1034. *The Dimroth Rearrangement. Part IV.*[1] *A Study of Facilitation by Electron-withdrawal. Alkylated 2-Alkyliminopyrimidines*

By D. J. Brown and J. S. Harper

The rates of Dimroth rearrangement of nuclear *N*-methylated 2- and 4-iminopyrimidines are increased by the electron-withdrawal provided by a 5-bromo-substituent, and much more by the greater electron-attracting power of a 5-nitro-group. 1-Benzyl-1,2-dihydro-2-methyliminopyrimidine largely rearranges into 2-benzylimino-1,2-dihydro-1-methylpyrimidine, but the reverse reaction is not detectable by ultraviolet-spectral means.

Unlike the pyrimidine analogues, 1,2-dihydro-2-imino-1-methylpyridine and its 5-chloro-, 3,5-dichloro-, and 5-cyano-derivatives do not rearrange. Only in its 3- and 5-nitro-derivatives is there sufficient localisation of π-electrons to permit easy rearrangement.

It has been shown[2] that the rate of Dimroth rearrangement of 1,2-dihydro-2-imino-1-methylpyrimidine (I) into 2-methylaminopyrimidine (II) is profoundly influenced by nuclear substitution: electron-withdrawing groups appear to facilitate the isomerisation, while electron-releasing groups do the reverse. This is also true of the few pteridine[3,4] and triazole[5] examples studied.

The present Paper further explores the rearrangement in three directions. The isomerisation rates for more 2-imino- and some 4-imino-pyrimidines are examined; 2-iminopyridines are shown to undergo rearrangement if sufficiently strong electron-withdrawal is provided by substitution; and evidence is advanced to suggest that alkylated alkyliminopyrimidines, *e.g.*, (III; R = Me, R′ = CH_2Ph) (III; R = CH_2Ph, R′ = Me), which cannot rearrange to formally aromatic structures, will isomerise towards the imine accommodating the larger alkyl group on extracyclic nitrogen (cf. the reversible interconversion,[6] *via* acetyl derivatives, of 3-methylcytosine and 2-hydroxy-4-methylaminopyrimidine).

Preparation of Compounds.—Electron-withdrawal in the pyrimidine imines was achieved with a 5-bromo- or 5-nitro-group. Thus, treatment of 2-amino-5-bromo-4,6-dimethylpyrimidine (made by an improved direct procedure) with methyl iodide gave 5-bromo-1,2-dihydro-2-imino-1,4,6-trimethylpyrimidine hydriodide (IV; R = R′ = Me), and 5-bromo-1-ethyl-1,2-dihydro-2-iminopyrimidine (IV; R = H, R′ = Et) was made similarly. Addition of these salts to warm ammonia caused immediate precipitation of the rearranged amines (V; R = R′ = Me) and (V; R = H, R′ = Et), respectively, which were distinguished from their imino-precursors by their relatively weakly basic strengths, and by direct comparison of the respective picrates.

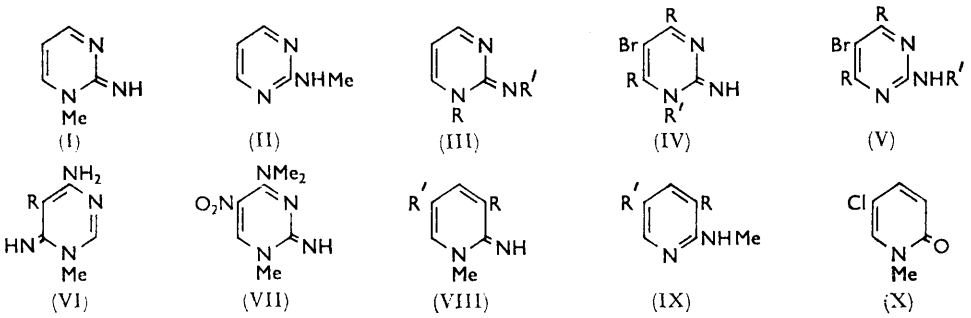
Previous attempts[7] to prepare 4-amino-1,6-dihydro-6-imino-1-methyl-5-nitropyrimidine (VI; R = NO_2) either by methylation or by nitration, led only to the rearranged product, 4-amino-6-methylamino-5-nitropyrimidine, because it was not then realised that rearrangement would occur extremely rapidly even at pH 8—9. By avoiding such mild alkalinity during the work-up procedure, the imine (VI; R = NO_2) has now been obtained as its hydriodide (and other salts). The picrate differed from that of the rearranged isomer. The related nitropyrimidine (VII) was prepared by first dimethylaminating 2,4-dichloro-5-nitropyrimidine to give 2-chloro-4-dimethylamino-5-nitropyrimidine, which

[1] Part III, D. D. Perrin and I. H. Pitman, *Austral. J. Chem.*, 1965, **18**, 763.
[2] D. J. Brown and J. S. Harper, *J.*, 1963, 1276.
[3] D. D. Perrin, *J.*, 1963, 1284.
[4] D. J. Brown and J. S. Harper, in "Pteridine Chemistry," Pergamon Press, Oxford, 1964, p. 217; R. B. Angier, *ibid.*, p. 230.
[5] O. Dimroth, *Annalen*, 1910, **377**, 127; B. R. Brown, D. E. Hammick, and S. G. Heritage, *J.*, 1953, 3820.
[6] T. Ueda and J. J. Fox, *J. Org. Chem.*, 1964, **29**, 1770; cf. I. Wempen, G. B. Brown, T. Ueda, and J. J. Fox, *Biochem.*, 1965, **4**, 54.
[7] D. J. Brown and N. W. Jacobsen, *J.*, 1960, 1978.

differed from the known [8] 4-chloro-2-dimethylamino-isomer, thereby confirming the structure. Subsequent amination gave 2-amino-4-dimethylamino-5-nitropyrimidine, which was then methylated. Position 1 is suggested as the site for this, by analogy with other 2,4-diaminopyrimidines,[9] and this is consistent with the fact [10] that when a solution of the cation is made alkaline, an extremely rapid Dimroth rearrangement occurs, to yield a solution with spectrum closely resembling that of 2-amino-4-dimethylamino-5-nitropyrimidine (the nearest model for the yet unknown 2-methylamino-homologue). However, *N*-3 in place of *N*-1 methylation cannot be positively excluded. An attempt [11] to make 4-amino-1,2-dihydro-2-imino-1-methyl-5-nitropyrimidine by nitration, for direct spectral comparison with compound (VII), was unsuccessful because rearrangement occurred during neutralisation, to yield the known [12] 4-amino-2-methylamino-5-nitropyrimidine.

