Keten Dithioacetals. Part 11.[1] Reaction of 3-Cyano-4-methylthio-2(1*H*)-pyridones with Hydrazine and Guanidine: Synthesis of Novel Substituted and Fused Pyrazolo[4,3-*c*]pyridone and Pyrido[4,3-*d*]pyrimidine derivatives

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The *N*-methylpyridones (2a—f) were prepared by alkylation of the pyridones (1a—f) with dimethyl sulphate, followed by heating the mixture of *N*-methyl (2) and *O*-methyl (3) products with methyl iodide. The pyrindone (4c), the quinolone (4d) and the benzoquinolone (5b) derivatives were prepared in the same manner. Treatment of the pyridones (2a—f) and (1a—i) with hydrazine in refluxing propan-2-ol yielded the respective pyrazolo-[4,3-*c*]pyridone derivatives (7a—o) in excellent yields, and the fused pyridones (4a—e) and (5a—d) afforded the respective fused pyrazolopyridone derivatives (8a—e) and (9a—d) in excellent yields under identical conditions. The reactions of the *N*-methylpyridones (2a—f), (4c—d), and (5b) with guanidine in the presence of 2 mol of sodium ethoxide similarly gave substituted and fused pyrido [4,3-*d*]pyrimidine derivatives (11a—f), (12a—b), and (13), respectively.

In Part 10,[1] we reported the reaction of α-oxoketen bisdithioacetals with *N*-methyl- and *N*-ethyl-cyanoacetamide, which yields a variety of substituted and fused 2,7-naphthyridine derivatives in excellent yields. The *N*-methylpyridones (2a—f) were shown to be the actual intermediates in this reaction; they react rapidly *in situ*

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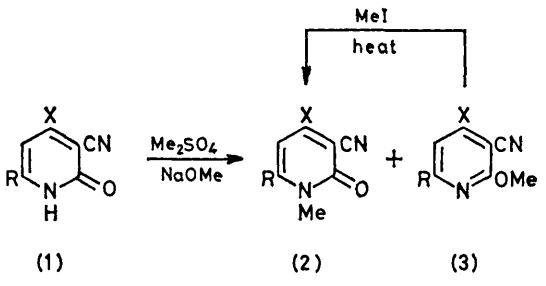
[1] Part 10, R. R. Rastogi, A. Kumar, H. Ila, and H. Junjappa, *J.C.S. Perkin I*, 1978, 554.

with more *N*-alkylcyanoacetamide anion to afford the 2,7-naphthyridines as the final products. These 3-cyano-4-methylthio-2(1*H*)-pyridones (2), with two reactive functional groups in adjacent positions, appeared attractive starting materials for the synthesis of fused heterocycles having a pyridone ring. Here we describe the synthesis of a number of substituted and fused pyrazolo[4,3-*c*]pyridone and pyrido[4,3-*d*]pyrimidine derivatives by the reactions of these pyridones with hydrazine and guanidine, respectively.

RESULTS AND DISCUSSION

Since attempts to isolate the pyridones (2a—f) from the reaction of *N*-methylcyanoacetamide with α-oxoketen



(1),(2),(3) a; R = Ph, X = SMe
b; R = *p*-MeC$_6$H$_4$, X = SMe
c; R = *p*-MeOC$_6$H$_4$, X = SMe
d; R = *p*-ClC$_6$H$_4$, X = SMe
e; R = *p*-BrC$_6$H$_4$, X = SMe
f; R = Me, X = SMe
(2g) R = Me, X = OMe
(2h) R = Me, X = OH

