Pyrimidine Reactions. Part XXV.[1] Synthesis and Piperidinolysis of Some Simple Fluoropyrimidines

By **Desmond J. Brown** * and **Paul Waring**, The John Curtin School of Medical Research, P.O. Box 334, Canberra City, Australia 2601

2-Fluoropyrimidine and its 4-methyl and 4,6-dimethyl derivatives are made by diazotization of the corresponding aminopyrimidines in fluoroboric acid. 4-Fluoro-2-methylpyrimidine, its 6-methyl isomer, and 4-fluoro-2,6-dimethylpyrimidine result from treatment of appropriate trimethylpyrimidin-4-ylammonium chlorides with aqueous potassium hydrogen difluoride. Second-order rate constants for piperidinolyses of the fluoropyrimidines and of 2-bromo-, 2-iodo-, and 4-chloro-5-methyl-pyrimidine indicate that the fluoropyrimidines react 60—200 times faster than other (corresponding) halogenopyrimidines at the same temperature. The u.v. and ^{1}H n.m.r. spectra are recorded and discussed.

SIMPLE 2- and 4-fluoropyrimidines have not been described. Hence they were omitted from a recent pilot study [2] of the relative reactivities of other such halogenopyrimidines towards aminolysis. We now report the synthesis of six 2- or 4-monofluoropyrimidines lacking other functional groups. In broad agreement with comparisons in the halogenonitrobenzenes [3,4] and with assorted data in a few heteroaromatic systems,[4-6] these fluoropyrimidines proved to be much more reactive than their chloro-, bromo-, or iodo-counterparts. So marked

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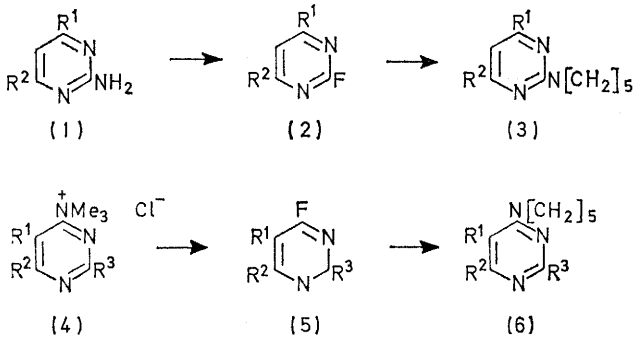
was the increase, that fluorine displacement by amines could not be followed by our previous method [2,7] using standardized preparative conditions without additional solvent. Accordingly we turned to dilute ethanolic piperidine so that the resulting second-order rate constants would be directly comparable with those of Chapman and Rees [8] for chloropyrimidines and with our new figures for 2-bromopyrimidine and for the recently synthesized [1] 2-iodopyrimidine.

Diazotization of the commercial aminopyrimidines (1; $R^1 = R^2 = H$) and (1; R^1 = Me, R^2 = H or Me)



(1) (2) (3)

(4) (5) (6)

in concentrated aqueous fluoroboric acid gave 2-fluoropyrimidine (2; $R^1 = R^2 = H$) and its homologues (2; R^1 = Me, R^2 = H or Me). The same procedure failed with 4-aminopyrimidines. However, 2,6-dimethylpyrimidin-4-yltrimethylammonium chloride (4; $R^1 = H$, $R^2 = R^3$ = Me), prepared [9] from the corresponding 4-chloropyrimidine with trimethylamine, reacted with cold aqueous potassium hydrogen difluoride to give an excellent yield of the fluorodimethylpyrimidine (5; R^1 = H, $R^2 = R^3$ = Me). Similar procedures were used to prepare the ammonio- and fluoro-pyrimidines (4 and 5; $R^1 = R^2 = H$, R^3 = Me), (4 and 5; $R^1 = R^3 = H$, R^2 = Me), and (4; R^1 = Me, $R^2 = R^3 = H$); attempts to convert the last mentioned ammonio-compound into its fluoro-analogue (5; R^1 = Me, $R^2 = R^3 = H$) failed.

In order to follow the piperidinolysis of the fluoropyrimidines spectrometrically, the corresponding piperidinopyrimidines were required: of these, only the dimethyl derivatives (3; $R^1 = R^2$ = Me) [8] and (6; $R^1 = H$, $R^2 = R^3$ = Me) [10] have been made previously in an analytically pure state; four others (3; R^1 = H or Me, $R^2 = H$),[8] (6; $R^1 = R^2 = H$, R^3 = Me),[8] and (6; $R^1 = R^3 = H$, R^2 = Me) [8,11] have been reported only as picrates or other derivatives; and the 5-methyl derivative (6; R^1 = Me, $R^2 = R^3 = H$) was unknown. We prepared all seven free bases from their known chloro-analogues.

