

## Synthesis of a Novel Series of 4-Arylpiperazinyl Derivatives Linked to a 2-(Pyridin-3-yl)-1*H*-benzimidazole as New Delavirdine Analogues

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A síntese de uma série de arilpiperazinas ligadas à estrutura 2-(piridina-3-il)-1*H*-benzo[*d*]imidazol, através de um linker alquílico é relatada. Os novos derivados 1-(2-(4-arilpiperazina-1-il)alquil)-2-(piridina-3-il)-1*H*-benzimidazol são estruturalmente relacionados à droga anti-HIV-1 Delavirdina e pertencem à família bis(heteroaril)piperazinas (BHAPs), um conhecido grupo de inibidores da transcriptase reversa HIV-1.

The synthesis of a series of substituted arylpiperazines linked to a 2-(pyridin-3-yl)-1*H*-benzo[*d*]imidazole scaffold through an alkylic linker is reported. The novel 1-(2-(4-arylpiperazin-1-yl)alkyl)-2-(pyridin-3-yl)-1*H*-benzimidazole derivatives are structurally related to the anti-HIV-1 drug Delavirdine and belong to the bis(heteroaryl)piperazines family (BHAPs), a well known HIV-1 reverse transcriptase inhibitors group.

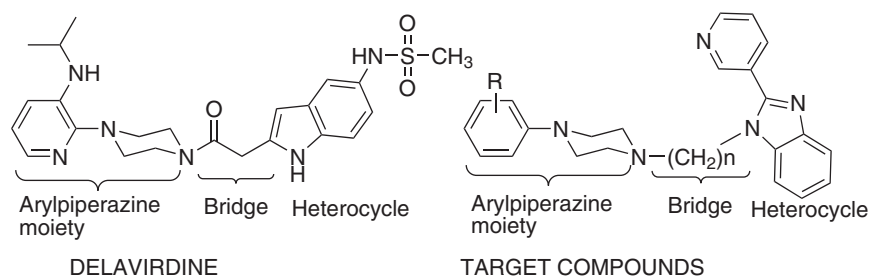
**Keywords:** arylpiperazinyl derivatives, benzo[*d*]imidazole, delavirdine analogues, alkylation

### Introduction

Non nucleoside HIV-1 reverse transcriptase inhibitors (NNRTIs) such as nevirapine, have been approved for the treatment of acquired immune deficiency syndrome (AIDS).<sup>1</sup> A major limitation of such treatment is the emergence of resistant virus with specific mutations in the reverse transcriptase (RT) gene. Therefore, the development of new active compounds has been the focus in many laboratories.<sup>2,3</sup>

The efforts along this line led to the discovery of the bis-(heteroaryl)piperazine (BHAP) class of HIV-1 reverse transcriptase inhibitors.<sup>4,5</sup> Delavirdine, a BHAP derivative and first-generation NNRTI is displayed in Figure 1.<sup>6</sup>

A variety of papers reporting the synthesis of Delavirdine analogues have been published up to the date.<sup>7,8</sup> However, structural modifications have been mainly focused on the 4-heteroaryl piperazine moiety, being the substitution of the indol ring by other heterocycles less explored.<sup>9</sup> To



**Figure 1.** Common structural pattern shared by Delavirdine and the target compounds.

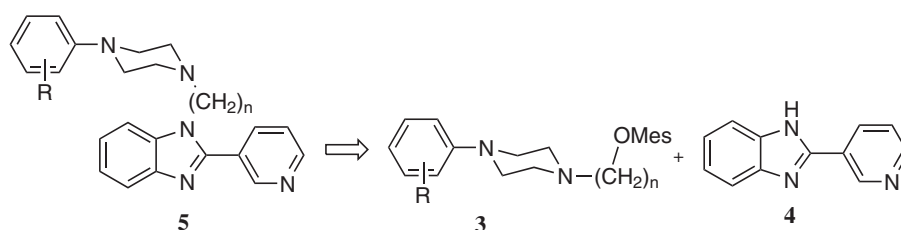
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the best of our knowledge, there is not any report about the synthesis of BHAPs containing benzimidazole as the heterocyclic framework. The main reason we adopted to use benzimidazole framework, is the well known bioisosteric equivalence of this ring, respect to 1(H)-Indole. Besides, preliminary docking studies carried out by our research group supported this bioisosteric change.

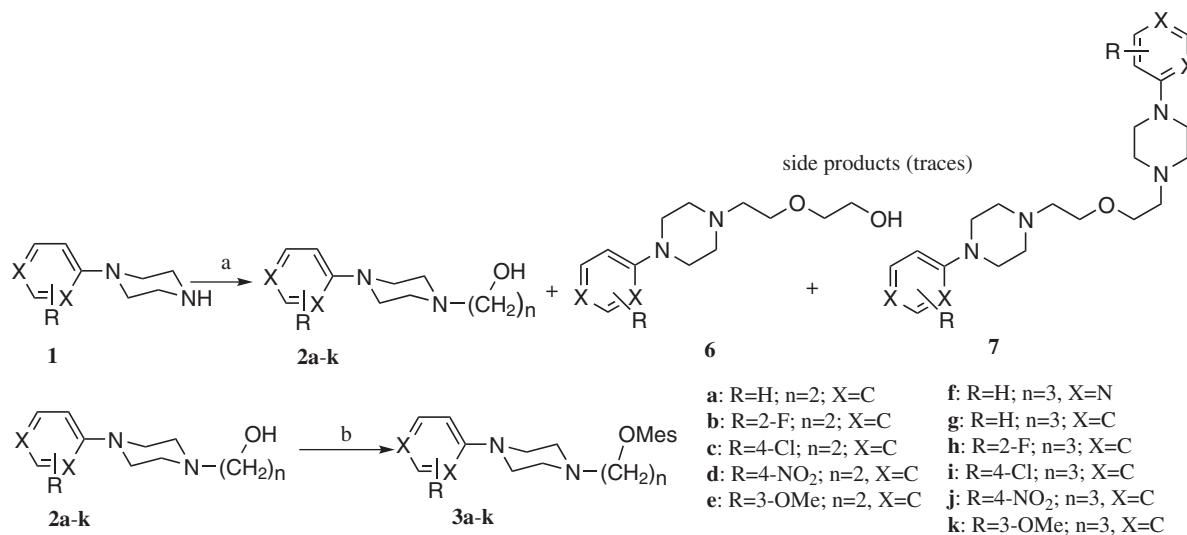
In this paper, we describe the synthesis of a new BHAP series combining two scaffolds, the 2-(pyridin-3-yl)-1*H*-benzo[*d*]imidazole and substituted 4-arylpiperazines linked by methylenic spacers. The structural similitude between Delavirdine and the target compounds is displayed in Figure 1.

## Results and Discussion

The Delavirdine analogues **5(a-k)** were prepared according to the retrosynthetic strategy displayed in scheme 1. We developed a general and useful synthesis of substituted 4-arylpiperazinyl ethyl (propyl) alcohol scaffolds **3(a-k)**, which were utilized for coupling reactions with 2-(pyridin-3-yl)-1*H*-benzo[*d*]imidazole **4** leading to the desired substituted target compounds.