SCHEME 1

dithioacetals were not successful,[1] efforts were made to prepare (2a—f) by alkylation of the readily available pyridones (1a—f). Treatment with dimethyl sulphate in the presence of sodium methoxide gave mixtures of *N*-methyl (2a—f) and *O*-methyl products (3a—f) in varying ratios (Scheme 1), which were separated by column chromatography. However, nearly quantitative conversion of the 2-methoxypyridines (3a—f) into the pyridones (2a—f) was achieved by heating the mixture of (2) and (3) with an excess of methyl iodide in a sealed tube at 140 °C for 8—10 h.[2] The physical data for compounds (2a—f) and (3a—f) are in Table 1 (spectral and analytical data are in Tables 1 and 7 of SUP 22249).* Alkylation of the pyrindone (4a) and quinolone (4b) derivatives with dimethyl sulphate under similar conditions yielded the respective *N*-methyl derivatives (4c) and (4d) exclusively, and the corresponding benzo[*h*]quinolone derivative (5a) afforded a mixture of (5b) and (6), which was thermally converted into (5b) as described above (spectral data in Table 2 of SUP 22249). Attempts to alkylate the pyridones (1g) and (1h) were not successful, probably because of simultaneous *N*-alkylation of the pyridine ring which leads to the formation of unidentified product mixtures.

TABLE 1

Physical data for 6-substituted *N*-methyl-3-cyano-4-methylthio-2(1*H*)-pyridones (2a—f) and 6-substituted 3-cyano-2-methoxy-4-methylthiopyridines (3a—e)

Product [a]	Reflux time/h	Yield (%)	M.p. (°C)	Formula
(2a)	3	42 (85) [b]	180	$C_{14}H_{12}N_2OS$
(2b)	3	41 (80) [b]	154—155	$C_{15}H_{14}N_2OS$
(2c)	3	42 (82) [b]	178—179	$C_{15}H_{14}N_2O_2S$
(2d)	4	28 (72) [b]	184—186	$C_{14}H_{11}ClN_2OS$
(2e)	4	23 (75) [b]	193—194	$C_{14}H_{11}BrN_2O$
(2f)	3	86 [b]	235—236	$C_9H_{10}N_2OS$
(3a)	3	25	144—145	$C_{14}H_{12}N_2OS$
(3b)	3	25	144—146	$C_{15}H_{14}N_2OS$
(3c)	3	20	154—156	$C_{15}H_{14}N_2O_2S$
(3d)	4	24	148—149	$C_{14}H_{11}ClN_2OS$
(3e)	4	19	152—154	$C_{14}H_{11}BrN_2O$

[a] Crystallization solvent EtOH. [b] Yields obtained after heating in the mixture of (2) and (3) with MeI.

TABLE 2

Physical data for *N*-methyl-3-cyano-4-methylthio-1,5,6,7-tetrahydro-2(1*H*)-pyrindone (4c); *N*-methyl-3-cyano-4-methylthio-5,6,7,8-tetrahydro-2(1*H*)-quinolone (4d); *N*-methyl-3-cyano-4-methylthio-5,6-dihydro-2(1*H*)-benzo[*h*]quinolone (5b); and 3-cyano-2-methoxy-4-methylthio-5,6-dihydrobenzo[*h*]quinoline (6)

Product [a]	Reflux time/h	Yield (%)	M.p. (°C)	Formula
(4c)	1.5	50	172—174	$C_{11}H_{12}N_2OS$
(4d)	2	70	165—166	$C_{12}H_{14}N_2OS$
(5b)	2.5	15 (75) [b]	198—200	$C_{16}H_{14}N_2OS$
(6)	2.5	37	104—106	$C_{16}H_{14}N_2OS$

[a] Crystallization solvent EtOH. [b] Yield obtained by thermal conversion of mixture of (5b) and (6).

The reaction of (2a—f) with hydrazine was in refluxing propan-2-ol gave 3-amino-1,5-dihydro-5-methyl-6-phenylpyrazolo[4,3-*c*]pyridin-4-one (7a) in 83% yield. Other substituted pyrazolo[4,3-*c*]pyridones (7a—f) were similarly prepared in 70—84% overall yields (Scheme 2). Whereas the pyridones (1a—i) did not react with the sodium salts of *N*-alkylcyanoacetamides, they reacted readily with hydrazine to yield the corresponding 5-unsubstituted pyrazolo[4,3-*c*]pyridones (7g—o) in excellent yield (Scheme 2).† The structures of all these compounds were confirmed with the help of spectral and analytical data (Tables 3 and 9 respectively of SUP

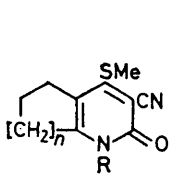
* Compound (2f) is a thio-analogue of the alkaloid ricinine (2g). Attempted preparation of (2g) by refluxing (2f) with sodium methoxide yielded only the hydrolysed product (2h). Attempts to convert (2f) into (2g) are in progress.

