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Pyridinium *N*-(2′-Azinyl)Aminides: Regioselective Synthesis of 2-Alkylaminoazines

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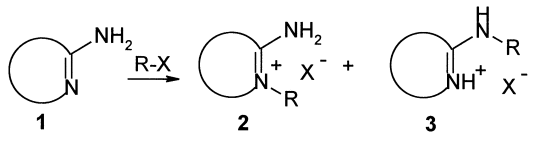
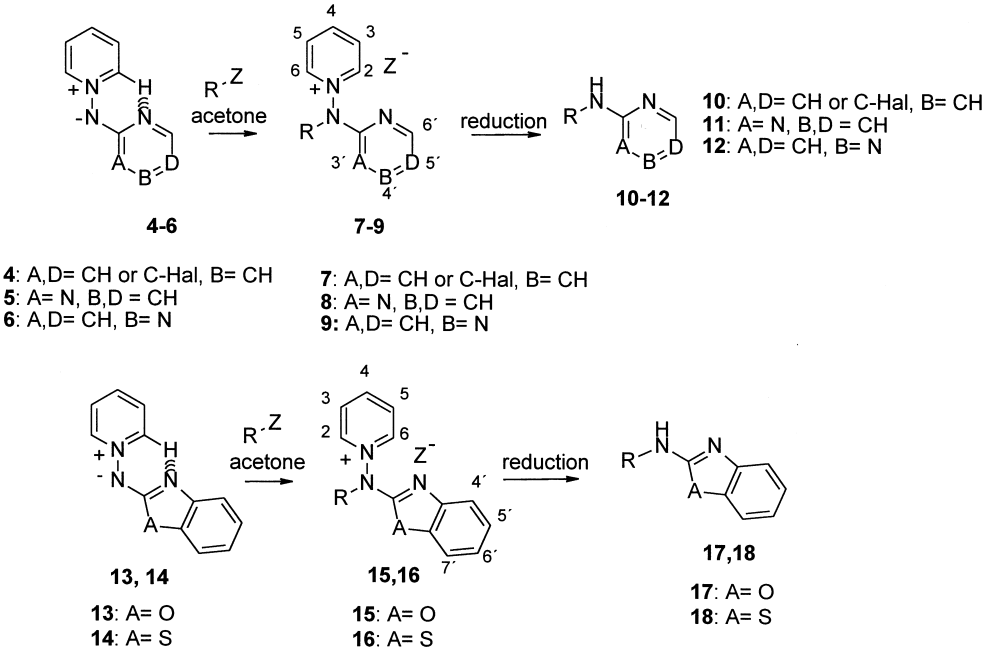
Abstract—The regioselective alkylation of pyridinium-*N*-(2′-azinil)aminides with alkyl halides under mild conditions is described. The alkylation, combined with a reduction of the N–N bond, allows an easy preparation of 2-alkylaminoazines.



Scheme 1.

The direct alkylation of heterocyclic amidines **1** is usually unsatisfactory as a preparative method, as it mainly occurs at the most basic endocyclic nitrogen.[1,2] In several cases, however, alkylation of these 1,3-dinucleophiles affords a mixture of N-endosubstituted **2** and N-exosubstituted **3** derivatives (Scheme 1), because the composition of the mixture is dependent upon the basicity of the heterocycle, the solvent and the steric effects at the exocyclic NH_2



Scheme 2.

Keywords: alkylation; amidines; pyridinium salts; ylids.

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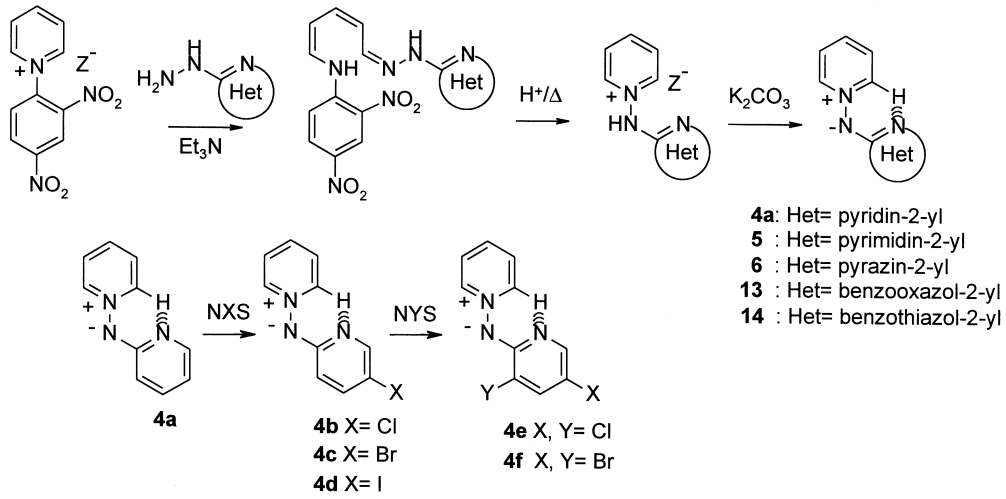
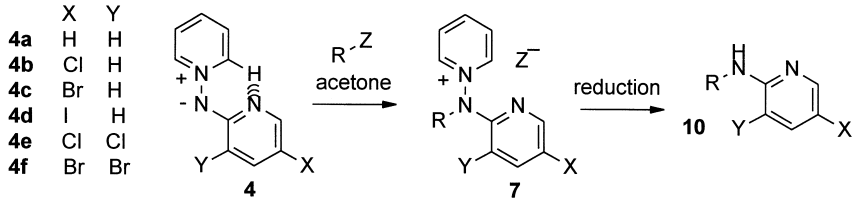


Scheme 3.



Scheme 4.

group. This is particularly evident with sterically hindered electrophiles.[3]

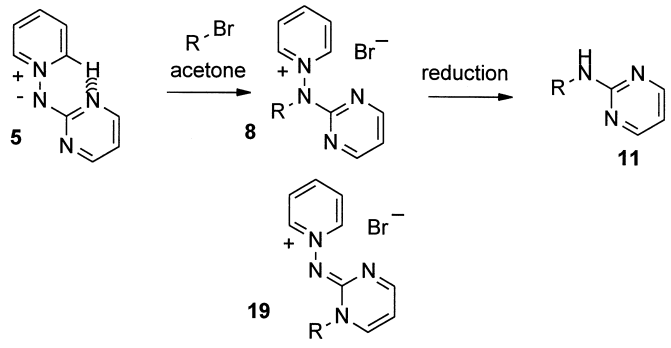
Generally, regioselectivity of the substitution reaction can be predicted by considering both HSAB theory and steric hindrance.[2,4,5] When reacted with primary halides other than benzyl chloride,[6] heterocyclic aminides yield only the endosubstituted isomer.

The exocyclic nitrogen of such systems can be rendered more basic by deprotonation, thus making its alkylation regioselective.[7,8] The metalation, however, might not be quantitative. As an alternative, activation of the exocyclic amino group facilitates deprotonation, and regioselective alkylation. Thus, *N*-acyl-aminopyridines[6] have been deprotonated with sodium amide and alkylated with methyl iodide,[9,10] yielding the 2-methylaminopyridines by hydrolysis. With other alkyl halides, obtained yields were lower. A similar procedure has been described using alcohols in the Mitsunobu reaction.[11] Alternative methods have been reported based on the easy reduction of aromatic aldimines, using heterocyclic fragments as leaving groups. Two-step

Table 1. Compounds **7a–r** and **10a–r** obtained

Compound **7**[a]	X	Y	R	Z	Yield (%)	Compound **10**[a]	Reagent	R	Yield (%)
a[20]	H	H	CH_3	I	75	**a**[24]	Zn/H^+	CH_3	75
b	Cl	H	CH_3	I	60	**b**[14]	Zn/H^+	CH_3	84
c	Br	H	CH_3	I	90	**c**	TEAF[b], Pt/C	CH_3	91
d	I	H	CH_3	I	95	**d**	TEAF, Pt/C	CH_3	62
e	Cl	Cl	CH_3	I	66	**e**[25]	Zn/H^+	CH_3	61
f	H	H	*n*-C_4H_9	Br	23	**f**[26]	TEAF, Pt/C	*n*-C_4H_9	99
g	Cl	H	*n*-C_4H_9	Br	62	**g**	TEAF, Pt/C	*n*-C_4H_9	96
h	Br	H	*n*-C_4H_9	Br	75	**h**	TEAF, Pt/C	*n*-C_4H_9	93
i	I	H	*n*-C_4H_9	Br	62	**i**	TEAF, Pt/C	*n*-C_4H_9	68
j	H	H	$C_6H_5CH_2$	Br	78	**j**[27]	Zn/H^+	$C_6H_5CH_2$	75
k	Cl	H	$C_6H_5CH_2$	Br	66	**k**[28]	TEAF, Pt/C	$C_6H_5CH_2$	80
l	Br	H	$C_6H_5CH_2$	Br	90	**l**	TEAF, Pt/C	$C_6H_5CH_2$	82
m	Cl	Cl	$C_6H_5CH_2$	Br	52	**m**[29]	TEAF, Pt/C	$C_6H_5CH_2$	74
n	Br	Br	$C_6H_5CH_2$	Br	71	**n**[29]	TEAF, Pt/C	$C_6H_5CH_2$	73
p	H	H	*p*-$BrC_6H_4CH_2$	Br	77	**p**[30]	Zn/H^+	*p*-$BrC_6H_4CH_2$	75
q	H	H	*p*-$MeC_6H_4CH_2$	Br	90	**q**[31]	Zn/H^+	*p*-$MeC_6H_4CH_2$	72
r	H	H	*p*-$O_2NC_6H_4CH_2$	Br	54	**r**	TEAF, Pt/C	*p*-$H_2NC_6H_4CH_2$	95

[a] Satisfactory microanalyses were obtained for all new compounds (C, H, N, and Halogens <0.40).
[b] TEAF: Triethylammonium formate.