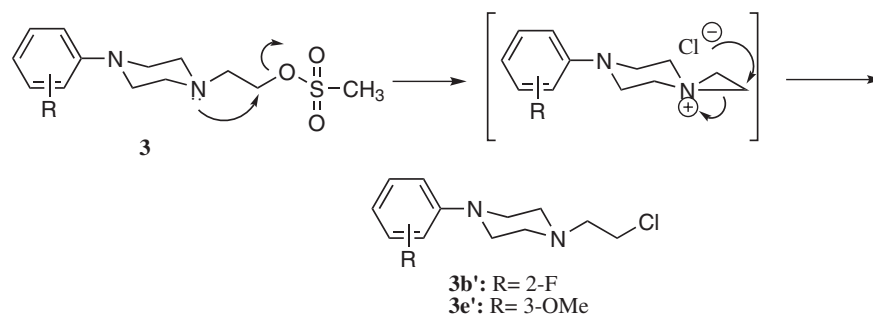
**Scheme 1.** Retrosynthetic strategy for the synthesis of **5(a-k)**.



**Scheme 2.** Synthesis of Phenylpiperazinyl alkyl methanesulphonates intermediates and side products detected as traces. Reagents and conditions. a. 1,2-Bromoethanol or 1,3-bromopropanol, acetone, triethylamine, continuous stirring, RT, 24 h; b. Methanesulfonyl chloride, dichloromethane, triethylamine, 0-5 °C, continuous stirring, RT, 4 h.

The intermediate arylpiperazinyl building blocks **3(a-k)** were synthesized as follows. Treatment of the appropriate substituted arylpiperazine **1** with 1-bromoethanol (1-bromopropanol) in acetone at room temperature, gave the corresponding alcohols **2(a-k)** in 40-54% yield along with the ethers **6** and **7** as minority side products (Scheme 2). The alcohols were easily purified by column chromatography, showing the characteristic hydroxyl spectral signals (IR:3590-3644 cm<sup>-1</sup>; <sup>1</sup>H-NMR, broad singlet δ<sub>OH</sub> 2.86-3.87). The <sup>1</sup>H-NMR spectra displayed also the piperazine and the methylene protons at high field (δ<sub>CH<sub>2</sub></sub> 1.70-3.87), supporting the presence of these functions.

Reaction of the alcohols **2a-k** with mesyl chloride and triethylamine in dichloromethane at 0 °C provided the respective mesylated alcohols **3a-k** in moderate to good yields (Scheme 2). The mesylation was mainly deduced by their IR spectra (absence of the hydroxyl signal and presence of the two characteristic SO<sub>2</sub> signals at 1348 and 1173 cm<sup>-1</sup>) and their <sup>1</sup>H-NMR spectra which displayed the singlet for the methyl group protons at δ: 2.78-3.08 ppm. Interestingly, the chloroethyl arylpiperazines **3b'** and **3e'** were obtained instead of the expected mesylated products.



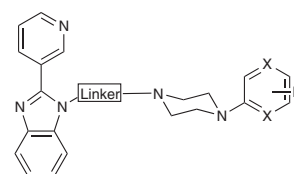
**Scheme 3.** A reasonable mechanistic proposal for the formation of chloroethyl arylpiperazines **3e** and **3b**.

A plausible mechanistic pathway (Scheme 3) probably involves the formation of an aziridinium intermediate generated by intramolecular attack of the basic piperazine nitrogen followed by an  $S_N2$  attack of the chloride anion.

Benzimidazole **4** was efficiently obtained by condensation of *o*-phenylenediamine **8** with 3-pyridine-carboxaldehyde in ethanol at room temperature. According to the literature,<sup>8</sup> the generation of benzimidazole **4** may be assumed to proceed through a three-step sequence: a) nucleophilic attack of the amino group onto the carbonylic carbon to give the imine intermediate **9**, b) intramolecular cyclization of **9** to the benzimidazolydine intermediate **10**, and c) aerobic oxidation to provide the benzimidazole ring **4** (Scheme 4).

Alkylation of the obtained benzimidazole moiety was readily accomplished using NaOH as the base in acetonitrile. As is shown in scheme 4, coupling of the benzimidazole anion with substituted alkyl arylpiperazines in the presence of triethylamine in acetonitrile at room temperature for 12 h, provided target compounds **5(a-k)** (Table 1) in low to moderate yields. <sup>1</sup>H-NMR analysis of **5a** displayed the four characteristic high field signals corresponding to the methylene protons of piperazine ring ( $\delta$ :3.10 and 2.50 ppm) and the linker chain ( $\delta$ :4.40 and

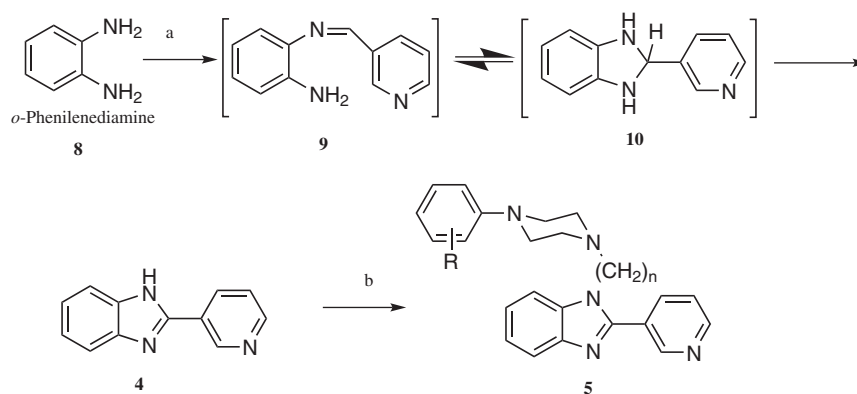
**Table 1.** Novel arylpiperazinil-benzimidazole derivatives obtained. Yields are expressed for pure products



Chemical Data for Compounds **5a-k**

Entry	Linker	R	X	Formula	Yield / %
5a	-(CH <sub>2</sub> ) <sub>2</sub> -	H	C	C <sub>24</sub> H <sub>25</sub> N <sub>5</sub>	45
5b	-(CH <sub>2</sub> ) <sub>2</sub> -	2-F	C	C <sub>24</sub> H <sub>24</sub> FN <sub>5</sub>	21
5c	-(CH <sub>2</sub> ) <sub>2</sub> -	4-Cl	C	C <sub>24</sub> H <sub>22</sub> ClN <sub>5</sub>	35
5d	-(CH <sub>2</sub> ) <sub>2</sub> -	4-NO <sub>2</sub>	C	C <sub>24</sub> H <sub>24</sub> N <sub>6</sub> O <sub>2</sub>	46
5e	-(CH <sub>2</sub> ) <sub>2</sub> -	3-OMe	C	C <sub>25</sub> H <sub>27</sub> N <sub>5</sub> O	20
5f	-(CH <sub>2</sub> ) <sub>2</sub> -	H	N	C <sub>22</sub> H <sub>23</sub> N <sub>7</sub>	38
5g	-(CH <sub>2</sub> ) <sub>3</sub> -	H	C	C <sub>25</sub> H <sub>27</sub> N <sub>5</sub>	48
5h	-(CH <sub>2</sub> ) <sub>3</sub> -	2-F	C	C <sub>25</sub> H <sub>26</sub> FN <sub>5</sub>	28
5i	-(CH <sub>2</sub> ) <sub>3</sub> -	4-Cl	C	C <sub>25</sub> H <sub>26</sub> ClN <sub>5</sub>	38
5j	-(CH <sub>2</sub> ) <sub>3</sub> -	4-NO <sub>2</sub>	C	C <sub>25</sub> H <sub>26</sub> N <sub>6</sub> O <sub>2</sub>	24
5k	-(CH <sub>2</sub> ) <sub>3</sub> -	3-OMe	C	C <sub>26</sub> H <sub>29</sub> N <sub>5</sub> O	33