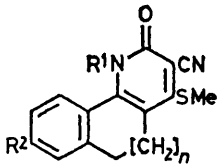
† The SMe group in the anion (1k) under basic conditions is apparently reluctant to undergo nucleophilic substitution,[3] but it is easily displaced by N_2H_4 in the oxo-form (1) under neutral conditions.[3] This is supported by the lack of reaction between N_2H_4 and 2-methoxypyridine (3a) under identical conditions.

[2] (*a*) E. C. Taylor, jun., A. J. Crovetti, and H. M. Loux, *J. Amer. Chem. Soc.*, 1955, **77**, 5445; (*b*) Leo A. Paquette and N. A. Nelson, *J. Org. Chem.*, 1962, **27**, 1085; (*c*) Leo A. Paquette and G. Slomp, *J. Amer. Chem. Soc.*, 1963, **85**, 765.

[3] R. G. Shepherd and J. L. Fedrick, *Adv. Heterocyclic Chem.*, 1965, **4**, 244.

22249). These 3-cyano-4-methylthio-2(1*H*)-pyridones are therefore useful intermediates for the preparation of a number of hitherto unknown 6-substituted 3-amino-pyrazolo[4,3-*c*]pyridone derivatives. Few syntheses of amino- or hydroxy-pyrazolo[4,3-*c*]pyridines [4-8] are described in the literature and most of them involve long and circuitous routes with low yields. The generality and the scope of this reaction is further illustrated by the preparation of the novel cyclopenta[*b*]pyrazolo[3,4-*d*]-pyridones (8a and c) and pyrazolo[4,3-*c*]quinolones (8b and d), derivatives which were obtained in 68—91% overall yields by the reactions of (4a—d) with hydrazine. The seven-membered homologue (8e) was similarly prepared from (4e) in 72% yield. The reactions of the benzo[*h*]quinolone derivatives (5a—c) with hydrazine yielded the novel benzo[*h*]pyrazolo[4,3-*c*]quinolone derivatives (9a—c) having a triazasteroidal skeleton. The corresponding benzocycloheptapyrazolopyridone derivative (9d) was prepared in the same manner from (5d) in 78% yield. Physical data for (8a—e) and (9a—d) are given in Tables 4 and 5 respectively. (Spectral and analytical data are in Table 4 of SUP 22249).





(6)

(4) a; $n = 1$; R = H
b; $n = 2$; R = H
c; $n = 1$; R = Me
d; $n = 2$; R = Me
e; $n = 3$; R = H

(5) a; $R^1 = R^2 = H$; $n = 1$
b; R^1 = Me, $R^2 = H$; $n = 1$
c; R^1 = MeO, $R^2 = H$; $n = 1$
d; $R^1 = R^2 = H$; $n = 2$

TABLE 3

Physical data for 6-substituted 1,5-dihydro-5-methyl-3-aminopyrazolo[4,3-*c*]pyridin-4-ones (7a—f) and 6-substituted 3-amino-1,5-dihydropyrazolo[4,3-*c*]pyridin-4-ones (7g—o)

Product	Reflux time/h	Yield (%)	Cryst. solvent	M.p. (°C)	Molecular formula
(7a)	1	83	EtOH	232	$C_{13}H_{12}N_4O$
(7b)	1	80	EtOH	274—276	$C_{14}H_{14}N_4O$
(7c)	1	84	EtOH	257—258	$C_{14}H_{14}N_4O_2$
(7d)	1.5	80	EtOH	266	$C_{13}H_{11}N_4OCl$
(7e)	1.5	78	EtOH	286—288	$C_{13}H_{11}BrN_4O$
(7f)	1.5	70	EtOH	338	$C_8H_{10}N_4O$
(7g)	1.5	88	AcOH	320	$C_{12}H_{10}N_4O$
(7h)	1.5	70	AcOH	335 (decomp.)	$C_{13}H_{12}N_4O$
(7i)	1.5	85	AcOH	378—380	$C_{13}H_{12}N_4O_2$
(7j)	2	90	AcOH	368—370	$C_{12}H_9ClN_4O$
(7k)	2	80	AcOH–H_2O	378—381	$C_{12}H_9BrN_4O$
(7l)	2	74	AcOH	368 (decomp.)	$C_7H_8N_4O$
(7m)	1.5	82	AcOH	374—376	$C_{11}H_9N_5O$
(7n)	1.5	86	AcOH	350 (decomp.)	$C_{11}H_9N_5O$
(7o)	2.5	79	AcOH	312—314	$C_{13}H_{12}N_4O$

