Aza-analogues of Pteridine. Part V.[1] 5-Alkylaminopyrimido[5,4-*e*]-*as*-triazines from 5-Alkyl or 5-Unsubstituted Analogues *via* 5,6-Adducts with Amines

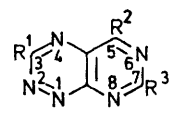
By **D. J. Brown** * and **T. Sugimoto**, Department of Medical Chemistry, John Curtin School of Medical Research, Canberra 2600, Australia

5-Alkylamino- and 5-dimethylamino-pyrimido[5,4-*e*]-*as*-triazines were formed by aerating the corresponding 5-unsubstituted or 5-alkyl-pyrimidotriazines, or their 1,2-dihydro-derivatives, in tetrahydrofuran containing an appropriate amine. The mechanism involved 5,6-addition of the amine and one or two oxidative steps, depending on the substrate. The method was used to make 5-propylaminopyrimidotriazine (1k) and its 3-methyl and 3,7-dimethyl derivatives; 5-dimethylaminopyrimidotriazine (1l) and its 3-methyl, 7-methyl, 3,7-dimethyl, and 7-methoxy-3-methyl derivatives; and 3-methyl-5-methylaminopyrimidotriazine(1r). Of these, the second, fifth, eighth, and ninth were made unambiguously by aminolyses of the corresponding methoxypyrimidotriazines; other structures were confirmed by u.v. and ^{1}H n.m.r. spectra. 1,2-Dihydro-3-methyl-5-propylpyrimidotriazine (2b) was made by cyclization of 4-(2-acetylhydrazino)-2-chloro-5-nitro-6-propylpyrimidine (3; R^1 = NH·NHAc, R^2 = Pr), prepared from its 2,4-dichloroanalogue and acetylhydrazine; other 1,2-dihydrosubstrates were made similarly or by established routes.

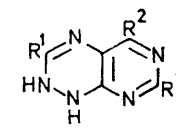
DIRECT amination of carbocyclic or heterocyclic nuclei usually involves the use of alkali-metal amides, hydroxylamine under alkaline conditions, *N*-halogeno-amines, or arenesulphonyl azides.[2] We now report the 5-alkylamination of simple 5-unsubstituted pyrimido[5,4-*e*]-*as*-triazines, *e.g.* (1a), by a new method involving use of alkylamines under mild conditions; the mechanism, involving covalent 5,6-addition of the amine followed by aerial oxidation of the adduct, has been implicated recently [1] in the more complicated conversion of 7-chloro-1,2-dihydropyrimidotriazines (2; R^3 = Cl) into 5,7-diaminopyrimidotriazines (1; $R^2 = R^3 = NH_2$) by ammonia. In addition, we report the conversion of 5-alkylpyrimidotriazines, *e.g.* (1b), into their 5-alkylamino-analogues by similar means. This reaction, involving loss of the *C*-alkyl group, is at least formally akin to the ready oxidative formation [3] of pteridin-4(or 7)-ones from the corresponding 4(or 7)-methylpteridines by a mechanism in which covalent 3,4(or 7,8)-hydration plays a role.

The required intermediate 1,2-dihydropyrimidotriazines (2) were synthesized by a route better than those[4,5] used previously. Thus, stirring the dichloropyrimidine (3; R^1 = Cl, R^2 = Me) with ethanolic formylhydrazine gave the formylhydrazinopyrimidine (3; R^1 = NH·NHCHO, R^2 = Me) which underwent dechlorination, reduction of the nitro-group, and subsequent acid-catalysed cyclization to give the dihydro-5-methylpyrimidotriazine (2c); in the same way, the isomer (2a) and its derivative (2b) were made *via* the acetylhydrazinopyrimidines (3; R^1 = NH·NHAc, R^2 = H or Pr).