2-Methylaminopyrimidine underwent benzylation to yield 1-benzyl-1,2-dihydro-2-methyliminopyrimidine (III; R = CH_2Ph, R′ = Me). The isomer (III; R = Me, R′ = CH_2Ph) was obtained by rearrangement, and also by methylation of 2-benzylaminopyrimidine, made from 2-chloropyrimidine. Other alkyl alkylimines were made similarly.

2-Amino-3-nitropyridine [13] (best prepared by aminating [14] commercial 2-chloro-3-nitropyridine) and methyl iodide gave 1,2-dihydro-2-imino-1-methyl-3-nitropyridine (VIII; R = NO_2, R′ = H), isolated as the pyridinium tri-iodide, as picrate, and as hydrochloride, Treatment with ammonia or sodium hydroxide caused almost instantaneous rearrangement to 2-methylamino-3-nitropyridine (IX; R = NO_2, R′ = H), the picrate of which differed from that of the imine. Tschitschibabin's inference [15] that methylation occurs directly on the amino-group, is therefore incorrect; a similar conclusion [16] in respect of the 5-nitro-isomer is confirmed. 5-Chloro-1,2-dihydro-2-imino-1-methylpyridine (VIII; R = H, R′ = Cl) and the dichloro-analogue (VIII; R = R′ = Cl) were made from the appropriate aminopyridine and methyl iodide, and were isolated as salts; the dichloro-imine was also isolated as a fairly stable free base. In each case, treatment with sodium



hydroxide caused hydrolysis rather than rearrangement, the potential products (IX; R = H, R′ = Cl) (IX; R = R′ = Cl) of which were synthesised by aminating 2,5-dichloro- and 2,3,5-trichloro-pyridine, respectively. 5-Cyano-1,2-dihydro-2-imino-1-methylpyridine (VIII; R = H, R′ = CN) was made by methylating 2-amino-5-cyanopyridine. It proved to be stable in alkali.

Discussion.—Our earlier postulation [2] that substitution by electron-withdrawing groups

[8] D. G. Saunders, *J.*, 1956, 3232; W. Pfleiderer and E. C. Taylor, *J. Amer. Chem. Soc.*, 1960, **82**, 3765.
[9] D. J. Brown and T. Teitei, *J.*, 1965, 755.
[10] D. D. Perrin and I. H. Pitman, personal communication.
[11] With N. W. Jacobsen.
[12] A. Albert, D. J. Brown, and G. Cheeseman, *J.*, 1952, 4219.
[13] W. T. Cornwell and E. C. Kornfeld, *J. Amer. Chem. Soc.*, 1942, **64**, 1695.
[14] G. B. Barlin, unpublished results.
[15] A. E. Tschitschibabin and A. W. Kirssanow, *Ber.*, 1928, **61**, 1223 (cf. Beilstein, **22**, II, 335).
[16] J. Geordeler and W. Roth, *Chem. Ber.*, 1963, **96**, 534.

would normally accelerate the Dimroth rearrangement, is upheld in the 2- and 4-imino-pyrimidines of Table 1. Thus, both 5-bromo-derivatives rearrange at 20° more quickly than do their respective unbrominated analogues [2] at 25°, and electron depletion of their π-layers is indicated by appreciable reduction in the pK_a value in each case. More marked are the effects of a nitro-group. The pK_a of 4-amino-1,6-dihydro-6-imino-1-methyl-pyrimidine (VI; R = H) is reduced by no less than 5 (logarithmic) units in its 5-nitro-derivative (VI; R = NO_2), and the corresponding increase in rate of rearrangement at

TABLE 1

Rearrangement rates of pyrimidine and pyridine imines

Pyrimidines	$t_{\frac{1}{2}}$ [a]
4-Amino-1,6-dihydro-6-imino-1-methyl	15 [b,c]
4-Amino-1,6-dihydro-6-imino-1-methyl-5-nitro	<0·1 [b,d]
1-Benzyl-2-benzylimino-1,2-dihydro	— [e]
1-Benzyl-1,2-dihydro-2-isopropylimino	<30 [f]
1-Benzyl-1,2-dihydro-2-methylimino	<90 [g]
2-Benzylimino-1,2-dihydro-1-isopropyl	∞ [h]
2-Benzylimino-1,2-dihydro-1-methyl	∞ [h]
5-Bromo-1,2-dihydro-2-imino-1,4,6-trimethyl	26 [b,i]
5-Bromo-1-ethyl-1,2-dihydro-2-imino	38 [b]
1,2-Dihydro-1-methyl-2-methylimino	— [j]
4-Dimethylamino-1,2(?2,3)-dihydro-1-imino-1(?3)-methyl-5-nitro	<0·1 [b,k]
1,2-Dihydro-2-imino-1-methylpyridines	
5-Chloro	∞
5-Cyano	∞ [b]
3,5-Dichloro	∞
3-Nitro	0·19 [b,l]
5-Nitro	0·17 [b,l]

[a] Time (min.) for appearance of half of rearranged product at 20° and pH 14. [b] Figures obtained by D. D. Perrin and I. H. Pitman with rapid-reaction techniques. [c] Corrected for cation present; pK_a *ca.* 12·7 (ref. 10), not 11·98 as previously recorded (ref. 7). [d] Strongly OH^--catalysed. At pH 10·1, $t_{\frac{1}{2}}$ = 2; at pH 9·6 (pK_a 7·6), $t_{\frac{1}{2}}$ = 3·9. [e] Slow ring-fission and other reactions; $t_{\frac{1}{2}}$ *ca.* 1500 for overall change at 247 mμ. [f] Maximum amount of 2-benzimino-isomer formed in *ca.* 30 min.; other slow reactions ensue. [g] Maximum rearrangement in *ca.* 90 min.; then other slow reactions. [h] No spectral change towards isomer. [i] At pH 12 and adjusted for cation present. Mild OH^- catalysis at higher pH values. [j] Slow ring-fission and other reactions; $t_{\frac{1}{2}}$ *ca.* 260 for overall change at 233 mμ. [k] Immeasurably rapid rearrangement. [l] At pH 11·5. Immeasurably rapid at pH 14 owing to strong OH^- catalysis.

pH 14 is ⩾150-fold, making it almost instantaneous at room temperature. The $t_{\frac{1}{2}}$ value for the reaction in very mildly alkaline buffer (pH 9·6) is slowed to 4 min., indicating considerable base catalysis. A similar relation is seen between the rearrangement of 4-dimethylamino-1,2-dihydro-2-imino-1-methylpyrimidine [2] ($t_{\frac{1}{2}}$ = 2000 min. at 25°) and its 5-nitro-derivative which rearranges so quickly at 20° that no estimate of pK_a value is even possible.[10]

Having but one ring-nitrogen atom to localise its π-electrons, 1,2-dihydro-2-imino-1-methylpyridine (VIII; R = R′ = H) does not undergo [17] Dimroth rearrangement like its pyrimidine analogue. However, it appeared [4,15] that the introduction of a nitro-group would facilitate such isomerisation, and the 5-nitro-derivative was indeed shown to rearrange,[16] although the first strict proof of this (mixed m. p. depression of both picrates, which melt within a few degrees of each other, and of both hydriodides) is now recorded. We have also extended this observation to the 3-nitro-isomer (VIII; R = NO_2, R′ = H), and the $t_{\frac{1}{2}}$ values indicate that rearrangement is virtually complete within a few seconds of making their solutions alkaline at room temperature. The extent of electron-withdrawal by the nitro-group is indicated by basic pK_a values of *ca.* 9 compared with >13 in the parent imine. In contrast, the insertion of a mildly electron-withdrawing chloro-substituent only reduced the pK_a value of the imine (VIII; R = H, R′ = Cl) to 12·3,

[17] A. E. Tschitschibabin, R. A. Konowalowa, and A. A. Konowalowa, *Ber.*, 1921, **54**, 814.