Scheme 5.

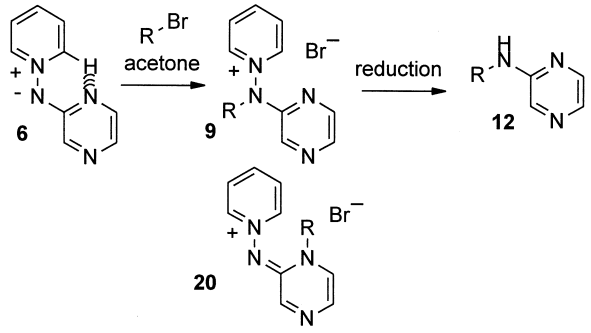
Table 2. Compound **8**, **19** and **11** obtained

Compound **8**, **19**	R[a]	Yield (a, b (%))	Compound **11**[b]	R	Yield (% from **8**)
a	$C_6H_5CH_2$	55, 25	**a**[25]	$C_6H_5CH_2$	67
b	*p*-$BrC_6H_4CH_2$	48, 24	**b**[30]	*p*-$BrC_6H_4CH_2$	65
c	*p*-$MeC_6H_4CH_2$	49, 24	**c**[14]	*p*-$MeC_6H_4CH_2$	76
d	*p*-$O_2NC_6H_4CH_2$	50, 25	**d**	*p*-$O_2NC_6H_4CH_2$	–

[a] All alkyl halides used as bromides.
[b] Satisfactory microanalyses were obtained for all new compounds (C, H, N <0.40).

sequences through benzotriazole[12–15] or indazole[16] derivatives have been described using these methods. More recently, methods employing palladium catalyzed cross-coupling reactions or amination of cuprates with *N*-alkylhydroxylamines were reported in the syntheses of *N*-alkylheteroarylamines.[17,18]

Going back to a classical approach, we planned to use a permanent nitride species, such as the pyridinium *N*-(2′-azinyl)aminides **4**–**6** (Scheme 2),[19–22] where the exocyclic nitrogen anion is stabilized by the presence of a pyridinium moiety. Moreover, the α-nuclear nitrogen, at least in pyridine derivatives, is partially blocked by an intramolecular hydrogen bond, making the alkylation regioselective.[20] This strategy has the advantage that the process should be compatible with nucleophile-sensitive groups in the azine ring without requiring strong bases. The final N–N bond reduction of the pyridinium salts **7**–**9** should allow the preparation of the corresponding 2-alkylaminoazines **10**–**12** (Scheme 2). Different azole-stabilized aminides **13**, **14**, obtained as described,[23] have been tested using the same strategy, with essentially the same results.



Scheme 6.

Preparation of starting amidines has been previously described from 2,4-dinitrophenyl pyridinium halide and the corresponding 2-heteroaryl hydrazine, producing the corresponding hydrazones (Scheme 3). Cyclization in acetic acid and treatment with potassium carbonate provide stable aminides **4a**,[20] **5**,[20] **6**,[20] and **14**[23] in good yield. Halogenation of **4a**, in very mild conditions, with *N*-halosuccinimides (NXS, X=Cl, Br, I) yields the haloderivatives **4b**–**f**[21] (Scheme 3).

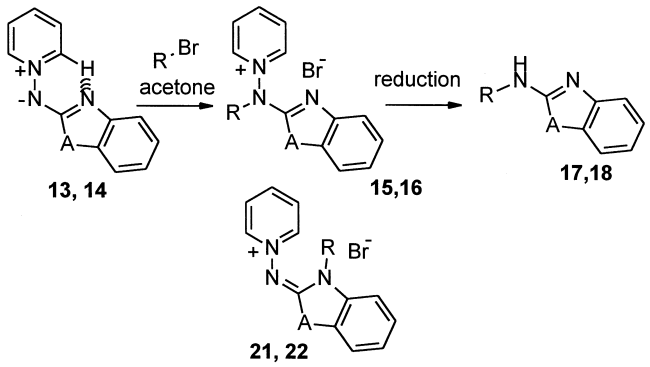
Results and Discussion

Different pyridyl-substituted aminides **4**[20,21] were reacted at room temperature with the corresponding alkyl halide to

Table 3. Compounds **9**, **20** and **12** obtained

Compound **9**, **20**	R[a]	Yield (a, b (%))	Compound **12**[b]	R	Yield (% from **9**)
a	$C_6H_5CH_2$	49, 25	**a**[32]	$C_6H_5CH_2$	74
b	*p*-$BrC_6H_4CH_2$	47, 23	**b**	*p*-$BrC_6H_4CH_2$	79
c	*p*-$MeC_6H_4CH_2$	49, 24	**c**	*p*-$MeC_6H_4CH_2$	55
d	*p*-$O_2NC_6H_4CH_2$	50, 25	**d**	*p*-$O_2NC_6H_4CH_2$	–

[a] All alkyl halides used as bromides.
[b] Satisfactory microanalyses were obtained for all new compounds (C, H, N <0.40).



Scheme 7.

Table 4. Compounds **15**, **16**, **21**, **22** and **17**, **18** obtained

Compound[a]	A	R[b]	Yield (a, b (%))	Compound[a]	A	R	Yield (%)
15, **21**	O	*p*-$MeC_6H_4CH_2$	67, traces	**17**	O	*p*-$MeC_6H_4CH_2$	93
16, **22**	S	*p*-$MeC_6H_4CH_2$	74, traces	**18**	S	*p*-$MeC_6H_4CH_2$	96

[a] Satisfactory microanalyses were obtained for all new compounds (C, H, N <0.40).
[b] All alkyl halides used as bromides.

produce *N*-alkyl-2′-pyridylaminopyridinium halides **7**. Either Zn/acetic acid treatment or reduction with formic acid/triethylamine in the presence of Pt/C,[21] afforded the 2-alkylaminopyridines **10** (Scheme 4). The two-step procedure is a general one and produced good results with a variety of substrates (Table 1).

The same process, when applied to pyrimidine-stabilized aminide **5**, again produced pyridinium salts **8** as the main product (Scheme 5, Table 2). The ring alkylated derivatives **19** appeared in roughly a 25% yield in the reaction mixture, indicating that the activation of the two ring nitrogens of the diazine, with only one of them blocked by the hydrogen bond, favor the formation of **19**. Compounds **8** and **19** can be perfectly discriminated in the reaction mixture with regard to ^{1}H NMR spectra. As expected, the final N–N fission of the regiosomeric mixture yielded the 2-alkylaminopyrimidines **11**.

The same scheme was applied to the alkylation of the pyrazine-stabilized aminide **6** (Scheme 6, Table 3) with essentially the same results. The presence of the ring alkylated compounds **20** in roughly 25% yield indicates that also the more π-deficient diazine ring could produce a weaker hydrogen bond, thus facilitating alkylation on the more nucleophilic ring nitrogen. No traces of the 4-N alkylated derivative were detected, indicating that electronic effects are dominant in the process. Again, the final N–N reduction afforded 2-alkylaminopyrazines **12** in good yield.

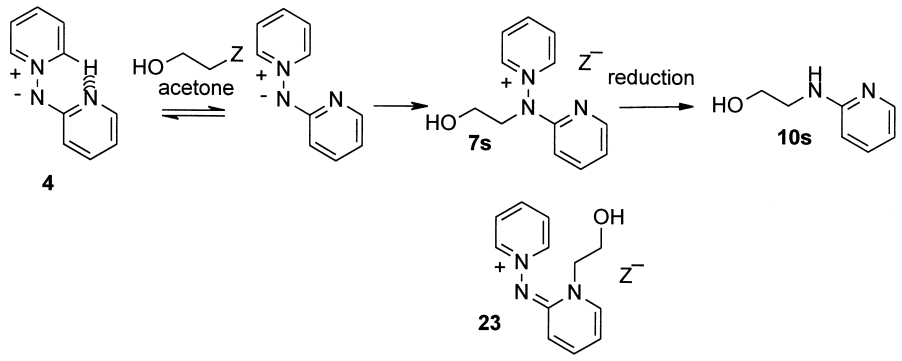
Other azole-stabilized aminides were tested in the alkylation process such as the benzazole derivatives **13** and **14** (Scheme 7, Table 4). The alkylation occurred mainly in the exocyclic nitrogen, producing salts **15** and **16**. The ring alkylated products **21** and **22** appeared only in trace amounts. Reduction of purified salts **15** and **16** yielded the expected 2-alkylaminobenzazoles **17** and **18**, respectively.

Other halides with different functions are being tested, but the very simple case of the reaction of the aminide **4a** with haloethanols (Scheme 8) should be cited. The presence of a hydroxy group in the alkyl halide contributes to weaken the hydrogen bond, facilitating the ring nitrogen alkylation process. Thus, although the salt **7s** was the main product, the ring alkylated product **23** was also obtained. The best results were obtained for Z=I. Varying the alkyl halide (Z=Br or Cl) considerably decreased the total yield, although the ratio **7s**:**23** essentially did not change (Table 5). Reduction of the isolated **7s** produced the alcohol **10s**.

