Preparation of Heteroaryl† Phenylmethanes and a ^{13}C and ^{15}N NMR Spectroscopic Study of their Conjugate Carbanions. Rotational Isomerism and Charge Maps of the Anions and Ranking of the Charge Demands of the Heterocycles

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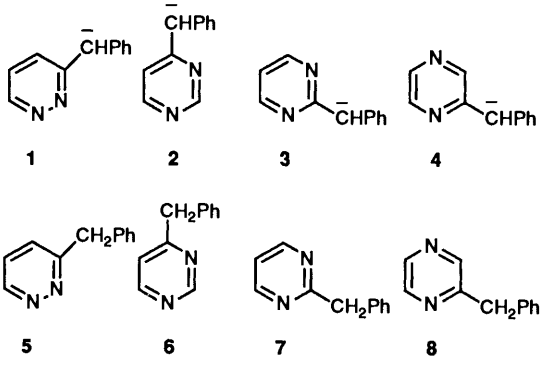
2-Benzylpyridazine, 4-benzylpyrimidine, 2-benzylpyrimidine and 2-benzylpyrazine, (**5–8**), have been prepared in order to study their ^{13}C and ^{15}N spectra and those of their conjugate carbanions (**1–4**). These systems are aza-homologues of the previously reported benzylpyridines and have been considered to evaluate the effect of aza-substitution upon rotational isomerism and charge maps in the anions. Two synthetic approaches have been followed: (i) decarboxylation of α-(heteroaryl)phenylacetic acids, in turn obtained by nucleophilic substitution of phenylacetonitrile anion on the pertinent halogenoazine (or a correspondingly available derivative); (ii) by nucleophilic substitution of benzyl(tributylphosphonium)ylide on the pertinent halogenoazine. The ^{13}C and ^{15}N NMR data for **1–4** indicate that, at room temperature, there is slow rotation about the bond between the carbanionic carbon and the carbon atom of the heterocycle: this generates geometrical isomerism in the anions **1–4**. The NMR data are treated with the π-charge–shift equations (1)–(4) to obtain the local variations of the π-electron density. By evaluating, in anions **1–4**, the fraction of π-charge transferred to the heterocycle from the carbanionic carbon it is possible to obtain the charge demands, c_x of the heterocycles, and thus rank them on the same scale as primary organic functionalities. It is found that the 4-pyrimidyl is the strongest electron-withdrawing heterocyclic residue, comparable with the acetyl group.

In a previous paper[1] we provided ^{13}C NMR spectroscopic evidence for considerable double-bond character in the bond between the heterocycle and the carbanionic carbon of carbanions of heteroaryl phenylmethanes (heteroaryl = 2- or 4-pyridyl or quinolyl). We found that the most favoured configuration of the double bond next to the ring nitrogen was the one with the phenyl ring *cis* to the heteroatom. The preliminary application of a ^{15}N shift–π-charge relationship, in addition to a well established, extended ^{13}C shift–π-charge relationship, provided a charge map in these systems.[2] Such charge maps offered a method for rating the charge demands of the groups next to the carbanionic centre. We defined[2,3] the charge demand of a group X (previously denoted as q_x, but from now on denoted as c_x‡) the fraction of π negative charge withdrawn by the group X. It resulted[2] that the charge demands, c_{py}, of the 2- and 4-pyridyl groups are indeed remarkable, and comparable to that of the methoxycarbonyl group.[3] Charge demands are a measure of the stabilization provided by charge delocalization in the heterocycle; therefore they allow a quantitative ranking of the electron-withdrawing capacities of aza-heterocycles.

Because of the above considerations, we have now extended the previous studies of benzyl carbanions substituted by pyridyl rings to benzyl carbanions substituted by heteroaromatic diazine rings. We report results for the anion **1** of 3-benzylpyridazine **5**, the anion **2** of 4-benzylpyrimidine **6**, the anion **3** of 2-benzylpyrimidine **7** and the anion **4** of 2-benzylpyrazine **8**.



In each case we found evidence for double-bond fixation between the carbanionic carbon and the heterocycle. The *Z* configuration of the double bond, with the phenyl ring facing the heterocyclic nitrogen atom, is strongly preferred. In comparison with pyridine, the effect of further aza-substitution in the diazine rings on the charge demand of the heterocycle is strongly dependent upon the position of substitution.

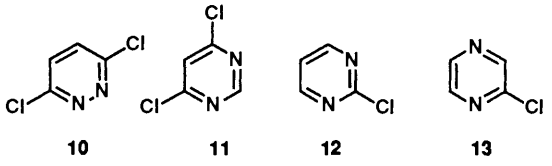
Results

Synthesis of the Benzylazines.—The benzylazines **5–8** are all known in the literature. Although a unified synthetic scheme was desirable, the reported syntheses vary with the type of heterocycle: the reason is often due to overall low yield in the final product. Some preparations are old and full characterization is often missing. For our purposes we needed large quantities (gram scale) of the benzylazines: for this reason we decided to investigate and systematize the synthetic approaches. The most frequently reported synthetic methods, often

† Heteroaryl = 2- and 4-pyrimidyl, pyridazin-3-yl and pyrazin-2-yl.
‡ Indeed, the symbol *q* usually denotes an electron density; accordingly q_c in eqn. (1) is the π-electron density residing on the carbanionic carbon, the previously reported q_{Ph}[3] is the π-electron density (total number of π electrons) residing on a phenyl group, *etc.* Since charge demands are *charges*, (the excess or the deficiency of electrons transferred from the charged site to adjacent substituents X) and not the total number of electrons delocalized or resident on the involved group, it seems no longer appropriate to identify such quantities by the symbol *q*. For this reason, from now on, we propose the symbol *c* for charge demands.

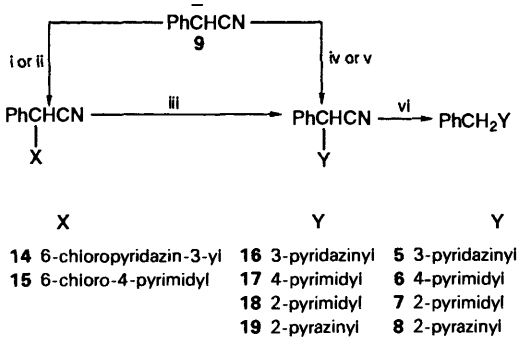
suggested by similar preparations of benzylpyridines, are the following. (*i*) The arylation of methyl azine carbanions,[4] a route originally proposed for the preparation of 2-benzylpyrazine.[5] (*ii*) The hydrolysis, followed by decarboxylation, of α-(heteroaryl)phenylacetonitriles, a route commonly used for pyridine derivatives.[1,6] (*iii*) The alkaline hydrolysis of benzyl pyridyl or quinolyl phosphonium ylides,[7] obtained by nucleophilic substitution of benzyl phosphonium ylides on the corresponding halogenoazines, a route applied to the synthesis of 2-benzylpyrimidine.[4] Method (*i*) is reported to offer low yields of compounds **5**,[4] **6**[4] and **8**.[5] Therefore, we have discarded it for preparative purposes.

