132.2 (C2″("6″)), 131.3 (C1″), 130.3 (C), 23.94 (Cβ≡), 86.5 (Cα≡), 45.2 (CH2), 21.3 (CH3). MS (EI, m/z): 443 (64, M⁺), 442 (26), 367 (17), 366 (69), 299 (27), 298 (100), 147 (37), 130 (39), 115 (26), 103 (21), 91 (42); HRMS (ESI-TOF, CH3OH): Calcd for C27H21F3N3: [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) νmax (cm⁻¹): 3402, 2917, 2849, 2200, 1609, 1569, 1559, 1506, 1498, 1248, 1173, 1030, 833, 816, 731, 698; ¹H NMR (300 MHz, CDCl3): δ 8.39 (1H, s, H6), 7.82 (2H, d, J 8.7 Hz, H2′(6′)), 7.44 (2H, d, J 8.2 Hz, H2″("6″)), 7.24 (5H, m, H2"("6″), H3″("5″) and H4″), 7.16 (2H, d, J 8.2 Hz, H3″("5″)), 6.96 (2H, d, J 8.7 Hz, H3′(5′)), 5.70 (1H, m, NH), 4.75 (2H, d, J 5.9 Hz, CH2), 3.83 (3H, s, OCH3), 2.36 (3H, s, CH3); ¹³C NMR (75 MHz, CDCl3): δ 159.7 (C4′), 153.0 (C2), 141.5 (C5), 139.8 (C4″), 138.9 (C1′), 137.7 (C6), 131.9 (C2″("6″)), 129.6 (C1′), 129.3 (C3″("5″)), 128.7 (C3″("5″)), 127.4 (two overlapped signals C4″ and C2″("6″)), 127.0 (C2′(6′)), 124.6 (C3), 118.5 (C1″), 114.1 (C3′(5′)), 96.7 (C5≡), 83.8 (Cα≡), 55.3 (OCH3), 45.2 (CH2), 21.6 (CH3). MS (EI, m/z): 405 (50, M⁺), 404 (16), 329 (24), 328 (100), 314 (44), 285 (18), 163 (23), 147 (15), 146 (46); HRMS (ESI-TOF, CH3OH): Calcd for C27H21F3N3O: [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) νmax (cm⁻¹): 3419, 2922, 2854, 2185, 1653, 1607, 1559, 1540, 1522, 1506, 1360, 1249, 1170, 1129, 1030, 946, 816, 729, 699; ¹H NMR (300 MHz, CDCl3): δ 8.34 (1H, s, H6), 7.83 (2H, d, J 8.8 Hz, H2′(6′)), 7.36 (7H, m, H2″("6″), H2″("6″), H3″("5″) and H4″), 6.95 (2H, d, J 8.8 Hz, H3′(5′)), 6.62 (2H, d, J 9.0 Hz, H3″("5″)), 5.73 (1H, br t, J 5.6 Hz, NH), 4.74 (2H, d, J 5.6 Hz, CH2), 3.82 (3H, s, OCH3), 2.98 (6H, s, NCH2); ¹³C NMR (75 MHz, CDCl3): δ 159.3 (C4′), 152.6 (C2), 150.4 (C4″), 141.0 (C5), 138.9 (C1″), 136.8 (C6), 133.0 (C2″("6″)), 130.3 (C1′), 128.5 (C3″("5″)), 127.2, 127.1 and 126.8 (C2′(6′), C4″ and C2′(6′)), 125.4 (C3), 113.9 (C3′(5′)), 111.5 (C3″("5″)), 110.4 (C1″), 98.4 (C5≡), 82.8 (Cα≡), 55.4 (OCH3), 45.2 (CH2), 40.2 (NCH3). MS (EI, m/z): 434 (83, M⁺), 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, CH₃OH): Calcd for C₂₈H₂₆N₄O: [M + H]+ 435.2179; Found 435.2174.

