Purine Studies. Part XI.[1] Condensation of Tetraethoxymethane and Similar Orthocarbonates with *ortho*-Diamines to give 8-Ethoxypurines and Related Fused Imidazoles

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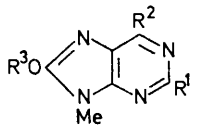
4,5-Diaminopyrimidines are converted by boiling tetraethoxy-, tetrapropoxy-, and tetrakismethylthio-methane into the corresponding 8-alkoxy- or 8-methylthio-purines. By conducting the first stage of the reaction at 25° in the presence of acetic acid, the intermediate diethoxymethyleneaminopyrimidines (3) may be isolated prior to thermal cyclization. 5,6-Diaminopyrimidine-2(and 4)-thiones normally undergo *S*-alkylation by the orthocarbonate as well as cyclization but, under acidic conditions, the 4-thiones yield 2-alkoxy-7-aminothiazolo[5,4-*d*]pyrimidines (4) instead of purines. Treatment of *o*-phenylenediamine, 2,3-diaminonaphthalene, and 2,3-diaminopyridine with a tetra-alkoxymethane gives the appropriate 2-alkoxylated benzimidazole (5; X = CH), naphth[2,3-*d*]-imidazole (6), or imidazo[4,5-*b*]pyridine (5; X = N). Ionization constants, u.v. absorption, and ^{1}H n.m.r. data are recorded and discussed.

TETRAETHOXYMETHANE (tetraethyl orthocarbonate) has recently proved effective for converting 5-amino-1,2,3-triazole-4-carbaldehydes into the corresponding 5-diethoxymethyleneamino-derivatives for cyclization by amines to 5-ethoxy-*v*-triazolo[4,5-*d*]pyrimidines;[2] also for converting 5-amino-4-hydrazinopyrimidines into their 4-diethoxymethylenehydrazino-analogues prior to cyclization and subsequent oxidation to 3-ethoxypyrimido[5,4-*e*]-*as*-triazines.[3] We now report the somewhat analogous use of tetraethoxy-,[4] tetrapropoxy-,[5] and tetrakismethylthio-methane [6] for converting 4,5-diaminopyrimidines into 8-alkoxy- or 8-alkylthio-purines, *e.g.* (1; R^3 = Pr) or (2; R^3 = SMe); 5-amino-6-methylaminopyrimidine-4-thione into 2-alkoxy-7-methylaminothiazolo[5,4-*d*]pyrimidines (4); *o*-phenylenediamine into 2-alkoxybenzimidazoles (5; X = CH); 2,3-diaminonaphthalene into 2-alkoxynaphth-[2,3-*d*]imidazoles (6); and 2,3-diaminopyridine into 2-alkoxyimidazo[4,5-*b*]pyridines (5; X = N).

When 5-amino-4-methylaminopyrimidine was boiled in tetraethoxymethane for several hours the purine (1a) resulted; in contrast, the isomeric 4-amino-5-methylaminopyrimidine gave the corresponding purine (2; R^1 = H, R^2 = Me, R^3 = OEt) only when 1 equiv. of glacial acetic acid was added to the reaction mixture. A similar procedure (without acetic acid) converted appropriate pyrimidines into the purines (1b—d) and (2; R^1 = Me, R^2 = H, R^3 = OEt) but with pyrimidines bearing an alkythio-group, it proved better (or even essential) to use mild conditions in the presence of acetic acid to give first the uncyclized 5-diethoxymethyleneamino-intermediates (3a and b) which underwent thermal cyclization to the purines (1e) and (1f), respectively. In extending this reaction to 4,5-diaminopyrimidinethiones, *S*-alkylation by the orthocarbonate frequently occurred as a side reaction: 5-amino-6-methylaminopyrimidine-4-thione gave the 8-ethoxy-6-ethylthiopurine (1f) or the 8-propoxy-6-propylthiopurine (1g), according to whether tetraethoxy- or tetrapropoxy-methane was used; and 5-amino-4-methyl-6-methylaminopyrimidine-2-thione gave first the *S*-alkylated intermediate (3c) and thence the purine (1h). Such *S*-alkylations have also been observed recently [7] when using the orthoesters of simple carboxylic acids in the presence of anhydrides. Although 4,5-diaminopyrimidine reacted with tetrakismethylthiomethane to give 8-methylthiopurine (2; R^1 = R^2 = H, R^3 = SMe) *via* the intermediate 4-amino-5-(bismethylthio)methyleneaminopyrimidine, the