The 'nitrile' route (*ii*) to benzylazines requires the action of phenylacetonitrile anion (**9**) on halogenoazines: the commercially available precursors are the chloro- or dichloro-azines **10–13**. This route appeared to us particularly attractive



10 **11** **12** **13**

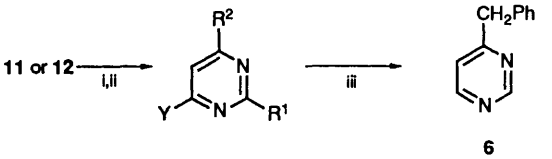
because it could provide us with α-(heteroaryl)phenylacetonitriles, the carbanions of which were interesting to us as part[8] of our investigation of the NMR spectra of carbanions.[1–3] In this case we needed substantial quantities of α-(heteroaryl)-phenylacetonitriles, useful both as substrates to be investigated, and as starting materials for the preparation of **5–8**. To optimize the yields we tried various conditions to generate this anion: sodium amide in toluene, tetrahydrofuran (THF) or *via* the dimsyl anion as a base in dimethyl sulphoxide (DMSO). Scheme 1 summarizes the 'nitrile' synthetic approach. The



Scheme 1 i, 3,6-dichloropyridazine **10**; ii, 4,6-dichloropyrimidine **11**; iii, H_2/Pd–C; iv, 2-chloropyrimidine **12**; v, 2-chloropyrazine **13**; vi, acidic hydrolysis (H_2SO_4 or hydrobromic acid).

action of phenylacetonitrile anion (**9**) on 3,6-dichloropyridazine (**10**) gave the α-(6-chloropyridazin-3-yl)phenylacetonitrile (**14**), on 4,6-dichloropyrimidine (**11**) the α-(6-chloro-4-pyrimidyl)-phenylacetonitrile (**15**) on 2-chloropyrimidine (**12**) the α-(2-pyrimidyl)phenylacetonitrile (**18**) and on 2-chloropyrazine (**13**) the α-pyrazin-2-ylphenylacetonitrile (**19**). The chloro derivatives **14** and **15** were hydrogenolysed with hydrogen on Pd–C in the presence of magnesium oxide[9] to give, in high yields, the nitriles **16** and **17**, respectively. Acidic hydrolysis (H_2SO_4 or hydrobromic acid) and simultaneous decarboxylation of the nitriles **16–19** gave the benzylazines **5–8**, respectively. We found that the hydrogenolysis of the chloro derivatives **14** and **15** should precede the acid-catalysed hydrolysis of the cyano group with simultaneous decarboxylation of the resulting carboxylic acids. This method avoids the formation of carbonyl compounds that originate from the concurrent hydrolysis of the ring chlorine atoms. While the preparation, hydrolysis and subsequent decarboxylation of the α-pyridazin-3-ylphenylacetonitrile (**16**) and of the α-pyrazin-2-ylphenylacetonitrile (**19**) proceeded with acceptable yields, we faced difficulties both in the isolation and in the hydrolyses of the α-(pyrimidyl)-phenyl acetonitriles **17** and **18**. In short, the method offered low yields in the desired products **6** and **7**. To obtain substantial quantities of the pyrimidine derivatives **6** and **7** we turned to method (*iii*) and found that it worked satisfactorily. Since compounds **5** and **8** could be adequately prepared by the 'nitrile' approach, their preparation *via* method (*iii*) was not investigated.

The 'ylide' approach for the preparation of the benzylpyrimidines **6** and **7** is summarized in Scheme 2. The action of



7 $R^1 = CH_2Ph$; $R^2 = Y = H$
20 $R^1 = H$; $R^2 = CH_2Ph$; $Y = Cl$

Scheme 2 *Reagents:* i, $PhCH^-P^+Bu_3$; ii, aq. Na_2CO_3; iii, H_2/Pd–C

benzyl tributylphosphonium ylide (prepared from the corresponding phosphonium chloride and butyllithium in dimethoxyethane) on 2-chloropyrimidine **12**, followed by basic hydrolysis, afforded a complex mixture from which we could isolate the 2-benzylpyrimidine **7** as a 1:1 complex with mercury(II) dichloride. We obtained the free base (32%) by the action of sodium sulphide under basic conditions. Similarly, the action of the same benzyl phosphonium ylide on 4,6-dichloropyrimidine (**11**) followed by basic hydrolysis gave, after chromatography, the 4-benzyl-6-chloropyrimidine **20** in 31% yield: hydrogenolysis with hydrogen on Pd–C, and in the presence of magnesium oxide,[9] afforded 4-benzylpyrimidine (**6**) in 76% yield.

NMR Shift Assignments.—The ^{13}C and ^{15}N NMR shifts of compounds **1–8** are reported in Table 1, relevant coupling constants of the heterocyclic moieties of anions **1–4** are collected in Table 2. To avoid possible ambiguities in NMR data interpretation we discuss the reported assignments in detail.

(a) ^{13}C *Shifts.* ^{13}C shift assignments in the neutral compounds **5–8** have been based on coupling constants[10a] and on known alkyl and aza substituent effects operating in the heterocycles.[11a,b] When ambiguities occur, a complete analysis of the spectrum has been performed and discrimination has been based on multiplicities of patterns and on values of the long range coupling constants (we omit to consider the $^1J_{C,H}$ coupling constants although we take them into account in describing the multiplicities reported later). Compound **5**: 126.61 ppm, C_{para}, double triplet, $^3J_{C,H(ortho)} = 4.3$ Hz; 126.88 ppm, C(4), double quartet, $^3J_{C,H(6)} \approx {}^3J_{C,H(\alpha)} \approx 5$ Hz, to be compared with $^3J_{C(4),H(6)} \approx 5.5$ Hz in pyridine and pyrimidine;[10b] 127.27 ppm, C(5), double broad doublet, $^2J_{C,H(6)} = 6.6$ Hz, to be compared with $^2J_{C(3),H(2)} = 8.5$ Hz and $^2J_{C(3),H(4)} = 0.9$ Hz in pyridine.[10c] Compound **6**: 157.18 ppm, C(6), double double doublet, $^2J_{C,H(5)} = 2.5$ Hz, $^3J_{C,H(2)} = 10.7$ Hz, to be compared with $^2J_{C(4),H(5)} = 1.9$ Hz and $^3J_{C(4),H(2)} = 10.4$ Hz in pyrimidine;[10b,c] 158.27 ppm, C(2), double doublet, $^3J_{C,H(6)} = 10.7$ Hz. Compound **8**: 142.55 ppm, C(5), double triplet, $^2J_{C,H(6)} \approx {}^3J_{C,H(3)} \approx 10.5$ Hz; 144.16 ppm, C(6), double doublet, $^2J_{C,H(5)} = 9.7$ Hz; 144.52 ppm, C(3), double double triplet, $^3J_{C,H(5)} = 9.7$ Hz and $^3J_{C,H(\alpha)} = 4.8$ Hz. In the anions **1–4**, the ^{13}C resonances of carbon atoms *para* to the carbanionic

Table 1 ^{13}C NMR shifts[a] and ^{15}N NMR shifts[b] of benzyldiazines **5–8** and conjugate carbanions **1–4** in DMSO[c]

