Dehydrogenation of 6-Azaquinazoline Derivatives. Formation of Unexpected Quinonediimine Intermediates[1]

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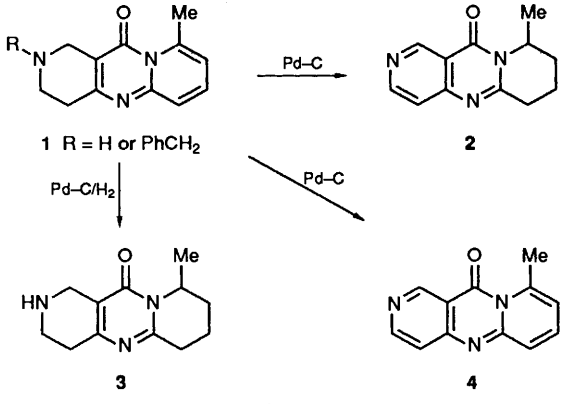
2,6-Disubstituted 5,6,7,8-tetrahydropyrido[4,3-*d*]pyrimidin-4(3*H*)-one (6-azaquinazoline) derivatives **7a–e** were synthesized from *N*-substituted 3-methoxycarbonyl-4-piperidones **5a, b** and amidines **6a–c**. Compounds **7a–d** and the debenzylated derivatives **8a–c** underwent dehydrogenation in xylene or in nitrobenzene in the presence of a palladium–carbon catalyst, furnishing products **9a, b** and **d** or **10a–c**, respectively. It was found that the formation of the two types of products, **9** or **10**, from the same molecules depends on the substituents at positions 2 and 6, and on the inert or oxidative character of the solvent used. The quinonediimine forms **9a, b** can be considered to be intermediates of the transformation **7a, b**→**10a, b**.

The synthesis of the partially saturated dipyrido[1,2-*a*:4,3-*d*]-pyrimidin-11-ones **1–4** (2-azapyracridones), a novel type of hetero ring system, was recently reported.[2,3] In the presence of palladium–carbon, these tricycles **1** were subjected to hydrogenation and/or dehydrogenation in refluxing cyclohexene, nitrobenzene or xylene (Scheme 1). Surprisingly, **1** (R = H)



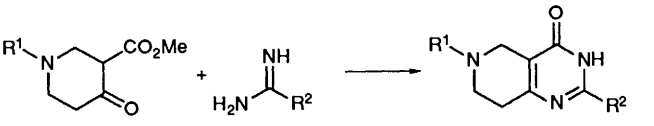
Scheme 1

gave not the expected pyridine derivative **4**, but the rearranged product **2** after a catalytic hydrogen-transfer process. In the hydrogen-donor cyclohexene the octahydro derivative **3** was formed, while in the hydrogen-acceptor nitrobenzene the pyridine compound **4** was formed, as sole product. However, the *N*-benzyl derivative **1** (R = $PhCH_2$) in xylene gave a mixture of **2** and **4**.

To extend the scope of these investigations, we set out to synthesize the bicyclic analogue 6-azaquinazoline derivatives **7a–e** and to investigate their hydrogenation and dehydrogenation. Investigations of this family of compounds was also stimulated by the fact that a number of recent publications have been concerned with the chemistry and the tumour cell growing activity of similar derivatives.[4–9]

Results

Since the description of the first 6-azaquinazoline derivative,[10] a number of methods have been developed for their synthesis.[11–17] There is current interest in these compounds as concerns their chemistry and pharmacology[18–23] and numerous patents have been granted in this field. For the synthesis of our target compounds **7a–e**, *N*-substituted-3-methoxycarbonyl-4-piperidones[24] **5a, b** were cyclized with amidines **6a–c** in basic medium (Scheme 2). Thus, numerous 6-azaquinazoline derivatives were prepared, particularly for pharmacological purposes.[25]



5a; R^1 = $PhCH_2$
5b; R^1 = Me

6a; R^2 = Ph
6b; R^2 = Me
6c; R^2 = 4-Py

7a; R^1 = $PhCH_2$, R^2 = 4-Ph
7b; R^1 = $PhCH_2$, R^2 = 4-Py
7c; R^1 = $PhCH_2$, R^2 = Me
7d; R^1 = Me, R^2 = Ph
7e; R^1 = R^2 = Me