In conclusion, the alkylation of heteroaryl-stabilized aminides, together with the reduction to break the N–N bond, produced a two-step method to yield the corresponding 2-alkylaminoazine or 2-aminoazole. The alkylation was very clean with pyridines, where the starting aminide has a stable hydrogen bond. The situation, however, is not as clear with diazines, where the ring nitrogen alkylation competes with the main process. In these cases the ring-alkylated product cannot be separated, but reduction of isomeric mixture afforded the corresponding 2-alkylaminoazines in good yield. The process was similar with benzazole-stabilized aminides, but in these cases the exocyclic N-alkylated products can be easily purified. The use of halohydrines also produced exocyclic nitrogen alkylation, but the presence of the hydroxy group favored the breaking of the hydrogen bond, so ring-alkylated products appeared as the secondary products.

Experimental

All melting points were determined in open capillary tubes, on a Electrothermal LA6304 and are uncorrected. IR spectra were obtained on a Perkin–Elmer 883 spectrometer. ^{1}H NMR spectra were obtained on a Varian Unity (300 MHz)



Scheme 8.

Table 5. Compounds **7s**, **23** and **10s** obtained

Compound[a]	Z	Ratio	Yield (a, b (%))	Compound	Reagent	Yield (%)
7s, **23**	Cl	3:1	16, 6	**10s**[33]	TEAF[b], Pt/C	85
7s, **23**	Br	3:1	27, 9			
7s, **23**	I	3:1	41, 13			

[a] Satisfactory microanalyses were obtained for all new compounds (C, H, N <0.40).
[b] TEAF: Triethylammonium formate.

spectrometer. Chemical shifts are expressed in ppm downfield from TMS. Elemental analyses were carried out on a Heraeus Rapid CHN analyzer and are within 0.4% of the theoretical values for all the new compounds described. All chemicals were of reagent grade and used without further purification. Ylides **4a**–**f**,[21] **5**[20], **6**[20] and **14**[23] have been previously described.

Preparation of pyridinium *N*-(2′-heteroaryl)aminides 4–6, 13 and 14

To a solution of *N*-(2′,4′-dinitrophenyl)pyridinium chloride (2.8 g, 0.01 mol) in ethanol (15 mL), the corresponding α-hydrazinoazine or azole (0.01 mol) in ethanol (5 mL) was added, followed by triethylamine (1.5 mL). The reaction mixture was stirred at room temperature for 15 min. The precipitate was filtered and washed with 10% hydrochloric acid (until the filtrate reached pH 5–6), then with methanol (30 mL) and finally with ether (30 mL). The crude hydrazone was suspended in glacial acetic acid (25 mL) and refluxed for 30 min until a clear solution was obtained. The mixture was then concentrated to dryness, the residue stirred in water (25 mL) and the insoluble material removed by filtration. The filtrate was decolorized with charcoal, acidified with 48% hydrobromic acid (0.02 mmol), then concentrated to dryness and the residue recrystallized from absolute ethanol. Addition of potassium carbonate (20 mmol), to a vigorously stirred solution of the corresponding *N*-(2′-heteroarylamino)pyridinium bromide (10 mmol) in acetone (45 mL) for 3 h, afforded after elimination of the inorganic salts and evaporation to dryness of the remaining solution, the corresponding aminides, which were recrystallized from adequate solvent.

***N*-(2′-benzooxazolyl)pyridinium aminide (13).** Yellow solid (1.75 g, 83%, dichloromethane/hexane), mp 195–198°C; [Found: C, 67.91; H, 4.44; N, 19.63. $C_{12}H_9N_3O$ requires C, 68.24; H, 4.29; N, 19.89%]; R_f (10% triethylamine/ethanol) 0.45; ν_{max}(KBr) 3045, 2994, 1627, 1479, 1358, 1002 cm^{-1}; δ_H (300 MHz. DMSO-d6) 9.39 (2H, dd, *J*=7.1, 1.2 Hz, *H*2(6)), 7.93 (1H, bt, *J*=7.6 Hz, *H*4), 7.84 (2H, dd, *J*=7.6, 7.1 Hz, *H*3(5)), 7.22 (1H, d, *J*=7.8 Hz, *H*4′), 7.12 (1H, d, *J*=7.8 Hz, *H*7′), 7.01 (1H, bt, *J*=7.8 Hz, *H*5′), 6.88 (1H, bt, *J*=7.8 Hz, *H*6′).

Reaction of aminides with alkyl halides

General method: To a solution of the corresponding aminide (10 mmol) in dry acetone (45 mL), the alkyl halide (11 mmol for benzyl halides and 16 mmol for iodomethane or *n*-butyl bromide) was added, and the mixture was stirred at room temperature until no starting material was detected by TLC (for **7f**–**i**, 36 h of reflux were necessary). The solid obtained was filtered, washed with acetone (5 mL), and recrystallized from the indicated solvent.

1-[(5-Chloropyridin-2-yl)methylamino]pyridinium iodide (7b). Reaction time, 2 h. Pale yellow solid (3.12 g, 90%, ethanol), mp 192–195°C; [Found: C, 38.22; H, 3.10; N, 11.99. $C_{11}H_{11}ClIN_3$ requires C, 38.04; H, 3.20; N, 12.11%]; R_f (10% triethylamine/ethanol) 0.15; ν_{max}(KBr) 3026, 1614, 1582, 1466, 1432, 1374, 1302 cm^{-1}; δ_H (300 MHz. DMSO-d6) 9.36 (2H, dd, *J*=7.2, 1.5 Hz, *H*2(6)), 8.81 (1H, tt, *J*=7.7, 1.5 Hz, *H*4), 8.34 (2H, dd, *J*=7.7, 7.2 Hz, *H*3(5)), 8.17 (1H, d, *J*=2.5 Hz, *H*6′), 7.99 (1H, dd, *J*=8.8, 2.5 Hz, *H*4′), 7.21 (1H, d, *J*=8.8 Hz, *H*3′), 3.75 (3H, s, *Me*).

1-[(5-Bromopyridin-2-yl)methylamino]pyridinium iodide (7c). Reaction time, 2 h. Pale yellow solid (3.51 g, 90%, methanol), mp 184–186°C; [Found: C, 33.49; H, 2.98; N, 10.49. $C_{11}H_{11}BrIN_3$ requires C, 33.73; H, 2.82; N, 10.75%];

R_f (10% triethylamine/ethanol) 0.15; ν_{max}(KBr) 3030, 3002, 1613, 1576, 1465, 1368, 1301, 1133 cm^{-1}; δ_H (300 MHz. DMSO-d6) 9.35 (2H, dd, *J*=7.0, 1.5 Hz, *H*2(6)), 8.80 (1H, tt, *J*=7.7, 1.5 Hz, *H*4), 8.34 (2H, dd, *J*=7.7, 7.0 Hz, *H*3(5)), 8.23 (1H, d, *J*=2.6 Hz, *H*6′), 8.08 (1H, dd, *J*=9.1, 2.6 Hz, *H*4′), 7.16 (1H, d, *J*=9.1 Hz, *H*3′), 3.74 (3H, s, *Me*).

1-[(5-Iodopyridin-2-yl)methylamino]pyridinium iodide (7d). Reaction time, 3 h. Pale yellow needles (3.00 g, 95%, methanol/water), mp 211–214°C; [Found: C, 30.32; H, 2.47; N, 9.40. $C_{11}H_{11}I_2N_3$ requires C, 30.09; H, 2.52; N, 9.57%]; R_f (10% triethylamine/ethanol) 0.15; ν_{max}(KBr) 3038, 3002, 1614, 1570, 1464, 1304 cm^{-1}; δ_H (300 MHz. DMSO-d6) 9.35 (2H, dd, *J*=6.6, 1.1 Hz, *H*2(6)), 8.79 (1H, tt, *J*=7.8, 1.1 Hz, *H*4), 8.36–8.30 (3H, m, *H*3(5), *H*6′), 8.18 (1H, dd, *J*=8.8, 2.2 Hz, *H*4′), 7.05 (1H, d, *J*=8.8 Hz, *H*3′), 3.72 (3H, s, *Me*).

1-[(3, 5-Dichloropyridin-2-yl)methylamino]pyridinium iodide (7e). Reaction time, 4 h. Pale yellow solid (2.51 g, 66%, methanol/ethyl acetate), mp 195–197°C; [Found: C, 34.37; H, 2.49; N, 10.80. $C_{11}H_{10}Cl_2IN_3$ requires C, 34.68; H, 2.65, N, 11.03%]; R_f (10% triethylamine/ethanol) 0.15; ν_{max}(KBr) 3430, 2992, 1478, 1438, 1412, 1378 cm^{-1}; δ_H (300 MHz. DMSO-d6) 9.36 (2H, d *J*=6.6 Hz, *H*2(6)), 8.75 (1H, t, *J*=7.6 Hz, *H*4), 8.52 (1H, d, *J*=2.0 Hz, *H*6′), 8.40 (1H, d, *J*=2.0 Hz, *H*4′), 8.26 (2H, dd, *J*=7.6, 6.6 Hz, *H*3(5)), 3.64 (3H, s, *Me*).