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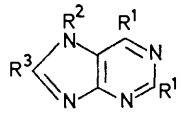
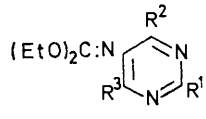


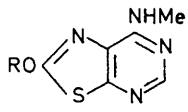
(2)

	R^1	R^2	R^3
a:	H	H	Et
b:	H	Cl	Et
c:	H	NMe_2	Et
d:	H	NHMe	Et
e:	H	SMe	Et
f:	H	SEt	Et
g:	H	SPr	Pr
h:	SEt	Me	Et

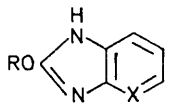


(3)

	R^1	R^2	R^3
a:	H	SMe	NHMe
b:	H	SEt	NHMe
c:	SEt	Me	NHMe
d:	H	H	NH_2
e:	H	Cl	NH_2



(4)



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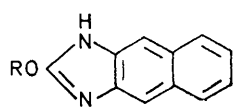

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same diamine and its 6-chloro-derivative with tetraethoxymethane gave only the pyrimidines (3d) and (3e), respectively, which we were unable to cyclize. When 5-amino-6-methylaminopyrimidine-4-thione was allowed to react with tetraethoxy- or tetrapropoxymethane (as above) but with acetic acid present, the thioxo- rather than the methylamino-substituent became involved in ring formation to give the thiazolo-[5,4-*d*]pyrimidines (4; R = Et or Pr) instead of the expected purines (1f and g) (*cf.* the analogous behaviour of similar diaminopyrimidinethiones with simple carboxylic acids as cyclizing agents [8,9]).

Under remarkably mild conditions, *o*-phenylenediamine and 2,3-diaminonaphthalene were converted by the appropriate tetra-alkoxymethanes (and acetic acid) into the benzimidazoles (5; R= Et or Pr, X = CH) and the naphthimidazoles (6; R = Et or Pr); under more vigorous conditions, 2,3-diaminopyridine underwent similar cyclization to the imidazo[4,5-*b*]pyridines (5; R = Et or Pr; X = N) but 3,4-diaminopyridine did not so react.

The basic strength of 8-ethoxypurine (expected to be similar to that of 8-methoxypurine,[9] pK_a 3·14), was raised a little in its 7-methyl (Table 1) (3·48) and 9-methyl [10] (3·45) derivatives and only one unit further by an additional powerfully electron-donating 6-substituent in the purines (1c and d) (pK_a 4·64 and 4·37, respectively). In contrast, the addition of 2 more *C*-methyl groups to 8-ethoxypurine gave the derivative (2; R^1 = Me, R^2 = H, R^3 = OEt), with pK_a 4·71. The appreciable base-weakening by insertion of a 6-methylthio-group [(1a) 3·45 ⟶ (1e) 1·82] suggested that the basic centre must be adjacent at N-1 for such a purely inductive effect to operate so strongly (*cf.* Reichman *et al.*[11]). The pK_a values for the thiazolo[5,4-*d*]-pyrimidines, benzimidazoles, and naphth[2,3-*d*]imidazoles proved comparable with those recorded for analogous members of the respective series.[9,12,13] The addition of a ring-nitrogen atom had the usual acid-strengthening effect in passing from the benzimidazole (5; R = Et, X = CH) (pK_a 11·60) to the imidazo[4,5-*b*]pyridine (5; R = Et, X = N) (pK_a 9·97) but also an unexpected small base-strengthening effect (4·39 ⟶ 4·58) which suggested a change of protonation site to the pyridine nitrogen atom. The acid-strengthening (inductive) effect of an 8-alkoxy-group on 7(9)-unsubstituted purines (*cf.* data in Table 1 and ref. 14) was appreciable.