The 1,2-dihydro-3-methylpyrimidotriazine (2a) was converted [5] by silver oxide into the aromatic analogue (1a). With propylamine in tetrahydrofuran, this gave the adduct (4; R^1 = Me, R^2 = H, R^3 = NHPr) which, without isolation, was aromatized by stirring with manganese dioxide or by a stream of dry air at room temperature; the structure of the product, 3-methyl-5-propylaminopyrimidotriazine (1d), was confirmed by unambiguous synthesis from its 5-methoxy-analogue [5] (1e) and propylamine. Similar amine adducts in the



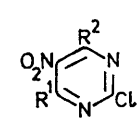
(1)



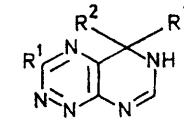
(2)

	R^1	R^2	R^3
a:	Me	H	H
b:	Me	Pr	H
c:	H	Me	H
d:	Me	NHPr	H
e:	Me	OMe	H
f:	Me	NMe_2	H
g:	H	H	H
h:	H	H	Me
i:	Me	H	Me

	R^1	R^2	R^3
j:	Me	H	OMe
k:	H	NHPr	H
l:	H	NMe_2	H
m:	H	NMe_2	Me
n:	Me	NHPr	Me
o:	Me	NMe_2	Me
p:	Me	NMe_2	OMe
q:	Me	Me	H
r:	Me	NHMe	H



(3)



(4)

pteridine series have defined aromatization under a variety of conditions.[6] Eventually we found that the 1,2-dihydropyrimidotriazine (2a) gave the propylamino-compound (1d) in one operation when simply stirred at 25° in tetrahydrofuran with propylamine in the presence of air. Any contribution to the oxidation of the 1,2- or 5,6-dihydro-intermediates by the peroxide associated with tetrahydrofuran must be unimportant because the reaction also proceeded satisfactorily in benzene. The 1,2-dihydropyrimidotriazine (2a) reacted similarly with

[1] Part IV, D. J. Brown and T. Sugimoto, *J. Chem. Soc.* (*C*), 1971, 2616.

[2] F. Möller, in 'Methoden der Organischen Chemie,' ed. E. Müller *et al.*, Georg Thieme Verlag, Stuttgart, 1957, vol. 11, part 1, p. 9; M. S. Gibson in 'The Chemistry of the Amino Group,' ed. S. Patai, Interscience, New York, 1968, p. 37; M. T. Leffler, *Org. Reactions*, 1947, **1**, 91.

[3] N. W. Jacobsen, *J. Chem. Soc.* (*C*), 1966, 1065.

[4] E. C. Taylor, J. W. Barton, and W. W. Paudler, *J. Org. Chem.*, 1961, **26**, 4961.

[5] M. E. C. Biffin, D. J. Brown, and T. Sugimoto, *J. Chem. Soc.* (*C*), 1970, 139.

[6] A. Albert and K. Ohta, *J. Chem. Soc.* (*C*), 1971, 2357; but *cf.* A. Albert, *J. Chem. Soc.*, 1955, 2690.

dimethylamine to give the known [7] dimethylamino-compound (1f), but with di- or tri-ethylamine it gave only pyrimidotriazin-5-one [7,8] in poor yield. The method was used also to convert the 1,2-dihydro-compounds [5] (2g—j) into the corresponding amines (2k—p); the last of these (2p) was made alternatively by preferential 5-dimethylaminolysis of the known [9] 5,7-dimethoxy-3-methylpyrimidotriazine.

Appropriately placed methyl groups prevent direct amination in pyridines [2] and hinder covalent hydration in pteridines [10] and related heterocycles.[11] However, we have found that a 5-alkyl group on a pyrimido[5,4-*e*]-*as*-triazine can be displaced by an alkylamine. Thus a fresh solution of 3-methyl-5-propylpyrimidotriazine (1b), prepared from the 1,2-dihydro-derivative (2b) and silver oxide, was stirred by a stream of air with propylamine to give the 3-methyl-5-propylaminopyrimidotriazine (1d). As soon as the solution of the aromatic compound (1b) was mixed with propylamine the u.v. spectrum [$\lambda_{max.}$ (cyclohexane) 220, *250*, *315*, 319, *326*, *332*, and 510 nm] changed to one [$\lambda_{max.}$ (MeOH) *240*, 276, 332, and 404 nm] resembling that [5] of 5,6-dihydro-5-methoxy-3-methylpyrimidotriazine (4; R^1 = Me, R^2 = H, R^3 = OMe), suggesting the presence of the (unisolable) covalent adduct (4; R^1 = Me, R^2 = Pr, R^3 = NHPr); thereafter the spectrum changed progressively (during oxidation) into that (Table 1) of the product (1d). It proved