1-(*n*-Butylpyridin-2-yl amino)pyridinium bromide (7f). White solid (0.71 g, 23%, ethanol), mp 99–100°C; [Found: C, 54.46; H, 6.13; N, 13.55. $C_{14}H_{18}BrN_3$ requires C, 54.56; H, 5.89; N, 13.63%]; R_f (10% triethylamine/ethanol) 0.15; ν_{max}(KBr) 3438, 3107, 2958, 2939, 1618, 1284 cm^{-1}; δ_H (300 MHz. DMSO-d6) 9.38 (2H, dd, *J*=6.6, 1.5 Hz, *H*2(6)), 8.83 (1H, tt, *J*=7.7, 1.5 Hz, *H*4), 8.36 (2H, dd, *J*=7.7, 6.6 Hz, *H*3(5)), 8.11 (1H, dd, *J*=5.1, 1.6 Hz, *H*6′), 7.85 (1H, ddd, *J*=8.8, 7.3, 1.6 Hz, *H*4′), 7.14 (1H, d, *J*=8.8 Hz, *H*3′), 7.07 (1H, dd, *J*=7.3, 5.1 Hz, *H*5′), 4.13 (2H, t, *J*=7.1 Hz, N-CH_2), 1.52–1.30 (4H, m, CH_2CH_2Me), 0.88 (3H, t, *J*=7.1 Hz, *Me*).

1-[*n*Butyl-(5-chloropyridin-2-yl)amino]pyridinium bromide (7g). White solid (2.12 g, 62%, ethanol), mp 199–201°C; [Found: C, 48.99; H, 4.88; N, 12.51. $C_{14}H_{17}ClBrN_3$ requires C, 49.07; H, 5.00; N, 12.26%]; R_f (10% triethylamine/ethanol) 0.15; ν_{max}(KBr) 3084, 2994, 2892, 1624, 1574, 1284, 872 cm^{-1}; δ_H (300 MHz. DMSO-d6) 9.37 (2H, dd, *J*=6.8, 1.3 Hz, *H*2(6)), 8.84 (1H, tt, *J*=7.8, 1.3 Hz, *H*4), 8.36 (2H, dd, *J*=7.8, 6.8 Hz, *H*3(5)), 8.18 (1H, d, *J*=2.6 Hz, *H*6′), 7.95 (1H, dd, *J*=9.0, 2.6 Hz, *H*4′), 7.18 (1H, d, *J*=9.0 Hz, *H*3′), 4.12 (2H, t, *J*=7.0 Hz, N-CH_2), 1.54–1.31 (4H, m, CH_2CH_2Me), 0.88 (3H, t, *J*=7.1 Hz, *Me*).

1-[(5-Bromopyridin-2-yl)*n*-butylamino]pyridinium bromide (7h). White solid (2.90 g, 75%, ethanol), mp 245–246°C; [Found: C, 43.46; H, 4.48; N, 10.98. $C_{14}H_{17}Br_2N_3$ requires C, 43.44; H, 4.43; N, 10.85%]; R_f (10% triethylamine/ethanol) 0.15; ν_{max} (KBr) 3415, 2988, 2962, 1614, 1364, 1221, 998 cm^{-1}; δ_H (300 MHz. DMSO-d6) 9.39 (2H, d, *J*=4.9 Hz, *H*2(6)), 8.84 (1H, t, *J*=7.7 Hz, *H*4), 8.37 (2H, bt, *J*=7.7 Hz, *H*3(5)), 8.24 (1H, d, *J*=2.6 Hz, *H*6′), 8.05 (1H, dd, *J*=8.8, 2.6 Hz, *H*4′), 7.15 (1H, d, *J*=8.8 Hz, *H*3′), 4.12 (2H, t, *J*=7.3 Hz, N-CH_2), 1.47–1.35 (4H, m, CH_2CH_2Me), 0.87 (3H, t, *J*=7.3 Hz, *Me*).

1-[*n*-Butyl(5-iodopyridin-2-yl)amino]pyridinium bromide (7i). White solid (2.68 g, 62%, ethanol), mp>300°C; [Found: C, 38.60; H, 3.75; N, 9.61. $C_{14}H_{17}BrIN_3$ requires C, 38.63; H, 3.65; N, 9.68%]; R_f (10% triethylamine/ethanol) 0.16; ν_{max}(KBr) 3424, 2988, 2930, 1614, 1572, 1270 cm^{-1}; δ_H (300 MHz. DMSO-d6) 9.34 (2H, d, *J*=5.9 Hz, *H*2(6)), 8.82 (1H, t, *J*=7.8 Hz, *H*4), 8.34 (3H, m, *H*3(5), *H*6′), 8.13 (1H, dd, *J*=9.0, 2.0 Hz, *H*4′), 7.00 (1H, d, *J*=9.0 Hz, *H*3′), 4.09 (2H, t, *J*=7.0 Hz, N-CH_2), 1.58–1.36 (4H, m, CH_2CH_2Me), 0.87 (3H, t, *J*=7.1 Hz, *Me*).

1-[Benzyl(pyridin-2-yl)amino]pyridinium bromide (7j). Reaction time, 48 h. White solid (2.67 g, 78%, ethanol), mp 107–109°C; [Found: C, 60.01; H, 4.70; N, 12.20. $C_{17}H_{16}BrN_3$ requires C, 59.81; H, 4.73; N, 12.32%]; R_f (10% triethylamine/ethanol) 0.17; ν_{max}(KBr) 3429, 3033, 1582, 1469, 1269, 786 cm^{-1}; δ_H (300 MHz. DMSO-d6) 9.36 (2H, dd, *J*=6.7, 1.3 Hz, *H*2(6)), 8.71 (1H, tt, *J*=7.8, 1.3 Hz, *H*4), 8.23 (2H, dd, *J*=7.8, 6.7 Hz, *H*3(5)), 8.17 (1H, dd, *J*=4.9, 1.8 Hz, *H*6′), 7.90 (1H, ddd, *J*=8.6, 7.1, 1.8 Hz, *H*4′), 7.41–7.37 (2H, m, *H*-Ph), 7.35–7.29 (3H, m, *H*-Ph), 7.27(1H, d, *J*=8.6 Hz, *H*3′), 7.14 (1H, dd, *J*=7.1, 4.9 Hz, *H*5′), 5.41 (2H, s, CH_2-N).

1-[Benzyl(5-chloropyridin-2-yl)amino]pyridinium bromide (7k). Reaction time, 48 h. White solid (2.48 g, 66%, ethanol), mp 143–145°C; [Found: C, 54.04; H, 3.97; N, 10.89. $C_{17}H_{15}ClBrN_3$ requires C, 54.21; H, 4.01; N, 11.16%]; R_f (10% triethylamine/ethanol) 0.17; ν_{max}(KBr) 3414, 3005, 2951, 1619, 1469, 1004 cm^{-1}; δ_H (300 MHz. CD_3OD) 9.13 (2H, d, *J*=6.6 Hz, *H*2(6)), 8.69 (1H, t, *J*=7.6 Hz, *H*4), 8.18–8.13 (3H, m, *H*3(5), *H*6′), 8.90 (1H, dd, *J*=8.8, 2.6 Hz, *H*4′), 7.41–7.37 (2H, m, *H*-Ph), 7.37–7.30 (3H, m, *H*-Ph), 7.27(1H, d, *J*=8.8 Hz, *H*3′), 5.36 (2H, s, CH_2-N).

1-[Benzyl(5-bromopyridin-2-yl)amino]pyridinium bromide (7l). Reaction time, 24 h. White solid (3.79 g, 90%, ethanol), mp 185–187°C; [Found: C, 48.50; H, 3.70; N, 10.09. $C_{17}H_{15}Br_2N_3$ requires C, 48.49; H, 3.59; N, 9.98%]; R_f (10% triethylamine/ethanol) 0.17; ν_{max}(KBr) 3440, 3005, 2937, 1618, 1461, 708 cm^{-1}; δ_H (300 MHz. CD_3OD) 9.33 (2H, d, *J*=5.5 Hz, *H*2(6)), 8.72 (1H, t, *J*=7.7 Hz, *H*4), 8.31 (1H, d, *J*=2.2 Hz, *H*6′), 8.25 (2H, bt, *J*=7.0 Hz, *H*3(5)), 8.12 (1H, dd, *J*=8.8, 2.2 Hz, *H*4′), 7.39–7.36 (2H, m, *H*-Ph), 7.34–7.29 (3H, m, *H*-Ph), 7.26 (1H, d, *J*=8.8 Hz, *H*3′), 5.39 (2H, s, CH_2-N).

1-[Benzyl(3, 5-dichloropyridin-2-yl)amino]pyridinium bromide (7m). This compound appeared as a hygroscopic solid, which was used in the next step without further purification. Reaction time, 48 h. (2.13 g, 52%), R_f (10% triethylamine/ethanol) 0.17; ν_{max} (KBr) 3472, 3006, 1581, 1470, 1280, 707 cm^{-1}; δ_H (300 MHz. CD_3OD) 9.29 (2H, d, *J*=6.6 Hz, *H*2(6)), 8.68 (1H, t, *J*=7.7 Hz, *H*4), 8.44 (1H, d, *J*=2.2, *H*6′), 8.18–8.13 (3H, m, *H*3(5), *H*4′), 7.49–7.46 (2H, m, *H*-Ph), 7.31–7.29 (3H, m, *H*-Ph), 5.23 (2H, s, CH_2-N).