TABLE 4

Physical data for 5-unsubstituted and 5-methyl-3-amino-5,6,7,8-tetrahydrocyclopenta[*b*]pyrazolo[3,4-*d*]pyridin-4(1*H*)-ones (8a and c); 5-unsubstituted and 3-amino-5-methyl-1,5,6,7,8,9-hexahydropyrazolo[4,3-*c*]quinolin-4-ones (8b and d); and 3-amino-5,6,7,8,9,10-hexahydro-cyclohepta[*b*]pyrazolo[3,4-*d*]pyridin-4(1*H*)-one (8e)

Product	Reflux time/h	Yield (%)	Cryst. solvent	M.p. (°C)	Formula
(8a)	1.5	68	EtOH	350 (decomp.)	$C_9H_{10}N_4O$
(8b)	1.5	70	EtOH	362 (decomp.)	$C_{10}H_{12}N_4O$
(8c)	1	80	EtOH	334—336	$C_{10}H_{12}N_4O$
(8d)	1	80	EtOH	328—330	$C_{11}H_{14}N_4O$
(8e)	2	72	EtOH–H_2O	270—272	$C_{11}H_{14}N_4O$

TABLE 5

Physical data for 1-amino-3,4,5,10-tetrahydronaphtho-[1,2-*b*]pyrazolo[3,4-*d*]pyridin-11-one (9a); 1-amino-10-methyl-3,4,5,10-tetrahydronaphtho[1,2-*b*]pyrazolo-[3,4-*d*]pyridin-11-one (9b); 1-amino-7-methoxy-3,4,-5,10-tetrahydronaphtho[1,2-*b*]pyrazolo[3,4-*d*]pyridin-11-one (9c); and 1-amino-4,5,6,11-tetrahydrobenzo-[6,7]cyclohept[1,2-*b*]pyrazolo[3,4-*d*]pyridin-12(3*H*)-one (9d)

Product	Reflux time/h	Yield (%)	Cryst. solvent	M.p. (°C)	Formula
(9a)	2	64	AcOH	360 (decomp.)	$C_{14}H_{12}N_4O$
(9b)	4	73	EtOH–EtOAc	100—102	$C_{15}H_{14}N_4O$
(9c)	2	68	AcOH	375	$C_{15}H_{14}N_4O_2$
(9d)	2.5	78	EtOH	348—350	$C_{15}H_{14}N_4O$

The 6-aminopyridones (10) remain unchanged on treatment with hydrazine in refluxing propan-2-ol.

[4] (*a*) E. C. Taylor and K. S. Hartke, *J. Amer. Chem. Soc.*, 1959, **81**, 2452, 2456; (*b*) T. Sato, *J. Org. Chem.*, 1959, **24**, 963; (*c*) M. D. Nair, S. R. Mehta, and S. M. Kalbah, *Indian J. Chem.*, 1967, **5**, 464.

[5] (*a*) G. M. Badger and R. P. Rao, *Austral. J. Chem.*, 1965, **18**, 379; (*b*) J. D. Bourzat, J. P. Marquet, A. Civier, and E. Bisagni, *Tetrahedron*, 1973, **29**, 441.

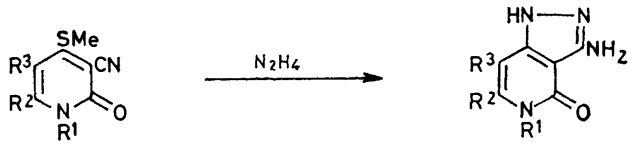
[6] T. Denzel and H. Höhn, *Arch. Pharm.*, 1973, **306**, 766.