	Diazine ring positions						Phenyl ring positions					
Compound	1	2	3	4	5	6	*ortho*	*meta*	*para*	*ipso*	CH_2/CH^-	^1J/Hz[d]
5	398.26	394.34	162.52	126.88	127.27	150.14	129.05	128.72	126.61	138.97	41.72	127.7
1	385.02	322.45	157.28	121.71	120.76	133.33	121.27	126.97	112.61	144.10	82.14	147.3
6	287.73	158.27	293.81	168.85	120.77	157.18	128.50	129.05	126.50	137.98	42.99	129.4
2	237.83	157.91	261.14	154.33	112.30	145.53	122.78	126.98	115.34	143.89	87.33	146.6
7	292.55	169.06	292.55	157.37	119.11	157.37	128.90	128.30	126.25	138.42	45.13	128.0
3	259.63[e]	162.52	245.74[e]	154.58[f]	97.70	154.26[f]	120.93	126.35	112.73	144.18	85.95	147.8
8	330.73	156.25	144.52	334.34	142.55	144.16	128.93	128.52	126.40	138.83	40.84	128.1
4	248.80	153.67	143.10	310.92	118.37	142.81	121.09	126.85	113.44	144.00	84.32	145.9

[a] Relative to Me_4Si (0.0 ppm). [b] Relative to liquid NH_3 (0.0 ppm), 380.23 ppm from neat nitromethane. [c] 0.5 mol dm^{-3} solutions. [d] Relative to the benzylic methylene or methine group. [e] Values can be exchanged. [f] Values can be exchanged.

Table 2 C–H Coupling constants (J/Hz) of the heterocyclic portion of anions **1–4**

Compound	Carbon	^1J	^2J	^3J
1	3	—	$J_{C,H(\alpha)} = J_{C,H(4)} = 3$	$J_{C,H(5)} = 6$
	4	158.3	—	$J_{C,H(\alpha)} = J_{C,H(6)} = 5.3$
	5	159.7	$J_{C,H(6)} = 8.1$	—
	6	178.1	$J_{C,H(5)} = 2.2$	$J_{C,H(4)} = 5.5$
	α	147.3	—	$J_{C,H(4)} = J_{C,H(o)} = 4.4$
2	2	184.0	—	$J_{C,H(6)} = 9.8$
	4	—	$J_{C,H(\alpha)} = J_{C,H(5)} = 2.8$	$J_{C,H(6)} = 6.7$; $J_{C,H(2)} = 9.7$
	5	156.2	$J_{C,H(6)} \approx 6.0$	$J_{C,H(\alpha)} \approx 6.0$
	6	165.4	$J_{C,H(5)} = 2.6$	$J_{C,H(2)} = 10.2$
	α	146.6	—	$J_{C,H(o)} = J_{C,H(5)} = 3.5$
3	2	—	—	$J_{C,H(4)} = J_{C,H(6)} = 10.9$
	4	167.4	$J_{C,H(5)} = 3.8$[a]	$J_{C,H(6)} = 5.4$[a]
	5	164.8	$J_{C,H(6)} = J_{C,H(4)} = 7.7$	—
	6	167.4	—	—
	α	147.8	—	—
4	2	—	$J_{C,H(3)} = 3.5$	$J_{C,H(6)} = 10.2$
	3	170.9	—	$J_{C,H(5)} \approx J_{C,H(\alpha)} = 6.6$
	5	177.9	$J_{C,H(6)} = 10.3$	$J_{C,H(3)} = 10.3$
	6	166.8	$J_{C,H(5)} = 10.4$	—
	α	145.9	—	—

[a] Uncertain assignment due to possible interchange of C(4) and C(6) chemical shifts

centre, both in the phenyl and in the heterocyclic rings, are those that are most efficiently shielded; the discrimination between the two rings of resonances present at similar frequencies has been based on signal intensities, and on vicinal and long-range coupling constants. When not straightforward, the following considerations provided unequivocal assignments. Anion **1**: 120.76 ppm, C(5), double doublet, $^2J_{C,H(6)} = 8.1$ Hz (see Table 2); 121.71 ppm, C(4), double triplet, $^3J_{C,H(6)} \approx {}^3J_{C,H(\alpha)} = 5.3$ Hz (see Table 2). Anion **4**: 142.81 ppm, C(6), double doublet, $^2J_{C,H(5)} = 10.4$ Hz (see Table 2); 143.10 ppm, C(3), double triplet, $^3J_{C,H(5)} \approx {}^3J_{C,H(\alpha)} = 6.6$ Hz (see Table 2); 144.00 ppm, C_{ipso}, triplet, $^3J_{C,H(meta)} = 6.8$ Hz. In the case of **3**, the anion of 2-benzylpyrimidine (**7**), the shift assignments to C-4 and C-6 are tentative.

(b) ^{15}N *Shifts*. Shift assignments to the two nitrogen atoms of the pyridazine **5**, of the pyrimidine **6**, and of the pyrazine **8** were based on the fact that alkyl substituents in the *ortho* or *para* positions are known to be more effective in shielding the ^{15}N resonance than *meta* substituents.[12] Also, *para* effects are reported to be usually stronger than *ortho* effects[12] (in the case of compound **6**). For the shift assignments to nitrogen atoms in the anions we assumed the following. In anions **1** (from **5**) and **4** (from **8**) one nitrogen atom is *ortho* and the other is *meta* to the carbanionic centre. By analogy with carbon shifts,[3] we assigned the most shielded resonance to the nitrogen in the *ortho* position with respect to the carbanionic centre. To assign the ^{15}N resonances to the nitrogen atoms 1 and 3 of anion **3** (from **7**) we reasoned as follows. In the anion of 4-benzylpyridine the phenyl group induces, by compression effects,[13] a shielding of *ca.* 9–10 ppm on the carbon atom of the heterocycle *cis* to it.[1] The same phenomenon is likely to occur when the *cis* atom is nitrogen. Indeed, the difference in the shifts of the two nitrogen atoms is of the same order of that reported above for carbon (14 ppm), and therefore we would assign the low-frequency resonance to the nitrogen atom facing (*cis*) the phenyl ring. To assign the ^{15}N resonances to the nitrogen atoms in the anion **2** (from **6**) we considered that the nitrogen atom *para* to the carbanionic centre would undergo the largest shielding, by analogy with values of the ^{15}N shifts of the anions of 2- and 4-benzylpyridine.[14] As expected, when the charge can partition between two *ortho* or an *ortho* and *para* positions (as in **3** and **2**, respectively), the chemical shift variation (shielding) of the *ortho* nitrogen (*ca.* 30 ppm) is much less than in the case where the charge