1-[Benzyl(3, 5-dibromopyridin-2-yl)amino]pyridinium bromide (7n). Reaction time, 48 h. White solid (3.55 g, 71%, methanol/ethyl acetate), mp 124–126°C; [Found: C, 40.80; H, 2.59; N, 8.71. $C_{17}H_{14}Br_3N_3$ requires C, 41.06; H, 2.84; N, 8.45%]; R_f (10% triethylamine/ethanol) 0.15; ν_{max} (KBr) 3020, 1668, 1612, 1421, 1365, 1046 cm^{-1}; δ_H (300 MHz. CD_3OD) 9.24 (2H, d, *J*=5.9 Hz, *H*2(6)), 8.62 (1H, t, *J*=7.7 Hz, *H*4), 8.59 (1H, d, *J*=1.8 Hz, *H*6′), 8.48 (1H, d, *J*=1.8 Hz, *H*4′), 8.09 (2H, dd, *J*=7.7, 5.9 Hz, *H*3(5)), 7.47–7.44 (2H, m, *H*-Ph), 7.32–7.30 (3H, m, *H*-Ph), 5.19 (2H, s, CH_2-N).

1-[4-Bromobenzyl(pyridin-2-yl)amino]pyridinium bromide (7p). Reaction time, 48 h. White solid (3.24 g, 77%, ethanol), mp 188–190°C; [Found: C, 48.57; H, 3.60; N, 10.10. $C_{17}H_{15}Br_2N_3$ requires C, 48.49; H, 3.59; N, 9.98%]; R_f (10% triethylamine/ethanol) 0.17; ν_{max} (KBr) 3429, 3033, 1582, 1269, 1172, 786 cm^{-1}; δ_H (300 MHz. DMSO-d6) 9.34 (2H, dd, *J*=6.7, 1.2 Hz, *H*2(6)), 8.76 (1H, bt, *J*=7.8 Hz, *H*4), 8.29 (2H, dd, *J*=7.8, 6.7 Hz, *H*3(5)), 8.19 (1H, dd, *J*=5.0, 1.9 Hz, *H*6′), 7.91 (1H, ddd, *J*=8.4, 7.4, 1.9 Hz, *H*4′), 7.55 (2H, d, *J*=8.4 Hz, *H*-Ph), 7.39 (2H, d, *J*=8.4 Hz, *H*-Ph), 7.21 (1H, d, *J*=8.4 Hz, *H*3′), 7.16 (2H, dd, *J*=7.4, 5.0 Hz, *H*5′), 5.40 (2H, s, CH_2-N).

1-[4-Methylbenzyl(pyridin-2-yl)amino]pyridinium bromide (7q). Reaction time, 96 h. White solid (3.20 g, 90%, ethanol), mp 192–194°C; [Found: C, 60.58; H, 4,79; N, 11.56. $C_{18}H_{18}BrN_3$ requires C, 60.83; H, 5.09; N, 11.83%]; R_f (10% triethylamine/ethanol) 0.18; ν_{max}(KBr) 3383, 3012, 2985, 1582, 1226, 780 cm^{-1}; δ_H (300 MHz. DMSO-d6) 9.29 (2H, dd, *J*=6.8, 1.3 Hz, *H*2(6)), 8.70 (1H, tt, *J*=7.9, 1.3 Hz, *H*4), 8.22 (2H, dd, *J*=7.9, 6.8 Hz, *H*3(5)), 8.16 (1H, dd, *J*=5.1, 1.8 Hz, *H*6′), 7.89 (1H, ddd, *J*=8.4, 7.2, 1.8 Hz, *H*4′), 7.27–7.21 (3H, m, *H*3′, *H*-Ph), 7.13 (1H, dd, *J*=7.2, 5.1 Hz, *H*5′), 7.11 (2H, d, *J*=7.7 Hz, *H*-Ph), 5.34 (2H, s, CH_2-N), 2.23 (3H, s, *Me*).

1-[4-Nitrobenzyl(pyridin-2-yl)amino]pyridinium bromide (7r). Reaction time, 48 h. White solid (2.09 g, 54%, ethanol), mp 185–187°C; [Found: C, 52.53; H, 4.03; N, 14.20. $C_{17}H_{15}BrN_4O_2$ requires C, 52.73; H, 3.90; N, 14.47%]; R_f (10% triethylamine/ethanol) 0.19; ν_{max} (KBr) 3355, 3026, 2951, 1595, 1425, 786 cm^{-1}; δ_H (300 MHz. DMSO-d6) 9.42 (2H, dd, *J*=6.8, 1.4 Hz, *H*2(6)), 8.80 (1H, tt, *J*=7.8, 1.4 Hz, *H*4), 8.32 (2H, dd, *J*=7.8, 6.8 Hz, *H*3(5)), 8.22–8.19 (3H, m, *H*6′, *H*-Ph), 7.89 (1H, ddd, *J*=8.5, 7.3, 1.7 Hz, *H*4′), 7.78 (2H, d, *J*=8.4 Hz, *H*-Ph), 7.17 (1H, dd, *J*=7.3, 5.0 Hz, *H*5′), 7.09 (1H, d, *J*=8.5 Hz, *H*3′), 5.59 (2H, s, CH_2-N).

1-[2-Hydroxyethyl(pyridyn-2-yl)amino]pyridinium bromide (7s). This compound appeared as a mixture with the regioisomer **23**. Separation by fractional crystallization (ethanol) provides the pure compound. Reaction time, 216 h. White solid (0.80 g, 27%, ethanol), mp 100–102°C; [Found: C, 48.40; H, 4.96; N, 14.27. $C_{12}H_{14}BrN_3O$ requires C, 48.67; H, 4.76; N, 14.19%]; R_f (10% triethylamine/ethanol) 0.17; ν_{max}(KBr) 3345, 3323, 3049, 2953, 1583, 1047, 885 cm^{-1}; δ_H (300 MHz. DMSO-d6) 9.36 (2H, dd, *J*=6.6, 1.5 Hz, *H*2(6)), 8.81 (1H, tt, *J*=7.9, 1.5 Hz, *H*4), 8.33 (2H, dd, *J*=7.9, 6.6 Hz, *H*3(5)), 8.09 (1H, dd, *J*=5.5, 1.8 Hz, *H*6′), 7.83 (1H, ddd, *J*=8.6, 7.1, 1.8 Hz, *H*4′), 7.09 (1H, d, *J*=8.6 Hz, *H*3′), 7.05 (1H, dd, *J*=7.1, 5.5 Hz, *H*5′), 4.95 (1H, t, *J*=5.1 Hz, O*H*), 4.23 (2H, t, *J*=5.1 Hz, CH_2-N), 3.68 (2H, q, *J*=5.1 Hz, CH_2-OH).

1-[1-(2-Hydroxyethyl)-1*H*-pyridin-2-ylideneamino]pyridinium bromide (23). White plates (0.27 g, 9%, ethanol), mp 168–170°C; [Found: C, 48.42; H, 4.96; N, 14.20. $C_{12}H_{14}BrN_3O$ requires C, 48.67; H, 4.76; N, 14.19%]; R_f (10% triethylamine/ethanol) 0.17; ν_{max}(KBr) 3323, 3293, 3059, 1639, 1550, 1071, 763 cm^{-1}; δ_H (300 MHz. DMSO-d6) 8.86 (2H, d, *J*=5.9 Hz, *H*2(6)), 8.44 (1H, t, *J*=7.7 Hz, *H*4), 8.13 (2H, dd, *J*=7.7, 5.9 Hz, *H*3(5)), 7.80 (1H, dd, *J*=6.5, 1.4 Hz, *H*6′), 7.46 (1H, ddd, *J*=9.1, 6.5, 1.4 Hz, *H*4′), 6.43 (1H, bt, *J*=6.5 Hz, *H*5′), 6.05 (1H, d, *J*=9.1 Hz, *H*3′), 4.98 (1H, t, *J*=5.5 Hz, O*H*), 4.20 (2H, t, *J*=5.5 Hz, CH_2-N), 3.84 (2H, q, *J*=5.5 Hz, CH_2-OH).

1-[Benzyl(pyrimidin-2-yl)amino]pyridinium bromide (8a). This compound appeared as a mixture with the regioisomer **19a** and was used in the next step without further purification. Reaction time, 24 h. (2.74 g, 75% total yield, 55% for **8a**), R_f (10% triethylamine/ethanol) 0.15, δ_H (300 MHz. DMSO-d6) 9.31 (2H, dd, *J*=6.9, 1.5 Hz, *H*2(6)), 8.75 (1H, t, *J*=7.7 Hz, *H*4); 8.64 (2H, d, *J*=4.8 Hz, *H*4′ (6′)); 8.26 (2H, dd, *J*=7.7, 6.9 Hz, *H*3(5)); 7.40–7.28 (5H, m, *H*-Ph); 7.22 (1H, t, *J*=4.8 Hz, *H*5′); 5.52 (2H, s, CH_2-N). *Regioisomer **19a*** (25%), R_f (10% triethylamine/ethanol) 0.15, δ_H (300 MHz. DMSO-d6) 8.87 (2H, dd, *J*=7.0, 1.6 Hz, *H*2(6)), 8.55 (1H, d, *J*=5.5 Hz, *H*4′); 8.45 (1H, d, *J*=6.1 Hz, *H*6′); 8.41 (1H, t, *J*=7.7 Hz, *H*4); 8.05 (2H, dd, *J*=7.7, 7.0 Hz, *H*3(5)); 7.51–7.40 (5H, m, *H*-Ph); 6.72 (1H, dd, *J*=6.1, 5.5 Hz, *H*5′); 3.39 (2H, s, CH_2-N).