The u.v. spectra (Table 1) of the purines and thiazolopyrimidines confirmed their structures by closely resembling recorded data [9,14] for analogous derivatives. The spectra for the naphthimidazoles (6) showed considerable fine structure, even in aqueous solution: their most intense peaks had log ε values approaching 5 (*cf.* ref. 13). The ^{1}H n.m.r. spectra (Table 2) were consistent with assigned structures and provided the only confirmation for the pyrimidine intermediates (3).

EXPERIMENTAL

Analyses were performed by the Australian National University Analytical Services Unit. The u.v. spectra were recorded on a Unicam SP 1800 instrument and peak data were checked on a manually operated instrument.

8-Alkoxypurines.—Each diaminopyrimidine was stirred in an excess of the appropriate tetra-alkoxymethane, with or without acetic acid (1 mol. equiv.), under the stated conditions. Concentration and/or refrigeration gave the crude product, which was purified by t.l.c. (chloroform–methanol), recrystallization, or sublimation. For example, 5-amino-4-methylaminopyrimidine [15] (0·47 g) was stirred for 6 h in refluxing tetraethoxymethane [4] (10 ml). Concentration under reduced pressure to *ca.* 2 ml and subsequent cooling gave a solid which was triturated with a little light petroleum and then recrystallized from ethanol to give 8-ethoxy-9-methylpurine (1a) (0·36 g), m.p. 99° (lit.,[10] 95—96°); u.v. spectra identical with those recorded.[10]

By such means, 4-amino-5-methylaminopyrimidine [16] (AcOH; 65°; 33 h) gave 8-*ethoxy*-7-*methylpurine* (2; R^1 = H, R^2 = Me, R^3 = OEt) (41%), m.p. 163° (from benzene) (Found: C, 54·2; H, 5·6; N, 31·6. $C_8H_{10}N_4O$ requires C, 53·9; H, 5·7; N, 31·4%); 5-amino-4-chloro-6-methylaminopyrimidine [15] (reflux; 44 h) gave 6-*chloro*-8-*ethoxy*-9-*methylpurine* (1b) (58%), m.p. 143° (from water) (Found: C, 45·5; H, 4·4; N, 26·7. $C_8H_9ClN_4O$ requires C, 45·2; H, 4·3; N, 26·3%); 5-amino-4-dimethylamino-6-methylaminopyrimidine [17] (reflux; 20 h) gave 6-*dimethylamino*-8-*ethoxy*-9-*methylpurine* (1c) (81%), m.p. 113° (t.l.c.; sublimation at 65° and 0·04 mmHg) (Found: C, 54·5; H, 6·7; N, 32·0. $C_{10}H_{15}N_5O$ requires C, 54·3; H, 6·8; N, 31·65%); 5-amino-4,6-bismethylaminopyrimidine [18] (reflux; 33 h) gave 8-*ethoxy*-9-*methyl*-6-*methylaminopurine* (1d) (70%), m.p. 151—152° (from ethanol after sublimation at 95° and 0·1 mmHg) (Found: C, 52·0; H, 6·0; N, 33·5. $C_9H_{13}N_5O$ requires C, 52·2; H, 6·3; N, 33·8%); 4,5-diamino-2,6-dimethylpyrimidine [19] (reflux; 8 h) gave a crude product which was fully cyclized by heating at 175° for 1 h before sublimation (130° at 0·1 mmHg) to give 8-*ethoxy*-2,6-*dimethylpurine* (2; R^1 = Me, R^2 = H, R^3 = OEt) (37%), m.p. >224° (decomp.) (Found: C, 56·0; H, 6·3; N, 29·3. $C_9H_{12}N_4O$ requires C, 56·2; H, 6·3; N, 29·15%); 5-amino-4-methylamino-6-methylthiopyrimidine [20] (AcOH; 25°; 6 h) gave 5-*diethoxymethyleneamino*-4-*methylamino*-6-*methylthiopyrimidine* (3a) (>90%), m.p. 116—117° (from ethanol) (Found: C, 48·9; H, 6·6; N, 20·8. $C_{11}H_{18}N_4O_2S$ requires C, 48·9; H, 6·7; N, 20·7%), which was cyclized by heating at 200° for 20 min to give 8-*ethoxy*-9-*methyl*-6-*methylthiopurine* (1e)

