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Synthesis of Amidines and Attempted Synthesis of Imidazoazines by Reactions of Lithiated β-Aminoazines with Nitriles

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Dedicated to Charles Rees on his retirement from the Hoffman Chair at Imperial College.

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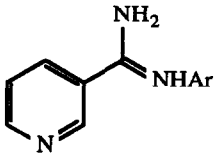
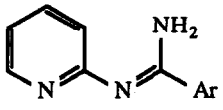
Abstract: *Deprotonation of 3-aminopyridine, followed by reaction of aromatic nitriles, gives* N-*(3-pyridyl)-benzamidines, and other β-aminoazines (pyridines, quinolines, pyrazines, pyrimidines) react similarly. Attempts to cyclise the amidines to, for example, 2-aryl-1*H*-imidazo[4,5-*b*]pyridines (5) met with limited success.*

Although a number of *N*-aryl derivatives of nicotinamidine (**1**) have been described,[1] as have *N*-(2-pyridyl)benzamidines (**2**),[2] the isomeric *N*-(3-pyridyl)benzamidines (**3**) and *N*-(4-pyridyl)benzamidines (**4**) have not. The omission in the case of the 3-pyridyl isomers (**3**) is surprising, in view of the relationship of the compounds to nicotinic acid, and the general interest in the biological activity of amidines. Besides their intrinsic interest, the amidines (**3**) might also be used to synthesise imidazopyridines (**5**), also of interest as deazapurines.



(1)



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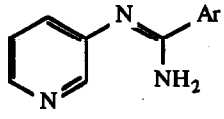

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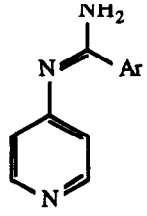

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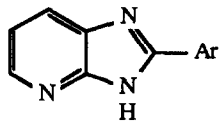
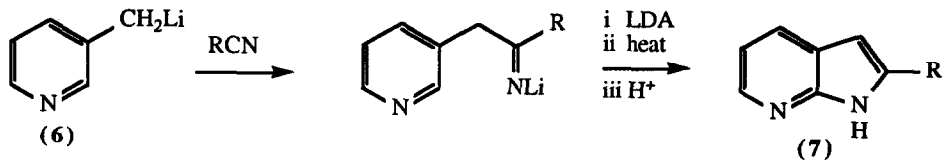


(5)

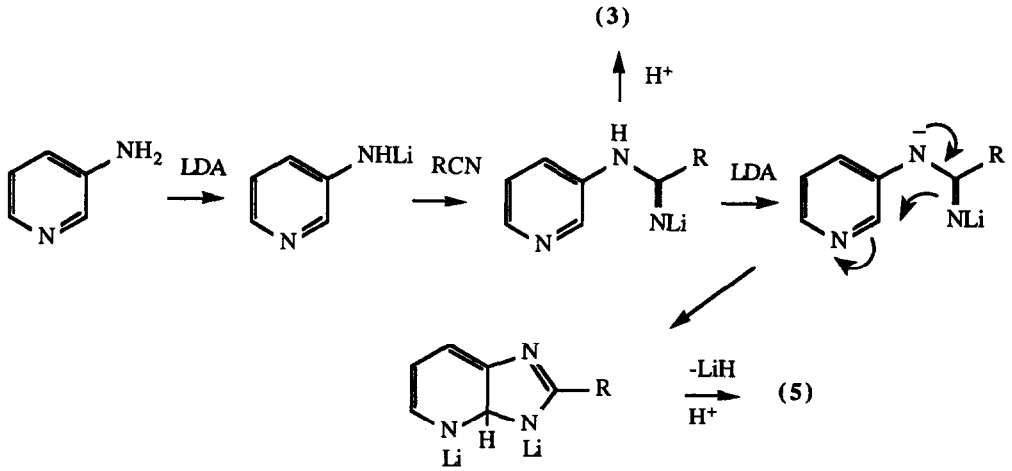
We have reported that the reaction of 3-(lithiomethyl)pyridine (**6**) with nitriles, followed by reaction with additional base, results in cyclisation to give pyrrolopyridines (**7**), as shown in Scheme 1.[3]



(6) (7)

Scheme 1

We envisaged that 3-aminopyridine might be used for analogous reactions, leading to the amidines (**3**) and/or the imidazopyridines (**5**), Scheme 2.