TABLE 2

Ionisation and ultraviolet spectra

	pK_a [a]	$\lambda_{max.}$ (mμ) (log ε)	pH
Pyrimidine derivative			
2-Amino-5-bromo-4,6-dimethyl		301(3·60), 235(4·17)	6·0
cation	3·35 ± 0·03	315(3·73), 235(4·19)	1·0
4-Amino-1,6-dihydro-6-imino-1-methyl-5-nitro		—	
cation	*ca.* 7·6	329(3·80), *293(3·55)*, 234(4·36)	4·0
2-Amino-4-dimethylamino-5-nitro		375(3·89), 273(4·06), 232(4·06)	7·0
cation	3·49 ± 0·03	330(3·44), 251(4·31)	1·0
2-Benzylamino		305(3·11), 236(3·97)	7·0
cation	3·56 ± 0·04 (M/1000)	316(3·23), 230(4·00)	1·0
1-Benzyl-2-benzylimino-1,2-dihydro		370(3·45), 246(4·24)	13·1
cation	10·60 ± 0·03	317(3·66), 232(4·24)	7·0
1-Benzyl-1,2-dihydro-2-isopropylimino		373(3·38), 245(4·14)	13·7
cation	11·55 ± 0·05	319(3·63), 232(4·21)	1·0
1-Benzyl-1,2-dihydro-2-methylimino		370(3·39), 242(4·15)	13·1
cation	11·17 ± 0·02	318(3·63), 229(4·54)	7·0
1-Benzyl-1,2-dihydro-2-oxo	—	305(3·77), 209(4·17)	7·0
2-Benzylimino-1,2-dihydro-1-isopropyl		371(3·44), 247(4·27)	13·2
cation	11·21 ± 0·05	317(3·65), 232(4·26)	1·0
2-Benzylimino-1,2-dihydro-1-methyl		364(3·41), 245(4·29)	13·1
cation	11·17 ± 0·02	315(3·63), 230(4·27)	7·0
2-Benzyloxy	—	263(4·26), *ca.* 206(4·31)	7·0
5-Bromo-1,2-dihydro-2-imino-1,4,6-trimethyl		—	
cation	11·0	316(3·72), 236(4·15)	5·0
5-Bromo-4,6-dimethyl-2-methylamino		314(3·53), 245(4·25)	7·0
cation	3·57 ± 0·02	327(3·67), 241(4·29)	−0·5
5-Bromo-2-ethylamino		327(3·37), 248(4·36)	7·0 [c]
cation	2·10 ± 0·04	340(3·47), 243(4·37)	−0·5
5-Bromo-1-ethyl-1,2-dihydro-2-imino		—	
cation	10·2	326(3·55), 237(4·25)	7·0
1,2-Dihydro-1-methyl-2-methylimino [d]		365(3·38), 241(4·22)	13·7
cation	11·74 ± 0·04	316(3·60), 227 (4·19)	7·0
1-Ethyl-1,2-dihydro-2-methylimino [d]		368(3·39), 243(4·22)	14·0
cation	—	319(3·59), 229(4·19)	7·0
2-Ethylimino-1,2-dihydro-1-methyl [d]		368(3·37), 243(4·23)	14·0
cation	—	317(3·66), 229(4·25)	7·0
2-Isopropylamino		308(3·39), 236(4·25)	7·0
cation	4·05 ± 0·04 (M/200)	317(3·50), 230(4·27)	1·0
Pyridine derivative			
2-Amino-5-cyano		*294(3·76)*, 264(4·32)	6·0
cation	3·46 ± 0·03	303(3·72), 256(4·27)	1·2
2-Amino-3,5-dichloro		312(3·65), 240(4·04)	7·0
cation	2·80 ± 0·01	326(3·81), *248(3·85)*, 242(3·94), *215(4·24)*, 211(4·28)	0·5
2-Amino-3-nitro			
cation	2·38 ± 0·04	—[e]	
2-Amino-5-nitro [f]		350(4·12), 220(3·92)	7·0
cation	2·83 ± 0·01	307(4·16), 212(4·03)	0·5
5-Chloro-1,2-dihydro-2-imino-1-methyl		344(3·51), *264(4·10)*, 258(4·16)	14·5
cation	12·30 ± 0·04	315(·370), 240(4·06)	7·0
5-Chloro-1,2-dihydro-1-methyl-2-oxo [g]	—	312(3·67), 235(3·97)	7·0
5-Chloro-2-hydroxy [h]		307(3·70), 233(4·02)	5·0
cation	0·01 ± 0·05	294(3·78), 223(3·85)	−2·0
anion	9·98 ± 0·03	307(3·64), 238(4·12)	14·0
5-Chloro-2-methylamino		315(3·50), 248(4·17)	7·5
cation	5·16 ± 0·04	320(3·71), 245(4·16)	3·0
5-Cyano-1,2-dihydro-2-imino-1-methyl		325(3·40), 282(4·34), 273(4·41), *267(4·31)*	13·0
cation	10·2	302(3·70), 256(4·27)	7·0
3,5-Dichloro-1,2-dihydro-2-imino-1-methyl		*365(3·58)*, 350(3·63), *263(3·98)*, 257(4·03), *249(3·92)*, 214(4·24)	12·4
cation	10·19 ± 0·02	324(3·81), *246(3·88)*, 242(3·91), *216(4·28)*, 211(4·33)	7·0