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(62%), m.p. 119° (Found: C, 48·3; H, 5·5; N, 25·3. $C_9H_{12}N_4OS$ requires C, 48·2; H, 5·4; N, 25·0%); 5-amino-6-methylaminopyrimidine-4-thione [20] (reflux; 9 h) gave *8-ethoxy-6-ethylthio-9-methylpurine* (1f) (54%), m.p. 79—80° (from light petroleum) (Found: C, 50·8; H, 6·0; N, 23·9. $C_{10}H_{14}N_4OS$ requires C, 50·4; H, 5·9; N, 23·5%) {the same pyrimidinethione [20] (1·5 g), N-potassium hydroxide (11 ml), and ethyl iodide (0·9 ml) were shaken for 3 h, set aside for 12 h, and then refrigerated; the *5-amino-4-ethylthio-6-methylaminopyrimidine* (1·64 g) had m.p. 91° [after recrystallization from water and drying (P_2O_5) at 65° and 760 mmHg] (Found: C, 45·6; H, 6·7; N, 30·5. $C_7H_{12}N_4S$ requires C, 45·65; H, 6·6; N, 30·4%); this pyrimidine (0·5 g), tetraethoxymethane (2·5 ml), and acetic acid (0·12 g) were stirred at 25—30° for 18 h; refrigeration gave *5-diethoxymethyleneamino-4-ethylthio-6-methylaminopyrimidine* (3b) (0·58 g), m.p. 94° (from light petroleum) (Found: C, 50·9; H, 7·1; N, 19·7. $C_{12}H_{20}N_4O_2S$ requires C, 50·7; H, 7·1; N, 19·7%); the diethoxymethylene derivative (0·1 g) was heated in a loosely stoppered tube at 195° for 20 min to give the purine (1f)}; 5-amino-4-methyl-6-methylaminopyrimidine-2-thione [21] (AcOH; reflux; 10 min) gave *5-diethoxymethyleneamino-2-ethylthio-4-methyl-6-methylaminopyrimidine* (3c) (81%), m.p. 124—125° (from ethanol) (Found: C, 52·4; H, 7·4; N, 18·9. $C_{13}H_{22}N_4O_2S$ requires C, 52·3; H, 7·4; N, 18·8%), and thence by heating at 170° for 40 min, *8-ethoxy-2-ethylthio-6,9-dimethylpurine* (1h) (68%), m.p. 79—80° (from ethanol) (Found: C, 52·6; H, 6·3; N, 22·6. $C_{11}H_{16}N_4OS$ requires C, 52·4; H, 6·4; N, 22·2%); and 5-amino-6-methylaminopyrimidine-4-thione [20] [$(PrO)_4C$; [5] 155°; 7 h] gave *9-methyl-8-propoxy-6-propylthiopurine* (1 g) (44%), m.p. 55° (from light petroleum) (Found: C, 54·5; H, 6·9; N, 21·3. $C_{12}H_{18}N_4OS$ requires C, 54·1; H, 6·8; N, 21·0%).

8-Methylthiopurine (2; $R^1 = R^2 = H$, $R^3 = SMe$).—4,5-Diaminopyrimidine [22] (0·5 g), tetrakismethylthiomethane [6] (0·9 g), and acetic acid (2 ml) were boiled under reflux with stirring for 2 h. The residue from concentration under reduced pressure solidified on trituration with ether (10 ml). The solid was washed with fresh ether (2 × 10 ml) and recrystallized from water to give *4-amino-5-(bismethylthiomethyleneamino)pyrimidine* (0·44 g), m.p. 157—158° (Found: C, 39·5; H, 4·9; N, 26·5. $C_7H_{10}N_4S_2$ requires C, 39·3; H, 4·7; N, 26·2%). This pyrimidine (0·2 g) was heated at 200° for 1 h. The residue crystallized from water to give 8-methylthiopurine, identified by mixed m.p. (258°) and u.v. spectra.[23]