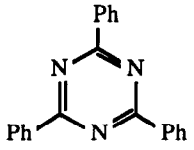


Scheme 2

Similar reactions might then be applied to the synthesis of amidines and fused imidazoles from other β-aminoazines.

Initial experiments with 3-aminopyridine and benzonitrile, using conditions similar to those used for the syntheses of 2-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine from 3-methylpyridine[3] were discouraging, yielding no

2-phenylimidazo[4,5-*b*]pyridine (**5**, Ar = Ph), only poor yields of *N*-(3-pyridyl)benzamidine (**3**, Ar = Ph), and small amounts of products including benzamide (presumably arising from hydrolysis of the amidine) and 2,4,6-triphenyl-1,3,5-triazine (**8**) (a known product of reactions of benzonitrile with strong bases).[4] These results are summarised in Table 1. Several variations in the conditions resulted in little improvement (see Table 1) and activation of the nitrile by aluminium trichloride[2] or boron trifluoride etherate was ineffective. However, with a solvent system comprising dimethylsulfoxide (DMSO) in THF, the yield of the amidine (**4**, Ar = Ph) rose to 77%. Although other syntheses of amidines by the reaction of metal amides with nitriles have been reported[5] (contrary to some recent statements[6]) the conditions required are evidently critical.



(**8**)

Table 1

Reactions of lithiated 3-aminopyridine with benzonitrile[a]

Solvent	Initial proportion of LDA (molar equiv.)	Second proportion of LDA (molar equiv.)	Temp. (°C)	Time (h)	Yield of amidine (3) R = Ph (%)	Other products (%)
THF	1	1	ambient	3	30	
THF	1.7	1.7	ambient	15	0	(TPT) (trace)
THF	1.7	1	46	4	0	(TPT) (trace)
THF	1.7	2	14	2	*b*	*b*
hexa-metapol:[a]	1	1	ambient	17	25	–
THF (1:3)	1[c]	1[d]	ambient	3.5	34	benzamide (22)
DMSO:THF	1	1	ambient	3	up to 63	
(1:10)	1	1	ambient	17-48	up to 77	

[a] Equimolar proportions of 3-aminopyridine and benzonitrile.

[b] Starting materials recovered.

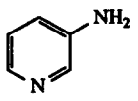
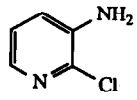
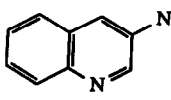
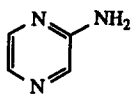
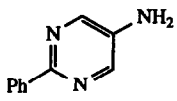
[c] Hexamethylphosphoric triamide.

[d] Potassium bis(trimethylsilyl)amide.

The LDA/DMSO/THF system was applied to the synthesis of amidines from 3-aminopyridine, 3-amino-2-chloropyridine, 3-aminoquinoline, 2-aminopyrazine, and 5-amino-2-phenylpyrimidine and benzonitriles. The results are summarised in Table 2. These reactions were not optimised, but it is clear from these results that the reaction works well for aromatic nitriles bearing electron-withdrawing substituents, but is less useful with, for example, 4-methoxybenzonitrile.