1-[4-Bromobenzyl(pyrimidin-2-yl)amino]pyridinium bromide (8b). This compound appeared as a mixture with the regioisomer **19b** and was used in the next step without further purification. Reaction time, 36 h. (3.04 g, 72% total yield, 48% for **8b**), R_f (10% triethylamine/ethanol) 0.15, δ_H (300 MHz. DMSO-d6) 9.31 (2H, d, *J*=5.5 Hz, *H*2(6)), 8.75 (1H, t, *J*=7.0 Hz, *H*4); 8.62 (2H, d, *J*=4.8 Hz, *H*4′ (6′)); 8.30 (2H, bt, *J*=7.3 Hz, *H*3(5)); 7.52 (2H, d, *J*=8.4 Hz, *H*-Ph); 7.35 (2H, d, *J*=8.4 Hz, *H*-Ph), 7.21 (1H, t, *J*=4.8 Hz, *H*5′); 5.48 (2H, s, CH_2-N). *Regioisomer **19b*** (24%), R_f (10% triethylamine/ethanol) 0.15, δ_H (300 MHz. DMSO-d6) 8.80 (2H, d, *J*=6.5 Hz, *H*2(6)), 8.56 (1H, d, *J*=5.4 Hz, *H*4′); 8.40 (1H, d, *J*=5.6 Hz, *H*6′); 8.33 (1H, t, *J*=7.5 Hz, *H*4); 8.05 (2H, dd, *J*=7.5, 6.5 Hz, *H*3(5)); 7.60 (2H, d, *J*=8.4 Hz, *H*-Ph); 7.45 (2H, d, *J*=8.4 Hz, *H*-Ph); 6.70 (1H, dd, *J*=5.6, 5.4 Hz, *H*5′); 5.29 (2H, s, CH_2-N).

1-[4-Methylbenzyl(pyrimidin-2-yl)amino]pyridinium bromide (8c). This compound appeared as a mixture with the regioisomer **19c** and was used in the next step without further purification. Reaction time, 36 h. (2.61 g, 73% total yield, 49% for **8c**), R_f (10% triethylamine/ethanol) 0.15, δ_H (300 MHz. DMSO-d6) 9.28 (2H, dd, *J*=7.0, 1.4 Hz, *H*2(6)), 8.75 (1H, tt, *J*=7.7, 1.4 Hz, *H*4); 8.63 (2H, d, *J*=5.1 Hz, *H*4′ (6′)); 8.26 (2H, dd, *J*=7.7, 7.0 Hz, *H*3(5)); 7.24–7.20 (3H, m, *H*5′, *H*-Ph); 7.10 (2H, d, *J*=7.7 Hz, *H*-Ph), 5.47 (2H, s, CH_2-N), 2.23 (3H, s, *Me*). *Regioisomer **19c*** (24%), R_f (10% triethylamine/ethanol) 0.15, δ_H (300 MHz. DMSO-d6) 8.80 (2H, d, *J*=6.5 Hz, *H*2(6)), 8.56 (1H, d, *J*=5.4 Hz, *H*4′); 8.41

(1H, d, *J*=5.7 Hz, *H*6′); 8.30 (1H, t, *J*=7.5 Hz, *H*4); 8.07 (2H, dd, *J*=7.5, 6.5 Hz, *H*3(5)); 7.40 (2H, d, *J*=7.7 Hz, *H*-Ph); 7.23 (2H, d, *J*=7.7 Hz, *H*-Ph); 6.69 (1H, dd, *J*=5.7, 5.4 Hz, *H*5′); 5.27 (2H, s, CH_2-N), 2.25 (3H, s, *Me*).

1-[4-Nitrobenzyl(pyrimidin-2-yl)amino]pyridinium bromide (8d). This compound appeared as a mixture with the regioisomer **19d** and was used in the next step without further purification. Reaction time, 12 h. (2.91 g, 75% total yield, 50% for **8d**), R_f (10% triethylamine/ethanol) 0.15, δ_H (300 MHz. DMSO-d6) 9.44 (2H, d, *J*=5.5 Hz, *H*2(6)), 8.81 (1H, t, *J*=7.7 Hz, *H*4); 8.62 (2H, d, *J*=4.8 Hz, *H*4′ (6′)); 8.34 (2H, dd, *J*=7.7, 5.5 Hz, *H*3(5)); 8.19 (2H, d, *J*=8.5 Hz, *H*-Ph); 7.75 (2H, d, *J*=8.5 Hz, *H*-Ph), 7.22 (1H, t, *J*=4.8 Hz, *H*5′); 5.66 (2H, s, CH_2-N). *Regioisomer **19d*** (25%), R_f (10% triethylamine/ethanol) 0.15, δ_H (300 MHz. DMSO-d6) 8.70 (2H, d, *J*=5.8 Hz, *H*2(6)), 8.59 (1H, d, *J*=5.5 Hz, *H*4′); 8.50 (1H, d, *J*=5.9 Hz, *H*6′); 8.38 (1H, t, *J*=7.7 Hz, *H*4); 8.24 (2H, d, *J*=8.5 Hz, *H*-Ph); 8.09 (2H, dd, *J*=7.7, 5.8 Hz, *H*3(5)), 7.70 (1H, d, *J*=8.5 Hz, *H*-Ph); 6.78 (1H, dd, *J*=5.9, 5.5 Hz, *H*5′); 5.45 (2H, s, CH_2-N).

1-[Benzyl(pyrazin-2-yl)amino]pyridinium bromide (9a). This compound appeared as a mixture with the regioisomer **20a** and was used in the next step without further purification. Reaction time, 48 h. (2.54 g, 74% total yield, 49% for **9a**), R_f (10% triethylamine/ethanol) 0.16, δ_H (300 MHz. DMSO-d6) 9.37 (2H, d, *J*=5.8 Hz, *H*2(6)), 8.83 (1H, t, *J*=7.8 Hz, *H*4); 8.78 (1H, s, *H*3′); 8.41 (1H, d, *J*=2.1 Hz, *H*5′); 7.29 (2H, bt, *J*=6.8, *H*3(5)), 8.25 (1H, d, *J*=2.1 Hz, *H*6′), 7.43–7.33 (5H, m, *H*-Ph); 5.52 (2H, s, CH_2-N). *Regioisomer **20a*** (25%), R_f (10% triethylamine/ethanol) 0.16, δ_H (300 MHz. DMSO-d6) 8.88 (2H, d, *J*=6.6 Hz, *H*2(6)), 8.76 (1H, t, *J*=7.7 Hz, *H*4); 8.70 (1H, d, *J*=1.5 Hz, *H*3′); 8.37 (1H, d, *J*=2.6 Hz, *H*5′); 8.28 (2H, dd, *J*=7.7, 6.6 Hz, *H*3(5)); 8.22 (1H, dd, *J*=2.6, 1.5 Hz, *H*6′), 7.53–7.37 (5H, m, *H*-Ph); 5.46 (2H, s, CH_2-N).

1-[4-Bromobenzyl(pyrazin-2-yl)amino]pyridinium bromide (9b). This compound appeared as a mixture with the regioisomer **20b** and was used in the next step without further purification. Reaction time, 36 h. (2.95 g, 70% total yield, 47% for **9b**), R_f (10% triethylamine/ethanol) 0.16, δ_H (300 MHz. DMSO-d6) 9.33 (2H, dd, *J*=6.6, 1.1 Hz, *H*2(6)), 8.76 (1H, tt *J*=7.7, 1.1 Hz, *H*4); 8.70 (1H, d, *J*=1.5 Hz, *H*3′); 8.37 (1H, d, *J*=2.6 Hz, *H*5′); 8.28 (2H, dd, *J*=7.7, 6.6 Hz, *H*3(5)), 8.22 (1H, dd, *J*=2.6, 1.5 Hz, *H*6′), 7.53 (2H, d, *J*=8.4 Hz, *H*-Ph); 7.37 (2H, d, *J*=8.4 Hz, *H*-Ph); 5.46 (2H, s, CH_2-N). *Regioisomer **20b*** (23%), R_f (10% triethylamine/ethanol) 0.16, δ_H (300 MHz. DMSO-d6) 8.80 (2H, d, *J*=6.6 Hz, *H*2(6)), 8.76 (1H, t, *J*=6.9 Hz, *H*4); 8.68 (1H, d, *J*=1.5 Hz, *H*3′); 8.39 (1H, d, *J*=2.6 Hz, *H*5′); 8.30 (2H, dd, *J*=6.9, 6.6 Hz, *H*3(5)); 8.23 (1H, dd, *J*=2.6, 1.5 Hz, *H*6′), 7.68 (2H, d, *J*=8.0 Hz, *H*-Ph); 7.60 (2H, d, *J*=8.0 Hz, *H*-Ph), 5.51 (2H, s, CH_2-N).