4-Amino-5-diethoxymethyleneaminopyrimidine (3d).—4,5-Diaminopyrimidine [22] (0·5 g), tetraethoxymethane (2·5 ml),

TABLE 1

Ionization data and u.v. spectra

Compound	pK_a [a]	$\lambda_{max.}$ (log ε) [b] [solvent or pH]
Purines		
8-OEt-7-Me	3·48 ± 0·02	274 (4·08) [1·0] 275 (4·05), *235* (3·48) [9·8]
6-Cl-8-OEt-9-Me		275 (4·00) *246*, (3·62) [MeOH]
6-NMe_2-8-OEt-9-Me	4·64 ± 0·01	*286* (4·19), 276 (4·24), 214 (4·33) [2·0] 278 (4·29), 217 (4·35) [8·4]
8-OEt-9-Me-6-NHMe	4·37 ± 0·05	*277* (4·19), 272 (4·22), *212* (4·34) [1·5] 270 (4·24), 210 (4·42) [7·0]
8-OEt-2,6-Me_2	4·71 ± 0·02 8·74 ± 0·01	279 (3·98), 215 (4·28) [1·0] 277 (3·97), *229* (3·96), *210* (4·27) [6·6] 282 (3·98), *220* (4·20) [11·9]
8-OEt-9-Me-6-SMe	1·82 ± 0·02	320 (4·28), *274* (3·53), 238 (4·16), [−1·0] 294 (4·23), *288* (4·22), 226 (4·21) [5·2]
8-OEt-6-SEt-9-Me	*c*	320 (4·28), *274* (3·63), 239 (4·16) [−1·0] 295 (4·26), *288* (4·22), 227 (4·20) [5·8]
8-OEt-2-SEt-6,9-Me_2		300 (3·68), 264 (3·85), 228 (3·99) [MeOH]
9-Me-8-OPr-6-SPr	*c*	320 (4·27), *274* (3·62), 239 (4·15) [−1·0] 295 (4·22), *287* (4·16), 228 (4·13) [5·5]
Others		
(4; R = Et)	*c*	*296* (3·91), 273 (4·12), *266* (4·07), 223 (4·25) [1·2] *297* (3·70), 272 (4·16), *267* (4·15), 218 (4·33) [6·7]
(4; R = Pr)	3·31 ± 0·01	*297* (3·92), 273 (4·13), *264* (4·07), 222 (4·27), [1·2] *296* (3·74), 271 (4·16), *265* (4·15), 218 (4·34) [8·0]
(5; R = Et, X = CH)	4·39 ± 0·02	275 (3·79), 269 (3·81), *221* (3·90) [2·0]
	11·60 ± 0·01	281 (3·69), 275 (3·74), *269* (3·35), *242* (3·38), 235 (3·75) [8·3] 283 (3·83), 245 (3·57), [14·0]
(5; R = Pr, X = CH)	*c*	276 (3·79), 270 (3·81), *223* (3·88) [1·0] 281 (3·73), 275 (3·78), 269 (3·65), *242* (3·68), 235 (3·79) [8·4] 283 (3·83), 244 (3·56) [14·0]
(6; R = Et)	4·07 ± 0·01	323 (3·80), 314 (3·76), 309 (3·79), 300 (3·81), *296* (3·78), 290 (3·71), *285* (3·70), *276* (3·55), *238* (4·80), 235 (4·82), *222* (4·68) [1·2]
	11·15 ± 0·01	327 (3·84), 319 (3·79), 313 (3·82), 306 (3·83), 240 (4·87) [8·1] 333 (3·85), *321* (3·81), 250 (4·82) [14·0]
(6; R = Pr)	*c*	323 (3·84), 314 (3·79), 309 (3·82), 300 (3·83), *296* (3·80), 290 (3·72), *285* (3·68), *276* (3·49), *238* (4·83), 235 (4·84), *222* (4·69) [1·2] 327 (3·91), 319 (3·87), 313 (3·89), 306 (3·89), 240 (4·91), [8·4] 334 (3·92), *321* (3·89), 250 (4·86), [14·0]
(5; R = Et, X = N)	4·58 ± 0·01	301 (4·21), 251 (3·33), *212* (3·92) [2·1]
	9·97 ± 0·04	286 (4·08), 230 (3·56) [7·4] 296 (4·09) [12·3]
(5; R = Pr, X = N)	*c*	301 (4·20), 251 (3·37), *212* (3·96) [2·0]