Scheme 2

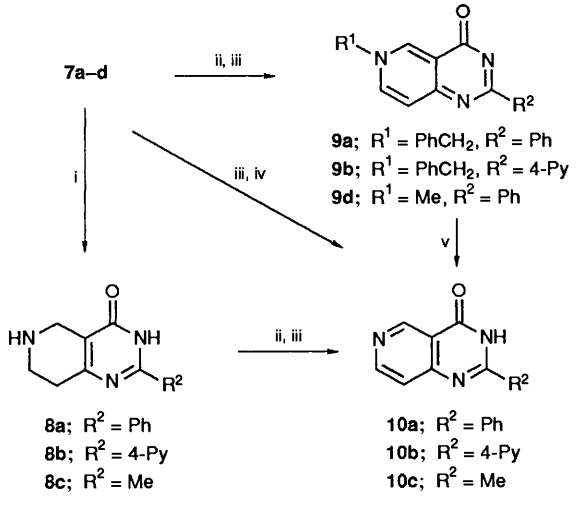
The 6-benzylazaquinazoline derivatives **7a–c** were debenzylated in the presence of a palladium–carbon catalyst under hydrogen, resulting in the *N*-unsubstituted compounds **8a–c** in high yields in strongly acidic medium (Scheme 3). A recent paper reported on unsuccessful attempts to debenzylate 2-methyl- **7c** and 2-phenyl-6-benzylazaquinazolines **7a**.[6] We assume that the very poor solubility of these compounds in neutral media might have caused the difficulty in the debenzylation. However, it is well known that the addition of acid improves hydrogenation.[26] Since **7a–e** do not dissolve even in hot cyclohexene, investigation of their dehydrogenation was performed in nitrobenzene and xylene with palladium–carbon catalysis. Dehydrogenation of **7a–d** and **8a–c** under oxidative conditions resulted in the respective quinonediimines **9a, b, d** or pyridines **10a–c** (Table 1). In contrast with the 2-aryl-substituted derivatives **7a, b**, the 2-methyl-substituted compound **7c** could not be converted into the corresponding quinonediimine, due to the electron-donor character of the methyl group. When the substituent at position 6 was methyl **7d**, only the quinonediimine derivative **9d** was obtained; when it was the easily removable hydrogen **8a–c**, only the pyridines **10a–c** were formed in xylene and nitrobenzene as well.

Owing to the effects of the solvents, the situation is more complicated for the 6-benzylazaquinazolin-4-ones **7a, b**. Both

Table 1 Dehydrogenation of **7a–e** and **8a–c**

Starting Compound				Product			
No.	R^1	R^2	Solvent[a]	No.	R^1	R^2	Yield[b] (%)
7a	$PhCH_2$	Ph	X	**10a**	—	Ph	58(iii)
			N	**9a**	$PhCH_2$	Ph	60(ii)
			N	**10a**	—	Ph	50(iv)
7b	$PhCH_2$	4-Py	X	**10b**	—	4-Py	55(iii)
			N	**9b**	$PhCH_2$	4-Py	61(ii)
			N	**10b**	—	4-Py	54(iv)
7c	$PhCH_2$	Me	N or X	**10c**	—	Me	63(iv), 66(iii)
7d	Me	Ph	N or X	**9d**	Me		57(ii), 52(iii)
7e	Me	Me	N or X	—	—	—	—
8a	H	Ph	N or X	**10a**	—	Ph	65(ii), 62(iii)
8b	H	4-Py	N or X	**10b**	—	4-Py	60(ii), 65(iii)
8c	H	Me	N or X	**10c**	—	Me	63(ii), 61(iii)

[a] N = nitrobenzene, X = xylene. [b] The method used is given in brackets. For the methods, see the footnotes to Scheme 3.



Scheme 3 *Conditions:* i, **7a–c** in MeOH–HCl with 10% Pd–C/H_2; ii, **7a–e** and **8a–c** in nitrobenzene with 10% Pd–C for 17 h; iii, **7a–e** and **8a–c** in xylene with 10% Pd–C; iv, **7a, b** in nitrobenzene with 10% Pd–C for 50 h; v, **9a** in MeOH with 10% Pd–C/H_2. For details, see Experimental section.

7a and **7b** could be transformed to **10a, b** in xylene, while the reaction in nitrobenzene under the same conditions resulted in **9a, b**. Nevertheless, **10a, b** could also be obtained in nitrobenzene, but only after an extended reaction time (Scheme 3, iv). This is a result of the mutual effects of the solvent used and the character of the substituents at positions 2 and 6.