N-Benzyl-N-[5-(1-benzo thiophen-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, CDCl₃): δ 8.39 (1H, s, H6), 8.32 (1H, dd, J 7.9 and 0.9 Hz, H4′), 7.88 (1H, dd, J 7.9 and 0.9 Hz, H7′), 7.67 (1H, s, H2′), 7.43 (7H, m, H2″(6″), H3″(5″), H4″ and H2‴(6‴)), 6.89 (4H, m, H5′, H6′ and H3‴(5‴)), 5.77 (1H, br. t, J 5.6 Hz, NH), 4.77 (2H, d, J 5.6 Hz, CH2), 3.82 (3H, s, CH3); ¹³C NMR (75 MHz, CDCl₃): δ 160.1 (C4″), 152.7 (C2), 140.3 (C5), 139.5 (C6), 138.4, 138.3 and 136.9 (C1″, C3″ and C7a′), 133.2 (C2‴(6‴)), 132.5 (C3a′), 128.3 (C3‴(5‴)), 127.5 (C4″), 127.0 (C2‴(6‴)), 126.8 (C3), 124.1. 124.0 and 123.9 (C2′, C5′ and C6′), 123.3 (C4″), 122.3 (C7′), 113.8 (C3‴(5‴)), 113.4 (C1′), 96.4 (Cβ≡), 82.7 (Cα≡), 54.9 (CH3), 44.7 (CH2). MS (EI, m/z): 447 (78, M+), 446 (20), 371 (29), 370 (100), 340 (19), 173 (39); HRMS (ESI-TOF, CH₃OH): Calcd for C₂₈H₂₆N₃O: [M + H]+ 442.1478; Found 442.1474.

Pyrrolo[2,3-b]pyridines (6) and pyrrolo[2,3-b]pyrazines (7). General procedure. AuCl₃ (3 mol%, 1·10⁻³ 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-1H-pyrrolo[2,3-b]pyridine (6a). Yellow solid (11.5 mg, 44%) mp 125–127 °C; IR (NaCl) ν max (cm⁻¹): 3029, 2923, 2852, 1601, 1495, 1472, 1447, 1410, 1361, 895, 823, 769, 698; ¹H NMR (500 MHz, CDCl₃): δ 8.55 (1H, d, J 2.1 Hz, H6), 8.09 (1H, d, J 2.1 Hz, H4), 7.63 (2H, dd, J 8.2 and 1.2 Hz, H2′(6′)), 7.46 (2H, dd, J 8.2 and 7.3 Hz, H3′(5′)), 7.35 (1H, t, J 7.3 and 1.2 Hz, H4′), 7.29 (2H, d, J 8.2 Hz, H2‴(6‴)), 7.18 (5H, m, H3″(5″), H4″(6″)) and H5″), 6.99 (2H, m, H2″(6″)), 6.57 (1H, s, H3), 5.57 (2H, s, CH2), 2.38 (3H, s, CH3); ¹³C NMR (75 MHz, CDCl₃): δ 148.8 (C7a), 142.8 (C2), 124.2 (C6), 139.8 (C1″), 138.5 and 138.4 (C1′ and C4′), 130.2 (C5), 130.1 (C1″), 129.3 (C2″(6″)), 129.1, 129.0 and 128.9 (C3″(5″), C3″(C5′) and C3‴(C5′)), 127.4 (C2‴(5″)), 127.0, 126.9 and 126.5 (C4, C4′ and C4″), 126.5 (C2″(6″)), 120.6 (C3a), 100.1 (C3), 46.1 (CH2), 21.3 (CH3). MS (EI, m/z): 374 (100, M+), 373 (81), 297 (36), 283 (20), 91 (12); HRMS (ESI-TOF, CH₃OH): Calcd for C₂₈H₂₄N₂: [M + H]+ 375.1856; Found 375.1867.

1-Benzyl-2-(4-methoxyphenyl)-5-phenyl-1H-pyrrolo[2,3-b]pyridine (6b). Yellow solid (11.8 mg, 43%) mp 122–124 °C; IR (NaCl) ν max (cm⁻¹): 3042, 2926, 1607, 1495, 1473, 1409, 1361, 1292, 1250, 1177, 1030, 835, 769, 699; ¹H NMR (300 MHz, CDCl₃): δ 8.59 (1H, d, J 2.2 Hz, H6), 8.13 (1H, d, J 2.2 Hz, H4), 7.68 (2H, br. d, J 7.3 Hz, H2′(6′)), 7.51 (2H, br. t, J 7.8 Hz, H3′(5′)), 7.39 (1H, m, H4′), 7.36 (2H, d, J 8.8 Hz, H2″(6″′)), 7.25 (3H, m, H3″(5″) and H4″), 7.04 (2H, br. d, J 7.3 Hz, H2″(6″′)), 6.95 (2H, d, J 8.8 Hz, H3″(5″′)), 6.58 (1H, s, H3), 5.60 (2H, s, CH2), 3.87 (3H, s, CH3); ¹³C NMR (75 MHz, CDCl₃): δ 159.8 (C4″), 148.7 (C7a), 142.5 (C2), 142.1 (C6), 139.7 (C1″), 138.5 (C1′), 130.5 (C2″(6″′)), 130.1 (C5), 128.8 and 128.5 (C3″(5″) and 130.5 (C2″(6″′))
C3′(C5′)), 127.3 (C2′(6′)), 127.0, 126.8 and 126.3 (C4, C4′ and C4″), 126.4 (C2″(6″)), 124.6 (C1″′), 120.6 (C3a), 114.0 (C3″′(5″′)), 99.8 (C3), 55.3 (CH3), 46.0 (CH2). MS (EI, m/z): 390 (100, M′′′), 389 (61), 314 (11), 313 (35), 299 (10), 283 (11), 256 (10), 255 (11), 91 (12); HRMS (ESI-TOF, CH3OH): Calcd for C27H23N2O: [M + H]+ 391.1805; Found 391.1826.