2.84 ppm), along with four aromatic doublets at low field ( $\delta$ : 9.10, 8.78, 8.22 and 7.92 ppm) typical of the pyridine ring attached to the 1*H*-benzimidazole system.



**Scheme 4.** Coupling of the benzimidazole moiety with substituted alkyl arylpiperazines. Reagents and conditions: a) 3-pyridinecarboxaldehyde, ethanol, room temp., 48 h; b) 2-(4-phenylpiperazin-1-yl)alkyl methanesulfonates or 1-(2-chloroethyl)-4-phenylpiperazines, acetonitrile, continuous stirring, RT, 12 h.

In summary, a convenient method for the synthesis of 1-(2-(4-Arylpiperazin-1-yl)alkyl)-2-(pyridin-3-yl)-1*H*-benzimidazole derivatives has been provided. Further studies on the application will be reported in due course.

## Experimental

All organic solvents used for the synthesis were of analytical grade. IR spectra were recorded on a Bruker Vector 22 spectrophotometer using KBr discs. <sup>1</sup>H and <sup>13</sup>C NMR spectra were obtained on Bruker APC-200 spectrometer using tetramethylsilane as internal reference. Column chromatography was performed on Merck silica gel 60 (70-230 mesh). Thin layer chromatography separations were performed on Merck Kieselgel 60 (70-230 mesh). Elemental analyses were carried out on a FISON EA 1108 CHNS-O analyzer.

### Synthesis of arylpiperazinyl alcohols 2(a-k). General procedure

A mixture of the commercial 4-arylpiperazines (6 mmol) and bromoethanol (bromopropanol) (6 mmol) and triethylamine (6 mmol) was stirred for 24 h in acetone (30 mL) at room temperature. The precipitate was filtered off and the filtrate was extracted with ethyl acetate (3 × 50 mL), subsequently dried over anhydrous MgSO<sub>4</sub> and evaporated under vacuum conditions. Column chromatography of the residue over silica gel (eluent EtOAc) afforded the corresponding alcohols. Spectral data for 2-(4-Arylpiperazin-1-yl) alcohols derivatives **2a-2c**, **2e**, **2g-2i** and **2k** were consistent with the assigned structures.<sup>10</sup>

#### 2-[4-(4-Nitrophenyl)piperazin-1-yl]ethanol (2d)

Yellow oil (40%), IR  $\nu_{\max}$ /cm<sup>-1</sup>: 3590 (OH), 1529 (NO<sub>2</sub>), 1292 (NO<sub>2</sub>). <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$  7.99 (d, 2H, *J* 8.1 Hz, H-3,5), 6.78 (d, 2H, *J* 8.9 Hz, H-2,6), 3.63 (t, 2H, *J* 9.8 Hz, CH<sub>2</sub>-1), 3.57-2.89 (m, 5H, 2×CH<sub>2</sub> pip., OH), 2.59-2.55 (m, 6H, 2×CH<sub>2</sub> pip., CH<sub>2</sub>-2). <sup>13</sup>C-NMR (CDCl<sub>3</sub>)  $\delta$  154.7, 137.8, 2×25.8, 2×112.5, 59.6, 58.2, 2×52.5, 2×46.8. Anal. Calc. for C<sub>12</sub>H<sub>17</sub>N<sub>3</sub>O<sub>3</sub>: C, 57.36; H, 6.82; N, 16.72. Found: C, 57.70; H, 7.01; N, 16.66%.

#### 2-(4-(Pyrazin-2-yl)piperazin-1-yl)ethanol (2f)

Yellow oil (44%), IR  $\nu_{\max}$ /cm<sup>-1</sup>: 3644 (OH), 1348 (C-N); <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$  8.39 (s, 1H, H-2), 7.97 (m, 1H, H-6), 7.49 (d, 1H, *J* 6.24 Hz, H-5), 3.56-3.51 (m, 6H, 2×CH<sub>2</sub> pip., CH<sub>2</sub>-1), 2.86 (1H, b.s., OH), 2.60-2.55 (m, 6H, 2×CH<sub>2</sub> pip., CH<sub>2</sub>-2); <sup>13</sup>C-NMR (CDCl<sub>3</sub>)  $\delta$  157.7, 130.9, 110, 65.1,

62.7, 57.8, 2×52.8, 2×46.6. Anal. Calc. for C<sub>10</sub>H<sub>16</sub>N<sub>4</sub>O: C, 57.67; H, 7.74; N, 26.90. Found: C, 57.55; H, 7.75; N, 26.82%.

#### 3-[4-(4-Nitrophenyl)piperazin-1-yl]propan-1-ol (2j)

Yellow oil (54%), IR  $\nu_{\max}$ /cm<sup>-1</sup>: 3630 (OH), 1527 (NO<sub>2</sub>); <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$  8.11 (d, 2H, *J* 11 Hz, H-3,5), 6.80 (d, 2H, *J* 9.4 Hz, H-2,6), 3.87-3.84 (m, 3H, CH<sub>2</sub>-1, OH), 3.53-3.44 (m, 4H, 2×CH<sub>2</sub>-pip.), 2.60 (m, 6H, 2×CH<sub>2</sub>-pip., CH<sub>2</sub>-3), 1.70 (m, 2H, CH<sub>2</sub>-2); <sup>13</sup>C-NMR (CDCl<sub>3</sub>)  $\delta$  154.7, 138.5, 2×125.9, 2×112.7, 58.3, 2×52.7, 52.4, 2×46.9, 28.7. Anal. Calc. for C<sub>13</sub>H<sub>19</sub>N<sub>3</sub>O<sub>3</sub>: C, 58.85; H, 7.22; N, 15.84. Found: C, 58.52; H, 7.34; N, 16.01%.

### Synthesis of 2-(4-Arylpiperazinyl) alkyl methanesulphonate derivatives 3(a-k). General procedure

Alcohols **2a-k** (2.4 mmol) were added to a solution of methanesulfonyl chloride (2.5 mmol) in dichloromethane (15 mL) and triethylamine (2.5 mmol) at 0 °C. The mixture was maintained with stirring for 4 h and then concentrated in vacuo. Purification of the crude by column chromatography CH<sub>2</sub>Cl<sub>2</sub> / AcOEt (1:2) as the eluent, afforded the title compounds (**3a-k**) as yellow oils in moderated yields (35-50%).