TABLE 1

U.v. spectra

Compound [a]	$\lambda_{max.}$ (log ε) [b]
(1d)	226 (4·16), 261 (3·93), *295* (3·30), 390 (3·85)
(1k)	226 (4·20), 256 (3·88), *300* (3·24), 392 (3·86)
(1l)	237 (4·20), 260 (3·82), *307* (3·34), 404 (3·87)
(1m)	235 (4·22), 268 (3·88), *300* (3·32), 402 (3·87)
(1n)	225 (4·16), 265 (3·99), *295* (3·34), 392 (3·82)
(1o)	236 (4·22), 272 (3·96), *300* (3·40), 404 (3·88)
(1p)	230 (4·21), 271 (4·01), *310* (3·21), 405 (3·86)
(1r)	225 (4·12), 260 (3·95), *300* (3·26), 390 (3·82)
(2a) [c]	222 (4·30), *250* (3·60), 332 (3·69)
(2b) [c]	225 (4·16), *250* (3·66), 334 (3·68)
(2c) [c]	218 (4·23), *245* (3·75), 337 (3·78)

[a] In ethanol except when indicated otherwise. [b] λ in nm; shoulders or inflections in italics. [c] In 0·1N-hydrochloric acid.

equally effective and more convenient to treat the 1,2-dihydro-compound (1b) with propylamine and air without prior aromatization. This variation was used to transform the 1,2-dihydro-derivatives (2b, c, and q) into the amines (1d, k, and l); analogous treatment of the dihydro-compound (2b) with commercial dimethylamine (now known to contain some methylamine) gave only the 5-methylaminopyrimidotriazine (1r), synthesized unambiguously by methylaminolysis of 5-methoxy-3-methylpyrimidotriazine (1e).[5] The u.v. and ^{1}H n.m.r.

TABLE 2

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

Compound [a]	δ Values [b] (p.p.m.)
(1d)	7-H: 9·20; 3-Me: 3·34; NPr: 4·5—3·9 (m), 2·3—1·6 (m), 1·15 (t, *J* 7)
(1k)	3-H: 10·54; 7-H: 9·26; NPr: 4·20 (q, *J* 7), 2·4—1·6 (m), 1·16 (t, *J* 7)
(1l)	3-H: 10·46; 7-H: 9·10; NMe_2: 4·38 and 4·00
(1m)	3-H: 10·50; NMe_2: 4·36 and 3·96; 7-Me: 2·99
(1n)	3-Me: 3·31; 7-Me: 3·00; NPr: 4·17 (q, *J* 7), 2·3—1·6 (m), 1·15 (t, *J* 7)
(1o)	NMe_2: 4·35 and 3·95; 3-Me: 3·29; 7-Me: 2·92
(1p)	OMe: 4·50; NMe_2: 4·39 and 3·95; 3-Me: 3·29
(1r)	7-H: 9·24; NMe: 3·72br; 3-Me: 3·22
(2a)	7-H: 8·38; 5-H: 6·55; 3-Me: 2·26
(2b)	7-H: 8·47; 3-Me: 2·30; Pr: 2·4—2·2 (m), 2·0—1·4 (m), 1·10 (t, *J* 7)
(2c)	7-H: 8·32; 3-H: 7·52; 5-Me: 2·12

[a] In $F_3C{\cdot}CO_2H$. [b] Singlets where unspecified; *J* in Hz.

spectra in the Tables confirm the structures of the products.