[7] (*a*) A. Dornow and H. V. Plessen, *Chem. Ber.*, 1966, **99**, 244; (*b*) S. Hunig and G. Kobrich, *Annalen*, 1958, **617**, 181.

[8] A. L. P. Hatt and J. D. R. Vass, *Chem. Comm.*, 1966, 293.

This is in line with the diminished electrophilicity of the pyridone ring due to the presence of an electron-donating amino-group.[3]

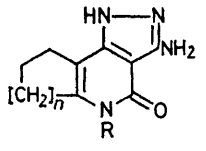
The reactions of the pyridones [(1a—i) and (2a—f)] with guanidine were next examined. When (1a) was refluxed with guanidine in the presence of 2 equiv. of sodium ethoxide in ethanol, starting material was recovered.† However, good yields of 2,4-diamino-6-methyl-7-phenylpyrido[4,3-*d*]pyrimidin-5(6*H*)-one (11a) were obtained when (2a) was treated with guanidine under identical conditions. The structure of (11a) was confirmed with the help of spectral and analytical data. Thus, the mass spectrum revealed a molecular-ion peak at *m/e* 267 ($C_{14}H_{13}N_5O$). The i.r. spectrum exhibited bands at 3 410 [unassociated $\nu_{asym}(NH_2)$], 3 305 [unassociated $\nu_{sym}(NH_2)$], 3 140 [associated $\nu(NH_2)$], and 1 625 and 1 593 [ν(CO) and $\delta(NH_2)$] cm^{-1}. There was no SMe signal in the n.m.r. spectrum, which had singlets at

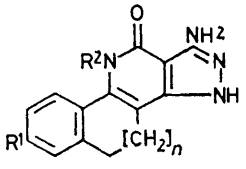


(1), (2a — f)
(1g) $R^1 = R^3 = H$, R^2 = 3-pyridyl
(1h) $R^1 = R^3 = H$, R^2 = 4-pyridyl
(1i) $R^1 = H$, R^2 = Me, R^3 = Ph

(7) a; R^1 = Me, R^2 = Ph, R^3 = H
b; R^1 = Me, R^2 = *p*-MeC_6H_4, R^3 = H
c; R^1 = Me, R^2 = *p*-$MeOC_6H_4$, R^3 = H
d; R^1 = Me, R^2 = *p*-ClC_6H_4, R^3 = H
e; R^1 = Me, R^2 = *p*-BrC_6H_4, R^3 = H
f; R^1 = Me, R^2 = Me, R^3 = H
g; $R^1 = R^3 = H$, R^2 = Ph
h; $R^1 = R^3 = H$, R^2 = *p*-MeC_6H_4
i; $R^1 = R^3 = H$, R^2 = *p*-$MeOC_6H_4$
j; $R^1 = R^3 = H$, R^2 = *p*-ClC_6H_4
k; $R^1 = R^3 = H$, R^2 = *p*-BrC_6H_4
l; $R^1 = R^3 = H$, R^2 = Me
m; $R^1 = R^3 = H$, R^2 = 3-pyridyl
n; $R^1 = R^3 = H$, R^2 = 4-pyridyl
o; $R^1 = H$, R^2 = Me, R^3 = Ph

SCHEME 2





(8) a; *n* = 1; R = H
b; *n* = 2; R = H
c; *n* = 1; R = Me
d; *n* = 2; R = Me
e; *n* = 3; R = H

(9) a; $R^1 = R^2 = H$; *n* = 1
b; $R^1 = H$, R^2 = Me; *n* = 1
c; R^1 = MeO, $R^2 = H$; *n* = 1
d; $R^1 = R^2 = H$; *n* = 2

(10) R^1 = H or Me, R^2 = aryl or CN

SCHEME 3

δ 3.16 (3 H, NMe) and 6.20 (1 H, 8-H) and a multiplet at δ 6.85—7.33 (5 H, aromatic). The pyridones (2b—f) similarly gave the pyridopyrimidines (11b—f) in 55—70% overall yields. The structures of compounds