Inspection of the u.v. spectra (Table 1) indicated appropriate analytical wavelengths for following the piperidinolyses. The resulting second-order rate constants (Table 2) indicated that 2-fluoropyrimidine reacted some 60, 120, and 200 times faster than its bromo-, chloro-, and iodo-analogues, respectively, at a given temperature; likewise, the methylated fluoropyrimidines (2; R^1 = Me, R^2 = H or Me) proved to be 75—90 times more reactive at 30° than their chloro-counterparts (ref. 8 and Table 2, respectively). Such enhanced reactivity in the fluoro-derivatives clearly arose from

TABLE 1

U.v. spectra

Pyrimidine [a]	Solvent [b]	Species	$\lambda_{max.}$(log ε) [c]
2-F	E	0	272(2·68), *253*(3·51), 248(3·62), 242(3·53)
2-F-4-Me	E	0	*275*(2·80), 250(3·79), 247(3·80)
2-F-4,6-Me_2	E	0	*257*(3·62), 250(3·82)
4-F-2-Me	E	0	240(3·34), 204(3·65)
4-F-6-Me	E	0	238(3·32), 206(3·62)
4-F-2,6-Me_2	E	0	240(3·43), 209(3·62)
2-Pip	1·3	+	330(3·48), 240(4·25)
4-Me-2-Pip	1·3	+	324(3·52), 240(4·28)
4,6-Me_2-2-Pip [d]	1·3	+	320(3·68), 240(4·26)
2-Me-4-Pip	4·0	+	264(4·22)
4-Me-6-Pip	4·0	+	269(4·29)
2,4-Me_2-6-Pip [e]	4·0	+	300(4·28)
5-Me-4-Pip	1·3	+	280(4·04)

[a] Pip = piperidino. [b] E = ethanol; figure = pH of aqueous solution. [c] Inflections and shoulders in italics; peaks <210 nm approximate. [d] $pK_a = 5·21 \pm 0·03$ (analytical λ 260 nm). [e] $pK_a = 8·02 \pm 0·04$ (analytical λ 275 nm).

their relatively low energies of activation: frequency factors varied but little throughout. The 4-fluoropyrimidines (5; $R^1 = R^2 = H$, R^3 = Me), (5; $R^1 = R^3 = H$, R^2 = Me), and (5; $R^1 = H$, $R^2 = R^3$ = Me) were over 100 times more reactive at 20° than their 4-chloro-analogues [8] and some 10 times more reactive at 20° than their nearest 2-fluoro-analogues (2; R^1 = Me, R^2 = H or Me), probably for the same reason. Each additional 2- or 4-methyl group decreased the reactivity of the 2- or 4-fluoropyrimidines *ca.* 3—4 fold. 4-Chloro-5-methylpyrimidine proved to be less than 1/3 as reactive as its 2- or 4-methyl-isomer [8] towards piperidine, a fact qualitatively parallel to the abnormally slow reaction of the same 5-methyl derivative with trimethylamine (see Experimental section).

The ^{1}H n.m.r. spectra (Table 3) of the fluoropyrimidines differed markedly from those of representative chloro-analogues (*cf.* ref. 12). Thus in the spectrum of 2-fluoropyrimidine (2; $R^1 = R^2 = H$), 4- and 6-H are represented by a quartet in which the *ortho*-proton coupling is 6 Hz and the *meta* proton–fluorine coupling (across N) is 1·7 Hz; 5-H also appears as a quartet in which the *ortho*-proton coupling and the *para*-proton–fluorine coupling are both 6 Hz. The methylated derivatives (2; R^1 = Me, R^2 = H or Me) have spectra consistent with that of their lower homologue. Although 4-fluoro-2-methylpyrimidine (5; $R^1 = R^2 = H$, R^3 =