EXPERIMENTAL

The ^{1}H n.m.r. spectra were obtained at 60 MHz and 33° (standard tetramethylsilane or sodium 3-trimethylsilylpropane-1-sulphonate as appropriate), and u.v. spectra were measured with a Unicam SP 800 spectrophotometer; peaks were checked on a manual SP 500 instrument.

1,2-*Dihydro*-3-*methyl*-5-*propylpyrimido*[5,4-e]-as-*triazine*.—Diethylaniline (130 ml) was added slowly to a suspension of 5-nitro-6-propyluracil [12] (80 g) in phosphoryl chloride (300 ml) gently boiling under reflux. The mixture was boiled for a further 1 h and the excess of phosphoryl chloride was distilled off under vacuum. The liquid residue was poured on crushed ice (*ca.* 1 kg) and stirred for 20 min. Extraction with ether (3 × 600 ml) and subsequent distillation of the water-washed and dried extract, gave 2,4-*dichloro*-5-*nitro*-6-*propylpyrimidine* (82 g), m.p. 43—44° after sublimation at 35° and 0·1 mmHg (Found: N, 17·85. $C_7H_7Cl_2N_3O_2$ requires N, 17·8%).

The dichloropyrimidine (20 g) and acetylhydrazine [13] were stirred in ethanol (200 ml) at 0° for 30 min. Sodium hydrogen carbonate (7·0 g) in water (150 ml) was added during 1 h with stirring. The precipitate was washed with a little cold water and then dried in air. Recrystallization from benzene gave 4-(2-*acetylhydrazino*)-2-*chloro*-5-*nitro*-6-*propylpyrimidine* (22 g), m.p. 156—157° (Found: C, 39·7; H, 4·5; N, 25·3. $C_9H_{12}ClN_5O_3$ requires C, 39·5; H, 4·4; 25·6%).

This pyrimidine (10 g) was hydrogenated over 10% palladium–charcoal (2 g) in methanol (300 ml) at 20° and *ca.* 760 mmHg for 3 h. The filtered solution was mixed with methanolic 10% hydrogen chloride (20 ml) and boiled for 20 min. Evaporation under reduced pressure and recrystallization of the residue from ethanol gave the *dihydro*-3-*methyl*-5-*propylpyrimidotriazine hydrochloride* (5·5 g), m.p. 222—224° (Found: C, 47·7; H, 6·3; N, 31·0. $C_9H_{13}N_5$,HCl requires C, 47·5; H, 6·3; N, 30·8%).

1,2-*Dihydro*-5-*methylpyrimido*[5,4-e]-as-*triazine*.— Crude 2-chloro-4-(2-formylhydrazino)-6-methyl-5-nitropyrimidine (14 g) was prepared from 2,4-dichloro-6-methyl-5-nitro-

[7] D. J. Brown and T. Sugimoto, *Austral. J. Chem.*, 1971, **24**, 633.
[8] C. Temple, C. L. Kussner, and J. A. Montgomery, *J. Org. Chem.*, 1969, **34**, 2102.
[9] D. J. Brown and T. Sugimoto, *J. Chem. Soc.* (*C*), 1970, 2661.
[10] A. Albert and F. Reich, *J. Chem. Soc.*, 1961, 127; A. Albert and C. F. Howell, *ibid.*, 1962, 1591.
[11] A. Albert and W. L. F. Armarego, *Adv. Heterocyclic Chem.*, 1965, **4**, 1.
[12] B. R. Baker and M. Kawazu, *J. Medicin. Chem.*, 1967, **10**, 316.
[13] G. Schöfer and N. Schwan, *J. prakt. Chem.*, 1895, **51**, 180.

pyrimidine [14] (15 g) and formylhydrazine [13] (4·5 g) by a method analogous to that for the acetylhydrazinopropylpyrimidine. Recrystallization gave only the known [7] 7-methyl-8-nitro-*s*-triazolo[4,3-*c*]pyrimidin-5-one, m.p. >300° (Found: C, 37·2; H, 2·8; N, 35·3. Calc. for $C_6H_5N_5O_3$: C, 36·9; H, 2·6; N, 35·9%). Hence the crude material (9·0 g) was hydrogenated and cyclized like its analogue to give the dihydro-5-methylpyrimidotriazine hydrochloride (4·7 g), m.p. 295° (decomp.), identified with authentic material [4] by mixed m.p. and i.r. spectra (Found: C, 38·8; H, 4·2; N, 37·9. Calc. for $C_6H_7N_5$,HCl: C, 38·8; H, 4·3; N, 37·7%).