1-Benzyl-5-(4-methoxyphenyl)-2-thiophen-3-yl-1H-pyrrolo[2,3-b]pyridine (6c). Yellow solid (18 mg, 65%) mp 132–134 °C; IR (KBr) νmax (cm⁻¹): 3102, 3059, 3032, 2963, 1607, 1522, 1474, 1407, 1361, 1293, 1182, 1028, 833, 757, 695; 1H NMR (300 MHz, CDCl3): δ 8.56 (1H, d, J 2.3 Hz, H6), 8.09 (1H, d, J 2.3 Hz, H4), 7.60 (2H, d, J 8.6 Hz, H2′(6′)), 7.40 (1H, dd, J 5.0 and 3.0 Hz, H5′′′), 7.29 (4H, m, H3′′′(5′′′), H4′′′ and H2′′′), 7.24 (1H, dd, J 5.0 and 1.6 Hz, H4′′′), 7.09 (2H, m, H2″(6″)), 7.06 (2H, d, J 8.6 Hz, H3′(5′)), 6.69 (1H, s, H3), 5.70 (2H, s, CH2), 3.90 (3H, s, CH3); 13C NMR (75 MHz, CDCl3): δ 158.9 (C4′), 148.4 (C7a), 142.3 (C6), 138.4 (C2), 137.3 (C1′), 132.6 and 132.2 (C1′′ and C3″′), 130.5 (C5), 128.7 and 128.4 (C2′′(6′) and C2″′(6″′)), 128.2 and 127.1 (C4″), 126.1 and 126.0 (C2″(6″) and two overlapped carbons signals C5″′ and C2″′), 123.7 (C4″′), 120.3 (C3a), 114.4 (C3″(5′′′)), 100.0 (C3), 55.4 (CH3), 46.0 (CH2). MS (EI, m/z): 396 (100, M′′′), 395 (61), 320 (14), 319 (57), 313 (11), 305 (12), 262 (12), 261 (12), 91 (29); HRMS (ESI-TOF, CH3OH): Calcd for C25H21N2OS: [M + H]+ 397.1369; Found 397.1372.

1-Benzyl-5-(4-methoxyphenyl)-2-(4-trifluoromethylphenyl)-1H-pyrrolo[2,3-b]pyridine (6d). Yellow solid (14.8 mg, 46%) mp 126–128 °C; IR (KBr) νmax (cm⁻¹): 3045, 2922, 1616, 1521, 1474, 1412, 1365, 1328, 1248, 1166, 1121, 1072, 852, 833, 766, 702; 1H NMR (300 MHz, CDCl3): δ 8.56 (1H, d, J 2.4 Hz, H6), 8.07 (1H, d, J 2.4 Hz, H4), 7.62 (2H, d, J 8.2 Hz, H3″″(5″″)), 7.55 (2H, d, J 8.6 Hz, H2′(6′)), 7.51 (2H, d, J 8.2 Hz, H2"″(6″″)), 7.20 (3H, m, H3″(5″′) and H4″′), 7.01 (2H, d, J 8.6 Hz, H3(5′)), 6.97 (2H, br. dd, J 7.3 and 2.0 Hz, H2″(6″′)), 6.64 (1H, s, H3), 5.58 (2H, s, CH2), 3.86 (3H, s, CH3); 13C NMR (75 MHz, CDCl3): δ 159.0 (C4′), 148.7 (C7a), 142.9 (C6), 140.8 (C2), 138.1 (C1′), 135.9 (C1″′), 132.0 (C1″′′), 130.3 (C5), 130.3 (c, 2JCF = 32.7 Hz, C4″′), 129.3, 128.6 and 128.4 (C2″″(6″′), C2′′(6′) and C3″″(C5″′)), 127.3 and 126.6 (C4 and C4″′), 126.6 (C2″(6″′)), 125.5 (c, 1JCF = 3.8 Hz, C3″″(C5″′)), 124.0 (c, 1JCF = 272 Hz, CF3), 120.3 (C3a), 114.4 (C3″(5′)), 101.5 (C3), 55.4 (CH3), 46.2 (CH2). MS (EI, m/z): 358 (100, M′′′), 382 (27), 313 (7), 91 (8); HRMS (ESI-TOF, CH3OH): Calcd for C28H22F3N2O: [M + H]+ 459.1679; Found 459.1661.