Table 2

Preparation of amidines

Aminoazine	Nitrile	Temp. of addition (°C)	Temp. (°C) and time (h) of reaction	Product	Yield (%)
	4-ClC_6H_4CN	- 40	- 20 → 0 (1) r.t. (2)	(**3**), Ar = 4-ClC_6H_4	68
	4-NCC_6H_4CN	- 40	r.t. (48)	(**3**), Ar = 4-NCC_6H_4	90
	4-$CH_3OC_6H_4CN$	- 40	- 20 (1.25) r.t. (15)	(**3**), Ar = 4-$CH_3OC_6H_4$	30[a]
	PhCN	- 40	r.t. (48)	(**9**), Ar = Ph	57[b]
	4-ClC_6H_4Cl	- 40	r.t. (48)	(**9**), Ar = 4-ClC_6H_4	51
	4-$CH_3OC_6H_4CN$	- 40	r.t. (48)	*c*	*c*
	PhCN	- 20	r.t. (17)	(**10**), Ar = Ph	52
	4-ClC_6H_4CN	- 40	r.t. (38)	(**10**), Ar = 4-ClC_6H_4	80
	4-$CH_3OC_6H_4CN$	- 40	r.t. (38)	(**10**), Ar = 4-$CH_3OC_6H_4$	45
	PhCN	- 20	r.t. (17)	(**11**), Ar = Ph	41
	4-ClC_6H_4CN	- 20	r.t. (17)	(**11**), Ar = 4-ClC_6H_4	51
	4-$CH_3OC_6H_4CN$	- 20	r.t. (17)	(**11**), Ar = 4-$CH_3OC_6H_4$	15
	PhCN	- 40	r.t. (19) + 50 (4)	(**12**)	50[d]

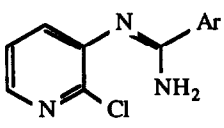
[a] 3-Aminopyridine (37%) recovered.

[b] 3-Aminopyridine (45%) recovered.

[c] None isolated.

[d] In this case, a better yield (79%) was obtained using THF as the solvent.

The amidines were susceptible to hydrolysis, and their tautomerism in solution resulted in broadening of their ^1H n.m.r. spectra. In the case of the amidine from 2-aminopyrazine and 4-chlorobenzonitrile, good crystals were obtained, and X-ray crystallography revealed that the amidine was in the form of the tautomer shown (**11**, Ar = 4-ClC_6H_4). The molecular structure is represented in the Figure and bond lengths and angles are listed in Table 3. One noteworthy feature of this structure is the proximity of N(1), H(1b) and N(3), which is consistent with hydrogen bonding. Hydrogen bonding was also suggested by the n.m.r. spectra of the *N*-pyrazinylbenzamidines, which showed signals for one or both of the NH protons at very low field.



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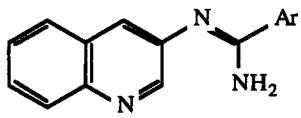

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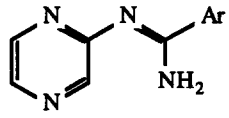

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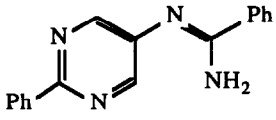

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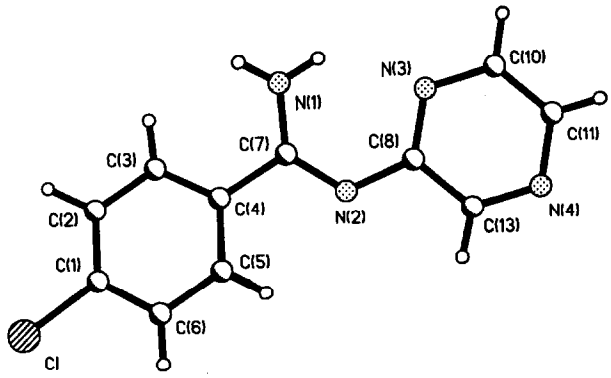
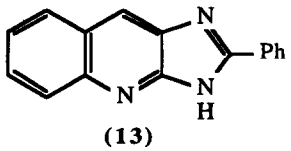


Figure. Molecular structure of **11** (Ar = 4-ClC_6H_4), showing the numbering scheme used

All attempts to obtain 2-phenylimidazo[4,5-*b*]pyridine (**5**, R = Ph) by cyclisation of the amidine (**3**, R = Ph), either *in situ*, or in a separate step, failed. Even the amidine (**9**, Ar = Ph) from 3-amino-2-chloropyridine gave the imidazopyridine (**3**, R = Ph) in only 7% yield on treatment with LDA. A low yield (18%) of the imidazopyridine (**5**, R = 4-ClC_6H_4) was also obtained by reaction of 3-aminopyridine with LDA and 4-chlorobenzonitrile, under the conditions described in the experimental section. Cyclisation was also achieved with 3-aminoquinoline, to give 2-phenyl-1*H*-imidazo[4,5-*b*]quinoline (**13**), an example of a rare ring system,[7] in 31% yield. The imidazoquinoline (**13**) was accompanied by a dimeric product (27%), for which we suggest the structure (**14**).