TABLE 6

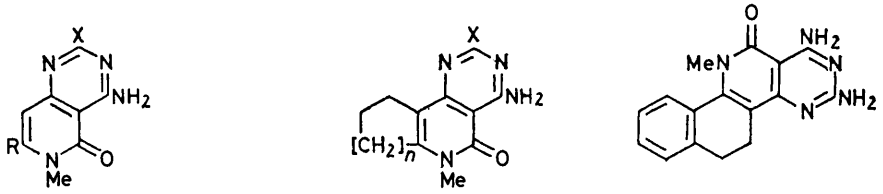
Physical data for 7-substituted 2,4-diamino-6-methylpyrido[4,3-*d*]pyrimidin-5(6*H*)-ones (11a—f); 4-amino-2-mercapto-6-methyl-7-*p*-bromophenylpyrido[4,3-*d*]-pyrimidin-5(6*H*)-one (11g); 2,4-diamino-6-methyl-6,7,-8,9-tetrahydrocyclopenta[5,6]pyrido[4,3-*d*]pyrimidin-5-one (12a); 2,4-diamino-6-methyl-7,8,9,10-tetrahydropyrimido[4,3-*c*]quinolin-5(6*H*)-one (12b); 4-amino-2-mercapto-6-methyl-7,8,9,10-tetrahydropyrimido[4,3-*c*]quinolin-5(6*H*)-one (12c); and 1,3-diamino-11-methyl-5,6-dihydrobenzo[*h*]pyrimido[5,4-*c*]quinolin-12(11*H*)-one (13)

Product[a]	Reflux time/h	Yield (%)	M.p. (°C)	Formula
(11a)	8	71	250—251	$C_{14}H_{13}N_5O$
(11b)	8	65	257—259	$C_{15}H_{15}N_5O$
(11c)	8	69	248—250	$C_{15}H_{15}N_5O_2$
(11d)	12	70	268—269	$C_{14}H_{12}ClN_5O$
(11e)	12	65	252—254	$C_{14}H_{12}BrN_5O$
(11f)	10	55	321—322	$C_9H_{11}N_5O$
(11g)	14	51	348—350	$C_{14}H_{11}BrN_4OS$
(12a)	8	31	349—350	$C_{11}H_{13}N_5O$
(12b)	2.5	68	287—289	$C_{12}H_{15}N_5O$
(12c)	10	53	326—328	$C_{12}H_{14}N_4OS$
(13)	14	41	154—156	$C_{16}H_{15}N_5O$

[a] Crystallization solvent EtOH.

† See footnote on page 858.

(11b—f) was in agreement with their spectral and analytical data (Tables 5 and 12, SUP 22249). In one experiment, when (2e) was treated with thiourea in the presence of 1 equiv. of sodium ethoxide in refluxing ethanol, the 2-mercaptopyridopyrimidine (11g) was obtained in 51% yield. The reactions of the pyrindone (4c) and the quinolone (4d) with guanidine, under identical conditions, afforded the corresponding 7,8-fused pyridopyrimidines (12a) and (12b), respectively, in good yields. The 2-mercapto-derivative (12c) was similarly prepared in 53% yield by the reaction of (4d) with thiourea. Extension of the reaction to the quinazolone (5b) afforded a novel pyridopyrimidine (13) in 41% yield (Scheme 4). The structures of (12a—c) and and (13) were confirmed by spectral and analytical data (Tables 6 and 12 of SUP 22249). From the above examples, it is apparent that the reaction of *N*-methyl-3-cyano-4-methylthio-2(1*H*)-pyridone with guanidine provides a useful and simple preparative route to a variety of pyrido[4,3-*d*]pyrimidine derivatives, some of which exhibit interesting pharmacological activity.[9] Reactions of these pyridones with other nucleophiles such as amines and active methylene compounds are under investigation.