When **9a** was subjected to debenzylation in an oxidative medium in xylene or nitrobenzene under the same conditions, no change was observed even after an extremely extended reaction time. Debenzylation usually needs hydrogen (for the formation of toluene[27]), and we accomplished the conversion of the 6-benzyl derivative **9a** to the 6-unsubstituted **10a** under reductive conditions (Scheme 3, v).

It is noteworthy that all attempts to achieve such dehydrogenation with the 2,6-dimethyl derivative **7e** were unsuccessful.

In our opinion, the formation of the respective quinonediimine forms **9** is hampered by the electron-donor 2-methyl substituent, as is the formation of the corresponding pyridines **10** by the 6-methyl group, which is difficult to remove. Further, the solvent (xylene or nitrobenzene, respectively) plays a basic role in the dehydrogenation of the 6-benzyl-substituted **7a** and **7b**.

If the present results are compared with those relating to the formation of partially saturated tricyclic compounds **2–4**, which can be regarded as 2,3-disubstituted-6-azaquinazoline derivatives, it is seen that a new form (the quinonediimine **9**) of 6-azaquinazoline derivatives has been prepared as an intermediate of the conversion of 5,6,7,8-tetrahydro derivatives **7a, b** to the 5,6,7,8-unsaturated compounds **10a, b**.

^{1}H and ^{13}C NMR Spectroscopic Investigation of **7–10**.—The structures of **7–10** were elucidated *via* their ^{1}H and ^{13}C NMR spectra. The ^{1}H NMR chemical shifts are given in the Experimental section, while the ^{13}C chemical shifts are compiled in Tables 2 and 3. Comparison of the ^{1}H NMR spectra unambiguously proves that compounds **8** are the corresponding debenzyl derivatives of compounds **7**. The absence of the ^{13}C signals of the *N*-benzyl group in **8** corroborate their structure. Beside the known substituent effects,[28] proton-coupled ^{13}C spectra and semiselective INEPT[29] measurements optimized for long-range couplings J(C,H) = 7 Hz were utilized to achieve a complete ^{13}C assignment. Fig. 1 shows an example of this method. When a selective pulse is applied to protons 7-H, 8-H and CH_3, respectively, only the signals of the carbon atoms appear individually in the INEPT spectra, and are long-range coupled with the selectively irradiated protons. The results of the INEPT experiments are summarized in Table 4.

The coupling between the NCH_2 protons and atoms C-1 and C-2,6 of the benzyl group allows the assignment of the group R^1. A distinction between the closely spaced quaternary atoms C-2 and C-8a was achieved *via* the long-range couplings J(C,H) of C-2 with the geminal or vicinal positioned CH_3 and protons 2,6-H of the group R^2. Atom C-8a is coupled with proton 7-H, which can be utilized for further support of their assignment. *Via* the coupling J(7-H,C-5), an unambiguous distinction between the C-5 and C-7 signals was achieved.

In **9** the arrangement of the double bonds in the pyrimidine ring is quite different from that in **7, 8** and **10**. The lower degree of conjugation in the quinonediimine intermediates **9** is reflected by the enhanced chemical shifts of the C-2, C-4 and C-8a signals.

Experimental

M.p.s were determined on a Boetius micro melting point apparatus and are uncorrected. IR spectra were recorded in potassium bromide discs on a Unicam SP 200 spectrometer; data are given in cm^{-1}. ^{1}H and ^{13}C NMR spectra were recorded in [$^2H_6$]-DMSO on Bruker AC-250 and JEOL FX-100 spectrometers, at room temperature, using Me_4Si as internal standard; J values are given in Hz. The catalyst used in the experiments was always 10% palladium–carbon (Fluka). All compounds gave satisfactory microanalyses (C, H, N).