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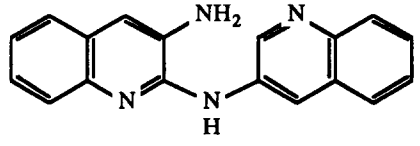

(14)

Experimental

For general directions, see ref. 3. 3-Aminopyridine, 3-aminoquinoline and 2-aminopyrazine were commercial materials and were dried and stored over molecular sieves. Solutions of lithium diisopropylamide (LDA) were prepared from diisopropylamine and butyllithium as described in ref. 3. 5-Amino-2-phenylpyrimidine was prepared by literature procedures[8] (CAUTION[9]).

***N*-(3-Pyridyl)benzamidine (3, R = Ph)** To a stirred solution of LDA (50 mmol) in THF (20 ml) plus DMSO (2 ml) at - 40°C was added 3-aminopyridine (2.8 g, 3.0 mmol) in THF (2-3 ml). The resulting suspension was stirred at 0°C for 30 min. and re-cooled to - 40°C; benzonitrile (3.0 ml, 30 mmol) was added dropwise by syringe. The mixture was stirred at below 0°C for 30 min., and at room temperature for 2 days. Ice-water (70 ml) was added, and the mixture was extracted with ether (5 x 20 ml). The combined extracts were dried and the solvents evaporated. Recrystallisation of the residue from ether-ethanol gave *N*-(3-pyridyl)benzamidine (3.63 g) and flash chromatography of the mother liquor gave a further 0.96 g (total yield 77%), m.p. 179.5-180° , δ (DMSO-d_6) 5.5 (2H, br s; NH_2) 6.2 (2H, br s) *ca* 6.4 (3H, 2 x br s), 7.0 (2H, br s), 7.2 (2H, br m), ν_{max} 3463, 3404, 3155 cm^{-1}. Found: M^+ at *m/z* 197.0957. $C_{12}H_{11}N_3$ requires 197.0953.

The procedure for the other preparations was similar, with variation in conditions as shown in Table 2. Spectroscopic and analytical data follow.

4-Chloro-*N*-(3-pyridyl)benzamidine (3, R = 4-ClC_6H_4), m.p. 162°C, δ (DMSO-d_6) 5.6 (2H, brs; NH_2), 6.5 (2H, br s), 6.65 (2H, d, J 7.5 Hz; 2,6-H), 7.2 (2H, d, J 7.5 Hz; 3,5-H), 7.5 (2H, br s). Found: $(M + 1)^+$ at *m/z* 231.0559 $C_{10}H_{11}ClN_3$ requires 231.0563.

4-Methoxy-*N*-(3-pyridyl)benzamidine (3, R = 4-$CH_3OC_6H_4$), m.p. 122.5-123.5°, δ (DMSO-d_6) 3.8 (3H, s; OCH_3), 4.9 (2H, br s; NH_2), 6.9 (2H, d, J 6 Hz; 3,5-H), 7.2 (2H, m, 2,6-H), 7.8 (2H, br s), 8.3 (2H, br s). Found: $(M + 1)^+$ at *m/z* 227.1052 $C_{13}H_{14}N_3O$ requires 227.1059.

4-Cyano-*N*-(3-pyridyl)benzamidine (3, R = 4-NCC_6H_4), m.p. 147-8°, δ ($CDCl_3$ + DMSO-d_6), 5.6 (2H, brs; NH_2), 7.1 (2H, brs), 7.5 (2H, d, J 8 Hz; 2,6-H), 7.9 (2H, d, J 8 Hz; 3,5-H), 8.1 (2H, br s), Found: $(M + 1)^+$ at *m/z* 223.0991 $C_{13}H_{11}N_4$ requires 223.0984.