5-Benzyl-6-(4-methoxyphenyl)-2-phenyl-5H-pyrrolo[2,3-b]pyrazine (7a). Yellow oil (12 mg, 44%); IR (NaCl) νmax (cm⁻¹): 3062, 3030, 2960, 2925, 2854, 1610, 1495, 1464, 1444, 1418, 1360, 1257, 1210, 1176, 1101, 1028, 935, 864, 835, 800, 695; 1H NMR (300 MHz, CDCl3): δ 8.67 (1H, s, H3), 8.02 (2H, br. d, J 7.2 Hz, H2′(6′)), 7.50 (2H, br. t, J 7.7 Hz, H3′(5′)), 7.36 (3H, m, H4′ and H2′′′(6″′)), 7.20 (3H, m, H3′(5′) and H4′′′), 6.99 (2H, m, H2″(6″′)), 6.94 (2H, d, J 9.0 Hz, H3″′(5″′)), 6.79 (1H, s, H7), 5.54 (2H, s, CH2), 3.84 (3H, s, CH3); 13C NMR (50.29 MHz, CDCl3): δ 160.4 (C4′), 147.2 (C6), 142.1 (C2), 137.7, 137.6, 137.1 and 136.1 (C4a, C7a, C1′ and C1″′), 134.9 (C3), 130.6 (C2′′′(6″′)), 128.9 and 128.6 6 (C3′(C5′) and C3″(C5″′)), 127.4 (C4′), 127.1 (C2′′′(6″′)), 126.8 (C4″′), 126.4 (C2″′(6″′)), 123.6 (C1″′), 114.2 (C3″′(C5″′)), 100.8 (C7), 55.4
(CH₃), 46.2 (CH₂). MS (EI, m/z): 391 (100, M⁺), 390 (9), 314 (15), 300 (9), 257 (14), 91 (4); HRMS (ESI-TOF, CH₃OH): Calcd for C₂₆H₂₁N₅O: [M + H]⁺ 392.1757; Found 392.1757.

5-Benzyl-2-(4-methylphenyl)-6-(4-trifluoromethylphenyl)-5H-pyrrolo[2,3-b]pyrazine (7b). Yellow solid (15.2 mg, 49%) mp 170–172 °C; IR (KBr) νmax (cm⁻¹): 3090, 3066, 3032, 2922, 2852, 1618, 1497, 1465, 1452, 1411, 1326, 1207, 1166, 1123, 1068, 1017, 851, 819, 722, 695; ¹H NMR (300 MHz, CDCl₃): δ 8.77 (1H, s, H3), 7.98 (2H, d, J 7.9 Hz, H2′(6′)), 7.72 (2H, d, J 8.4 Hz, H3′′(5′′)), 7.60 (2H, d, J 8.4 Hz, H2′′(6′′)), 7.37 (2H, br. d, J 7.9 Hz, H3′(5′)), 7.27 (3H, m, H3′(5′) and H4′), 7.01 (2H, m, H2′′(6′′)), 6.93 (1H, s, H7), 5.60 (2H, s, CH₂), 2.47 (3H, s, CH₃); ¹³C NMR (125 MHz, CDCl₃): δ 146.1 (C2), 142.9 and 142.8 (C6 and C4a), 139.7 and 139.6 (C7a and C1′), 137.0 (C4′), 136.1 (C3), 134.6 (C1′), 130.8 (C1″), 129.9 and 129.6 (C3′(5′) and (C2′′(6′′)), 128.9 (C3′(5′′)), 127.8 (C4′), 127.3 (C2′(6′)), 126.4 (C2′′(6′′)), 125.8 (c, 3JCF = 3.7 Hz, C3′′(5′′)), 102.1 (C7), 46.5 (CH₂), 21.4 (CH₃), (CF₃ and C4′ were not clearly identified); ³⁹F NMR (282 MHz, CDCl₃): δ –62.7 (CF₃). MS (EI, m/z): 443 (100, M⁺), 442 (54), 366 (13), 352 (28), 298 (14), 91 (26); HRMS (ESI-TOF, CH₃OH): Calcd for C₂₇H₂₁F₃N₃: [M + H⁺] 444.1682; Found 444.1674.