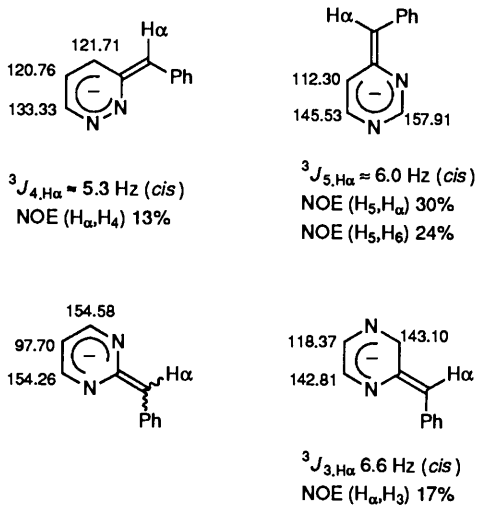


Fig. 1

Table 3 Shielding contributions A_x (ppm) of heteroaryl substituents at C(β) in β-substituted styrenes

Substituent	^{13}C(β) shift	A_X[a]	Ref.
H	113.2	0.00	*b*
Pyridazin-3-yl	124.7	11.5	*c*
2-Pyrimidyl	127.1	13.9	*c*
4-Pyrimidyl	123.7	10.5	*c*
Pyrazinyl	123.7	10.5	*c*

[a] Positive values mean lowfield displacements. [b] H. O. Kalinowski, S. Berger and S. Braun, *Carbon-13 NMR Spectroscopy*, John Wiley & Sons, Chichester, 1988, p. 161. [c] H. P. Erb and T. Bluhm, *Org. Magn. Reson.*, 1980, **14**, 285.

partitions between *ortho* and *meta* positions, as in **1** and **4** (70–80 ppm).

Geometrical Isomerism in the Anions **1–4** *of Benzylazines* **5–8**.—The magnetic non-equivalence, both of C(4) and C(6) and of N(1) and N(3), in the anion **3** (from **7**) provides the most straightforward evidence for geometrical isomerism in this system. Previously, we used,[1] as a discriminating stereochemical probe, the size of the nuclear Overhauser effect (NOE) between the proton bonded to the carbanionic centre and protons bonded to the *ortho* and *ortho'* positions with respect to the carbanionic methine group. The NOE experiment was performed by irradiating the carbanionic proton. We decided to run the same set of experiments on benzyl anions **1**, **2** and **4** and the results are reported in Fig. 1. Also, we previously used[1] the size of the $^3J_{C,H}$ coupling constant between the proton bonded to the carbanionic carbon and the heteroaromatic carbon atom in the allylic-type position as a discriminating probe for assigning the relative stereochemistry of these two atoms. The present case, however, is different from the pyridyl case, because the benzyl group is always bonded to a carbon atom having a nitrogen atom in its *ortho* position. There is therefore only one $^3J_{C,H}$ coupling constant with carbon atoms of the heterocyclic moiety. We have now based our stereochemical assignments on the discriminative *Z* and *E* values of $^3J_{C,H}$ reported[15] for alkenic systems. Both the $^3J_{C,H}$ and NOE data in Fig. 1 for anions **1**, **2** and **4** agree with a *Z* configuration (with the phenyl ring positioned on the same side of the nitrogen atom). Obviously, because of the lack of protons in the *ortho,ortho'* positions with respect to the benzyl residue in anion **3**, no stereochemical assignments can be made about the two different nitrogen atoms on the basis of the above cited stereochemical probes. In the preceding section we made a tentative assignment on the basis of 'compression' effects.

Charge Maps.—To calculate the charge maps of the anions **1–4**, and thus the charge demands c_X of the four azine rings, we used eqns. (1) and (2) for carbon and either eqn. (3) or (4) for nitrogen. Eqn. (1) gives the actual π-electron density on the

$$\delta(^{13}C) = 122.8 + \Sigma A_i - 160(q^{\pi}_C - 1) \quad (1)$$

$$\Delta\delta(^{13}C) = -160\,\Delta q^{\pi}_C \quad (2)$$

$$\Delta\delta(^{15}N) = -626.76\,\Delta q^{\pi}_N \quad (3)$$

$$\Delta\delta(^{15}N) = -366.34\,\Delta q^{\pi}_N \quad (4)$$

carbanionic carbon, while eqn. 2 provides the variation of π-electron density on aromatic and heteroaromatic carbon atoms.[3] Eqn. (1) requires the knowledge of the shielding effects, A_i, exerted on the carbanionic centre by the phenyl group (A_{Ph} = 13 ppm[16]) and by the heterocyclic azine (A_X with X = heterocycle). These last A_X values are collected in Table 3 and have been obtained as the difference of the ^{13}C shift of the β carbon of the β-heteroarylstyrene and the same carbon of styrene itself, following a procedure already used. In fact, we have shown[17] that these systems, in addition to the vinyl systems CH_2=CHX, are good models for obtaining the A_X values.

Eqn. (3) is based on the relationship (5) obtained by plotting Fliszár's[18] ^{15}N π-electron densities calculated in pyridine,

$$\delta(^{15}N) = 347.35 - 626.76\,(q^{\pi}_N - 1) \quad (5)$$

$$\delta(^{15}N) = 345.41 - 366.34\,(q^{\pi}_N - 1) \quad (6)$$

pyrimidine, pyrazine and *sym*-triazine *vs.* the corresponding ^{15}N shifts. We have already used this relationship for charge mapping in the anions of benzylpyridines.[2] The ^{15}N shift of pyridazine does not seem to obey relation (5).* Eqn. (4) is based on the excellent (r = 0.995) relationship (6) obtained by plotting ^{15}N π-electron densities[20] (*ab initio* calculated at the RHF/6-31G+ level) in ten neutral and anionic pyridine derivatives, *vs.* the corresponding ^{15}N shifts. Table 4 reports the variations of the π-electron densities for each *i*th position on going from the neutral to the anion on applying, to the ^{13}C and ^{15}N shifts of Table 1, eqns. (1)–(3) and eqn. (4) as an alternative to eqn. (3). In Table 5 we give the experimental π-electron densities, q, on the carbanionic carbon, on the phenyl group, and on the heterocycle, respectively q_C, q_{Ph} and q_{Het}. Their sum, reported in the 5th column, should approach the total number of 14 π-electrons present in the system. The last column of Table 5 reports the charge demand of heterocycles as c_{Het} = $8 - q_C - q_{Ph}$. Obviously, this value is different from ($q_{Het} - 6$); in fact, to make fruitful comparisons with the previously calculated[3,17] charge demands of electron-withdrawing groups X (X = CN, COR, SO_nR, NO_2, *etc.*), the present c_{Het} must be calculated in a similar manner. Since it has been so far impossible to perform any empirical evaluation of the π-electron densities (q_X) of the above X groups, the c_{Het} values must also be independent of the calculation of the π-electron density (q_{Het}) of the heterocycle.

* In fact, the ^{15}N shift is too low-field in comparison with the shifts of the other heterocyclic azines. We have indications that this is due both to the presence of the N–N bond, instead of the C–N bond of the other azines, and to the low-field displacement caused by the sp^2 electron pairs on the two vicinal nitrogen atoms.[19] Examples of this phenomenon may be traced for ^{13}C shifts of carbon atoms adjacent to alkenic carbanions (*e.g.* vinyllithium, phenyllithium, *etc.*,[11c]).