***N*-(2-Chloro-3-pyridyl)benzamidine** (9, Ar = Ph), m.p. δ ($CDCl_3$) 5.0 (2H, brs, NH_2), 7.0 (1H, m; pyridyl, 5-H), 7.2 (1H, m, pyridyl 4-H), 7.4 (3H, m), 7.8 (2H, m, 2,6-H), 7.9 (1H, dd, J 4.5, 1.3 Hz; pyridyl 6-H). Found: $(M + 1)^+$ at *m/z* 232.0663. $C_{12}H_{11}ClN_3$ requires 232.0642.

4-Chloro-*N*-(2-chloro-3-pyridyl)benzamidine (9, Ar = 4-ClC_6H_4), m.p. 168.5-169.5°, δ ($CDCl_3$) 4.9 (2H, brs; NH_2), 7.20 (1H, dd, J 8, 4.5 Hz, pyridyl 5-H), 7.3 (1H, dd, J 8, 1.3 pyridyl 4-H), 7.4 (2H, d, J 8.4 Hz; 2,6-H), 7.8 (2H, d, J 8.4 Hz; 3,5-H), 8.2 (1H, dd, J 4.5, 1.3 Hz; pyridyl 6-H). Found: M^+ at *m/z* 265.0160. $C_{12}H_9Cl_2N_3$ requires 265.0174.

***N*-(Quinolin-3-yl)benzamidine(10**, R = Ph), m.p. 168-9°C δ ($CDCl_3$) 5.0 (2H, br s; NH_2), 7.4 (4H, m), 7.6 (1H, t, J 7.5 Hz; 4-H), 7.65 (1H, s; quinolinyl 4-H), 7.7 (1H, d, J 8 Hz; quinolinyl 5-H), 7.9 (2H, d, J 6.8 Hz; 2,6-H), 8.1 (1H, d, J 8.3 Hz; quinolinyl 8-H), 8.7 (1H, s; quinolinyl 2-H). Found: M^+ at *m/z* 247.1106 $C_{16}H_{13}N_3$ requires 247.1109.

4-Chloro-*N*-(quinolin-3-yl)benzamidine (**10**, R = 4-ClC_6H_4), m.p. 198°C δ ($CDCl_3$) 5.0 (2H, br s; NH_2), 7.45 (2H, d, J 8 Hz; 2.6-H) overlapping 7.45 (1H, t, J 8 Hz, quinolinyl 7-H), 7.6 (1H, s; quinolinyl 4-H), 7.7 (1H, d, J 7.9 Hz; quinolinyl 5-H), 7.8 (2H, d, J 8 Hz; 3,5-H), 8.0 (1H, d, J 8.4 Hz; quinolinyl 8-H), 8.6 (1H, s; quinolinyl 2-H). Found: C, 68.45; H, 4.3; N, 15.0. $C_{16}H_{12}ClN_3$ requires C, 67.9; H, 4.4; N, 14.6%.

4-Methoxy-*N*-(quinolin-3-yl)benzamidine (**10**, Ar = 4-$CH_3OC_6H_4$), m.p. 166-7°C. δ ($CDCl_3$) 3.8 (3H, s; OMe), 5.1 (2H, br s; NH_2), 6.9 (2H, d, J 7.5 Hz; 3,5-H), 7.4 (1H, m; quinolinyl 6 or 7-H), 7.6 (1H, m; quinolinyl 6 or 7-H), 7.7 (2H, d, J 7.5 Hz; 2,6-H), 7.9 (1H, d, J 8.3 Hz; quinolinyl 5-H), 8.0 (1H, d, J 8.3 Hz; quinolinyl 8-H), 8.6 (1H, s; quinolinyl 2-H). Found: C, 73.6; H, 5.1; N, 15.1. $C_{17}H_{15}N_3O$ requires C, 73.6; H, 5.45; N, 15.2%.

***N*-(2-Pyrazinyl)benzamidine** (**11**, Ar = Ph), m.p. 164°C, δ ($CDCl_3$ + DMSO-d_6) 5.5 (1H, very br s; NH), 7.4 (3H, m; ArH), 7.9 (2H, dd, J 7.5, 1.5 Hz; 2,6-H), 8.1 (1H, d, J 2.7 Hz; pyrazinyl H), 8.3 (1H, d, J 2.6 Hz; pyrazinyl H), 8.6 (1H, s; pyrazinyl 6-H), 10.2 (1H, very br s; NH). Found: $[M + 1]^+$ at *m/z* 199.0978. $C_{11}H_{11}N_4$ requires 199.0984.