TABLE 2 (*Continued*)

	pK_a [a]	$\lambda_{max.}$ (mμ) (log ε) [b]	pH
3,5-Dichloro-1,2-dihydro-1-methyl-2-oxo [g]	—	*340(3·54)*, 322(3·80), *315(3·78)*, *246(3·68)*, 239(3·80), 208(4·39)	7·0
3,5-Dichloro-2-methylamino cation	3·06 ± 0·01	322(3·64), 250(4·15)	7·0
		345(3·63), 311(3·81), *253(4·01)*, 248(4·07), 213(4·30)	0·8
1,2-Dihydro-2-imino-1-methyl [i] cation	13·25 ± 0·03 [j]	299(3·73), 230(3·86)	7·0
1,2-Dihydro-2-imino-1-methyl-3-nitro cation	9·0	357(3·81), 263(3·53), *230(3·66)*	4·0
1,2-Dihydro-2-imino-1-methyl-5-nitro ation	9·3	304(4·12), 215(3·96)	5·0
2-Methylamino-3-nitro cation	2·46 ± 0·02	423(4·35), 266(3·65), 223(4·35)	5·0
		376(3·81), 269(3·78), 212(4·29)	0·2
2-Methylamino-5-nitro cation	2·79 ± 0·04	372(4·21), *305(3·60)*, 223(3·97)	7·0
		313(4·16), 214(4·04)	0·5

[a] Measured at 20° spectrometrically or potentiometrically (molarity given) by methods in ref. 19. Figures without spread are approximated from unpublished values (ref. 10) obtained by rapid reaction techniques. [b] Inflexions in italics. Data for unstable free bases will be published by D. D. Perrin and I. H. Pitman. [c] Buffer contained 5% ethanol. [d] Hydriodide: I^- concentration balanced in reference cell. [e] For spectra see G. B. Barlin, *J.*, 1964, 2150. [f] "Fluka" sample, recrystallised (carbon) from water, m. p. 187° (A. Tschitschibabin, *J. Russ. Phys. Chem. Soc.*, 1914, **46**, 1236, though *Chem. Zentr.*, 1915, I, 1066, gives 188°). [g] Prep. from A. Binz and C. Räth, *Annalen*, 1931, **486**, 71. [h] Prep. ref. 34. [i] Prep. ref. 17. [j] Cf. 12.2 given by S. J. Angyal and C. L. Angyal, *J.*, 1952, 1462.

and no detectable rearrangement took place. Thus, in 3N-potassium hydroxide the spectrum of the imine gradually approximated to that of an authentic specimen of its hydrolysis product (X), but showed no contribution from the curve of 5-chloro-2-methylaminopyridine, determined from authentic material. Hydrolysis was 75% complete at 25° in 8 days; at 98° in *ca.* 15 min. The addition of two such chloro-substituents to give the imine (VIII; R = R′ = Cl) reduced the pK_a value to 10·2, but still no rearrangement occurred in alkali; indeed, much of the free base was recovered unchanged after heating for 10 min. at 98° in buffer of pH 14. Substitution of 1,2-dihydro-2-imino-1-methylpyridine by a 5-cyano-group again reduced the pK_a to 10·2, and again no rearrangement occurred in alkali. It is therefore clear that before Dimroth rearrangement will occur, the parent pyridine (VIII; R = R′ = H) needs electron-localising substituents powerful enough to reduce its basic strength to a value well below pK_a 10.

Preliminary examination revealed that the spectra of 1-ethyl-1,2-dihydro-2-methyliminopyrimidine [2] (III; R = Et, R′ = Me) and the isomer [2] (III; R = Me, R′ = Et) were all but identical, and could therefore not be used to follow any interchange of the isomers in alkali. However, the related pair, 1-benzyl-1,2-dihydro-2-methyliminopyrimidine and its isomer (III; R = Me, R′ = CH_2Ph) showed just sufficient difference in the intensity and position of their peaks at 242 and 245 mμ, respectively, to make it possible to follow any interchange semi-quantitatively. At pH 14 and 20°, the 242-mμ peak of the 1-benzyl isomer shifted bathochromically and increased in intensity until, after 90 min., it approximated in position and height to the 245-mμ peak of its isomer; thereafter, the peak fell slowly with no appreciable change in $\lambda_{max.}$ value. The inference, that the 1-benzylpyrimidine had been converted largely into its 2-benzylimino-isomer, was tested by isolating the picrate of the latter from a similar experiment on a preparative scale. When the experiment was reversed by starting with the 2-benzylimine, no detectable change in $\lambda_{max.}$ occurred, and the 245-mμ peak merely fell at a rate comparable with the second (slow) change mentioned above.* From a parallel preparative-scale experiment only the benzylimine picrate could be isolated. It is therefore suggested that, if an equilibrium is attained at all, it strongly favours the isomer having the benzyl group on the

* 1-Benzyl-2-benzylimino-1,2-dihydropyrimidine and 1,2-dihydro-1-methyl-2-methyliminopyrimidine, which cannot rearrange, showed comparable behaviour in this respect (cf. a purine analogue [18]).

[18] H. G. Windmueller and N. O. Kaplan, *J. Biol. Chem.*, 1961, **236**, 2716.
[19] A. Albert and E. P. Serjeant, "Ionization Constants of Acids and Bases," Methuen, London, 1962.

extracyclic nitrogen atom. The experiments were repeated using 1-benzyl-1,2-dihydro-2-isopropyliminopyrimidine and its isomer (III; R = Pr^i, R′ = CH_2Ph) in which each methyl group had been replaced by an isopropyl group, more comparable with the benzyl group in its capacity sterically to hinder, for example, ring-closure. The pattern remained the same: only the 1-benzylpyridimidine could be shown to rearrange.

All the above alkylamines at pH 14 slowly develop during 10 hr. a flat peak at 310—320 mμ, which then wanes over several days. This probably indicates some hydrolysis to the 2-oxo-analogues, for 1-benzyl-1,2-dihydro-2-oxopyrimidine at pH 14 has an initial peak at 308 mμ, which waxes and shifts to 312 mμ and then wanes slowly. 1-Benzyl-1,2-dihydro-2-isopropyliminopyrimidine is uniquely characterised by the rapid development, in 4 min. at pH 14, of a small peak at 324 mμ, which then undergoes a small hypsochromic shift to 320 mμ and slowly decays.

Experimental

Analyses were done by Dr. J. E. Fildes and her staff. Ionisation constants were measured by methods described by Albert and Serjeant.[19] All compounds were checked for chromatographic homogeneity. Alkylations requiring a sealed tube were rocked and heated in a modified version of Gabriel's furnace.[20]

2-*Amino*-5-*bromo*-4,6-*dimethylpyrimidine*.—Bromine (5·3 ml.) was slowly added with stirring to 2-amino-4,6-dimethylpyrimidine [21] (12·5 g.), powdered calcium carbonate (5 g.), and water (100 ml.) at 50—55°. After a further hour, the solution was adjusted with ammonia to pH 8—9 and refrigerated. The bromopyrimidine (86%) had m. p. 184° (from ethanol) (lit.,[22] 47%; m. p. 187—188° corr.).