Table 4 Variations of the local π-electron densities for each *i*th position on going from the neutral benzyldiazines **5–8** to the conjugate anions **1–4**[a]

Compound		Diazine ring positions						Phenyl ring positions			
Neutral	Anion	1	2	3	4	5	6	*ortho*	*meta*	*para*	*ipso*
5	**1**	0.021[b] 0.036[c]	0.115[b] 0.196[c]	0.033	0.032	0.041	0.105	0.049	0.011	0.088	−0.032
6	**2**	0.080[b] 0.136[c]	0.002	0.052[b] 0.089[c]	0.091	0.053	0.073	0.036	0.013	0.070	−0.037
7	**3**	0.052[b] 0.090[c]	0.041	0.075[b] 0.128[c]	0.017	0.134	0.019	0.050	0.012	0.084	−0.036
8	**4**	0.131[b] 0.224[c]	0.016	0.009	0.037[b] 0.064[c]	0.151	0.008	0.049	0.010	0.081	−0.032

[a] Positive values correspond to an increment of π-electron density. [b] Values obtained by using eqn. (3). [c] Values obtained by using eqn. (4).

Table 5 Experimental π-electron densities (q) for conjugate anions **1–4** of benzyldiazines **5–8**, and charge demands (c) of heteroaryl substituents

Compd.	q_{Ph}[a]	q_{Het}[b]	q_C[c]	$q_{Ph} + q_{Het} + q_C$[d]	c_{Het}[e]
1	6.176	6.347[f] 6.443[g]	1.407	13.930[f] 14.026[g]	0.417
2	6.131	6.351[f] 6.444[g]	1.368	13.850[f] 13.943[g]	0.501
3	6.172	6.338[f] 6.429[g]	1.398	13.908[f] 13.999[g]	0.430
4	6.167	6.352[f] 6.472[g]	1.387	13.906[f] 14.026[g]	0.446

[a] π-Electron density resident on the phenyl ring. [b] π-Electron density resident on the diazine ring. [c] π-Electron density resident on the carbanionic carbon. [d] Total π-electron density of the anionic system (to be compared with the theoretical value of 14 π-electrons). [e] Charge demand of the heteroaryl substituent in the benzylic anion. [f] Values obtained by using eqn. (3). [g] Values obtained by using eqn. (4).

Discussion

π-Charge–Shift Relationships and Charge Demands of the Heterocycles.—Chemical shifts depend upon the charge (and thus the electron density) residing on the atom under consideration: the slope (sensitivity) has opposed signs for σ and π-electron density.[21] In eqns. (1) and (2) the ^{13}C shift (or its variation) is forced to depend only upon the π-electron density (or its variation); analogously, in eqns. (3) and (4), the ^{15}N shift variation must depend only upon the variation of the nitrogen π-electron density. To include the σ dependence of the chemical shift into the π term is certainly an oversimplification, and the reported NMR shift treatment may not take account of rigorous theoretical considerations. However, eqns. (1) and (2) have a considerable predictive power,[2,22] account satisfactorily for the variation of the total number of π-electrons in carbonaceous systems,[16] and provide results in general agreement with intuition.

Several π-charge–^{15}N shift relationships have been proposed previously,[12] but eqns. (3) and (4), although based on different calculations, appear to provide a self-consistent charge map picture. The range (80 ppm) and number (n = 4) of ^{15}N shifts treated by relationship (5) are smaller than those (range = 190 ppm, and n = 10) treated by relationship (6). It is worth noting that, despite the very large difference in slopes, relationships (5) and (6) provide very similar values for the intercept: its value of 345 or 347 ppm corresponds to the ^{15}N shift of a trigonal, dicoordinated nitrogen atom bearing an electron pair in an sp^2 orbital, orthogonal to the p orbital occupied by one electron (thus with q^{π}_N = 1). The large difference in slope results from a large difference in the π-electron densities computed by the two approaches. Within the limits of acceptance and reliability we pointed out before, it seems that eqn. (4) provides a better fit; in fact its use in the $\Sigma(q_{Ph} + q_{Het} + q_C)$ affords a value of π-electrons present in the anions **1–4** closer to the theoretical value of 14.

The values of charge demands of heterocycles c_{Het} reported in Table 5 deserve some comment. As stated before, these values are different from $6 - q_{Het}$. This divergence is intrinsic in the definition of $c_{Het} = 8 - q_{Ph} - q_C$ and of $q_{Het} = 6 + \Delta q^{\pi}$. In fact, Δq^{π} depends upon the chosen π-charge–shift relationship. Our target was the comparison of the ability of various substituents to withdraw π negative charge from a carbanionic centre: this is indeed the definition of charge demand. We are aware that the q_{Ph} and q_C values may suffer from the application of approximations, however, within the limits of acceptance and reliability already pointed out, it should be conceded that the c_X values reported here (and previously[2,3]) are affected to the same extent, and will therefore be internally consistent. We believe that a reasonable limit of confidence of the reported c_X values is ±0.015 electrons.

With this perspective in mind, it is important to note that the c_{Het} value of the pyrazinyl, the pyridazin-3-yl and 2-pyrimidyl groups are not very different from the c_{Het} value of the pyridyl residue (c_X = 0.41[3]). This means that, in comparison with the pyridyl ring, the second substitution of a carbon with a nitrogen atom in a *meta* or in the *ortho* positions with respect to the benzylic carbanionic centre, has a small effect. In contrast, the second substitution of a carbon with a nitrogen atom in the *para* position with respect to the carbanionic centre, substantially increases the charge demand: thus, the 4-pyrimidyl ring is the most electron-withdrawing group among the heterocycles considered herein. Indeed, it is as efficient as the acetyl group (c_{COMe} = 0.50[3]).

A similar series of comparisons involves the c_{Ph} value, reported[3] to be 0.268 in the diphenyl methyl carbanion. Substitution of an *ortho* or *para* carbon atom with nitrogen (to obtain the 2- or 4-pyridyl system) increases the c_X value by *ca.* 0.13 electrons. Substitution of a second carbon atom with nitrogen in the *ortho* position (to obtain the 2-pyrimidyl system) is not as efficient as the first substitution. We would ascribe the small increase of $c_{2\text{-pyrimidyl}}$ relative to $c_{2\text{-pyridyl}}$ to the already discussed saturation phenomena.[2,22] Results indicate that the

second substitution of a carbon with a nitrogen atom in the *para* position (to obtain the 4-pyrimidyl group) is less sensitive to saturation effects (increase of $c_{4\text{-pyrimidyl}}$ relative to c_{pyridyl} of 0.09 electrons). The fact that the 4-pyrimidyl group is more electron-withdrawing than the 2-analogue, may be rationalised by considering that, towards nucleophilic substitution with piperidine, the 4-chloropyrimidine is more reactive than the 2-chloro analogue by one order of magnitude.[23] Under the same conditions, 2-chloropyrimidine is more reactive than 2-chloropyridine by six orders of magnitude:[23] this fact is not consistent with the corresponding c_X values reported here.