Table 2 ^{13}C NMR chemical shifts of **7** and **8**

	δ_C						
	7a	**7b**[a]	**7c**	**7d**	**8a**	**8b**[a]	**8c**
C-2	154.1	152.8	155.7	154.0	154.0	154.7	155.6
C-4	161.3	161.7	160.8	161.1	161.9	161.7	161.5
C-4a	117.5	119.0	116.3	117.3	118.6	117.2	118.0
C-5	48.8	48.9	48.6	50.9	41.5	41.3	41.5
C-7	49.2	49.3	49.1	51.1	42.1	41.7	42.3
C-8	31.3	31.3	31.1	31.1	30.8	29.7	30.9
C-8a	158.7	159.0	158.3	158.3	158.7	158.0	158.6
R^2	132.3	140.0	20.7	132.3	132.6	142.0	20.8
	128.4	121.5		128.4	128.4	121.4	
	127.4	150.4		127.4	127.4	150.1	
	131.2			131.2	131.2		
R^1	61.5	61.6	61.5	45.1			
	138.1	138.1	138.1				
	128.7	129.0	128.6				
	128.1	128.4	128.1				
	126.9	127.3	126.9				

[a] For R^2 = pyridyl **7b** and **8b**, we followed the same numbering as for R^2 = phenyl **7a** and **8a** in order to make comparison of the data easier.

Table 3 ^{13}C NMR chemical shifts of **9** and **10**

	δ_C					
	9a	**9b**[a]	**9d**	**10a**	**10b**[a]	**10c**
C-2	169.7	168.1	169.5	156.9	155.3	159.6
C-4	169.7	169.9	169.9	161.5	161.5	160.9
C-4a	117.3	117.8	117.1	116.5	117.0	116.5
C-5	145.6	146.2	146.6	149.3	149.5	149.1
C-7	141.2	141.7	142.2	153.3	153.6	153.0
C-8	122.9	123.4	122.4	120.4	120.7	119.7
C-8a	160.2	160.3	159.9	153.6	153.2	153.7
R^2	138.4	145.9	138.6	132.1	139.4	21.7
	128.7	122.4	128.7	128.1	121.9	
	127.9	150.1	128.1	128.6	150.3	
	131.0		131.1	132.1		
R^1	61.2	61.5	45.9			
	128.4	128.6				
	131.0	129.2				
	128.9	129.0				

[a] For R^2 = pyridyl (**9b** and **10b**), we followed the same numbering as for R^2 = phenyl (**9a** and **10a**) in order to make comparison of the data easier.

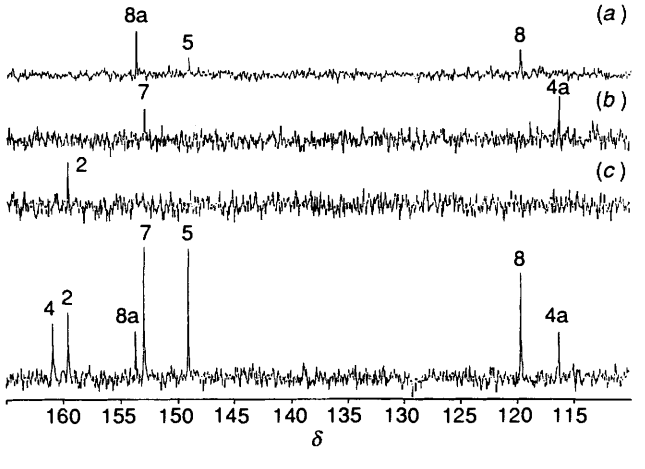


Fig. 1 Semiselective INEPT measurements on **10c**. Selectively irradiated at (*a*) H-7, (*b*) H-8 and (*c*) CH_3 protons. Bottom, broad band decoupled ^{13}C spectrum.

Table 4 Proton–carbon connectivity *via* semiselective INEPT, J(C,H) = 7 Hz

	Proton	Carbon
7b[a]	R^2, 6-H	C-2
7c	R^2 NCH_2	C-5, C-7, R^1 C-1, R^1 C-2,6
8c	R^2 CH_3	C-2
	7-H	C-5, C-8a
9b[c]	5-H	C-4, C-7, C-8a
	7-H	C-5, C-8, C-8a
	8-H	C-4a, C-7
	R^2 2,6-H	C-2, R^2 C-3, 5
	R^1 NCH_2	C-5, C-7, R^1 C-2,6
9d	5-H	C-4, C-4a, C-7, C-8a
	8-H	C-4a, C-7
10b[a]	8-H	C-4a, C-7
	R^2 2,6-H	C-2
10c	7-H	C-8, C-8a
	8-H	C-4a, C-7
	R^2 CH_3	C-2

[a] For R^2 = pyridyl **7b** and **8b**, we followed the same numbering as for R^2 = phenyl **7a** and **8a** in order to make comparison of the data easier.