4-Chloro-*N*-(2-pyrazinyl)benzamidine (**11**, Ar = 4-ClC_6H_4), m.p. 202°C δ ($CDCl_3$) 7.4 (2H, d, J 8.5 Hz; 2,6-H), 7.9 (2H, d, J 8.6 Hz; 3,5-H), 8.1 (1H, d, J 2.8 Hz; pyrazinyl H), 8.2 (1H, dd, J 2.6, 1.4 Hz; pyrazinyl H), 8.5 (1H, d, J 1.2 Hz; pyrazinyl 6-H), 9.7-10.5 (2H, br s, NH_2). Found: M^+ at *m/z* 232.0509. $C_{11}H_9ClN_4$ requires 232.0519.

X-Ray Crystallographic Analysis Data. *Crystal data* $C_{11}H_9N_4Cl$, M = 232.7, orthorhombic, a = 5.683(3), b = 9.798(5), c = 19.027(8) Å U = 1059.5(9) $Å^3$, spacegroup $Pc2_1b$, Z = 4, Dc = 1.459 Mg/m^3, μ (Mo-Kα) = 0.333 mm^{-1}, λ = 0.71073 Å, F(000) = 480, crystal size 0.4 x 0.3 x 0.2 mm. *Data Collection* All data were collected on a Siemens R3m/V diffractometer with Mo-Kα radiation graphite monochromated and using ω-2ϑ scan mode. Three reflections measured every 100 reflections showed no significant change in intensity. The 2ϑ range was 3° - 55° and the index range was $0 \le h \le 7$, $0 \le k \le 12$, $-24 \le l \le 24$. 2944 reflections were collected, of which 1307 were unique (R_{int} = 0.024) and 1212 satisfied the criterion $F > 4.0\sigma(F)$ and were used in the refinement. *Structure Determination and Refinement* The structure was solved by direct methods and refined by full matrix least square routines [quantity minimized $[w(F_o-F_c)^2]$. All non-hydrogen atoms were allowed to vibrate anisotropically. The hydrogen atoms were found from difference maps and their positional parameters refined with fixed isotropic thermal parameters. At convergence R = 0.029 and wR = 0.036 where $w^{-1} = \sigma^2(F) + 0.004F^2$. The values of R and wR for all data were 0.033 and 0.037 respectively. The goodness-of-fit was 1.31; the largest Δ/σ was 0.001 with a data to parameter ratio of 7:1. The final difference maps showed no features greater or less than 0.17 $eÅ^{-3}$. Table 3 lists the fractional atomic coordinates and Table 5 the bond lengths and bond angles respectively. All calculations were performed using the SHELXTL-PLUS program suite.[10] Full crystallographic data are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, UK.

Table 3 Atomic coordinates ($x10^4$) and equivalent isotropic displacement coefficients ($Å^2 \times 10^3$)

	x	y	z	U(eq)
Cl	1418 (1)	5162	5555(1)	42(1)
N(1)	6536(4)	8575(2)	2860(1)	31(1)
N(2)	8380(3)	6399(2)	2810(1)	27(1)
N(3)	9849(4)	7873(2)	1894(1)	33(1)
N(4)	13412(3)	5926(2)	1673(1)	32(1)
C(1)	3003(4)	5817(3)	4840(1)	29(1)
C(2)	2106(4)	6907(3)	4466(1)	32(1)
C(3)	3365(4)	7394(3)	3890(1)	31(1)

C(4)	5489(4)	6793(3)	3688(1)	25(1)
C(5)	6325(4)	5683(3)	4076(1)	31(1)
C(6)	5099(4)	5196(3)	4657(1)	33(1)
C(7)	6890(4)	7291(3)	3074(1)	25(1)
C(8)	9937(4)	6725(2)	2276(1)	26(1)
C(10)	11557(5)	8042(3)	1415(1)	38(1)
C(11)	13331(5)	7106(3)	1308(1)	34(1)
C(13)	11740(4)	5758(3)	2149(1)	30(1)