Geometrical Isomerism in the Azine Benzyl Anions.—The data reported (Table 1 and Scheme 3) clearly indicate the occurrence of geometrical isomerism in benzyl anions **1–4**; only one isomer is present and the *Z* relationship of the phenyl ring in relation to the heterocyclic nitrogen atom is firmly documented, in analogy with the case of benzyl anions α-substituted by pyridine rings.[1] So far, we do not know the reason for this preference. The conditions under which we chose to record the NMR spectra of the anions (excess of base in the form of dimsyl anion) did not permit us to perform high-temperature experiments to investigate the coalescence temperature, at which free rotation would occur around the bond linking the carbanionic and heterocyclic carbon atoms, as the dimsyl anion apparently decomposes around 55–60 °C.[24] In any case, the reported geometrical isomerism is convincing evidence that the relatively strong π-bond order between the carbon atoms of the anion and of the heteroaromatic residue is associated with extensive negative charge delocalization onto the heteroaromatic ring. The geometrical isomerism in systems **1–4** necessarily imposes the sp^2 configuration of the carbanionic carbon. Since the chemical shift and the $^1J_{C,H}$ value of the benzylic carbon of anions **1–4** are comparable with those of other benzyl anions, and in particular of the diphenylmethyl carbanion,[3] this is *a posteriori* evidence that in the other benzyl carbanions exhibiting similar NMR parameters, the carbanionic carbon is also trigonal, despite the missing evidence for geometrical isomerism. Also, it can be noted that the π-electron density, q_C, at the carbanionic carbon in the anions **1–4** is only slightly smaller than in the diphenylmethyl carbanion (q_C = 1.428) (with respect to this last system the Δq_C values for anions **1–4** are 0.021, 0.060, 0.030 and 0.041 electrons, respectively). This is an indication that minute variations of the π-electron density at the carbanionic carbon are sufficient for observing (or not) the isomerism around the bond linking the carbanionic carbon to the heterocycle: thus, q_C is a relatively insensitive probe for predicting the occurrence of geometrical isomerism. As discussed earlier, a better, more sensitive, probe appears to be the charge demand, c_X. So far, we can propose that, to observe room temperature geometrical isomerism in carbanions, at least one substituent with $c_X > 0.40$ should be present (as in carbanions substituted by pyridyl and heterocyclic azine groups); with substituents with $c_X < 0.27$ (as in diphenylmethyl carbanion) no room-temperature isomerism can be detected.

Experimental

^{1}H NMR shifts were recorded on a Varian 90 MHz instrument, using Me_4Si as internal standard. ^{13}C and ^{15}N spectra were recorded at 27 °C on a Varian XL-300 spectrometer, operating at 75.47 and 30.45 MHz, respectively, and using 0.50 mol dm^{-3} solutions in Me_2SO. ^{13}C NMR shifts were measured relative to Me_4Si and ^{15}N NMR shifts were measured relative to aniline, both as external standards. The aniline standard was checked against neat nitromethane and the chemical shifts are reported to liquid NH_3, using the conversion factor of 380.23 ppm for the chemical shift of neat nitromethane. Acquisition parameters for ^{15}N measurements (gated decoupled experiment) were: spectral width 15 000 Hz, 32K data points, pulse delay of 20 s, pulse angle of *ca.* 70° for 30 μs, zero filling (once) and line broadenings of 1–3 Hz, number of transients of 2000–3000. The [$^2H_6$]-Me_2SO solvent provided the internal deuterium lock; anion solutions in Me_2SO (10 mm o.d. tubes) were provided with an internal 5 mm coaxial tube containing neat [$^2H_6$]Me_2SO. Elemental analyses were performed on a Perkin-Elmer 240 instrument by the microanalysis laboratory of our department. M.p.s are uncorrected. Anhydrous solvents (dimethoxyethane, THF, benzene) were prepared by continuous distillation over sodium sand, in the presence of benzophenone and under nitrogen until the blue of sodium ketyl was permanent. Extracts were dried over Na_2SO_4. Anions were prepared following the procedure already described.[16] Coupling constant values, *J*, are given in Hz throughout.

α(6-Chloropyridazin-3-yl)phenylacetonitrile (**14**).—Pure, powdery sodium amide (1.45 g, 37 mmol), was obtained by placing an aliquot of a 50% suspension of sodium amide in toluene in a flask under nitrogen and evaporating the solvent under reduced pressure. The amide was suspended in anhydrous THF (25 cm^3) and, with stirring and under a nitrogen atmosphere, was added dropwise a solution of phenylacetonitrile (4.36 g, 37 mmol) in the same solvent (20 cm^3), maintaining the temperature below 15 °C. After 15 min at room temperature, the reaction mixture was cooled to 0 °C and added dropwise to a solution of 3,6-dichloropyridazine (**10**) (2.79 g, 18.7 mmol) in THF (25 cm^3). After the temperature had returned to ambient, stirring was continued for a further 30 min and the reaction mixture was poured onto ice and neutralised with aqueous NH_4Cl. The mixture was extracted with methylene dichloride (5 × 60 cm^3) and the solvent was removed from the dried extracts to leave the product as a white solid (3.54 g, 15.4 mmol, 82.3%), m.p. 125–126 °C (MeOH) (Found: C, 62.6; H, 3.4; N, 18.1. $C_{12}H_8ClN_3$ requires C, 62.8; H, 3.5; N, 18.3%); $\delta_H(CDCl_3)$ 7.3–7.6 (7 H, m, Ar) and 5.7 (1 H, s, benzylic CH).

α-(6-Chloro-4-pyrimidyl)phenylacetonitrile (**15**).—To a suspension of sodium amide (5 g, 128.2 mmol) in anhydrous THF (20 cm^3), prepared from a 50% suspension in toluene as described for the preparation of **14**, was added a solution of phenylacetonitrile (7.74 g, 66.1 mmol) in the same solvent (30 cm^3), dropwise with stirring, under a nitrogen atmosphere and with the temperature below 15 °C. After 15 min at room temperature, the reaction mixture was cooled to 0 °C and a solution of 4,6-dichloropyrimidine (**11**) (8.91 g, 59.8 mmol) in the same solvent (30 cm^3) was added dropwise; the reaction mixture was then brought to room temperature and stirred for 1 h. After being poured onto ice, 10% hydrochloric acid was added to pH *ca.* 7 and the mixture was extracted with methylene dichloride (3 × 60 cm^3); the solvent was removed from the dried extracts to leave an oil (11 g) which was submitted to flash chromatography (hexane–AcOEt, 8.5:1.5) on silica gel to provide the product (4.06 g, 17.7 mmol, 29.6%), b.p. 160 °C/0.05 mmHg (Found: C, 62.8; H, 3.3; N, 18.2. $C_{12}H_8ClN_3$ requires C, 63.0; H, 3.1; N, 18.4%); $\delta_H(CDCl_3)$ 9.0 (1 H, s, 2-H of the pyrimidyl ring), 7.40 (6 H, m, 5-H of the pyrimidyl ring and protons of the phenyl ring) and 5.28 (1 H, s, benzylic CH).