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TABLE 2

Kinetic data for the reaction of halogenopyrimidines with piperidine in ethanol

Pyrimidine	10^2k_2/l mol^{-1} sec^{-1} 40°	30°	20°	15°	10°	E/kcal mol^{-1} [a]	$\log_{10} A$ [a]
2-F	14·4 ± 0·3	7·18 ± 0·2	4·04 ± 0·1 4·01 ± 0·1 [b]			9·7	5·8
2-F-4-Me	4·27 ± 0·05 4·25 ± 0·05 [b]	2·59 ± 0·07 2·60 ± 0·01 [b]	1·48 ± 0·04			9·7	5·4
2-F-4,6-Me$_2$	1·38 ± 0·03	0·81 ± 0·01	0·45 ± 0·01 0·44 ± 0·01 [b]			10·3	5·2
4-F-2-Me			17·7 ± 0·2	13·3 ± 0·4 13·2 ± 0·4 [b]	10·8 ± 0·2	8·0	5·2
4-F-6-Me		21·7 ± 0·4 [c]	12·6 ± 0·3 12·4 ± 0·3 [b]	10·5 ± 0·2	7·7 ± 0·2	8·2	5·2
4-F-2,6-Me$_2$			4·29 ± 0·1 4·26 ± 0·1 [b]	3·22 ± 0·07	2·56 ± 0·05	8·6	5·0
2-Cl [d]	0·129	0·069	0·033			12·4	5·7
2-Br	0·250 ± 0·008 0·248 ± 0·006 [b]	0·125 ± 0·002	0·061 ± 0·002			12·9	6·4
2-I	0·082 ± 0·001	0·0388 ± 0·0006	0·0186 ± 0·0007 0·0182 ± 0·0006 [b]			13·6	6·4
4-Cl-5-Me	0·146 ± 0·003	0·0710 ± 0·0002	0·0348 ± 0·0002			13·7	6·3
2-Cl-4,6-Me$_2$		0·0111 ± 0·0002 0·0112 [d]					

[a] Accuracy *ca.* ±0·3. [b] Using half-concentrations of pyrimidine and piperidine. [c] At 25°. [d] Data from ref. 8.

Me) has chemical shifts similar to those of its chloro-analogue, 6-H is represented in the fluoro-compound by a quartet with the usual (6 Hz) *ortho*-proton coupling and a *meta*-proton–fluorine coupling (across C) of no less than 12 Hz; 5-H has an *ortho*-proton–fluorine coupling of only 3 Hz (*cf.* the unproven assignment of J values in the ^{19}F n.m.r. spectrum of 2-fluoroquinoline [13]). The proton signals from the 4-fluoropyrimidines (5; R^1 = H, R^2 = Me, R^3 = H or Me) were too poorly resolved at 33° for analysis at 60 MHz.

TABLE 3

^{1}H N.m.r. spectra

Pyrimidine [a]	δ(J/Hz)
2-F	8·75 (q, $J_{4(6),5}$ 6, $J_{4,F}$ 1·7, 4,6-H$_2$), 7·40 (q, $J_{4,5}$, 6, $J_{5,F}$ 6, 5-H)
2-Cl	8·65 (d, J 6, 4,6-H$_2$), 7·30 (t, J 6, 5-H)
2-F-4-Me	8·63 (q, $J_{5,6}$, 6, $J_{4,F}$, 1·7, 6-H), 7·35 (t, $J_{5,6}$ 6, $J_{5,F}$, 6, 5-H), 2·50 (s, Me)
2-F-4,6-Me$_2$	7·04 (d, $J_{5,F}$ 6, 5-H), 2·40 (s, Me$_2$)
4-F-2-Me	8·97 (q, $J_{5,6}$ 6, $J_{6,F}$ 12, 6-H), 6·96 (q, $J_{5,6}$ 6, $J_{5,F}$ 3, 5-H), 2·73 (s, Me)
4-Cl-2-Me	8·60 (d, J 6, 6-H), 7·25 (d, J 6, 5-H), 2·75 (s, Me)
4-F-6-Me	8·80br (s, 2-H), 7·00br (s, 5-H), 2·60 (s, Me)
4-F-2,6-Me$_2$	6·70br (s, 5-H), 2·65 (s, 2-Me), 2·55 (s, 6-Me)
4-Cl-2,6-Me$_2$	7·10 (s, 5-H), 2·67 (s, 2-Me), 2·50 (s, 6-Me)
2-Pip	8·19 (d, J 6, 4,6-H$_2$), 6·30 (t, J 6, 5-H), 3·77 (m, 2′,2′,6′,6′-H$_4$), 1·65br (s, 3′,3′,4′,4′,5′,5′-H$_6$)
4-Me-2-Pip	8·05 (d, J 6, 6-H), 6·15 (d, J 6, 5-H), 3·75 (m, 2′,2′,6′,6′-H$_4$), 2·25 (s, Me), 1·60br (s, 3′,3′,4′,4′,5′,5′-H$_6$)
4,6-Me$_2$-2-Pip	6·08 (s, 5-H), 3·75 (2′,2′,6′,6′-H$_4$), 2·20 (s, Me$_2$), 1·65 (3′,3′,4′,4′,5′,5′-H$_6$)
2-Me-4-Pip	8·15 (d, J 6, 6-H), 6·35 (d, J 6, 5-H), 3·60 (m, 2′,2′,6′,6′-H$_4$), 2·50 (s, Me), 1·64br (s, 3′,3′,4′,4′,5′,5′-H$_6$)
4-Me-6-Pip	8·52 (s, 2-H), 6·38 (s, 5-H), 3·60 (m, 2′,2′,6′,6′-H$_4$), 2·32 (s, Me), 1·65br (s, 3′,3′,4′,4′,5′,5′-H$_6$)
2,4-Me$_2$-6-Pip	6·10 (s, 5-H), 3·60 (m, 2′,2′,6′,6′-H$_4$), 2·38 (s, 2-Me), 2·22 (s, 4-Me), 1·64br (s, 3′,3′,4′,4′,-5′,5′-H$_6$)
5-Me-4-Pip	8·63 (s, 2-H), 8·15 (s, 6-H), 3·45 (m, 2′,2′,6′,6′-H$_4$), 2·20 (s, Me), 1·64br (s, 3′,3′,4′,4′,5′,5′-H$_6$)