#### 2-(4-Phenylpiperazin-1-yl)ethyl methanesulphonate (3a)

(48%), IR  $\nu_{\max}$ /cm<sup>-1</sup>: 1347(SO<sub>2</sub>), 1172 (SO<sub>2</sub>); <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$  7.30 (t, 2H, *J* 8.0 Hz, H-3, 5), 6.94 (m, 3H, H-2,4,6), 3.83 (t, 2H, *J* 7.0 Hz, CH<sub>2</sub>-1), 3.44-3.20 (m, 4H, 2×CH<sub>2</sub> pip.), 2.98 (s, 3H, CH<sub>3</sub>), 2.89 (t, 2H, *J* 7.2 Hz, CH<sub>2</sub>-2), 2.70 (t, 4H, *J* 5.1 Hz, 2×CH<sub>2</sub> pip.); <sup>13</sup>C-NMR (CDCl<sub>3</sub>)  $\delta$  151.2, 2×129.3, 119.9, 2×116.1, 65.3, 59.8, 2×53.2, 2×49.4, 37.1. Anal. Calc. for C<sub>13</sub>H<sub>20</sub>N<sub>2</sub>O<sub>3</sub>S: C, 54.91; H, 7.09; N, 9.85. Found: C, 55.02; H, 7.11; N, 10.02%.

#### 1-(2-Chloroethyl)-4-(2-fluorophenyl)piperazine (3b')

(35%), IR  $\nu_{\max}$ /cm<sup>-1</sup>: 1007 (C-F), 728 (C-Cl); <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$  7.18-6.85 (m, 3H, H-3,4,5), 6.68-6.57 (m, 1H, H-6), 3.73 (t, 2H, *J* 13.5 Hz, CH<sub>2</sub>-1), 3.25 (t, 4H, *J* 9.5 Hz, 2×CH<sub>2</sub> pip.), 2.89 (m, 6H, 2×CH<sub>2</sub> pip., CH<sub>2</sub>-2); <sup>13</sup>C-NMR (CDCl<sub>3</sub>)  $\delta$  158.16 (d, 2C, *J*<sub>C-F</sub> 337 Hz), 151.78, 124.6, 123.1, 122.9, 119.1, 116.4, 115.9, 59.5, 2×53.2, 2×49.7, 39.9. Anal. Calc. for C<sub>12</sub>H<sub>16</sub>ClFN<sub>2</sub>: C, 59.38; H, 6.64; N, 11.54. Found: C, 59.49; H, 6.67; N, 11.38%.

#### 2-[4-(4-Chlorophenyl)piperazin-1-yl]ethyl methane-sulphonate (3c)

(38%), IR  $\nu_{\max}$ /cm<sup>-1</sup>: 1349 (SO<sub>2</sub>), 1173 (SO<sub>2</sub>), 933 (C-Cl); <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$  7.30 (d, 2H, *J* 8.4 Hz, H-3,5), 6.91 (d, 2H, *J* 8.4 Hz, H-2,6), 4.18 (m, 2H, CH<sub>2</sub>-1),

3.52-3.37 (m, 4H, 2×CH<sub>2</sub> pip.), 3.32-2.80 (m, 9H, 2×CH<sub>2</sub> pip., CH<sub>2</sub>-2, CH<sub>3</sub>); <sup>13</sup>C-NMR (CDCl<sub>3</sub>) δ 149.3, 130.9, 2×129.4, 2×118.6, 66.2, 2×52.6, 2×49.7, 38.7, 29.7. Anal. Calc. for C<sub>13</sub>H<sub>19</sub>ClN<sub>2</sub>O<sub>3</sub>S: C, 48.97; H, 6.01; N, 8.79. Found: C, 49.05; H, 6.14; N, 8.72%.

*2-[4-(4-Nitrophenyl)piperazin-1-yl]ethyl methane-sulphonate (3d)*

(35%), IR  $\nu_{\max}$ /cm<sup>-1</sup>: 1348 (SO<sub>2</sub>), 1173 (SO<sub>2</sub>), 1529, 1292 (NO<sub>2</sub>); <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ 8.20 (d, 2H, *J* 7.9 Hz, H-3,5), 6.90 (d, 2H, *J* 7.2 Hz, H-2,6), 3.81 (t, 2H, *J* 11.5 Hz, CH<sub>2</sub>-1), 3.52-3.39 (m, 4H, 2×CH<sub>2</sub> pip), 3.29-2.78 (m, 9H, 2×CH<sub>2</sub> pip., CH<sub>2</sub>-2, CH<sub>3</sub>); <sup>13</sup>C-NMR (CDCl<sub>3</sub>) δ 153.8, 137.5, 2×125.8, 2×113.7, 63.4, 55.2, 2×52.6, 2×50.1, 37.9. Anal. Calc. for C<sub>13</sub>H<sub>19</sub>N<sub>3</sub>O<sub>5</sub>S: C, 47.41; H, 5.81; N, 12.76. Found: C, 47.12; H, 5.61; N, 12.59%.

*1-(2-Chloroethyl)-4-(3-methoxyphenyl)piperazine (3e')*

(37%), IR  $\nu_{\max}$ /cm<sup>-1</sup>: 2835 (CO-CH<sub>3</sub>), 728 (C-Cl); <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ 7.22 (dd, 1H, *J*<sub>1</sub> 8.3 Hz, *J*<sub>2</sub> 2.6 Hz, H-5), 6.61-6.22 (m, 3H, H-4,5,6), 3.82-3.71 (m, 5H, CH<sub>2</sub>-2, OCH<sub>3</sub>), 3.60 (t, 2H, *J* 11.9 Hz, CH<sub>2</sub>-1), 3.38-3.20 (m, 4H, 2×CH<sub>2</sub>-pip.), 2.67 (t, 4H, *J* 10 Hz, 2×CH<sub>2</sub>-pip.); <sup>13</sup>C-NMR (CDCl<sub>3</sub>) δ 160.6, 152.5, 129.8, 108.9, 104.6, 102.6, 97.34, 59.7, 55.2, 2×53.1, 2×49.3, 37.9. Anal. Calc. for C<sub>14</sub>H<sub>19</sub>ClN<sub>2</sub>O: C, 61.29; H, 7.52; N, 11.00. Found: C, 60.94; H, 7.65; N, 11.32%.