5-*Bromo*-1,2-*dihydro*-2-*imino*-1,4,6-*trimethylpyrimidine*.—The above amine (2·0 g.) and methyl iodide (10 ml.) were rocked at 110° for 3 hr. After refrigeration, the solid (2·7 g.) was removed, washed with ether, and recrystallised from ethanol. The *iminopyrimidine hydriodide* had m. p. *ca.* 240° (decomp.) (Found: N, 12·35. $C_7H_{11}BrIN_3$ requires N, 12·2%). The *hydrochloride*, m. p. 250° (decomp.) was crystallised from methanol by adding hot ethyl acetate. (Found: N, 16·7. $C_7H_{11}BrClN_3$ requires N, 16·6%). The *picrate* (from water) had m. p. 191—192° (Found: C, 35·2; H, 2·9. $C_{13}H_{13}BrN_6O_7$ requires C, 35·05; H, 2·9%).

5-*Bromo*-4,6-*dimethyl*-2-*methylaminopyrimidine*.—The above hydrochloride (0·25 g.) was warmed for 3 min. in 2N-ammonia (10 ml.). The resulting solid sublimed (100°/0·1 mm.) to give the *methylaminopyrimidine* (0·15 g.), m. p. 130° (Found: N, 19·6. $C_7H_{10}BrN_3$ requires N, 19·45%). Its *picrate* (from ethanol) had m. p. 164° (Found: C, 35·1; H, 3·05. $C_{13}H_{13}BrN_6O_7$ requires C, 35·05; H, 2·9%).

5-*Bromo*-1,2-*dihydro*-2-*imino*-1-*methylpyrimidine*.—The methylation of 2-amino-5-bromopyrimidine must be done at 110° in a sealed tube, not by heating under reflux as previously recorded.[2]

5-*Bromo*-1-*ethyl*-1,2-*dihydro*-2-*iminopyrimidine*.—2-Amino-5-bromopyrimidine [23] (3·6 g.) and ethyl iodide (36 ml.) were rocked at 120—130° for 40 hr. The crude solid was dissolved in hot methoxyethanol (25 ml.) and hot ethyl acetate (50 ml.) was added. The resulting *imine hydriodide* (4·3 g.) had m. p. 240° (decomp.) (Found: C, 22·1; H, 2·8; N, 12·6. $C_6H_9BrIN_3$ requires C, 21·85; H, 2·75; N, 12·7%). The *hydrochloride* (from methanol–ether) had m. p. 258° (decomp.) (Found: N, 17·5. $C_6H_9BrClN_3$ requires N, 17·6%), and the *picrate* (from water), m. p. 195° (Found: C, 33·3; H, 2·5. $C_{12}H_{11}BrN_6O_7$ requires C, 33·4; H, 2·6%).

5-*Bromo*-2-*ethylaminopyrimidine*.—15N-Ammonia (5 ml.) was added to the above hydriodide (1·1 g.) dissolved in hot water (10 ml.). The resulting solid sublimed (90°/0·01 mm.) to give 5-*bromo*-2-*ethylaminopyrimidine* (80%), m. p. 122° (Found: C, 35·4; H, 4·1; N, 20·9. $C_6H_8BrN_3$ requires C, 35·65; H, 4·0; N, 20·8%). Its *picrate* (from ethanol) had m. p. 158° (Found: C, 33·2; H, 2·7. $C_{12}H_{11}N_6O_7$ requires C, 33·4; H, 2·6%).

4-*Amino*-1,6-*dihydro*-6-*imino*-1-*methyl*-5-*nitropyrimidine*.—4,6-Diamino-5-nitropyrimidine [24]

[20] S. Gabriel, *Ber.*, 1905, **38**, 630.
[21] A. Combes and C. Combes, *Bull. Soc. chim. France*, 1892, [3], **7**, 788.
[22] J. P. English, J. H. Clark, J. W. Clapp, D. Seeger, and R. H. Ebel, *J. Amer. Chem. Soc.*, 1946, **68**, 453.
[23] C. Ziegler, U.S.P. 2,609,372/1952 (*Chem. Zentr.*, 1953, **124**, 5934).
[24] D. J. Brown, *J. Soc. Chem. Ind.*, 1950, **69**, 353.

(6 g.) and methyl iodide (60 ml.) were rocked at 135—145° for 6 hr. The solid was extracted with boiling ethanol (450 ml.), and ether (peroxide-free; 1800 ml.) was slowly added to the warm solution. The crude product (6·8 g.) was recrystallised from ethanol (50 parts) containing a few drops of hydriodic acid. The *imine hydriodide* had m. p. *ca.* 223° (decomp.) (Found: C, 20·3; H, 2·9. $C_5H_8IN_5O_2$ requires C, 20·2; H, 2·7%). The *hydrochloride* (from methanol–ether) had m. p. 270—280° (decomp.) (Found: Cl, 17·15; N, 34·4. $C_5H_8ClN_5O_2$ requires Cl, 17·2; N, 34·1%), and the *picrate*, m. p. 212—214° (from water) (Found: C, 33·3; H, 2·6. $C_{11}H_{10}N_8O_9$ requires C, 33·2; H, 2·5%).

When the hydriodide was dissolved in hot water and treated with aqueous ammonia, 4-amino-6-methylamino-5-nitropyrimidine [7] (m. p. and mixed m. p. 248°) was precipitated. It showed no chromatographic spot corresponding to 4-amino-1,6-dihydro-1-methyl-5-nitro-6-oxopyrimidine (which has m. p. 284°; not 184° as recorded [25]), thus precluding any appreciable hydrolysis of the imine. The *picrate*, made by addition of aqueous picric acid to a solution of the rearranged base in N-hydrochloric acid, crystallised from methoxyethanol as needles, m. p. 265° (decomp.) (Found: C, 33·1; H, 2·6. $C_{11}H_{10}N_8O_9$ requires C, 33·2; H, 2·5%).

2-*Chloro*-4-*dimethylamino*-5-*nitropyrimidine*.—2,4-Dichloro-5-nitropyrimidine [26] (13·5 g.) in dioxan (50 ml.) was stirred at 15° while dimethylamine (43 ml. of 30% aqueous solution adjusted to pH 8 with acetic acid) was added dropwise. After a further 2 hr., water (150 ml.) was added; refrigeration and recrystallisation from ethanol gave the *amine* (8·8 g.), m. p. 116—117° (Found: C, 35·5; H, 3·55. $C_6H_7ClN_4O_2$ requires C, 35·55; H, 3·5%). On prolonged refrigeration, 2,4-bisdimethylamino-5-nitropyrimidine (1·5 g.) was deposited, m. p. 90° (from light petroleum) (lit.,[27] 88—92°).