[a] Measured spectrometrically (A. Albert and E. P. Serjeant, 'Determination of Ionization Constants,' Chapman and Hall, London, 1971) at 20° and concentrations $<10^{-3}$M in buffers of 10^{-2}M ionic strength (D. D. Perrin, *Austral. J. Chem.*, 1963, **16**, 572) without thermodynamic corrections. [b] Inflections and shoulders in italics. [c] Ionization assumed to approximate to that of homologue.

[21] D. J. Brown, P. W. Ford, and K. H. Tratt, *J. Chem. Soc.* (*C*), 1967, 1445.

[22] D. J. Brown, *J. Appl. Chem.*, 1952, **2**, 239.

[23] A. Albert and D. J. Brown, *J. Chem. Soc.*, 1954, 2060; S. F. Mason, *ibid.*, p. 2071.

TABLE 2

^{1}H N.m.r. spectra [a]

	δ Values
Purines	
8-OEt-9-Me	8·87 (s, 2-H), 8·81 (s, 6-H), 4·71 (q, *J* 7, CH_2), 3·66 (s, 9-Me), 1·51 (t, *J* 7, CMe)
8-OEt-7-Me	9·01 (s 2-H), 8·58 (s, 6-H), 4·79 (q, *J* 7, CH_2), 3·63 (s, 7-Me), 1·53 (t, *J* 7, CMe)
6-Cl-8-OEt-9-Me	8·58 (s, 2-H), 4·75 (q, *J* 7, CH_2) 3·65 (s 9-Me), 1·53 (t, *J* 7, CMe)
6-NMe_2-8-OEt-9-Me	8·36 (s, 2-H), 4·60 (q, *J* 7, CH_2), 3·54 (s, 9-Me), 3·46 (s, NMe_2), 1·47 (t, *J* 7, CMe)
8-OEt-9-Me-6-NHMe	8·39 (s, 2-H), 4·57 (q, *J* 7, CH_2), 3·58 (s, 9-Me), 3·16 (d, *J* 5, 6-NMe), 1·47 (t, *J* 7, CMe)
8-OEt-2,6-Me_2	4·67 (q, *J* 7, CH_2), 2·78 (s, 2-Me), 2·70 (s, 6-Me), 1·48 (t, *J* 7, Me of Et)
8-OEt-9-Me-6-SMe	8·64 (s, 2-H), 4·68 (q, *J* 7, CH_2), 3·64 (s, 9-Me), 2·71 (s, SMe), 1·49 (t, *J* 7, CMe)
8-OEt-6-SEt-9-Me	8·61 (s, 2-H), 4·68 (q, *J* 7, OCH_2), 3·58 (s, 9-Me), 3·38 (q, *J* 7, SCH_2), 1·49 (t, *J* 7, Me of OEt), 1·43 (t, *J* 7, Me of SEt)
8-OEt-2-SEt-6,9-Me_2	4·65 (q, *J*, 7, OCH_2), 3·56 (s, 9-Me), 3·24 (q, *J* 7, SCH_2), 2·64 (s, 6-Me), 1·50 (t, *J* 7, Me of OEt), 1·41 (t, *J* 7, Me of SEt)
9-Me-8-OPr-6-SPr	8·61 (s, 2-H), 4·59 (t, *J* 7, OCH_2), 3·59 (s, 9-Me), 3·37 (t, *J* 7, SCH_2), 1·87 (m, both C·CH_2), 1·07 (t, *J* 7, both CMe)
8-SMe [b]	8·94 (s, 2-H), 8·84 (s, 6-H), 2·77 (s, Me)
Pyrimidines [c]	
5-NH_2-4-SEt-6-NHMe	8·27 (s, 2-H), 5·20br (s, NH_2), 3·20 (q, *J* 7, CH_2), 3·01 (d, *J* 5, NMe), 1·33 (t, *J* 7, C-Me)
5-De-4-SEt-6-NHMe	8·30 (s, 2-H), 4·32 (q, *J* 7, both OCH_2), 3·15 (q, *J* 7, SCH_2), 3·00 (d, *J* 5, NMe), 1·33 (t, *J* 7, all CMe)