*2-(4-Pyrazin-2-yl-piperazin-1-yl)ethyl methanesulphonate (3f)*

(37%), IR  $\nu_{\max}$ /cm<sup>-1</sup>: 1347 (SO<sub>2</sub>), 1171 (SO<sub>2</sub>); <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 8.35 (s, 1H, H-6), 8.08 (d, 1H, *J* 8 Hz, H-4), 6.44 (d, 1H, *J* 8.5 Hz, H-3), 4.26 (t, 2H, *J* 11.0 Hz, CH<sub>2</sub>-1), 3.80 (m, 4H, 2 × CH<sub>2</sub> pip), 3.03-2.86 (m, 5H, CH<sub>2</sub>-2, CH<sub>3</sub>), 2.63-2.48 (m, 4H, 2 × 2 × CH<sub>2</sub> pip). <sup>13</sup>C RMN (CDCl<sub>3</sub>) δ 162.3, 159.1, 156.5, 103.6, 53.6, 2×52.0, 2×49.8, 46.7, 42.1. Anal. Calc. for C<sub>11</sub>H<sub>18</sub>N<sub>4</sub>O<sub>3</sub>S: C, 46.14; H, 6.34; N, 19.57. Found: C, 45.94; H, 6.45; N, 19.82%.

*3-[4-(3-Methoxyphenyl)piperazin-1-yl]propyl methane-sulphonate (3g)*

(35%), IR  $\nu_{\max}$ /cm<sup>-1</sup>: 1347 (SO<sub>2</sub>), 1173 (SO<sub>2</sub>); <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ 7.30 (t, 2H, *J* 8.4 Hz, H-3,5), 6.96 (m, 3H, H-2,4,6), 4.31 (m, 2H, CH<sub>2</sub>-1), 3.2 (t, 4H, *J* 5 Hz, 2×CH<sub>2</sub>-pip.), 2.90 (s, 3H, CH<sub>3</sub>), 2.63-2.43 (m, 6H, 2×CH<sub>2</sub>-pip., CH<sub>2</sub>-3), 2.10-1.90 (m, 2H, CH<sub>2</sub>-2); <sup>13</sup>C-NMR (CDCl<sub>3</sub>) δ 160.6, 151.1, 129.5, 119.7, 116, 68.5, 55.0, 53.9, 2×53.1, 2×48.9, 37.8, 26.9. Anal. Calc. for C<sub>14</sub>H<sub>22</sub>N<sub>2</sub>O<sub>3</sub>S: C, 56.35; H, 7.43; N, 9.39; O. Found: C, 56.47; H, 7.76; N, 9.12%.

*3-[4-(2-Fluorophenyl)piperazin-1-yl]propyl methane-sulphonate (3h)*

(50%), IR  $\nu_{\max}$ /cm<sup>-1</sup>: 1348 (SO<sub>2</sub>), 1170 (SO<sub>2</sub>), 1010 (C-F); <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ 7.28-6.87 (m, 4H, H-3,4,5,6), 3.82 (t, 2H, *J* 10.2 Hz, CH<sub>2</sub>-1), 3.47 (m, 4H, 2×CH<sub>2</sub>-pip.), 3.36-2.92 (m, 9H, 2×CH<sub>2</sub>-pip., CH<sub>2</sub>-3, CH<sub>3</sub>), 2.12-1.90 (m, 2H, CH<sub>2</sub>-2); <sup>13</sup>C-NMR (CDCl<sub>3</sub>) δ 158.10 (d, 2C, *J*<sub>C-F</sub> 318 Hz), 153.10, 137.5, 124.4, 118.9, 116.2, 115.9, 68.4, 62.4, 59.4, 53.9, 2×53.2, 2×45.5, 39.7, 26.7. Anal. Calc. for C<sub>14</sub>H<sub>21</sub>FN<sub>2</sub>O<sub>3</sub>S: C, 53.15; H, 6.69; N, 8.85. Found: C, 52.73; H, 6.66; N, 8.24%.

*3-[4-(4-Chlorophenyl)piperazin-1-yl]propyl methane-sulphonate (3i)*

(50%), IR  $\nu_{\max}$ /cm<sup>-1</sup>: 1350 (SO<sub>2</sub>), 1178 (SO<sub>2</sub>), 938 (C-Cl); <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ 7.41 (d, 2H, *J* 12.3 Hz, H-3,5), 6.94 (d, 2H, *J* 8.8 Hz, H-2,6), 3.71 (t, 2H, *J* 5.8 Hz, CH<sub>2</sub>-1), 3.50 (m, 4H, 2×CH<sub>2</sub>-pip), 3.36-2.92 (m, 6H, 2×CH<sub>2</sub>-pip., CH<sub>2</sub>-3), 2.87 (s, 3H, CH<sub>3</sub>), 2.25-2.00 (m, 2H, CH<sub>2</sub>-2); <sup>13</sup>C-NMR (CDCl<sub>3</sub>) δ 147.9, 2×129.4, 126.9, 2×118.5, 66.9, 2×52.1, 2×46.8, 41.6, 39.6, 26.5. Anal. Calc. for C<sub>14</sub>H<sub>21</sub>ClN<sub>2</sub>O<sub>3</sub>S: C, 50.52; H, 6.36; N, 8.42. Found C<sub>14</sub>H<sub>21</sub>ClN<sub>2</sub>O<sub>3</sub>S: C, 49.97; H, 6.72; N, 8.14%.

*3-[4-(4-Nitrophenyl)piperazin-1-yl]propyl methane-sulphonate (3j)*

(46%), IR  $\nu_{\max}$ /cm<sup>-1</sup>: 1351 (SO<sub>2</sub>), 1173 (SO<sub>2</sub>); <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ 8.11 (d, 2H, *J* 6.5 Hz, H-3,5), 6.80 (d, 2H, *J* 9.5 Hz, H-2,6), 4.28 (t, 2H, *J* 6.2 Hz, H-1), 3.65-3.43 (m, 4H, 2×CH<sub>2</sub>-pip), 3.32-2.92 (m, 6H, 2×CH<sub>2</sub>-pip., CH<sub>2</sub>-2), 2.88 (s, 3H, CH<sub>3</sub>), 2.26 (t, 2H, *J* 6.6 Hz, H-2); <sup>13</sup>C-NMR (CDCl<sub>3</sub>) δ 150.8, 137.9, 2×125.9, 2×112.7, 68.12, 2×52.6, 2×46.9, 37.5, 29.7. Anal. Calc. for C<sub>14</sub>H<sub>21</sub>N<sub>3</sub>O<sub>5</sub>S: C, 48.97; H, 6.16; N, 12.24. Found: C, 49.14; H, 6.28; N, 12.09%.

*3-[4-(3-Methoxyphenyl)piperazin-1-yl]propyl methane-sulphonate (3k)*

(37%), IR  $\nu_{\max}$ /cm<sup>-1</sup>: 1349 (SO<sub>2</sub>), 1170 (SO<sub>2</sub>), 2835 (C-H); <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ 7.22 (dd, 1H, *J*<sub>1</sub> 8.2 Hz, *J*<sub>2</sub> 2.86 Hz, H-5), 6.61-6.21 (m, 3H, H-4,5,6), 4.30 (t, 2H, *J* 6.3 Hz, H-1), 3.82 (d, 3H, *J* 9.6 Hz, H-2), 3.75 (s, 3H, OCH<sub>3</sub>), 3.25 (t, 4H, *J* 9.8 Hz, 2×CH<sub>2</sub>-pip.), 2.9-2.5 (m, 6H, CH<sub>2</sub>-pip, CH<sub>2</sub>-3), 2.18 (t, 2H, *J* 6.7 Hz, H-2); <sup>13</sup>C-NMR (CDCl<sub>3</sub>) δ 160.4, 148.2, 129.8, 108.9, 104.6, 102.6, 68.3, 55.2, 53.9, 2×53.1, 2×48.9, 37.3, 26.4. Anal. Calc. for C<sub>15</sub>H<sub>24</sub>N<sub>2</sub>O<sub>4</sub>S: C, 54.86; H, 7.37; N, 8.53. Found: C, 54.49; H, 7.65; N, 8.24%.