1-[4-Methylbenzyl(pyrazin-2-yl)amino]pyridinium bromide (9c). This compound appeared as a mixture with the regioisomer **20c** and was used in the next step without further purification. Reaction time, 36 h. (2.61 g, 73% total yield, 49% for **9c**), R_f (10% triethylamine/ethanol) 0.16, δ_H (300 MHz. DMSO-d6) 9.30 (2H, d, *J*=6.2 Hz, *H*2(6)), 8.80 (1H, t *J*=6.9 Hz, *H*4); 8.76 (1H, s, *H*3′); 8.37 (1H, d, *J*=2.5 Hz, *H*5′); 8.26 (2H, dd, *J*=6.9, 6.2 Hz, *H*3(5)), 8.22 (1H, d, *J*=2.5 Hz, *H*6′), 7.26 (2H, d, *J*=7.7 Hz, *H*-Ph); 7.11 (2H, d, *J*=7.7 Hz, *H*-Ph); 5.43 (2H, s, CH_2-N), 2.23 (3H, s, *Me*). *Regioisomer **20c*** (24%), R_f (10% triethylamine/ethanol) 0.16, δ_H (300 MHz. DMSO-d6) 8.85 (2H, d, *J*=7.0 Hz, *H*2(6)), 8.80 (1H, t, *J*=6.6 Hz, *H*4); 8.72 (1H, d, *J*=1.5 Hz, *H*3′); 8.39 (1H, d, *J*=2.7 Hz, *H*5′); 8.30 (2H, dd, *J*=7.0, 6.6 Hz, *H*3(5)); 8.23 (1H, dd, *J*=2.7, 1.5 Hz, *H*6′), 7.50 (2H, d, *J*=7.7 Hz, *H*-Ph); 7.26 (2H, d, *J*=7.7 Hz, *H*-Ph), 5.45 (2H, s, CH_2-N), 2.30 (3H, s, *Me*).

1-[4-Nitrobenzyl(pyrazin-2-yl)aminolpyridinium bromide (9d). This compound appeared as a mixture with the regioisomer **20d** and was used in the next step without further purification. Reaction time, 36 h. (2.91 g, 75% total yield, 50% for **9d**), R_f (10% triethylamine/ethanol) 0.16, δ_H (300 MHz. DMSO-d6) 9.53 (2H, d, *J*=5.5 Hz, *H*2(6)), 8.83 (1H, t *J*=7.9 Hz, *H*4); 8.64 (1H, d, *J*=1.5 Hz, *H*3′); 8.39 (1H, d, *J*=2.7 Hz, *H*5′); 8.36 (2H, dd, *J*=7.9, 5.5 Hz, *H*3(5)), 8.25 (1H, dd, *J*=2.7, 1.5 Hz, *H*6′), 8.20 (2H, d, *J*=8.8 Hz, *H*-Ph); 7.82 (2H, d, *J*=8.8 Hz, *H*-Ph); 5.74 (2H, s, CH_2-N). *Regioisomer **20d*** (25%), R_f (10% triethylamine/ethanol) 0.16, δ_H (300 MHz. DMSO-d6) 8.80 (2H, d, *J*=5.7 Hz, *H*2(6)), 8.69 (1H, t, *J*=8.0 Hz, *H*4); 8.64 (1H, d, *J*=1.5 Hz, *H*3′); 8.39 (1H, d, *J*=2.7 Hz, *H*5′); 8.35 (2H, dd, *J*=8.0, 5.7 Hz, *H*3(5)); 8.28 (2H, d, *J*=8.8 Hz, *H*-Ph); 8.20 (1H, dd, *J*=2.7, 1.5 Hz, *H*6′), 7.85 (2H, d, *J*=8.8 Hz, *H*-Ph), 6.15 (2H, s, CH_2-N).

1-[Benzooxazol-2-yl-(4-methyl-benzyl)amino]pyridinium bromide (15). Reaction time, 144 h. White solid (2.65 g, 67%, ethanol), mp 108–115°C; [Found: C, 60.70; H, 4.34; N, 10.37. $C_{20}H_{18}BrN_3O$ requires C, 60.62; H, 4.58; N, 10.60%]; R_f (10% triethylamine/ethanol) 0.17; ν_{max}(KBr) 3295, 3050, 1540, 1071, 927, 760 cm^{-1}; δ_H (300 MHz. DMSO-d6) 8.50 (2H, d, *J*=5.5 Hz, *H*2(6)), 8.85 (1H, t, *J*=7.9 Hz, *H*4), 8.36 (2H, dd, *J*=7.9, 5.5 Hz, *H*3(5)), 7.65 (1H, d, *J*=7.7 Hz, *H*4′), 7.52 (1H, d, *J*=7.3 Hz, *H*7′), 7.40–7.20 (2H, m, *H*5′, *H*6′), 7.31 (2H, d, *J*=8.1 Hz, *H*-Ph), 7.15 (2H, d, *J*=8.1 Hz, *H*-Ph), 5.46 (2H, s, CH_2-N), 2.25 (3H, s, *Me*).

1-[Benzothiazol-2-yl-(4-methyl-benzyl)amino]pyridinium bromide (16). Reaction time, 144 h. White solid (3.05 g, 74%, ethanol), mp 198–200°C; [Found: C, 57.93; H, 4.44; N, 10.38. $C_{20}H_{18}BrN_3S$ requires C, 58.26; H, 4.40; N, 10.19%]; R_f (10% triethylamine/ethanol) 0.17; ν_{max}(KBr), 3049, 2995, 1610, 1540, 1071, 760 cm^{-1}; δ_H (300 MHz. DMSO-d6) 9.60 (2H, d, *J*=5.7 Hz, *H*2(6)), 8.85 (1H, t, *J*=7.8 Hz, *H*4), 8.38 (2H, dd, *J*=7.8, 5.7 Hz, *H*3(5)), 8.02 (1H, d, *J*=8.1 Hz, *H*4′), 7.58 (1H, d, *J*=8.1 Hz, *H*7′), 7.41–7.38 (1H, m, *H*5′ or *H*6′), 7.39 (2H, d, *J*=7.9 Hz, *H*-Ph), 7.32–7.28 (1H, m, *H*5′ or *H*6′), 7.19 (2H, d, *J*=7.9 Hz, *H*-Ph), 5.45 (2H, s, CH_2-N), 2.28 (3H, s, *Me*).

Reduction of substituted *N*-alkyl *N*-(2′-pyridyl)-pyridinium salts

Method A: A solution of the corresponding pyridinium salt (1 mmol) in glacial acetic acid (15 mL) and zinc dust

(10 mmol) was stirred at room temperature for 5 h. When almost all the zinc had disappeared, another portion of zinc (10 mmol) was added and the mixture was kept stirring for 24 h more. The resulting suspension was passed through a cellite column, and eluted with acetic acid (2×2 mL). The eluate was evaporated in vacuo and the product was purified by chromatography on silica gel (ethyl acetate/hexane), crystallized and identified.

(5-Bromo-pyridin-2-yl) methyl-amine (10c). White solid (0.17 g, 91%, hexane), mp 67–70°C; [Found: C, 38.20; H, 4.05; N, 15.11. $C_6H_7BrN_2$ requires C, 38.53; H, 3.77; N, 14.98%]; R_f (50% ethyl acetate/hexane) 0.60; ν_{max}(KBr), 3260, 3090, 1598, 1530, 1380 cm^{-1}; δ_H (300 MHz. DMSO-d6) 8.00 (1H, d, *J*=3.5 Hz, *H*6), 7.47 (1H, dd, *J*=8.9, 3.5 Hz, *H*4), 6.67 (1H, bs, N-*H*), 6.41 (1H, d, *J*=8.9 Hz, *H*3), 2.72 (3H, d, *J*=4.8 Hz, *Me*).

Method B: Platinum on charcoal (5%) (75 mg) was suspended into a solution of the pyridinium salts (0.31 mmol) in CH_3CN (3 mL) and cooled in an ice bath. Formic acid (98%, 0.5 mL), and then triethylamine (4.5 mL) in the same solvent (2.5 mL) were added dropwise. The reaction mixture was stirred at 0°C for 1 h and at room temperature for a further 4 h. The resulting suspension was filtered through Celite, the filtrate evaporated and the residue dissolved in water, made basic with solid potassium carbonate and extracted with ethyl acetate (3×15 mL). The combined organic phases were dried over $MgSO_4$, filtered and evaporated to dryness. The residue was purified by column chromatography on silica gel (ethyl acetate/hexane). The corresponding 2-aminoheterocycle was purified by crystallization and identified.

(5-Iodo-pyridin-2-yl) methyl-amine (10d). White solid (45 mg, 62%, hexane), mp 94–95°C; [Found: C, 30.50; H, 3.05; N, 12.11. $C_6H_7IN_2$ requires C, 30.79; H, 3.01; N, 11.97%]; R_f (50% ethyl acetate/hexane) 0.60; ν_{max}(KBr), 3256, 1594, 1524, 1452, 1430, 1378, 1162 cm^{-1}; δ_H (300 MHz. DMSO-d6) 8.10 (1H, d, *J*=2.4 Hz, *H*6), 7.56 (1H, dd, *J*=8.8, 2.4 Hz, *H*4), 6.67 (1H, bs, N-*H*), 6.33 (1H, d, *J*=8.8 Hz, *H*3), 2.70 (3H, d, *J*=4.8 Hz, *Me*).

***n*-Butyl(5-chloropyridin-2-yl)amine (10g).** White solid (55 mg, 96%, hexane), mp 53–54°C; [Found: C, 58.75; H, 7.37; N, 14.98. $C_9H_{13}ClN_2$ requires C, 58.54; H, 7.10; N, 15.17%]; R_f (50% ethyl acetate/hexane) 0.60; ν_{max}(KBr), 3260, 2962, 2932, 1600, 1478, 1448 cm^{-1}; δ_H (300 MHz. $CDCl_3$) 8.03 (1H, d, *J*=2.6 Hz, *H*6), 7.37 (1H, dd, *J*=9.0, 2.6 Hz, *H*4), 6.33 (1H, d, *J*=9.0 Hz, *H*3), 4.51 (1H, d, *J*=5.7 Hz, N-*H*), 3.24 (2H, dt, *J*=7.1, 5.7 Hz, C*H*$_2$-N), 1.61 (2H, q, *J*=7.1 Hz, C*H*$_2$–CH_2N), 1.44 (2H, sx, *J*=7.1 Hz, C*H*$_2$–Me), 0.97 (3H, t, *J*=7.1 Hz, *Me*).