5-De-2-SEt-4-Me-6-NHMe	4·30 (q, *J* 7, both OCH_2), 3·16 (q, *J* 7, SCH_2), 2·99 (d, *J* 5, NMe), 2·11 (s, 4-Me), 1·39 (m, Me of SEt and both OEt)
5-De-4-NHMe-6-SMe	8·36 (s, 2-H), 4·33 (q, *J* 7, both CH_2), 3·02 (d, *J* 5, NMe), 2·51 (s, SMe), 1·36 (t, *J* 7, both CMe)
4-NH_2-5-De	8·26 (s, 2-H), 8·19 (s, 6-H), 5·54br (s, NH_2), 4·26 (q, *J* 7, both CH_2), 1·32 (t, *J* 7, both Me)
4-NH_2-6-Cl-5-De	8·15 (s, 2-H), 5·32br (s, NH_2), 4·35 (q, *J* 7, both CH_2), 1·34 (t, *J* 7, both Me)
4-NH_2-5-Bm	8·42 (s, 2-H), 8·00 (s, 6-H), 5·30br (s, NH_2), 2·55 (s, both Me)
Others	
(4; R = Et)	8·47 (s, 5-H), 4·58 (q, *J* 7, CH_2), 3·19 (d, *J* 5, NMe), 1·47 (t, *J* 7, CMe)
(4; S = Pr)	8·44 (s, 5-H), 4·45 (t, *J* 7, SCH_2), 3·15 (d, *J* 5, NMe), 1·87 (sext., *J* 7, C·CH_2), 1·03 (t, *J* 7, CMe)
(5; R = Et, X = CH)	7·25 (m, 4,5,6,7-H_4), 4·63 (q, *J* 7, CH_2), 1·44 (t, *J* 7, Me)
(5; R = Pr, X = CH)	7·30 (m, 4,5,6,7-H_4), 4·55 (t, *J* 7, OCH_2), 1·86 (sext., *J* 7, C·CH_2), 0·99 (t, *J* 7, Me)
(6; R = Et) [b]	7·86 (m), 7·38 (m), 4·59 (q, *J* 7, CH_2), 1·42 (t, *J* 7, Me)
(6; R = Pr)	7·80 (m), 7·37 (m), 4·58 (t, *J* 7, OCH_2), 1·88 (sext., *J* 7, C·CH_2), 1·02 (t, *J* 7, Me)
(5; R = Et, X = N)	8·27 (q, $J_{5,6}$ 5, $J_{5,7}$ 1·4, 5-H), 7·88, (q, $J_{6,7}$ 8, $J_{5,7}$ 1·4, 7-H), 7·18 (q, $J_{5,6}$, 5, $J_{6,7}$ 8, 6-H), 4·70 (q, *J* 7, CH_2), 1·51 (t, *J* 7, Me)
(5; R = Pr, X = N)	8·22 (q, $J_{5,6}$ 5, $J_{5,7}$ 1·4, 5-H), 7·86 (q, $J_{6,7}$ 8, $J_{5,7}$ 1·4, 7-H), 7·15 (q, $J_{5,6}$ 5, $J_{6,7}$ 8, 6-H), 4·58 (t, *J* 7, OCH_2), 1·94 (sext., *J* 7, C·CH_2), 1·07 (t, *J* 7, Me)

[a] Measured at 60 MHz and 33° in $CDCl_3$ (except as otherwise indicated); Me_4Si as internal standard; *J* values in Hz. [b] In $(CD_3)_2SO$. [c] De = $(EtO)_2C{:}N$; Bm = $(MeS)_2C{:}N$.

and acetic acid (0·28 g) were heated and stirred under reflux for 30 min. The solid (0·68 g) which was deposited on refrigeration was triturated with N-potassium hydroxide and then washed with water to give the *diethoxymethylene derivative*, m.p. 109—110° (Found: C, 51·1; H, 6·9; N, 26·4. $C_9H_{14}N_4O_2$ requires C, 51·4; H, 6·7; N, 26·65%).