α-Pyridazin-3-ylphenylacetonitrile (**16**).—A solution of compound **14** (3.54 g, 15.4 mmol) in 95% ethanol (250 cm^3) was added to a suspension of Pd–C (10%) (0.90 g) and magnesium oxide (2 g, 50 mmol) in ethanol–water (1:1 by vol) (40 cm^3), and the mixture was subjected to hydrogenation at room temperature and pressure. After the theoretical volume of hydrogen was consumed (377 cm^3), the mixture was filtered and

evaporated to dryness to afford the product[25] as a yellowish solid (2 g, 10.25 mmol, 66.6%), m.p. 136–137 °C (Found: C, 73.7; H, 4.6; N, 21.4. Calc. for $C_{12}H_9N_3C$, 73.8; H, 4.6; N, 21.5%); δ_H($CDCl_3$, 200 MHz) 9.2 (1 H, dd, $J_{5,6}$ 3.6, $J_{4,6}$ 1.8, 6-H) and 7.6–7.3 (7 H, m, the remaining aromatic protons), 5.7 (1 H, s, benzylic proton).

α-(4-*Pyrimidyl*)*phenylacetonitrile* (**17**).—A solution of α-(6-chloro-4-pyrimidyl)phenylacetonitrile (**15**) (4.06 g, 17.7 mmol) in 95% ethanol (180 cm^3), was added to a suspension of 10% Pd–C (1 g) and magnesium oxide (1.56 g, 39 mmol) in a 1:1 mixture of 95% ethanol–water (50 cm^3). The mixture was subjected to hydrogenation at room temperature and pressure and the reaction was stopped after 426 cm^3 of hydrogen had been consumed. The mixture was filtered, and the solution was concentrated under reduced pressure to 20 cm^3. Diethyl ether was added to obtain the product as a yellowish solid (2.44 g, 12.5 mmol, 71%), m.p. 100–102 °C (EtOH–H_2O, 2:1) (Found: C, 73.7; H, 4.45; N, 21.6. $C_{12}H_9N_3$ requires C, 73.8; H, 4.7; N, 21.5%); δ_H($CDCl_3$) 9.24 (1 H, s, 2-H of the pyrimidyl ring), 8.75 (1 H, d, J_{AB} 7, 6-H), 7.4 (6 H, m, 5-H and phenyl ring protons) and 5.30 (1 H, s, benzylic proton).

α-(2-*Pyrimidyl*)*phenylacetonitrile* (**18**).—To pure, powdery sodium amide (1.55 g, 39.7 mmol), obtained from a 50% suspension in toluene as previously described for the preparation of **14** was rapidly added anhydrous DMSO (39.7 cm^3), with stirring, and under a nitrogen atmosphere. The solution obtained (1 mol dm^{-1} in dimsyl anion) was degassed under reduced pressure from ammonia before being added dropwise to a solution of phenylacetonitrile (4.21 g, 36 mmol) in the same solvent (10 cm^3), maintaining the temperature below 20 °C. A solution of 2-chloropyrimidine (**12**) (2.06 g, 18 mmol) in DMSO (20 cm^3) was then added to the red solution of phenylacetonitrile anion, maintaining the temperature below 25 °C. After being stirred for 15 min, the reaction mixture was poured onto ice, neutralized with 1 mol dm^{-3} hydrochloric acid, and extracted with diethyl ether (5 × 100 cm^3). The extracts were washed with brine and the solvent was removed from the dried extracts to leave an oil (4.05 g). The product was obtained, after two purifications by flash chromatography on silica gel (AcOEt–CH_2Cl_2, 2:1) as a yellowish solid (1 g, 5.12 mmol, 28.5%), m.p. 63–64 °C; after treatment with diisopropyl ether the white compound had m.p. 65 °C (lit.,[26] b.p. 170 °C/2 mmHg; lit.,[27] m.p. 90–91 °C) (Found: C, 73.9; H, 4.55; N, 21.65. $C_{12}H_9N_3$ requires: C, 73.8; H, 4.7; N, 21.5%); δ_H($CDCl_3$) 8.7 (2 H, d, 4-H and 6-H of the pyrimidine ring), 7.2–7.4 (6 H, m, 5-H and phenyl ring protons) and 5.4 (1 H, s, benzylic proton).

α-*Pyrazin*-2-*ylphenylacetonitrile* (**19**).—To a suspension of sodium amide (4.76 g, 122 mmol) in anhydrous THF (35 cm^3), prepared from a 50% suspension in toluene as described for the preparation of **14**, was added a solution of phenylacetonitrile (14.3 g, 122 mmol) in the same solvent (35 cm^3), dropwise, with stirring under a nitrogen atmosphere, with the temperature kept below 20 °C. After 15 min at room temperature, the deep red reaction mixture was cooled to 0 °C and a solution of 2-chloropyrazine (**13**) (7 g, 61 mmol) in the same solvent (20 cm^3) was added dropwise; the reaction mixture was then brought to room temperature and stirred for 2 h. After being poured onto ice, 10% hydrochloric acid was added to pH *ca.* 7 and the mixture was extracted with chloroform (4 × 70 cm^3); the solvent was removed from the dried extracts to leave a residue which, when taken up with diethyl ether (3 cm^3), gave the product[27,28] as a white solid (8.71 g, 44.7 mmol, 73.3%) m.p. 130 °C (lit.,[27] m.p. 132–133 °C) (Found: C, 73.3; H, 4.5; N, 21.2. Calc. for $C_{12}H_9N_3$: C, 73.8; H, 4.7; N, 21.5%); δ_H($CDCl_3$) 8.70 (1 H, s, 3-H), 8.52 (2 H, s, 5-H and 6-H), 7.3–7.6 (5 H, m, phenyl ring protons) and 5.35 (1 H, s, benzylic proton).

3-*Benzylpyridazine* (**5**).—A mixture of 48% hydrobromic acid (40 cm^3) and α-pyridazin-3-ylphenylacetonitrile (**16**) (1.5 g, 7.7 mmol) was heated at 110 °C for 3 h. The mixture was then poured onto ice, neutralized with aqueous ammonia and extracted with methylene dichloride (3 × 60 cm^3). The solvent was removed from the dried extracts to give a red–brown oil which was purified by Kugelrohr distillation (170 °C/0.5 mmHg) to give the product[4] as a white solid m.p. 40–42 °C (0.536 g, 3.15 mmol, 41%) (Found: C, 77.8; H, 5.8; N, 16.7. Calc. for $C_{11}H_{10}N_2$ C, 77.6; H, 5.9; N, 16.5%); δ_H($CDCl_3$) 9.05 (1 H, dd, $J_{5,6}$ 3.7, $J_{4,6}$ 2, 6-H), 7.30 (7 H, m, 4-H, 5-H and phenyl ring protons) and 4.35 (2 H, s, benzylic proton).