2-*Amino*-4-*dimethylamino*-5-*nitropyrimidine*.—The above chloropyrimidine (5 g.) was heated at 140° for 6 hr. in ethanolic ammonia (10%; 50 ml.). The residue from evaporation was triturated with water (10 ml.). The remaining solid (4·0 g.) was dissolved in 0·2N-hydrochloric acid (110 ml.) at 25° and the solution, filtered from a residue, was treated with a little charcoal. The precipitate formed on adjustment to pH 10 with ammonia was recrystallised from propanol to give the *diamine* (1·2 g.), m. p. 142—143° (Found: C, 39·4; H, 5·1. $C_6H_9N_5O_2$ requires C, 39·3; H, 4·95%).

2-*Amino*-4-*dimethylamino*-5-*nitropyrimidine Methiodide*.—The pyrimidine (0·2 g.) methyl iodide (2 ml.) and propanol (5 ml.) were heated under reflux for 18 hr. After refrigeration, the solid (0·26 g.) recrystallised from ethanol to give the *methiodide*, m. p. *ca.* 236° (decomp.) (Found: C, 25·75; H, 3·85. $C_7H_{12}IN_5O_5$ requires C, 25·85; H, 3·7%).

2-*Benzylaminopyrimidine*.—2-Chloropyrimidine [28] (8·6 g.), benzylamine (11·0 g.), and ethanol (50 ml.) were heated under reflux for 2 hr. The residue from evaporation was extracted with boiling light petroleum (b. p. 80—100°; 3 × 150 ml.). The extracts were evaporated, and the residue, twice recrystallised, gave 2-benzylaminopyrimidine (8·8 g.), m. p. 82—83° (lit.,[29] 83—84°) (Found: C, 71·65; H, 6·1; N, 22·7. Calc. for $C_{11}H_{11}N_3$: C, 71·3; H, 6·0; N, 22·7%).

2-*Isopropylaminopyrimidine*.—2-Chloropyrimidine [28] (5·73 g.), isopropylamine (9·1 g.), and ethanol (40 ml.) were heated under reflux for 8 hr. The residue from evaporation was extracted with boiling light petroleum (b. p. 80—100°; 3 × 50 ml.) and distillation of the extracts gave 2-*isopropylaminopyrimidine* (3·8 g.), b. p. 92—93°/12 mm. and m. p. 27—28° (Found: C, 61·05; H, 8·0; N, 30·5. $C_7H_{11}N_3$ requires C, 61·3; H, 8·1; N, 30·6%). Its *picrate* (from ethanol) had m. p. 173—174° (Found: C, 42·8; H, 3·9. $C_{13}H_{14}N_6O_7$ requires C, 42·6; H, 3·85%).

1-*Benzyl*-1,2-*dihydro*-2-*oxopyrimidine*.—2-Hydroxypyrimidine [30] (0·48 g.), ethanolic 2N-potassium hydroxide (10 ml.), and benzyl chloride (2·53 g.) were set aside at 25° for 18 hr. The mixture was adjusted with concentrated hydrochloric acid to pH 5—6, heated to boiling, and filtered from salt. The residue from evaporating the filtrate crystallised from ethyl acetate (7 ml.) to give 1-*benzyl*-1,2-*dihydro*-2-*oxopyrimidine* (0·25 g.), m. p. 138—139° (Found: C, 71·3; H, 5·6; N, 15·2. $C_{11}H_{10}N_2O$ requires C, 70·95; H, 5·4; N, 15·05%).

2-*Benzyloxypyrimidine*.—Sodium (1·15 g.) was allowed to react with an excess of benzyl

[25] D. J. Brown and J. S. Harper, *J.*, 1961, 1298.
[26] N. Whittaker, *J.*, 1951, 1565.
[27] W. E. Fidler and H. C. S. Wood, *J.*, 1956, 3311.
[28] I. C. Kogon, R. Minin, and C. G. Overberger, *Org. Synth.*, 1955, **35**, 34.
[29] T. Matsukawa, K. Shirakawa, and H. Kawasaki, *J. Pharm. Soc. Japan*, 1951, **71**, 895.
[30] R. R. Hunt, J. F. W. McOmie, and E. R. Sayer, *J.*, 1959, 525.

alcohol on a steam-bath. The sodium salt, obtained by evaporation *in vacuo*, was suspended in ether (55 ml.) containing 2-chloropyrimidine [28] (5·7 g.). After 10 days, salt was removed and the filtrate evaporated. The residue was fractionally distilled, and twice redistilled, to give 2-*benzyloxypyrimidine*, b. p. 115°/0·4 mm., n_D^{20} 1·5735 (Found: C, 70·6; H, 5·4; N, 15·0. $C_{11}H_{10}N_2O$ requires C, 70·95; H, 5·4; N, 15·05%).

1-*Benzyl*-1,2-*dihydro*-2-*methyliminopyrimidine*.—Benzyl iodide [31] (4·0 g.), 2-methylaminopyrimidine [32] (1·25 g.), and ethanol (15 ml.) were set aside in the dark at 25° for 12 days. The mixture was concentrated on a steam-bath under vacuum and the semi-solid was triturated with ether (4 × 50 ml.). The insoluble residue was dissolved in ethanol (5 ml.) and ethyl acetate (70 ml.) slowly added. Refrigeration gave a pale yellow crystalline solid (1 g.) which was recrystallised thrice from ethanol–ethyl acetate (1 : 1) to give the colourless *hydriodide* (0·3 g.), m. p. 165—166° (Found: C, 44·4; H, 4·2; N, 12·9. $C_{12}H_{14}IN_3$ requires C, 44·0; H, 4·3; N, 12·8%).

The *hydrochloride* made from it was identified by mixed m. p. with that made as follows: 2-methylaminopyrimidine (1·4 g.) and benzyl chloride (7 ml.) were heated on a steam-bath for 14 hr. Refrigeration gave a solid which, recrystallised from ethanol (5 ml.), had m. p. 208—209° (Found: C, 61·2; H, 6·0; N, 17·8. $C_{12}H_{14}ClN_3$ requires C, 61·1; H, 6·0; N, 17·8%). The *picrate* had m. p. 134—135° (from water) (Found: C, 50·9; H, 3·7; $C_{18}H_{16}N_6O_7$ requires C, 50·5; H, 3·8%).

2-*Benzylimino*-1,2-*dihydro*-1-*methylpyrimidine*.—(*a*) 2-Benzylaminopyrimidine (1·0 g.) and methyl iodide (5 ml.) were heated under reflux for 10 hr. The residue from evaporation was recrystallised from ethanol to give the *pyrimidine hydriodide* (1·25 g.), m. p. 183—185° (Found: C, 44·3; H, 4·4; N, 12·9. $C_{12}H_{14}IN_3$ requires C, 44·0; H, 4·3; N, 12·8%). The *hydrochloride* (from ethanol–ethyl acetate; 1 : 4) had m. p. 207° (decomp.) (Found: C, 61·05; H, 5·8; N, 17·8. $C_{12}H_{14}ClN_3$ requires C, 61·1; H, 6·0; N, 17·8%) and the *picrate*, m. p. 167—168° (from water) (Found: C, 50·2; H, 3·75. $C_{15}H_{16}N_6O_7$ requires C, 50·5; N, 3·8%).