6-*Benzyl*-2-*phenyl*-5,6,7,8-*tetrahydro*-3H-*pyrido*[4,3-d]*pyrimidin*-4-*one* **7a**.—*N*-Benzyl-3-methoxycarbonyl-4-piperidone hydrochloride[24] **5a** (1.42 g, 5 mmol) was dissolved in dry ethanol (20 cm^3). A solution of the appropriate amidine hydrochloride **6a** (0.78 g, 5 mmol) in dry ethanol (10 cm^3) and then a solution of metallic sodium (0.69 g, 30 mmol) in dry ethanol (10 cm^3) were added. The mixture was stirred at 100 °C for 12 h, then evaporated to dryness, and the residue was suspended in water, filtered off and washed with water and acetone. The product was recrystallized from ethanol, m.p. 244–247 °C (lit.,[18] m.p. 245 °C); yield: 62%; ν_{max}/cm^{-1} 700, 1550 and 1640; δ_H 2.74 (4 H, m, 7,8-H_2), 3.28 (2 H, s, 5-H_2), 3.71 (2 H, s, R^1 NCH_2), 7.25–7.40 (5 H, m, R^1 Ph), 7.40–7.60 (3 H, R^2 3,4,5-H) and 8.06 (2 H, dm, R^2 2,6-H).

6-*Benzyl*-2-(4-*pyridyl*)-5,6,7,8-*tetrahydro*-3H-*pyrido*[4,3-d]-*pyrimidin*-4-*one* **7b**. This was prepared as described for **7a** from the appropriate amidine hydrochloride **6c** (0.79, 5 mmol), m.p. 222–223 °C (MeOH); yield: 65% (Found: C, 71.4; H, 5.6; N, 17.8. $C_{19}H_{18}N_8N_4O$ requires C, 71.7; H, 5.7; N, 17.6%); ν_{max}/cm^{-1} 700, 1600 and 1640; δ_H 2.75 (4 H, s, 7,8-H_2), 3.28 (2 H, s, 5-H_2), 3.68 (2 H, s, R^1 NCH_2), 7.30–7.40 (5 H, m, R^1 Ph), 8.00 (2 H, dm, R^2 2,6-H) and 8.75 (2 H, R^2 3,5-H).

6-*Benzyl*-2-*methyl*-5,6,7,8-*tetrahydro*-3H-*pyrido*[4,3-d]*pyrimidin*-4-*one* **7c**. This was prepared as described for **7a** from the appropriate amidine hydrochloride **6b** (0.47 g, 5 mmol). M.p. 194–197 °C (EtOH) (lit.,[18] m.p. 195–197 °C); yield. 60%; ν_{max}/cm^{-1} 700, 1610 and 1670. δ_H 2.22 (3 H, s, R^2 CH_3), 2.56 (2 H, t, 8-H_2), 2.66 (2 H, t, 7-H_2), 3.17 (2 H, s, 5-H_2), 3.65 (2 H, s, R^1 NCH_2) and 7.25–7.35 (5 H, m, R^1 Ph).

6-*Methyl*-2-*phenyl*-5,6,7,8-*tetrahydro*-3H-*pyrido*[4,3-d]*pyrimidin*-4-*one* **7d**. This was prepared as described for **7a** from 3-methoxycarbonyl-*N*-methyl-4-piperidone hydrochloride[24] **5b** (1.04 g, 5 mmol) and the appropriate amidine hydrochloride **6a** (0.78 g, 5 mmol). M.p. 229–230 °C (MeCH), (lit.,[10] m.p. 225–227 °C); yield: 65%, ν_{max}/cm^{-1} 690, 1530 and 1630; δ_H 2.38 (3 H, s, R^1 CH_3), 2.67 (4 H, m, 7,8-H_2), 3.26 (2 H, s, 5-H_2), 7.40–7.60 (3 H, m, R^2 3,4,5-H) and 8.07 (2 H, dm, R^2 2,6-H).

2,6-*Dimethyl*-5,6,7,8-*tetrahydro*-3H-*pyrido*[4,3-d]*pyrimidin*-4-*one* **7e**. This was prepared as described for **7a** from 3-methoxycarbonyl-*N*-methyl-4-piperidone hydrochloride[24] **5b** (1.04 g, 5 mmol) and the appropriate amidine hydrochloride **6b** (0.47 g, 5 mmol). M.p. 215–218 °C (MeOH) (lit.,[19] m.p. 215–216 °C); yield: 56%; ν_{max}/cm^{-1} 690, 1600 and 1630.