[a] Halogenopyrimidines in $CDCl_3$; piperidinopyrimidines in CCl_4.

EXPERIMENTAL

Elemental analyses were done by the Australian National University Analytical Services Unit. U.v. spectra were recorded on a Unicam SP 1800 spectrophotometer but the peaks were checked manually. Ionization constants were obtained spectrometrically [14] at 20° using concentrations below 10^{-3}M in buffers [15] of 10^{-2}M ionic strength by Mr. I. Hawkins; thermodynamic corrections were not applied. The ^{1}H n.m.r. spectra were measured by Mr. S. E. Brown at 60 MHz and 33° using tetramethylsilane as internal standard.

Rate Measurements.—Accurately prepared ethanolic solutions of the halogenopyrimidine (*ca.* 10^{-2}M) and of anhydrous piperidine (*ca.* 4×10^{-2}M) were allowed to reach the required temperature. Equal volumes of each solution were mixed and thermostatted while 10—15 samples (2·00 ml each) were withdrawn at appropriate intervals to span >90% of the reaction. Each sample was diluted immediately to 250 ml with either 5×10^{-2}M-hydrochloric acid (for 2-halogenopyrimidines) or acetate buffer of pH 4·5 (for 4-fluoropyrimidines) to arrest the reaction. The concentration of piperidinopyrimidine (cation) present was measured spectrometrically (*cf.* Table 1) at its predetermined $\lambda_{max.}$ (where the halogeno-substrate had no absorption). The second-order rate constants (k_2) were derived from equation (1) in which a = [piperidine], b = [halogeno-

$$k_2t = \{\ln [b(a - DF/\varepsilon)]/[a(b - DF/\varepsilon)]\}/(a - b) \quad (1)$$

pyrimidine], t = time, D = optical density, F = dilution factor (usually 125), and ε = molar absorption of piperidinopyrimidine. In every run the standard deviation of k_2 was <3% between 5 and 80% reaction. The u.v. spectrum

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of every sample at t_∞ (>24 h) was virtually indistinguishable from that of an appropriate concentration of the authentic piperidinopyrimidine cation. The spectra of every halogenopyrimidine in ethanol (without piperidine) was unchanged for at least 24 h at 25°. Every piperidinolysis was repeated at one temperature using half-concentration of both reactants: the resulting k_2 values proved to be within ±1% of those already determined. This spectrometric method gave a k_2 value for 2-chloro-4,6-dimethylpyrimidine identical (within experimental error) with that obtained by Chapman and Rees[8] using a titrimetric method (see Table 2).

2-Fluoropyrimidine (2; $R^1 = R^2 = H$).—Sodium nitrite (3·8 g) in water (15 ml) was added during 30 min to a stirred solution of 2-aminopyrimidine (2·5 g) in aqueous fluoroboric acid (43%; 90 ml) maintained at −10 to −15°. Stirring and cooling were continued for a further 20 min and during subsequent adjustment of the mixture to pH 6—7 using 10N-sodium hydroxide. The solution was extracted with ether (4 × 50 ml). It proved essential to shake the extract thoroughly with aqueous potassium carbonate (2%; 10 ml) followed by water (2 × 10 ml) prior to dehydration over calcium sulphate. Distillation then gave the *fluoropyrimidine*, b.p. 75° at 20 mmHg, m.p. 25° (from light petroleum) (Found: C, 48·7; H, 3·1; F, 19·3; N, 28·5. $C_4H_3FN_2$ requires C, 49·0; H, 3·1; F, 19·4; N, 28·6%). The yield of distilled product varied from 25 to 50%.