(*b*) 1-Benzyl-1,2-dihydro-2-methyliminopyrimidine hydrochloride (0·7 g.) was stirred for 1·5 hr. at 20—22° in N-sodium hydroxide (15 ml.) and ethanol (45 ml.). The solution was adjusted to pH 4—5 with hydrochloric acid and evaporated to dryness *in vacuo*. The residue was extracted with ethanol–ethyl acetate (1 : 4; 3 × 25 ml.). The solid remaining after evaporation of the extracts was dissolved in water (30 ml.) and treated with saturated (20°) aqueous picric acid (14 ml.). After refrigeration, the benzyliminopyrimidine picrate (0·25 g.) had m. p. 165°, undepressed on admixture with authentic material. The filtrate was treated with more picric acid solution (14 ml.). Refrigeration gave the 1-benzylpyrimidine picrate (0·13 g.) identified by mixed m. p. 131°.

When the 2-benzyliminopyrimidine hydrochloride was treated similarly in sodium hydroxide, fractional precipitation with picric acid did not yield any of the 1-benzylpyrimidine picrate, but gave 50% recovery of starting material as picrate.

1-*Benzyl*-2-*benzylimino*-1,2-*dihydropyrimidine*.—2-Benzylaminopyrimidine (2·0 g.) and benzyl chloride (10 ml.) were heated on a steam-bath for 24 hr. Evaporation to dryness *in vacuo* and recrystallisation from ethanol–ethyl acetate (1 : 4), gave the *benzyliminopyrimidine hydrochloride* (2·2 g.), m. p. 164—165° (Found: C, 69·4; H, 6·1; N, 13·4. $C_{18}H_{18}ClN_3$ requires C, 69·3; H, 5·8; N, 13·5%).

1-*Benzyl*-1,2-*dihydro*-2-*isopropyliminopyrimidine*.—2-Isopropylaminopyrimidine (1·5 g.) and benzyl chloride (8 ml.) were heated on a steam-bath for 30 hr. The residue from distillation *in vacuo* was recrystallised twice from ethanol–ethyl acetate (1 : 4) to give the *benzylpyrimidine hydrochloride* (0·8 g.), m. p. 168—169° (Found: C, 64·0; H, 6·8; N, 15·9. $C_{14}H_{18}ClN_3$ requires C, 63·7; H, 6·9; N, 15·9%).

2-*Benzylimino*-1,2-*dihydro*-1-*isopropylpyrimidine*.—2-Benzylaminopyrimidine (2·0 g.) and isopropyl iodide (12·0 ml.) were heated on a steam-bath for 14 days. Refrigeration and filtration gave red crystals (1·75 g.) which recrystallised from ethanol to give the colourless *benzyliminopyrimidine hydriodide*, m. p. 210—211° (Found: C, 47·4; H, 5·1; N, 11·8. $C_{14}H_{18}IN_3$ requires C, 47·3; H, 5·1; N, 11·8%). Its hygroscopic *hydrochloride* (from dioxan) had m. p. 137—138° (Found: N, 15·7. $C_{14}H_{18}ClN_3$ requires N, 15·9%).

1,2-*Dihydro*-2-*imino*-1-*methyl*-3-*nitropyridine*.—2-Amino-3-nitropyridine [13,14] (1 g.) and methyl iodide (5 ml.) were rocked at 115° for 4 hr. The black solid was washed with ether,

[31] G. Kumpf, *Annalen*, 1884, **224**, 96.
[32] D. J. Brown and L. N. Short, *J.*, 1953, 331.

triturated with hot ethanol (3 ml.), and then recrystallised from ethanol. The iodine-like crystals (0·7 g.) of *1,2-dihydro-2-imino-1-methyl-3-nitropyridinium triodide* had m. p. 145° (decomp.) (Found: C, 14·0; H, 1·55; I, 70·8. $C_6H_8I_3N_3O_2$ requires C, 13·5; H, 1·5; I, 71·5%).

2-Amino-3-nitropyridine (3 g.), methyl iodide (15 ml.), and ethanol (30 ml.) were rocked at 100° for 4 hr. The residue from evaporation *in vacuo*, was dissolved in aqueous sodium hydrogen sulphite (4%; 75 ml.), and saturated aqueous picric acid (450 ml.) was added. Adjustment to pH 5·5 with sodium hydrogen carbonate, and refrigeration, gave the crude picrate (5·0 g.; m. p. *ca.* 140°). After eight recrystallisations from water (33 parts), *1,2-dihydro-2-imino-1-methyl-3-nitropyridine picrate* (1·8 g.) had m. p. 169—170° (Found: C, 37·9; H, 2·7. $C_{12}H_{10}N_6O_9$ requires C, 37·7; H, 2·6%).

Dry hydrogen chloride was passed into a suspension of pure picrate (0·85 g.) in anhydrous benzene (20 ml.) until the solid was colourless. The benzene was decanted, replaced by fresh solvent, and hydrogen chloride again passed. Recrystallisation from ethanol–ethyl acetate (1 : 1) gave a colourless product (dihydrochloride ?) which rapidly became yellow when kept at room temperature *in vacuo*. After 2 hr., followed by heating at 100° for 2 hr., the bright yellow *(mono)hydrochloride* (0·18 g.) had m. p. 230° (decomp.) (Found: C, 38·1; H, 4·3. $C_6H_5ClN_3O_2$ requires C, 38·0; H, 4·3%).

2-Methylamino-3-nitropyridine.—The above imine picrate (0·3 g.) was dissolved in hot water and the solution adjusted to pH 10 with sodium hydroxide. After refrigeration, the solid was dried and sublimed. The rearranged base (0·03 g.) had m. p. 63—64° (lit.,[15] 63—64°). Its *picrate* (from water) had m. p. 158°, depressed on admixture with the isomeric imine picrate (Found: C, 37·9; H, 2·5. $C_{12}H_{10}N_6O_9$ requires C, 37·7; H, 2·6%).

1,2-Dihydro-2-imino-1-methyl-5-nitropyridine.—2-Amino-5-nitropyridine (5 g.), ethanol (50 ml.), and methyl iodide (25 ml.) were heated under reflux for 20 hr. The hydriodide (6·5 g.) was filtered off, and had m. p. 214° (decomp.) (lit.,[15,16,33] 205—207°; and 227° corr. on a Kofler-hot-stage apparatus) before and after recrystallising from methanol–ether (Found: C, 25·8; H, 2·85. Calc. for $C_6H_8IN_3O_2$: C, 25·65; H, 2·9%). The *hydrochloride* (from methanol–ethyl acetate) had m. p. 265° (decomp.) (Found: C, 37·9; H, 4·4; Cl, 18·8. $C_6H_8ClN_3O_2$ requires C, 38·0; H, 4·25; Cl, 18·7%) and the picrate, m. p. 191° (lit.,[16] 192°).