2-*Phenyl*-5,6,7,8-*tetrahydro*-3H-*pyrido*[4,3-d]*pyrimidin*-4-*one* **8a**.—(i) The *N*-benzyl derivative **7a** (3.17 g, 10 mmol) was

dissolved in hydrochloric acid–MeOH (1:10, 50 cm^3). The catalyst (50 mg) was added, and the resulting suspension was stirred and refluxed under hydrogen for 10 h. After removal of the catalyst, the solvent was evaporated off. The residual crude crystalline product was recrystallized from ethanol, m.p. 214–216 °C, the 2 HCl salt melts at 323–326 °C (lit.,[6] m.p. 325 °C); yield: 91%; ν_{max}/cm^{-1} 670, 1520 and 1600; δ_H 2.58 (2 H, t, 8-H_2), 2.99 (2 H, t, 7-H_2), 3.60 (2 H, s, 5-H_2), 7.40–7.60 (3 H, m, R^2 3,4,5-H) and 8.07 (2 H, dm, R^2 2,6-H).

2-(4-*Pyridyl*)-5,6,7,8-*tetrahydro*-3H-*pyrido*[4,3-d]*pyrimidin*-4-*one* **8b**. This was prepared as described for **8a** from the *N*-benzyl derivative **7b** (3.18 g, 10 mmol). M.p. 244–246 °C (MeOH); yield: 87% (Found: C, 63.2; H, 5.5; N, 24.3. $C_{12}H_{12}N_4O$ requires C, 63.2; H, 5.3; N, 24.6%); ν_{max}/cm^{-1} 1380, 1500 and 1590. δ_H 2.67 (2 H, t, 8-H_2), 3.12 (2 H, t, 7-H_2), 3.71 (2 H, s, 5-H_2), 8.03 (2 H, dm, R^2 2,6-H) and 8.70 (2 H, dm, R^2 3,5-H).

2-*Methyl*-5,6,7,8-*tetrahydro*-3H-*pyrido*[4,3-d]*pyrimidin*-4-*one* **8c**. This was prepared as described for **8a** from the *N*-benzyl derivative **7c** (2.55 g, 10 mmol). The product was recrystallized from methanol, m.p. 184–187 °C, the 2 HCl salt melts at 325–328 °C (lit.,[6] m.p. 327 °C); yield 83%; ν_{max}/cm^{-1} 1530, 1550 and 1600; δ_H 2.21 (3 H, s, R^2 CH_3), 2.38 (2 H, t, 8-H_2), 2.87 (2 H, t, 7-H_2) and 3.44 (2 H, s, 5-H_2).

6-*Benzyl*-2-*phenylpyrido*[4,3-d]*pyrimidin*-4-*one* **9a**.—(ii) Compound **7a** (0.96 g, 3 mmol) and the catalyst (400 mg) were suspended in nitrobenzene (40 cm^3). The mixture was kept at 125–130 °C for 17 h and filtered while still hot. After being left overnight at room temperature, the separated *crystals* were collected, m.p. 272–275 °C (Found: C, 76.5; H, 4.9; N, 13.6. $C_{20}H_{15}N_3O$ requires C, 76.7; H, 4.8; N, 13.4%); ν_{max}/cm^{-1} 1490, 1580 and 1620; δ_H 5.70 (2 H, s, R^1 NCH_2), 7.40–7.55 (7 H, m, R^1 Ph and R^2 3,5-H), 7.69 (1 H, d, 8-H), 8.43 (2 H, dm, R^2 2,6-H), 8.56 (1 H, dd, 7-H) and 9.40 (1 H, d, 5-H).

6-*Benzyl*-2-(4-*pyridyl*)*pyrido*[4,3-d]*pyrimidin*-4-*one* **9b**. This was prepared as described for **9a** from **7b** (0.96 g, 3 mmol), m.p. 275–279 °C (Found: C, 72.8; H, 4.8; N, 17.9. $C_{19}H_{14}N_4O$ requires C, 72.6; H, 4.5; N, 17.8%); ν_{max}/cm^{-1} 1500, 1590 and 1630; δ_H 5.77 (2 H, s, R^1 NCH_2), 7.40–7.55 (5 H, m, R^1 Ph), 7.79 (1 H, d, 8-H), 8.27 (2 H, dm, R^2 2,6-H), 8.65 (1 H, dd, 7-H), 8.74 (2 H, dm, R^2 3,5-H) and 9.51 (1 H, d, 5-H).