*Equivalent isotropic U defined as one third of the trace of the orthogonalized U_{ij} tensor

H-Atom coordinates ($x10^4$) and isotropic displacement coefficients ($Å^2 \times 10^3$)

	x	y	z	U(eq)
H(1A)	5845(52)	9169(39)	3120(17)	50
H(1B)	7323(53)	8838(36)	2506(19)	50
H(2)	537(53)	7399(36)	4639(15)	50
H(3)	2670(52)	8179(37)	3655(16)	50
H(5)	7703(55)	5234(37)	3938(15)	50
H(6)	5737(47)	4468(36)	4907(18)	50
H(10)	11490(50)	8901(42)	1146(16)	50
H(11)	14507(55)	7229(35)	1000(17)	50
H(13)	11696(45)	4916(39)	2408(18)	50

Table 4 Bond lengths and bond angles

Bond lengths (Å)			
Cl-C(1)	1.752 (2)	N(1)-C(7)	1.337 (3)
N(2)-C(7)	1.316 (3)	N(2)-C(8)	1.385 (3)
N(3)-C(8)	1.341 (3)	N(3)-C(10)	1.341 (3)
N(4)-C(11)	1.350 (4)	N(4)-C(13)	1.323 (3)
C(1)-C(2)	1.381 (4)	C(1)-C(6)	1.383 (3)
C(2)-C(3)	1.393 (3)	C(3)-C(4)	1.397 (3)
C(4)-C(5)	1.397 (3)	C(4)-C(7)	1.495 (3)
C(5)-C(6)	1.392 (3)	C(8)-C(13)	1.416 (3)
C(10)-C(11)	1.378 (4)		
Bond angles (°)			
C(7)-N(2)-C(8)	122.5(2)	C(8)-N(3)-C(10)	116.4(2)
C(11)-N(4)-C(13)	115.8(2)	Cl-C(1)-C(2)	119.6(2)
Cl-C(1)-C(6)	118.5(2)	C(2)-C(1)-C(6)	121.9(2)
C(1)-C(2)-C(3)	118.8(2)	C(2)-C(3)-C(4)	121.1(2)
C(3)-C(4)-C(5)	118.4(2)	C(3)-C(4)-C(7)	122.5(2)
C(5)-C(4)-C(7)	119.0(2)	C(4)-C(5)-C(6)	121.1(2)
C(1)-C(6)-C(5)	118.7(2)	N(1)-C(7)-N(2)	127.2(2)
N(1)-C(7)-C(4)	117.7(2)	N(2)-C(7)-C(4)	115.1(2)
N(2)-C(8)-N(3)	124.6(2)	N(2)-C(8)-C(13)	115.7(2)
N(3)-C(8)-C(13)	119.7(2)	N(3)-C(10)-C(11)	123.3(3)
N(4)-C(11)-C(10)	121.2(2)	N(4)-C(13)-C(8)	123.6(2)

4-Methoxy-*N*-(2-pyrazinyl)benzamidine (**11**, Ar = 4-$CH_3OC_6H_4$), m.p. 128°C δ ($CDCl_3$) 3.8 (3H, s, OMe), 6.9 (2H, d, J 8.8 Hz; 3,5-H), 7.8 (2H, d, J 8.8 Hz; 2,6-H), 8.0 (1H, d, J 2.7 H; pyrazinyl 3-H), 8.1 (1H, m, pyrazinyl H), 8.5 (1H, s, pyrazinyl 6-H). Found: M^+ at *m/z* 228.1098. $C_{12}H_{12}N_4O$ requires 228.1011.

***N*-(2-Phenylpyrimidin-5-yl)benzamidine** (**12**) m.p. 158-9°C δ ($CDCl_3$) 5.0 (2H, br s; NH_2), 7.45 (6H, m; ArH), 7.8 (2H, d, J 8 Hz; phenyl *o*-H), 8.3 (2H, d, J 8, 2 Hz, 2-phenyl *o*-H), 8.5 (2H, s; pyrimidinyl 4,6-H). Found: $[M + 1]^+$ at *m/z* 275.1273. $C_{17}H_{15}N_4$ requires 275.1297.