*Synthesis of 1-[2-(4-Arylpiperazin-1-yl)alkyl]-2-(pyridin-3-yl)-1H-benzimidazoles 5a-k. General procedures*

A solution of 2-(pyridin-3-yl)-1H-benzimidazole **4** (0.15 g, 0.75 mmol) in acetonitrile was stirred with NaOH

for 2 hours. The benzimidazole anion afforded was added to a solution of the corresponding arylpiperazinyl alkyl methanesulphonate derivatives **3** (0.70 mmol) in acetonitrile (12 mL). The mixture was stirred at room temperature for 12 hours and concentrated in vacuo. Purification of the crude by column chromatography with dichloromethane as the eluent afforded the target compounds **5a-k** as yellow oils.

*1-[2-[4-(4-Phenylpiperazin-1-yl)ethyl]-2-pyridin-3-yl]-1H-benzimidazole (5a)*

(45%), IR  $\nu_{\max}/\text{cm}^{-1}$ : 2885 (C-H), 1338 (C-N).  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  9.10 (d, 1H,  $J$  2.1 Hz, H-2 pyr.), 8.78 (d, 1H,  $J$  4.9 Hz, H-4 pyr.), 8.22 (d, 1H,  $J$  7.9 Hz, H-6 pyr.), 7.92 (d, 1H,  $J$  8.5 Hz, H-5-pyr.), 7.53-7.14 (m, 6H, Ar), 6.85 (m, 3H, H-2,4,6), 4.40 (t, 2H,  $J$  6.5 Hz,  $\text{CH}_2$ -1), 3.10 (t, 4H,  $J$  4.9 Hz,  $2\times\text{CH}_2$ -pip.), 2.84 (t, 2H,  $J$  6.5 Hz,  $\text{CH}_2$ -2), 2.50 (t, 4H,  $J$  5.1 Hz,  $2\times\text{CH}_2$  pip.).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  151.3, 150.7, 149.9, 143.3, 137.2, 135.6,  $2\times 129.1$ ,  $2\times 123.6$ , 123.4,  $2\times 120.3$ , 119.9,  $2\times 116.1$ , 110.2, 57.2,  $2\times 53.6$ ,  $2\times 48.9$ , 42.9. Anal. Calc. for  $\text{C}_{24}\text{H}_{25}\text{N}_5$ : C, 75.17; H, 6.57; N, 18.26. Found: C, 75.36; H, 6.42; N, 18.22%.

*1-[2-[4-(2-Fluorophenyl)piperazin-1-yl]ethyl]-2-pyridin-3-yl-1H-benzimidazole (5b)*

(21%), IR  $\nu_{\max}/\text{cm}^{-1}$ : 1321 (C-N), 1007 (C-F);  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  9.10 (d, 1H,  $J$  1.4 Hz, H-2 pyr.), 8.78 (d, 1H,  $J$  4.8 Hz, H-4 pyr.), 8.24 (d, 1H,  $J$  7.9 Hz, H-6 pyr.), 7.92 (d, 1H,  $J$  7.8 Hz, H-5-pyr.), 7.62-7.21 (m, 6H, Ar), 7.12-6.85 (m, 2H, H-4,6), 4.40 (t, 2H,  $J$  6.5 Hz,  $\text{CH}_2$ -1), 2.97 (t, 4H,  $J$  4.9 Hz,  $2\times\text{CH}_2$ -pip.), 2.84 (t, 2H,  $J$  6.5 Hz,  $\text{CH}_2$ -2), 2.50 (m, 4H,  $J$  4.9 Hz,  $2\times\text{CH}_2$  pip.).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  158.10 (d, 2C,  $J_{\text{C-F}}$  318 Hz), 153.10, 151.1, 150.7, 149.9, 143.2, 137.2, 135.6, 124.5, 124.4, 123.6, 123.4, 122.9, 122.7, 122.5, 120.2, 118.9, 116.3, 115.9, 110.2, 57.2,  $2\times 53.7$ ,  $2\times 50.3$ . Anal. Calc. for  $\text{C}_{24}\text{H}_{24}\text{FN}_5$ : C, 71.80; H, 6.03; N, 17.44. Found: C, 72.14; H, 6.14; N, 17.62%.

*1-[2-[4-(4-Chlorophenyl)piperazin-1-yl]ethyl]-2-pyridin-3-yl-1H-benzimidazole (5c)*

(35%), IR  $\nu_{\max}/\text{cm}^{-1}$ : 1317 (C-N), 933 (C-Cl);  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 9.11 (d, 1H,  $J$  2.1 Hz, H-2 pyr.), 8.78 (d, 1H,  $J$  4.9 Hz, H-4-pyr.), 8.25 (d, 1H,  $J$  7.9 Hz, H-6 pyr.), 7.91 (d, 1H,  $J$  7.1 Hz, H-5-pyr.), 7.54-7.16 (m, 6H Ar) 7.11-6.87 (m, 2H, H-2,6) 4.41 (t, 2H,  $J$  6.4 Hz,  $\text{CH}_2$ -1), 3.10 (t, 4H,  $J$  5 Hz,  $2\times\text{CH}_2$ -pip.), 2.88 (t, 2H,  $J$  12 Hz,  $\text{CH}_2$ -2), 2.56 (t, 4H,  $J$  9.8 Hz,  $2\times\text{CH}_2$ -pip.).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  151.7, 150.8, 147.2, 137.2, 134.4, 132.5,  $2\times 128.9$ , 124.4 123.6, 123.5, 123.4, 122.9, 120.3,  $2\times 117.3$ , 110.2, 58.2, 57.1,  $2\times 53.5$ ,  $2\times 48.9$ , 42.9. Anal. Calc. for  $\text{C}_{24}\text{H}_{22}\text{ClN}_5$ : C, 68.97; H, 5.79; N, 16.76. Found: C, 69.02; H, 5.62; N, 17.00%.