6-*Methyl*-2-*phenylpyrido*[4,3-d]*pyrimidin*-4-*one* **9d**. This was prepared as described for **9a** from **7d** (0.72 g, 3 mmol), m.p. 315–317 °C (Found: C, 70.7; H, 4.9; N, 17.5. $C_{14}H_{11}N_3O$ requires C, 70.9; H, 4.7; N, 17.7%); ν_{max}/cm^{-1} 1510, 1610 and 1660; δ_H 4.19 (3 H, s, R^1 CH_3), 7.40–7.50 (3 H, m, R^2 3,4,5-H), 7.66 (1 H, d, 8-H), 8.42 (1 H, dd, 7-H), 8.44 (2 H, dm, R^2 2,6-H) and 9.20 (1 H, d, 5-H).

This product **9d** was also prepared by method iii, as described below for **10a**.

2-*Phenyl*-3H-*pyrido*[4,3-d]*pyrimidin*-4-*one* **10a**.—(iii) Compound **7a** (0.96 g, 3 mmol) and the catalyst (400 mg) were suspended in xylene (40 cm^3). The mixture was kept at 125–130 °C for 17 h and filtered while still hot. After being left overnight at room temperature, the separated crystals were collected, m.p. 286–288 °C (lit.,[13] m.p. 284–286 °C); ν_{max}/cm^{-1} 1590, 1690 and 1710; δ_H 7.50–7.65 (3 H, m, R^2 3,4,5-H), 7.59 (1 H, d, 8-H), 8.82 (3 H, dm, 7-H and R^2 2,6-H) and 9.30 (1 H, d, 5-H).

This product **10a** was also prepared by method (iv). Compound **7a** (0.96 g, 3 mmol) and the catalyst (400 mg) were suspended in nitrobenzene (40 cm^3). The mixture was kept at 125–130 °C for 50 h and filtered while still hot. After being left overnight, the crystals of **10a** were collected.

Product **10a** was also prepared from the *N*-unsubstituted compound **8a** (0.92 g, 4 mmol) according to methods ii and iii.

Method v *for preparation of* **10a** *from* **9a**. Compound **9a** (0.93 g, 3 mmol) was dissolved in a mixture of methanol (50 cm^3) and the catalyst (50 mg). After being stirred for 4 h at room temperature under hydrogen, the catalyst and the solvent were removed. The crystalline residue was recrystallized from xylene, giving **10a** in 85% yield.

2-(4-*Pyridyl*)-3H-*pyrido*[4,3-d]*pyrimidin*-4-*one* **10b**. This was prepared as described for **10a** by methods iii and iv from **7b** (0.96 g, 3 mmol), m.p. 304–308 °C (Found: C, 64.4; H, 3.7; N, 24.9. $C_{12}H_8N_4O$ requires C, 64.3; H, 3.6; N, 25.0%); ν_{max}/cm^{-1} 1550, 1600 and 1680; δ_H 7.68 (1 H, d, 8-H), 8.11 (2 H, dm, R^2 2,6-H), 8.83 (2 H, dm, R^2 3,5-H), 8.88 (1 H, d, 7-H) and 9.33 (1 H, d, 5-H).

Product **10b** was also prepared from the *N*-unsubstituted compound **8b** (0.92 g, 4 mmol) according to methods ii and iii.

2-*Methyl*-3H-*pyrido*[4,3-d]*pyrimidin*-4-*one* **10c**. This was prepared as described for **10a** by methods iii and iv from **7c** (0.78 g, 3 mmol), m.p. 308–310 °C (lit.,[13] m.p. 309–310 °C); ν_{max}/cm^{-1} 1470, 1600 and 1690; δ_H 2.39 (3 H, R^2 CH_3), 7.46 (1 H, d, 8-H), 8.76 (1 H, d, 7-H) and 9.22 (1 H, d, 5-H).

Product **10c** was also prepared from the *N*-unsubstituted compound **8c** (0.85 g, 5 mmol) according to methods ii and iii.

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