2-Phenyl-1*H*-imidazo[4,5-*b*]pyridine (**5**, Ar = Ph) To a stirred solution of LDA (10.3 mmol) in THF (40 ml) at - 40°C was added in three portions a solution of 2-chloro-*N*-(2-pyridyl)benzamidine (1.92 g, 5.15 mmol) in THF (9 ml). After 30 min. the mixture was warmed to room temperature and then heated at 55°C overnight. The mixture was cooled and worked up *via* addition of water (40 ml), ether extraction and gradient elution flash chromatography to give (i) 2-phenyl-1*H*-imidazo[4,5-*b*]pyridine (70 mg, 7%), m.p. *ca.* 282°C

dec. (lit. m.p. 285-286°C[10]), δ ($CDCl_3$ + DMSO-d_6), 7.19 (1H, dd, J 8, 4.9 Hz; 5-H), 7.50 (3H, m; Ph). 7.98 (1H, br s; 4-H), 8.29 (1H, brs, 6-H), 13.1 (0.3 H, s; 3-H of tautomer), 13.5 (0.7H, s; 1-H) and (ii) starting material (160 mg, 13%).

2-(4-Chlorophenyl)-1*H*-imidazo[4,5-*b*]pyridine (**5**, Ar = 4-ClC_6H_4). To a stirred solution of LDA (5 mmol) in THF (20 ml) at 0°C was added a solution of 3-aminopyridine (280 mg, 3 mmol) in THF (3 ml), to give a pale green suspension. After 30 min. 4-chlorobenzonitrile (410 mg, 3 mmol) was added and the mixture was stirred at 0°C for 1 h. A second portion of LDA (5 mmol) in THF (20 ml) was added. The mixture was stirred at 0°C for 15 min. and at 60°C for 6 h. Conventional hydrolysis and work-up followed by flash chromatography (silica, Et_2O) gave 2-(4-chlorophenyl)-1*H*-imidazo[4,5-*b*]pyridine (121 mg, 18%), dec. *ca.* 315°C. δ ($CDCl_3$ + DMSO-d_6) 7.1 (1H, dd, J 7.9, 4.8 Hz; 5-H), 7.5 (2H, d, J 8.6 Hz; ArH), 7.9 (1H, br s; 4-H), 8.2 (2H, d, J 8.6 Hz; ArH), 8.3 (1H, br s; 6-H), 9.7 and 10.5 (total 1H, br; 1-H + 3-H of tautomer). Found: M^+ at *m/z* 229.0403. $C_{12}H_8{}^{35}ClN_3$ requires 229.0407.

2-Phenyl-1*H*-imidazo[4,5-*b*]quinoline (**13**) To a stirred solution of LDA (10 mmol) in THF (20 ml) at -40°C was added 3-aminoquinoline (865 mg, 6 mmol) to give a greenish-yellow solution. After 45 min, benzonitrile (0.60 ml, 6 mmol) was added and the mixture was stirred at <-10°C for 2 h. A second portion of LDA (10 mmol) was added, and the mixture was heated to 50°C and stirred at that temperature for 17 h. Conventional work-up followed by chromatography (silica, Et_2O) gave i) 2-phenyl-1*H*-imidazo[4,5-*b*]quinoline (450 mg, 31%), cream solid, dec. *ca* 290°C, δ ($CDCl_3$ + DMSO-d_6) 7.35-7.6 (8H, m), 7.7-8.05 (1H, m), 8.3 (1H, m), 10.3 (1H, br; 1-H). Found: $[M + 1]^+$ at *m/z* 246.1036. $C_{16}H_{12}N_3$ requires 246.1031, and ii) a deep yellow solid, possibly 3-amino-2-(quinolin-3-ylamino)quinoline (462 mg, 27%), m.p. 235°C, δ ($CDCl_3$ + DMSO-d_6) 6.3-6.6 (3H, br, NH), 7.3-7.5 (7H, m), 7.52 (2H, m), 7.8 (2H, d, J 7.2 Hz). Found: M^+ at *m/z* 286.1218. $C_{18}H_{14}N_4$ requires 286.1210.

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