2-Fluoro-4-methylpyrimidine (2; $R^1 = Me$, $R^2 = H$).—2-Amino-4-methylpyrimidine (19·1 g) in fluoroboric acid (240 ml) was treated similarly with sodium nitrite (28·5 g) in water (90 ml) to give the *fluoro(methyl)pyrimidine* (31%), b.p. 56° at 17 mmHg (Found: C, 53·3; H, 4·8; F, 17·05; N, 24·7. $C_5H_5FN_2$ requires C, 53·6; H, 4·5; F, 16·95; N, 25·0%).

2-Fluoro-4,6-dimethylpyrimidine (2; $R^1 = R^2 = Me$).—In a similar way 2-amino-4,6-dimethylpyrimidine (8 g), fluoroboric acid (80 ml), sodium nitrite (9·5 g), and water (30 ml) gave the *fluoro(dimethyl)pyrimidine* (26%), b.p. 70° at 20 mmHg (Found: C, 56·8; H, 5·5; F, 15·2; N, 22·3. $C_6H_7FN_2$ requires C, 57·1; H, 5·6; F, 15·1; N, 22·2%).

4-Fluoro-2,6-dimethylpyrimidine (5; $R^1 = H$, $R^2 = R^3 = Me$).— 2,6-Dimethylpyrimidin-4-yltrimethylammonium chloride[9] (10 g) was dissolved in a solution of potassium hydrogen difluoride (25 g) in water (90 ml) at 5°. Diethyl ether (100 ml) was added immediately and the two layers were stirred sufficiently vigorously to cause mixing at their interface without intimate mixture as a whole. After such treatment for 4 h at 5°, the ether layer was removed and the aqueous layer was extracted with ether (3 × 20 ml). The combined ether solutions were washed with aqueous potassium carbonate (2%; 10 ml) followed by water (2 × 10 ml) and then dehydrated over calcium sulphate. Evaporation and subsequent distillation gave the *fluoro(dimethyl)pyrimidine* (95%), b.p. 72° at 21 mmHg (Found: C, 57·05; H, 5·65; N, 22·05. $C_6H_7FN_2$ requires C, 57·1; H, 5·6; N, 22·2%).

4-Fluoro-2-methylpyrimidine (5; $R^1 = R^2 = H$, $R^3 = Me$).—6-Chloro-2-methylpyrimidin-4-one[16] (4 g) was hydrogenated during 4 h over palladium–charcoal (10%; 0·3 g) in ethanol (50 ml) containiug sodium hydroxide (1 g). Filtration and evaporation of the filtrate gave 2-methylpyrimidin-4-one (90%), m.p. 210° (from ethyl acetate) (lit.,[17] 212—213°), which was then converted[8,17] into 4-chloro-2-methylpyrimidine. This material (3 g) was added slowly to anhydrous benzene (30 ml) containing trimethylamine (4 g). After 2 days at 20—25° the solid was filtered off and washed with a little benzene followed by ether prior to analysis. The hydroscopic *trimethyl-2-methylpyrimidin-4-ylammonium chloride* (4; $R^1 = R^2 = H$, $R^3 = Me$) (91%) had m.p. 155—157° (decomp.) (Found: C, 48·1; H, 7·7; N, 20·95. $C_8H_{14}ClN_3,0·75H_2O$ requires C, 47·8; H, 7·8; N, 20·9%). Treatment as above with potassium hydrogen difluoride gave *4-fluoro-2-methylpyrimidine* (50%), b.p. 32—34° at 20 mmHg (Found: C, 53·6; H, 4·7; N, 24·9. $C_5H_5FN_2$ requires C, 53·6; H, 4·5; N, 25·0%).

4-Fluoro-6-methylpyrimidine (5; $R^1 = R^3 = H$, $R^2 = Me$).—4-Chloro-6-methylpyrimidine[8] was converted as its isomer above (but during 5 days) into *trimethyl-6-methylpyrimidin-4-ylammonium chloride* (87%), m.p. 169—172° (decomp.) (Found: C, 51·7; H, 7·6; N, 22·7. $C_8H_{14}ClN_3$ requires C, 51·2; H, 7·5; N, 22·4%), and thence into *4-fluoro-6-methylpyrimidine* (55%), b.p. 43° at 20 mmHg (Found: C, 53·0; H, 5·1; N, 24·7. $C_5H_5FN_2$ requires C, 53·6; H, 4·5; N, 25·0%).