*1-[2-[4-(4-Nitrophenyl)piperazin-1-yl]ethyl]-2-pyridin-3-yl-1H-benzimidazole (5d)*

(46%), IR  $\nu_{\max}/\text{cm}^{-1}$ : 1529 ( $\text{NO}_2$ ), 1292 ( $\text{NO}_2$ ), 1324 (C-N);  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  9.10 (d, 1H,  $J$  1.5 Hz, H-2 pyr.), 8.78 (d, 1H,  $J$  4.8 Hz, H-4 pyr.), 8.23 (m, 1H, H-6 pyr.), 8.12 (d, 1H,  $J$  6.5 Hz, H-3,5), 7.91 (d, 1H,  $J$  7.1 Hz, H-5-pyr.), 7.69-7.36 (m, 5H, Ar), 6.89 (d, 2H,  $J$  9.5 Hz, H-2,6), 4.40 (t, 2H,  $J$  12.6 Hz,  $\text{CH}_2$ -1), 3.15 (t, 4H,  $J$  10.2 Hz,  $2\times\text{CH}_2$ -pip.), 2.85 (t, 2H,  $J$  12.6 Hz,  $\text{CH}_2$ -2), 2.50 (t, 4H,  $J$  10.1 Hz,  $2\times\text{CH}_2$  pip.).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  154.6, 150.7, 149.9, 147.5, 137.2, 134.2, 130.8,  $2\times 125.9$ , 124.7, 123.6, 123.4, 122.9, 120.4,  $2\times 112.8$ , 110.1, 58.4, 57.3  $2\times 53.1$ ,  $2\times 47.9$ , 39.8. Anal. Calc. for  $\text{C}_{24}\text{H}_{24}\text{N}_6\text{O}_2$ : C, 67.27; H, 5.65; N, 19.61. Found: C, 66.93; H, 5.42; N, 19.42%.

*1-[2-[4-(3-Methoxyphenyl)piperazin-1-yl]ethyl]-2-pyridin-3-yl-1H-benzimidazole (5e)*

(20%), IR  $\nu_{\max}/\text{cm}^{-1}$ : 2883 (C-H), 1313 (C-N);  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  9.10 (d, 1H,  $J$  2.1 Hz, H-2 pyr.), 8.78 (d, 1H,  $J$  4.9 Hz, H-4 pyr.), 8.22 (d, 1H,  $J$  7.9 Hz, H-6 pyr.), 7.92 (d, 1H,  $J$  7.1 Hz, H-5-pyr.), 7.62-7.12 (m, 5H, Ar), 6.61-6.21 (m, 3H, H-4,5,6), 4.40 (t, 2H,  $J$  6.6 Hz,  $\text{CH}_2$ -1), 3.86 (s, 3H,  $\text{OCH}_3$ ), 3.15 (t, 4H,  $J$  5.0 Hz,  $2\times\text{CH}_2$ -pip.), 2.84 (t, 2H,  $J$  13 Hz,  $\text{CH}_2$ -2), 2.58 (t, 4H,  $J$  5.1 Hz,  $2\times\text{CH}_2$  pip.).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  160.6, 152.4, 150.7, 149.9, 147.2, 143.2, 137.2, 135.6, 129.8, 127.3, 123.6, 123.4, 122.9, 120.3, 110.2, 108.9, 104.5, 102.6, 57.2, 55.2,  $2\times 53.6$ ,  $2\times 48.9$ , 42.9. Anal. Calc. for  $\text{C}_{25}\text{H}_{27}\text{N}_5\text{O}$ : C, 72.61; H, 6.58; N, 16.94. Found: C, 72.76; H, 6.23; N, 16.82%.

*1-(2-(4-(Pyrazin-2-yl)piperazin-1-yl)ethyl)-2-(pyridin-3-yl)-1H-benzimidazole (5f)*

(38%), IR  $\nu_{\max}/\text{cm}^{-1}$ : 2856 (C-H), 1311 (C-N);  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  9.10 (d, 1H,  $J$  2.1 Hz, H-2 pyr.), 8.78 (d, 1H,  $J$  4.8 Hz, H-4 pyr.), 8.36-8.21 (m, 2H, H-2 pyr., H-6 pyr.), 7.91 (d, 1H,  $J$  9.0 Hz, H-5-pyr.), 7.76-7.31 (m, 5H, Ar), 6.50 (t, 1H,  $J$  4.1 Hz, H-6), 4.42 (t, 2H,  $J$  6.6 Hz,  $\text{CH}_2$ -1), 3.17 (t, 4H,  $J$  4.9 Hz,  $2\times\text{CH}_2$ -pip.), 2.83 (t, 2H,  $J$  6.4 Hz,  $\text{CH}_2$ -2), 2.49 (t, 4H,  $J$  5 Hz,  $2\times\text{CH}_2$  pip.).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  162.3, 157.7, 156.2, 150.7, 149.9, 147.5, 143.3, 137.1, 135.6, 129.8, 127.5, 123.4, 122.9, 120.3, 110.7, 110.0, 57.3,  $2\times 53.4$ ,  $2\times 48.4$ , 42.8. Anal. Calc. for  $\text{C}_{22}\text{H}_{23}\text{N}_7$ : C, 68.55; H, 6.01; N, 25.44. Found: C, 68.36; H, 6.26; N, 25.23%.

*1-[3-(4-Phenylpiperazin-1-yl)propyl]-2-pyridin-3-yl-1H-benzimidazole (5g)*

(48%), IR  $\nu_{\max}/\text{cm}^{-1}$ : 2875 (C-H), 1306 (C-N);  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  9.10 (d, 1H,  $J$  2.2 Hz, H-2 pyr.), 8.78 (d, 1H,  $J$  4.9 Hz, H-4 pyr.), 8.22 (d, 1H,  $J$  8 Hz, H-6 pyr.), 7.89 (d, 1H,  $J$  9.2 Hz, H-5-pyr.), 7.53-7.20 (m, 6H, Ar), 6.95

(m, 3H, H-2,4,6), 4.40 (t, 2H, *J* 7.8 Hz, CH<sub>2</sub>-1), 3.16 (t, 4H, *J* 9.8 Hz, 2×CH<sub>2</sub>-pip.), 2.50 (t, 4H, *J* 9.9 Hz, 2×CH<sub>2</sub> pip.), 2.37 (t, 2H, *J* 6.6 Hz, CH<sub>2</sub>-3), 1.91 (m, 2H, CH<sub>2</sub>-2). <sup>13</sup>C-NMR (CDCl<sub>3</sub>) δ 151.1, 150.7, 150.4, 149.7, 147.6, 143.1, 136.9, 135.7, 134.4, 2×129.4, 127.6, 123.6, 123.1, 122.9, 120.1, 119.8, 2×116.1, 54.6, 2×53.1, 2×49.7, 29.8. Anal. Calc. for C<sub>25</sub>H<sub>27</sub>N<sub>5</sub>: C, 75.54; H, 6.85; N, 17.62. Found: C, 75.31; H, 6.90; N, 17.79%.