4-*Amino*-6-*chloro*-5-*diethoxymethyleneaminopyrimidine* (3e).—4,5-Diamino-6-chloropyrimidine [24] (0·2 g), tetraethoxymethane (1·8 g), and acetic anhydride (0·2 g) were stirred under reflux until the mixture was homogeneous (*ca.* 5 min). Refrigeration gave the *chloro*-5-*diethoxymethyleneaminopyrimidine* (0·16 g), m.p. 111—112° (from ethanol) (Found: C, 44·3; H, 5·4; N, 22·8. $C_9H_{13}ClN_4O_2$ requires C, 44·2; H, 5·4; N, 22·9%).

2-*Alkoxy*-7-*methylaminothiazolo*[5,4-d]*pyrimidines*.—5-Amino-6-methylaminopyrimidine-4-thione [20] (0·5 g), tetraethoxymethane (5 g), and acetic acid (0·2 g) were stirred at 80° for 4 h and then chilled. The solid was washed with cold light petroleum, subjected to t.l.c. [silica; chloroform–acetone (9 : 1)], and then sublimed (80° at 0·02 mmHg) to give the 2-*ethoxy*-7-*methylaminothiazolopyrimidine* (4; R = Et) (0·26 g), m.p. 141° (Found: C, 46·0; H, 4·8; N, 26·6. $C_8H_{10}N_4OS$ requires C, 45·7; H, 4·8; N, 26·65%). Use of tetrapropoxymethane at 95° for 1 h gave the 7-*methylamino*-2-*propoxythiazolopyrimidine* (4; R = Pr) (0·41 g), m.p. 131—132° (from ethanol) (Found: C, 48·3; H, 5·4; N, 25·3. $C_9H_{12}N_4OS$ requires C, 48·2; H, 5·4; N, 25·0%).

2-*Alkoxylated Fused Imidiazoles*.—As in the purine series, *o*-phenylenediamine (AcOH; 30°; 30 min) gave 2-ethoxybenzimidazole (5; R = Et, X = CH) (73%), m.p. 166—167° (lit.,[25] 160—166°), identified by its i.r. spectrum; [26] also 2-*propoxybenzimidazole* (5; R = Pr, X = CH) (93%), m.p. 164—165° (Found: C, 68·1; H, 6·8; N, 16·0. $C_{10}H_{12}N_2O$ requires C, 68·2; H, 6·9; N, 15·9%). Similarly, 2,3-diaminonaphthalene (AcOH; 30°; 90 min) gave 2-*ethoxynaphth*[2,3-d]*imidazole* (6; R = Et) (>90%), m.p. 241—242° (from ethanol) (Found: C, 74·0; H, 5·6; N, 13·0. $C_{13}H_{12}N_2O$ requires C, 73·6; H, 5·7; N, 13·2%) and its 2-*propoxy-homologue* (6; R = Pr) (>90%), m.p. 167—168° (from aqueous ethanol) (Found: C, 74·5; H, 6·2; N, 12·5. $C_{14}H_{14}N_2O$ requires C, 74·3; H, 6·2; N, 12·4%); and 2,3-diaminopyridine (155°; 80 min) gave 2-*ethoxyimidazo*[4,5-b]*pyridine* (5; R = Et, X = N) (57%), m.p. 148—150° (from acetone) (Found: C, 59·5; H, 5·6; N, 26·0. $C_8H_9N_3O$ requires C, 58·9; H, 5·6; N, 25·75%) and the 2-*propoxy-homologue* (5; R = Pr, X = N) (82%), m.p. 121° (Found: C, 61·1; H, 6·3; N, 23·8. $C_9H_{11}N_3O$ requires C, 61·0; H, 6·3; N, 23·7%).

We thank Drs. W. L. F. Armarego and J. H. Lister for discussions; Mr. S. E. Brown for measuring the n.m.r. spectra; and the Australian National University for supporting R. K. L. as a scholar.

[3/1777 *Received*, 24*th August*, 1973]

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