2-Methylamino-5-nitropyridine.—Treatment of the above hydrochloride (0·38 g.) in warm water (4 ml.) with 15N-ammonia (1 ml.) immediately gave the methylamino-compound (0·3 g.) which (from methanol) had m. p. 180° (lit.,[16,33] 180—181°). Its *hydriodide*, prepared in ether and recrystallised from ethanol (containing a drop of hydriodic acid) by addition of ether, had m. p. *ca.* 130°, depressed on admixture with the above hydriodide (Found: C, 25·55; H, 3·0. $C_6H_8IN_3O_2$ requires C, 25·65; H, 2·9%). The picrate [16,33] had m. p. 197°, depressed on admixture with the imine picrate above. Hydrolysis of the methylamine (cf.[15]) gave 2-hydroxy-5-nitropyridine, m. p. 182° undepressed on admixture with authentic material made [15] from 2-amino-5-nitropyridine.

5-Chloro-1,2-dihydro-2-imino-1-methylpyridine.—2-Amino-5-chloropyridine (5 g.) was heated under reflux with methyl iodide (50 ml.) for 18 hr. The solid (10 g.), recrystallised from ethanol, gave the *iminopyridine hydriodide* (78%), m. p. 230° (decomp.) (Found: N, 10·3. $C_6H_8ClIN_2$ requires N, 10·35%). Prepared from it using silver chloride, the *hydrochloride* (from propanol) had m. p. 240° (Found: N, 15·6. $C_6H_8Cl_2N_2$ requires N, 15·6%).

5-Chloro-2-methylaminopyridine.—2,5-Dichloropyridine [34] (1·5 g.) was heated with ethanolic methylamine (30%; 15 ml.) at 160° for 3 hr. The solution, concentrated to small volume *in vacuo*, was stirred with methanolic sodium methoxide (20 ml.; sodium, 0·25 g.) and then treated with carbon dioxide. The filtered solution was evaporated, and the residue extracted with ether (3 × 50 ml.). Removal of solvent and two sublimations (50°/0·05 mm.) gave *5-chloro-2-methylaminopyrimidine* (1·05 g.), m. p. 66—67° (Found: C, 50·6; H, 4·9; N, 19·8. $C_6H_7ClN_2$ requires C, 50·5; H, 4·95; N, 19·65%). Evaporation of a solution of the base in hydrochloric acid gave the *hydrochloride*, m. p. 191° (from ethanol) (Found: C, 40·1; H, 4·5; N, 15·6. $C_6H_8Cl_2N_2$ requires C, 40·2; H, 4·5; N, 15·6%).

3,5-Dichloro-1,2-dihydro-2-imino-1-methylpyridine.—2-Amino-3,5-dichloropyridine [34] (3 g.) and methyl iodide (30 ml.) were heated under reflux for 36 hr. Evaporation, and recrystallisation of the residue from ethanol gave the *methylpyridine hydriodide* (2·1 g.), m. p. 217—218° (decomp.)

[33] A. E. Tschitschibabin and R. A. Konowalowa, *Ber.*, 1925, **58**, 1712.

[34] A. E. Tschitschibabin and A. Jegorow, *J. Russ. Phys. Chem. Soc.*, 1928, **60**, 683 (*Chem. Zentr.*, 1928, II, 1670).

(Found: C, 23·6; H, 2·45; N, 9·1. $C_6H_7Cl_2IN_2$ requires C, 23·6; H, 2·3; N, 9·2%). The *hydrochloride* (from ethanol–ethyl acetate; 1 : 2) had m. p. 234—235° (decomp.) (Found: C, 33·5; H, 3·4; N, 13·0. $C_6H_7Cl_3N_2$ requires C, 33·75; H, 3·3; N, 13·1%). The hydriodide (1·8 g.) was shaken with N-potassium hydroxide (36 ml.) until the resulting oil solidified. The yellow *base* (0·5 g.) had m. p. 84—85° (from light petroleum) (Found: C, 40·65; H, 3·65; N, 15·8. $C_6H_6Cl_2N_2$ requires C, 40·7; H, 3·4; N, 15·8%). Except for some darkening, the base was unchanged after heating at 220—230° for 3 min.

3,5-*Dichloro*-2-*methylaminopyridine*.—2,3,5-Trichloropyridine [34] (4 g.) and ethanolic methylamine (30%; 10 ml.) were heated at 150° for 3 hr. The residue from evaporation at normal pressure was dissolved in N-hydrochloric acid (35 ml.) and treated with carbon. The base was liberated with ammonia, and recrystallised from water containing 33% ethanol. After sublimation, the *methylaminopyrimidine* had m. p. 51—52° (Found: C, 40·65; H, 3·5; N, 15·6. $C_6H_6Cl_2N_2$ requires C, 40·7; H, 3·4; N, 15·8%).

5-*Cyano*-1,2-*dihydro*-2-*imino*-1-*methylpyridine*.—2-Amino-5-cyanopyridine was made from 2-amino-5-bromopyridine essentially as described by Caldwell *et al.*,[35] but the reaction was carried out on a 5-g. scale in a 500-ml. vessel fitted with a 3-cm. diameter cold-finger. A vacuum was applied as soon as the reaction began to subside (about 2 min.), and the product quickly sublimed.

This amine (1 g.) and methyl iodide (10 ml.) were rocked at 100° for 4 hr. The residue from evaporation recrystallised from ethanol to give the colourless *hydriodide* (1·15 g.), m. p. 238—239° (decomp.) (Found: C, 32·4; H, 3·1; N, 16·15. $C_7H_8IN_3$ requires C, 32·2; H, 3·1; N, 16·1%). The *hydrochloride* had m. p. 270—275° (decomp.) (from 95% ethanol) (Found: C, 49·7; H, 4·8; N, 25·0. $C_7H_8ClN_3$ requires C, 49·6; H, 4·75; N, 24·8%), and the *picrate*, m. p. 243—244° (from water) (Found: C, 42·9; H, 2·7. $C_{13}H_{10}N_6O_7$ requires C, 43·1; H, 2·8%).

When the hydriodide (0·2 g.) was added to 2·5N-sodium hydroxide, and the mixture set aside for 75 min., unchanged imine was isolated as the above picrate (0·28 g.).

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[35] W. T. Caldwell, F. T. Tyson, and L. Lauer, *J. Amer. Chem. Soc.*, 1944, **66**, 1479.