*1*-{3-[4-(2-Fluorophenyl)piperazin-1-yl]propyl}-2-pyridin-3-yl-1*H*-benzimidazole (**5h**)

(28%), IR ν<sub>max</sub>/cm<sup>-1</sup>: 1225 (C-N), 1007 (C-F); <sup>1</sup>H-NMR(CDCl<sub>3</sub>) δ 9.10 (d, 1H, *J* 3Hz, H-2 pyr.), 8.80 (d, 1H, *J* 6.6 Hz, H-4 pyr.), 8.23 (d, 1H, *J* 7.9 Hz, H-6 pyr.), 7.91 (d, 1H, *J* 5.3 Hz, H-5-pyr.), 7.61-7.21 (m, 6H, Ar), 7.12-6.86 (m, 2H, Ar), 4.41 (t, 2H, *J* 7.1 Hz, H CH<sub>2</sub>-1), 3.20 (t, 4H, *J* 4.5 Hz, CH<sub>2</sub>-2×CH<sub>2</sub>-pip.), 2.50 (t, 4H, *J* 4.9 Hz, 2×CH<sub>2</sub> pip.), 2.36 (t, 2H, *J* 6.7 Hz, CH<sub>2</sub>-3), 1.97 (t, 2H, *J* 13.8 Hz, CH<sub>2</sub>-2). <sup>13</sup>C-NMR (CDCl<sub>3</sub>) δ 158.10 (d, 2C, *J*<sub>C-F</sub> 318 Hz), 153.10, 150.7, 147.4, 143.1, 139.1, 136.9, 135.7, 134.4, 127.1, 124.5, 123.9, 123.3, 122.9, 120.1, 118.9, 116.3, 116.9, 115.9, 110.4, 54.7, 2×53.2, 2×50.4, 50.4, 29.9. Anal. Calc. for C<sub>25</sub>H<sub>26</sub>FN<sub>5</sub>: C, 72.27; H, 6.31; N, 16.85. Found: C, 71.99; H, 6.67; N, 16.49%.

*1*-{3-[4-(4-Chlorophenyl)piperazin-1-yl]propyl}-2-pyridin-3-yl-1*H*-benzimidazole (**5i**)

(38%), IR ν<sub>max</sub>/cm<sup>-1</sup>: 1227 (C-N), 933 (C-Cl); <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ 9.10 (d, 1H, *J* 2.5 Hz, H-2 pyr.), 8.78 (d, 1H, *J* 4.8 Hz, H-4 pyr.), 8.22 (d, 1H, *J* 8.0 Hz, H-6 pyr.), 7.90 (d, 1H, *J* 7.4 Hz, H-5-pyr.), 7.52-7.14 (m, 6H, Ar), 7.11-6.87 (m, 2H, H-2,6), 4.41 (m, 2H, H CH<sub>2</sub>-1), 3.15 (m, 4H, CH<sub>2</sub>-2×CH<sub>2</sub>-pip.), 2.48 (m, 4H, 2×CH<sub>2</sub> pip.), 2.32 (m, 2H, CH<sub>2</sub>-3), 2.0 (m, 2H, CH<sub>2</sub>-2). <sup>13</sup>C-NMR (CDCl<sub>3</sub>) δ 151.6, 150.8, 147.3, 137.1, 134.5, 132.7, 2×129.0, 127.5, 124.2, 123.6, 123.5, 123.3, 122.9, 120.3, 2×118.3, 110.2, 58.4, 57.1, 2×53.7, 2×49.1, 29.7. Anal. Calc. for: C<sub>25</sub>H<sub>26</sub>ClN<sub>5</sub>: C, 69.51; H, 6.07; N, 16.21. Found: C, 69.27; H, 6.14; N, 15.99%.

*1*-{3-[4-(4-Nitrophenyl)piperazin-1-yl]propyl}-2-pyridin-3-yl-1*H*-benzimidazole (**5j**)

(24%), IR ν<sub>max</sub>/cm<sup>-1</sup>: 1530 (NO<sub>2</sub>), 1296 (NO<sub>2</sub>). <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ 9.10 (d, 1H, *J* 1.5 Hz, d, H-2 pyr.), 8.78 (d, 1H, *J* 4.9 Hz, H-4 pyr.), 8.22 (m, 1H, H-6 pyr.), 8.13 (d, 1H, *J* 6.7 Hz, H-3,5), 7.90 (d, 1H, *J* 6.9 Hz, H-5-pyr.), 7.68-7.36 (m, 5H, Ar), 6.89 (d, 2H, *J* 9.4 Hz, H-2,6), 4.40 (t, 2H, *J* 7.1 Hz, CH<sub>2</sub>-1), 3.23 (t, 4H, *J* 5.0 Hz, 2×CH<sub>2</sub>-pip.), 2.48 (t, 4H, *J* 5.2 Hz, 2×CH<sub>2</sub> pip.), 2.35 (t, 2H, *J* 6.3 Hz, CH<sub>2</sub>-3), 2.10 (bs, 2H, *J* 6.8 Hz, CH<sub>2</sub>-2). <sup>13</sup>C-NMR (CDCl<sub>3</sub>) δ 154.6, 150.7, 149.9, 147.5, 137.2, 136.7, 134.2, 130.8, 2×125.9,

124.7, 123.6, 123.4, 122.9, 120.4, 2×112.8, 110.1, 58.4, 57.3, 2×53.1, 2×47.9, 22.8. Anal. Calc. for C<sub>25</sub>H<sub>26</sub>N<sub>6</sub>O<sub>2</sub>: C, 67.86; H, 5.92; N, 18.99. Found: C, 68.14; H, 5.69; N, 19.23%.

*1*-{3-[4-(3-Methoxyphenyl)piperazin-1-yl]propyl}-2-pyridin-3-yl-1*H*-benzimidazole (**5k**)

(33%), IR ν<sub>max</sub>/cm<sup>-1</sup>: 2835 (C-H), 1315 (C-N); <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ 9.10 (d, 1H, *J* 2.19 Hz, H-2 pyr.), 8.78 (d, 1H, *J* 4.9 Hz, H-4 pyr.), 8.21 (d, 1H, *J* 7.9 Hz, H-6 pyr.), 7.91 (d, 1H, *J* 5.5 Hz, H-5-pyr.), 7.63-7.13 (m, 5H, Ar), 6.61-6.24 (m, 3H, H-4,5,6), 4.40 (t, 2H, *J* 7.3 Hz, H CH<sub>2</sub>-1), 3.86 (s, 3H, OCH<sub>3</sub>), 3.17 (t, 4H, *J* 5.0 Hz, 2×CH<sub>2</sub>-pip.), 2.50 (t, 4H, *J* 5 Hz, 2×CH<sub>2</sub> pip.), 2.36 (t, 2H, *J* 6.5 Hz, CH<sub>2</sub>-3), 2.0 (b.s., 2H, *J* 13.8 Hz, CH<sub>2</sub>-2). <sup>13</sup>C-NMR (CDCl<sub>3</sub>) δ 160.8, 152.3, 150.7, 150.0, 147.2, 143.3, 137.1, 136.6, 135.6, 129.8, 127.3, 123.6, 123.3, 122.9, 120.3, 110.4, 109.0, 104.6, 102.6, 57.3, 55.2, 2×53.6, 2×48.9, 22.9. Anal. Calc. for C<sub>26</sub>H<sub>29</sub>N<sub>5</sub>O: C, 73.04; H, 6.84; N, 16.38. Found: C, 72.89; H, 6.98; N, 16.78%.

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## Supplementary Information

Supplementary data are available free of charge at <http://jbcbs.sbj.org.br>, as PDF file.

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