4-*Benzylpyrimidine* (**6**).—(a) *By hydrogenolysis of* 4-*benzyl*-6-*chloropyrimidine* (**20**). Butyllithium (28.6 cm^3 of a 1.6 mol dm^{-3} solution in hexane) was slowly added to a stirred suspension of benzyl tributylphosphonium chloride[29] (15.04 g, 45.74 mmol) in anhydrous dimethoxyethane (40 cm^3), under nitrogen, with the temperature kept below −35 °C. The temperature was gradually raised to ambient and the reaction mixture stirred for 1 h before being cooled again to −35 °C and slowly added to a solution of 4,6-dichloropyrimidine (**11**) (3.1 g, 20.8 mmol) in the same solvent (20 cm^3). The temperature was slowly raised to ambient and the reaction mixture was stirred for 12 h. Saturated aqueous Na_2CO_3 (50 cm^3) was then added to the reaction mixture, which was heated to reflux for 5 h. The cooled solution was then extracted with diethyl ether (4 × 100 cm^3), and the solvent was removed from the dried extracts under reduced pressure to give a residue (9.94 g) which, upon flash chromatography (CH_2Cl_2–AcOEt, 2:1) gave practically pure 4-*benzyl*-6-*chloropyrimidine* (**20**) (1.6 g, 7.82 mmol, 38%) as an oil which was used without further purification in the next stage. δ_H($CDCl_3$) 8.9 (1 H, s, 2-H), 7.4–7.2 (5 H, m, phenyl ring protons), 7.1 (1 H, s, 5-H) and 4.1 (2 H, s, CH_2). To a suspension of Pd–C (10%) (0.5 g) in water (20 cm^3) and 95% ethanol (20 cm^3) was added a suspension of magnesium oxide (0.95 g, 23.6 mmol) in ethanol (20 cm^3), containing the oily 4-benzyl-6-chloropyrimidine (**20**) (1.6 g, 7.82 mmol) obtained as describe above. The mixture was hydrogenated at room temperature and ambient pressure (*ca.* 30 min). The mixture was filtered from the catalyst which was then washed with methylene dichloride (10 cm^3); the washings were added to the solution which was concentrated under reduced pressure. The aqueous residue was extracted with diethyl ether (40 cm^3) and the solvent was removed from the dried extracts to leave the practically pure product[4] (1.01 g, 5.94 mmol, 76%) b.p. 90 °C/0.01 mmHg (Found: C, 77.2; H, 5.8; N, 16.6. Calc. for $C_{11}H_{10}N_2$ C, 77.6; H, 5.9; N, 16.5%); δ_H($CDCl_3$) 9.08 (1 H, s, 2-H of the pyrimidine ring), 8.50 (1 H, AB system, d, $J_{5,6}$ 7, 6-H), 7.33–7.15 (5 H, m, phenyl ring protons), 7.04 (1 H, d, 5-H) and 4.05 (2 H, s, CH_2).

(b) via *Nitrile route*. α-(4-Pyrimidyl)phenylacetonitrile (**17**) (1.65 g, 8.5 mmol) in 48% hydrobromic acid (45 cm^3) was heated at 110 °C for 90 min. The reaction mixture was poured onto ice, neutralized with conc. aqueous ammonia and extracted with CH_2Cl_2 (3 × 40 cm^3). The solvent was removed from the dried extracts leaving a residue which was purified by flash chromatography on silica gel (Et_2O–AcOEt–hexane, 4:3:3) to give the product (780 mg, 4.58 mmol, 54%).

2-*Benzylpyrimidine* (**7**).—(a) via *Phosphonium route*. To a stirred suspension of benzyl tributylphosphonium chloride[29] (6.57 g, 20 mmol) in anhydrous dimethoxyethane (40 cm^3), was in hexane, 20 mmol), under nitrogen and maintaining the temperature between −35 °C and −30 °C. After 1 h at the same

temperature 2-chloropyrimidine (**12**) (1.04 g, 9.1 mmol) in dimethoxyethane (10 cm^3) was added. The temperature was gradually raised to ambient and the reaction mixture was further magnetically stirred for 48 h. The new ylide was then hydrolysed by adding aqueous sodium carbonate (0.5 mol dm^{-3}; 40 cm^3) and refluxing the mixture for 3 h. The mixture was then concentrated under reduced pressure, acidified to pH 1 with 10% hydrochloric acid, extracted with diethyl ether (3 × 100 cm^3) and the extracts were discarded. The aqueous solution was then made alkaline with 30% sodium hydroxide and again extracted with diethyl ether (3 × 100 cm^3). The solvent was removed from the dried extracts under reduced pressure to leave a brown oil (2.5 g), which was treated with a solution of mercury(II) chloride (4 g, 14.73 mmol) in ethanol (20 cm^3). The resulting white precipitate (2.1 g) was the adduct of 2-benzylpyrimidine with mercury(II) chloride, m.p. 90 °C (Found: C, 29.8; H, 2.4; N, 6.1. $C_{11}H_{10}HgN_2Cl_2$ requires C, 29.9; H, 2.3; N, 6.3%). A suspension of the adduct in water (10 cm^3) was then treated for 30 min with a solution of $Na_2S{\cdot}9H_2O$ (0.79 g, 3.24 mmol) in water (5 cm^3), in the presence of some sodium carbonate. The mercury(II) sulphide was filtered off and washed with diethyl ether (2 × 20 cm^3); the solution was also extracted with the same solvent (3 × 15 cm^3). The solvent was removed from the dried extracts to leave the practically pure 2-*benzylpyrimidine*[4] (**7**) (0.49 g, 2.88 mmol, 32%), b.p. 110 °C/0.05 mmHg (lit.,[30] b.p. 97–99 °C/2 mmHg) (Found: C, 77.2; H, 5.8; N, 16.6. Calc. for $C_{11}H_{10}N_2$, C, 77.6; H, 5.9; N, 16.5%); $\delta_H(CDCl_3)$ 8.6 (2 H, AB_2 system, d, $J_{4,5}$ 4.56, 4-H and 6-H of the pyrimidine ring), 7.5–7.3 (5 H, m, phenyl ring protons), 7.1 (1 H, t, 5-H) and 4.3 (2 H, s, CH_2).

(b) via *Nitrile route*. α-(2-Pyrimidyl)phenylacetonitrile (**18**) (0.4 g, 2.05 mmol) in 48% hydrobromic acid (5 cm^3) was heated at 60 °C for 4 h; the mixture was poured onto ice, neutralized with conc. aqueous ammonia and extracted with methylene dichloride (3 × 50 cm^3). The dried extracts were evaporated to dryness and the residue was purified by flash chromatography (AcOEt–CH_2Cl_2, 2:1) to give the product (0.2 g, 1.17 mmol, 57%).

2-*Benzylpyrazine* (**8**).—A solution of α-pyrazin-2-ylphenylacetonitrile (**19**) (6 g, 30.7 mmol) in 60% H_2SO_4 (100 cm^3) was heated under reflux for 3 h. The reaction mixture was poured onto ice, neutralized with conc. aqueous ammonia and extracted with chloroform (3 × 60 cm^3). The dried extracts were evaporated to dryness to leave an oil which was purified by distillation to give the product[4,5] (3.34 g, 19.6 mmol, 63.8%), b.p. 150 °C/0.07 mmHg (lit.,[5] b.p. 107–108 °C/1.3 mmHg) (Found: C, 77.6; H, 5.9; N, 16.5. Calc. for $C_{11}H_{10}N_2$ C, 77.8; H, 5.7; N, 16.5%); $\delta_H(CDCl_3)$ 8.55 (2 H, s, 5-H and 6-H), 8.3 (1 H, s, 3-H), 7.4–7.3 (5 H, m, phenyl ring protons) and 4.2 (2 H, s, benzylic proton).

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