***n*-Butyl(5-bromopyridin-2-yl)amine (10h).** White solid (66 mg, 93%, hexane), mp 51–52°C; [Found: C, 47.02; H, 5.87; N, 12.46. $C_9H_{13}BrN_2$ requires C, 47.18; H, 5.87; N, 12.46%]; R_f (50% ethyl acetate/hexane) 0.60; ν_{max}(KBr), 3257, 2958, 2930, 1592, 1446, 1287 cm^{-1}; δ_H (300 MHz. $CDCl_3$) 8.08 (1H, d, *J*=2.2 Hz, *H*6), 7.46 (1H, dd, *J*=8.8, 2.2 Hz, *H*4), 6.28 (1H, d, *J*=8.8 Hz, *H*3), 3.22 (2H, t, *J*=7.3 Hz, C*H*$_2$-N), 1.59 (2H, q, *J*=7.3 Hz, C*H*$_2$–CH_2N), 1.41 (2H, sx, *J*=7.3 Hz, C*H*$_2$–Me), 0.95 (3H, t, *J*=7.3 Hz, *Me*).

***n*-Butyl(5-iodopyridin-2-yl)amine (10i).** White solid (58 mg, 68%, hexane), mp 55–56°C; [Found: C, 38.93; H, 4.77; N, 9.99. $C_9H_{13}IN_2$ requires C, 39.15; H, 4.75; N, 10.15%]; R_f (50% ethyl acetate/hexane) 0.60; ν_{max}(KBr), 3417, 3250, 1593, 1446, 1154, 812 cm^{-1}; δ_H (300 MHz. $CDCl_3$) 8.20 (1H, d, *J*=2.4 Hz, *H*6), 7.59 (1H, dd, *J*=8.8, 2.4 Hz, *H*4), 6.22 (1H, d, *J*=8.8 Hz, *H*3), 4.52 (1H, bs, N-*H*), 3.21 (2H, t, *J*=7.3 Hz, C*H*$_2$-N), 1.43 (2H, q, *J*=7.3 Hz, C*H*$_2$–CH_2N), 1.40 (2H, sx, *J*=7.3 Hz, C*H*$_2$–Me), 0.94 (3H, t, *J*=7.1 Hz, *Me*).

Benzyl(5-bromopyridin-2-yl)amine (10l). White solid (67 mg, 82%, hexane), mp 120–122°C; [Found: C, 54.78; H, 4.43; N, 10.88. $C_{12}H_{11}BrN_2$ requires C, 54.77; H, 4.21; N, 10.65%]; R_f (50% ethyl acetate/hexane) 0.60; ν_{max} (KBr), 3223, 1604, 1578, 1452, 1392, 1143 cm^{-1}; δ_H (300 MHz. $CDCl_3$) 8.13 (1H, d, *J*=2.6 Hz, *H*6), 7.46 (1H, dd, *J*=8.8, 2.6 Hz, *H*4), 7.34–7.27 (5H, m, *H*-Ph), 6.29 (1H, d, *J*=8.8 Hz, *H*3), 4.49 (1H, bs, N-*H*), 4.48 (2H, d, *J*=5.7 Hz, C*H*$_2$-N).

(4-Aminobenzyl)pyridin-2-yl-amine (10r). White solid (59 mg, 95%, hexane), mp 85–87°C; [Found: C, 72.65; H, 6.39; N, 21.20. $C_{12}H_{13}N_3$ requires C, 72.34; H, 6.58; N, 21.09%]; R_f (50% ethyl acetate/hexane) 0.60; ν_{max}(KBr) 3402, 3332, 3243, 3016, 1608, 1513, 1069, 822 cm^{-1}; δ_H (300 MHz. DMSO-d6) 7.94 (1H, dd, *J*=4.8, 1.8 Hz, *H*6), 7.32 (1H, ddd, *J*=8.5, 7.0, 1.8 Hz, *H*4), 6.98 (2H, d, *J*=8.5 Hz, *H*-Ph), 6.72 (1H, t, *J*=5.8 Hz, N-*H*), 6.49 (2H, d, *J*=8.5 Hz, *H*-Ph), 6.46–6.42 (2H, m, *H*3, *H*5), 4.91 (2H, s, N*H*$_2$), 4.24 (2H, d, *J*=5.8 Hz, C*H*$_2$-N), *m*/*z* (EI) 199 (31, M^+), 121 (6), 106 (100), 93 (16), 78 (11), 51 (4).

(4-Bromobenzyl)pyrazin-2-yl-amine (12b). White solid (65 g, 79%, hexane), mp 113–115°C; [Found: C, 50.30; H, 3.61; N, 16.20. $C_{11}H_{10}BrN_3$ requires C, 50.19; H, 3.83; N, 15.95%]; R_f (ethyl acetate) 0.70; ν_{max}(KBr), 3246, 3003, 1583, 1325, 1200, 1004 cm^{-1}; δ_H (300 MHz. DMSO-d6) 7.94 (1H, d, *J*=1.5 Hz, *H*3), 7.88 (1H, dd, *J*=2.7, 1.5 Hz, *H*5), 7.64 (1H, d, *J*=2.7 Hz, *H*6), 7.60 (1H, t, *J*=5.8 Hz, N-*H*), 7.48 (2H, d, *J*=8.4 Hz, *H*-Ph), 7.25 (2H, d, *J*=8.4 Hz, *H*-Ph), 4.42 (2H, d, *J*=5.8 Hz, C*H*$_2$-N), *m*/*z* (EI) 263, 265 (37, 36,M^+), 184 (54), 169 (100).

(4-Methylbenzyl)pyrazyn-2-yl-amine (12c). White solid (34 mg, 55%, hexane), mp 78–80°C; [Found: C, 72.10; H, 6.70; N, 21.08. $C_{12}H_{13}N_3$ requires C, 72.32; H, 6.58; N, 21.10%]; R_f (ethyl acetate) 0.70; ν_{max}(KBr), 3230, 2995, 1583, 1331, 1050, 828 cm^{-1}; δ_H (300 MHz. DMSO-d6) 7.92 (1H, d, *J*=1.5 Hz, *H*3), 7.88 (1H, dd, *J*=2.9, 1.5 Hz, *H*6), 7.62 (1H, d, *J*=2.9 Hz, *H*5), 7.50 (1H, t, *J*=5.8 Hz, N-*H*), 7.18 (2H, d, *J*=7.7 Hz, *H*-Ph), 7.09 (2H, d, *J*=7.7 Hz, *H*-Ph), 4.39 (2H, d, *J*=5.8 Hz, C*H*$_2$-N), 2.24 (2H, s, *Me*). *m*/*z* (EI) 199 (19, M^+), 184 (6), 105 (100), 77 (23), 52 (8).

Benzooxazol-2-yl-(4-methyl-benzyl)-amine (17). White solid (69 mg, 93%, hexane), mp 148–150°C; [Found: C, 75.90; H, 6.00; N, 11.08. $C_{15}H_{14}N_2O$ requires C, 75.61; H, 5.92; N, 11.76%]; R_f (ethyl acetate) 0.70; ν_{max}(KBr), 3430,

2980, 1616, 1481, 1050, 927 cm^{-1}; δ_H (300 MHz. DMSO-d6) 8.40 (1H, t, *J*=6.4 Hz, N*H*), 7.31 (1H, bd, *J*=7.5 Hz, *H*4), 7.24 (2H, d, *J*=8.1 Hz, *H*-Ph), 7.21 (1H, bd, *J*=7.7 Hz, *H*7), 7.12 (2H, d, *J*=8.1 Hz, *H*-Ph), 7.10–7.07 (1H, m, *H*5 or *H*6), 6.98–6.94 (1H, m, *H*5 or *H*6), 4.44 (2H, d, *J*=6.4 Hz, CH_2-N), 2.25 (3H, s, *Me*).

Benzothiazol-2-yl-(4-methyl-benzyl)-amine (18). White solid (76 mg, 96%, hexane), mp 184–186°C; [Found: C, 71.02; H, 5.50; N, 11.20. $C_{15}H_{14}N_2S$ requires C, 70.83; H, 5.55; N, 11.01%]; R_f (ethyl acetate) 0.70; ν_{max}(KBr), 3330, 2995, 1565, 1413, 1331, 1050 cm^{-1}; δ_H (300 MHz. DMSO-d6) 8.43 (1H, t, *J*=5.7 Hz, N*H*), 7.64 (1H, dd, *J*=7.9, 1.3 Hz, *H*4), 7.35 (1H, dd, *J*=8.1, 1.1 Hz, *H*7), 7.24 (2H, d, *J*=8.1 Hz, *H*-Ph), 7.19–7.17 (1H, m, *H*5 or *H*6), 7.13 (2H, d, *J*=8.1 Hz, *H*-Ph), 7.00–6.97 (1H, m, *H*5 or *H*6), 4.51 (2H, d, *J*=5.7 Hz, CH_2-N), 2.26 (3H, s, *Me*).

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