(11) a; R = Ph, X = NH_2
b; R = *p*-MeC_6H_4, X = NH_2
c; R = *p*-$MeOC_6H_4$, X = NH_2
d; R = *p*-ClC_6H_4, X = NH_2
e; R = *p*-BrC_6H_4, X = NH_2
f; R = Me, X = NH_2
g; R = *p*-BrC_6H_4, X = SH

(12) a; *n* = 1; X = NH_2
b; *n* = 2; X = NH_2
c; *n* = 2; X = SH

(13)

SCHEME 4

EXPERIMENTAL

M.p.s were determined on a Townson and Mercer apparatus (capillary method). The i.r. spectra were recorded on Perkin-Elmer 137, 177, and 337 spectrophotometers, and the u.v. spectra were obtained on a Perkin-Elmer 202 spectrophotometer. The n.m.r. spectra were recorded on a Varian A-60D spectrometer with $SiMe_4$ as internal reference. Mass spectra were recorded with a Hitachi RMU-6E spectrometer fitted with a direct inlet system. Spectral and analytical data are in Supplementary Publication No. SUP 22249 (21 pp.).*

Starting Materials.—All the pyridones (1a—i), (4a—b), (4e) (5a), (5c), and (5d) were prepared by the general method reported earlier [10] from the appropriate keten dithioacetal and cyanoacetamide in the presence of sodium isopropoxide.

Alkylation of the Pyridones (1a—f): *General Method for the Preparation of Substituted and Fused* N-*Methyl*-3-*cyano*-4-*methylthio*-2(1H)-*pyridones*.—The pyridone (1a) was alkylated with dimethyl sulphate in the presence of sodium methoxide as reported previously.[1] The pyridones (1b—f) were alkylated in a similar manner and the mixtures of *N*-methyl (2b—e) and *O*-methyl products (3b—e) were separated by column chromatography on silica gel (Table 1). The mixture of (2f) and (3f) could not be separated by column chromatography and was used as such for further reactions.

The benzoquinoline derivatives (5b) and (6) were obtained in the same manner, whereas methylation of (4a) and (4b) gave the respective *N*-alkylated products (4c) and (4d) exclusively (Table 2).

General Method for the Thermal Conversion of Mixtures of N-*Methyl* (2) *and* O-*Methyl Products* (3) *into* N-*Methylpyridones* (2).—A mixture of (2a) and (3a) (0.51 g, 0.002 mol) and MeI (6.5 ml, 0.1 mol) was heated in a steel bomb at 140—150 °C for 10—12 h. After cooling, the excess of MeI was removed *in vacuo* and the light brown solid was purified by column chromatography to yield (2a) (0.43 g, 85%).

The pyridones (2b—f) and (5b) were also obtained in this manner (Table 1).

General Method for the Preparation of Substituted and Fused Pyrazolo[4,3-*c*]*pyridones*.—A solution of the pyridone (0.005 mol) and hydrazine hydrate (99%; 5 ml) in propan-2-ol (20 ml) was refluxed for 1—2 h. Evaporation, followed by treatment of the residue with cold water, gave pale coloured solids, which were filtered off and purified by crystallization.

All the pyrazolo[4,3-*c*]pyridones (7a—o), (8a—c), and (9a—d) were prepared by this procedure (Tables 3—5).

General Method for the Preparation of Substituted and Fused Pyrido[4,3-d]*pyrimidines*.—To a solution of sodium ethoxide [prepared by dissolving sodium (0.46 g, 0.02 mol) in ethanol (50 ml) guanidine nitrate (1.22 g, 0.01 mol) was added and the mixture was stirred for 10—15 min. The appropriate *N*-methylpyridone (0.01 mol) was then added and the mixture was refluxed for 8—12 h. The solvent was

* For details see Notice to Authors No. 7, *J.C.S. Perkin I*, 1977, Index issue.

[9] A. G. Ismail and D. G. Wibberley, *J. Chem. Soc.* (*C*), 1967, 2613; 1968, 2705, and references therein.

[10] Part 9, R. R. Rastogi, A. Kumar, H. Ila, and H. Junjappa, *J.C.S. Perkin I*, 1978, 549.

removed under reduced pressure, and the residue was quenched with crushed ice; the solid which separated was filtered off and purified by crystallization.

The pyrimidines (11a—f), (12a—b), and (13) were prepared by this procedure (Table 6). The corresponding 2-mercaptopyrimidines (11g) and (12c) were obtained by treatment of the respective pyridones (2e) and (4d) (0.01 mol) with thiourea (0.01 mol) under identical conditions.

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