Trimethyl-5-methylpyrimidin-4-ylammonium Chloride (4; $R^1 = Me$, $R^2 = R^3 = H$).— 6-Chloro-5-methylpyrimidin-4-one[16] was dechlorinated as its 2-methyl isomer above to give 5-methylpyrimidin-4-one (85%), m.p. 149—150° (lit.,[18] 153—154°) which was converted[19] into 4-chloro-5-methylpyrimidine. This chloro-compound (5·7 g), anhydrous benzene (60 ml), and trimethylamine (8 g) were left at 20—25° in a stoppered flask for 18 weeks. The white solid was filtered off, washed with benzene, and dried *in vacuo*: the hygroscopic *5-methylpyrimidinylammonium chloride* (2·5 g) had m.p. 186—187° (decomp.) (Found: C, 48·0; H, 7·3; N, 20·5. $C_8H_{14}ClN_3,0·75H_2O$ requires C, 47·8; H, 7·8; N, 20·9%). Evaporation of the benzene filtrate (still smelling strongly of trimethylamine) gave unchanged chloro-compound (2·7 g).

Piperidinopyrimidines.—2-Chloropyrimidine[20] (3·0 g), piperidine (4·5 g), and ethanol (20 ml) were heated under reflux for 1 h. Evaporation, extraction of the residual slurry with ether (3 × 20 ml), drying of the extract (Na_2SO_4), and distillation gave *2-piperidinopyrimidine* (3; $R^1 = R^2 = H$) (60%), b.p. 120° at 16 mmHg (Found: C, 66·2; H, 8·0; N, 25·75. $C_9H_{13}N_3$ requires C, 66·2; H, 8·1; N, 25·8%).

In a similar way, the 2-chloro-4-methyl compound[21] gave *4-methyl-2-piperidinopyrimidine* (3; $R^1 = Me$, $R^2 = H$) (65%), b.p. 125—126° at 13 mmHg (Found: C, 67·55; H, 8·6; N, 23·9. $C_{10}H_{15}N_3$ requires C, 67·8; H, 8·5; N, 23·7%); the 2-chloro-4,6-dimethyl compound[22] gave 4,6-dimethyl-2-piperidinopyrimidine (3; $R^1 = R^2 = Me$) (64%), m.p. 62—63° (lit.,[8] 62°) (Found: C, 69·3; H, 8·9; N, 22·25. Calc. for $C_{11}H_{17}N_3$: C, 69·1; H, 9·0; N, 22·0%); the 4-chloro-6-methyl compound[23] gave *4-methyl-6-piperidinopyrimidine* (6; $R^1 = R^3 = H$, $R^2 = Me$) (80%), b.p. 148—149° at 17 mmHg (Found: C, 67·1; H, 8·6; N, 23·5.

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$C_{10}H_{15}N_3$ requires C, 67·8; H, 8·5; N, 23·7%); the 4-chloro-2-methyl compound [8,17] gave *2-methyl-4-piperidinopyrimidine* (6; $R^1 = R^2 = H$, $R^3 = Me$) (69%), b.p. 150—151° at 20 mmHg (Found: C, 67·5; H, 8·6; N, 23·6. $C_{10}H_{15}N_3$ requires C, 69·8; H, 8·5; N, 23·7%); the 4-chloro-2,6-dimethyl compound [24] gave 2,4-dimethyl-6-piperidinopyrimidine (6; $R^1 = H$, $R^2 = R^3 = Me$) (60%), b.p. 154° at 18 mmHg (lit.,[10] 110° at 10^{-3} mmHg) (Found: C, 68·7; H, 8·9; N, 22·1. Calc. for $C_{11}H_{17}N_2$: C, 69·1; H, 9·0; N, 22·0%); and the 4-chloro-5-methyl compound (see above), gave (after heating under reflux for 24 h) *5-methyl-4-piperidinopyrimidine* (6; $R^1 = Me$, $R^2 = R^3 = H$) (50%), b.p. 148—150° at 15 mmHg (Found: C, 67·2; H, 8·4; N, 23·85. $C_{10}H_{15}N_3$ requires C, 67·8; H, 8·5; N, 23·7%).

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