5-Benzyl-2-(4-methoxyphenyl)-6-(4-methylphenyl)-5H-pyrrolo[2,3-b]pyrazine (7c). White solid (16.9 mg, 59%) mp 144–146 °C; IR (KBr) νmax (cm⁻¹): 3020, 1609, 1559, 1516, 1461, 1415, 1249, 1213, 1181, 1146, 1033, 839, 808, 728, 696; ¹H NMR (300 MHz, CDCl₃): δ 8.66 (1H, s, H3), 8.02 (2H, d, J 8.8 Hz, H2′(6′)), 7.37 (2H, d, J 8.2 Hz, H2′′(6′′)), 7.26 (5H, m, H2′′(6′′), H3′′(5′) and H4′), 7.05 (4H, m, H3′(5′) and H3′′(5′′)), 6.81 (1H, s, H7), 5.57 (2H, s, CH₂), 3.90 (3H, s, OCH₃), 2.43 (3H, s, CH₃); ¹³C NMR (75 MHz, CDCl₃): δ 159.8 (C4′), 147.2 and 146.6 (C6 and C2), 141.4, 139.0 (two overlapped signals) and 137.5 (C4a, C7a, C1″ and C4″), 134.4 (C3), 130.7 (C1′′), 129.2, 128.9, 128.4 and 128.1 (C2′(6′), C2′′(6′′), C3′(5′) and C3′′(5′′)), 128.4 (C4′), 126.3 C2′′(6′′), 114.2 (C3′(5′)), 101.1 (C7), 55.4 (OCH₃), 46.2 (CH₂), 21.5 (CH₃). MS (EI, m/z): 405 (100, M⁺), 328 (17), 315 (10), 314 (31), 299 (21), 298 (21), 271 (23), 146 (22), 91 (39); HRMS (ESI-TOF, CH₃OH): Calcd for C₂₇H₂₃F₃N₃: [M + H⁺] 406.1914; Found 406.1910.

2-(1-Benzothiophen-3-yl)-5-benzyl-6-(4-methoxyphenyl)-5H-pyrrolo[2,3-b]pyrazine (7d). Yellow solid (15 mg, 48%) mp 131–133 °C; IR (KBr) νmax (cm⁻¹): 2957, 2924, 2853, 1608, 1492, 1467, 1355, 1257, 1247, 1203, 1174, 1028, 841, 760, 729, 708, 695; ¹H NMR (500 MHz, CDCl₃): δ 8.63 (1H, s, H3), 8.48 (1H, d, J 8.0 Hz, H4′), 7.92 (1H, d, J 7.5 Hz, H7′), 7.80 (1H, s, H2′), 7.45 (1H, ap. td, J 7.1 and 1.1 Hz, H5′), 7.39 (3H, m, H6′ and H2′′(6′′)), 7.24 (3H, m, H3′(5′) and H4′), 7.03 (2H, br. d, J 6.4 Hz, H2′(6′)), 6.95 (2H, d, J 8.7 Hz, H3′′(5′′)), 6.80 (1H, s, H7), 5.31 (2H, s, CH₂), 3.84 (3H, s, CH₃); ¹³C NMR (125 MHz, CDCl₃): δ 160.4 (C4″), 147.0 (C6), 144.8 (C2), 141.5 (C4a), 140.8 (C7a), 139.4 (C7a), 137.7 and 137.6 (C1′″ and C3a′), 136.3 (C3), 135.1 (C3′), 130.6 (C2′′(6′′)), 128.7 (C3′(5′)), 127.4 (C4″), 126.5 (C2′(6′)), 125.6 (C2′), 124.7 and 124.6 (C5′ and C6′), 124.0 (C4″), 123.7 (C1′″), 123.7 (C7′), 114.2 (C3′′(5′′)), 101.1 (C7), 55.4 (CH₃), 46.1 (CH₂). MS (EI, m/z): 447 (100, M⁺), 356 (33), 313 (26), 172 (22); HRMS (ESI-TOF, CH₃OH): Calcd for C₂₈H₂₂N₃O: [M + H⁺] 448.1487; Found 448.1478.
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