1,2-*Dihydro*-3-*methylpyrimido*[5,4-e]-as-*triazine*.— 4-(2-Acetylhydrazino)-2-chloro-5-nitropyrimidine [1] (2·0 g) was similarly hydrogenated and cyclized to give the *dihydro*-3-*methylpyrimidotriazine dihydrochloride* (1·5 g). m.p. >300° (Found: N, 31·6. $C_6H_7N_5$,2HCl requires N, 31·5%).

3-*Methyl*-5-*propylaminopyrimido*[5,4-e]-as-*triazine*.— (*a*) 5-Methoxy-3-methylpyrimidotriazine [5] (0·5 g), propylamine (0·5 g), and ethanol (50 ml) were boiled under reflux for 2 h. The residue from evaporation was recrystallized (charcoal) from ethanol to give the 3-*methyl*-5-*propylaminopyrimidotriazine* (0·47 g), m.p. 181—182° (Found: C, 52·9; H, 6·1; N, 41·3. $C_9H_{12}N_6$ requires C, 52·9; H, 5·9; N, 41·15%).

(*b*) 1,2-Dihydro-3-methylpyrimidotriazine dihydrochloride (0·9 g), anhydrous triethylamine (0·8 g), and anhydrous tetrahydrofuran (150 ml) were stirred for 10 min. Silver oxide (3 g) and barium oxide (10 g) were added and stirring was continued for 10 h at 25°. The filtered solution of 3-methylpyrimidotriazine was then stirred with anhydrous propylamine (2 g) and manganese dioxide (9 g) for 8 h at 25°. Filtration, evaporation, and recrystallization gave the same product (0·56 g) as in (*a*).

(*c*) Free 1,2-dihydro-3-methylpyrimidotriazine [5] (0·8 g) was oxidized by stirring for 6 h with silver oxide (4 g) and barium oxide (10 g) in tetrahydrofuran (150 ml). The filtered solution and propylamine (3·0 g) were stirred in air (moisture excluded) for 30 h to give (after work-up) the same product (0·61 g).

(*d*) 1,2-Dihydro-3-methylpyrimidotriazine (0·5 g), propylamine (5 g), barium oxide (10 g), and anhydrous tetrahydrofuran (100 ml) were stirred by a stream of dry air for 24 h at 25°. Filtration *etc.* gave the same product (0·32 g); when benzene replaced tetrahydrofuran the yield was 0·23 g.

(*e*) 1,2-Dihydro-3,5-dimethylpyrimidotriazine hydrochloride [5] (0·68 g), propylamine (7·5 g), barium oxide (10 g), and tetrahydrofuran (200 ml) were aerated as in (*d*) for 100 h to give the same product (0·3 g), m.p. 181° (Found: C, 52·9; H, 6·3; N, 41·0%).

(*f*) 1,2-Dihydro-3-methyl-5-propylpyrimidotriazine hydrochloride (0·74 g) was treated as in (*e*) for 20 h to give the same product (0·53 g). In benzene, the yield was 0·37 g (Found: C, 53·1; H, 6·1; N, 41·4%).

(*g*) The same substrate (0·8 g) was oxidized as in (*c*). Isolation of 3-methyl-5-propylpyrimidotriazine from part of the red filtrate (of characteristic u.v. spectrum: Table 1) was unsuccessful owing to decomposition on attempted sublimation. The remaining solution, mixed with propylamine (5 ml), exhibited a spectrum (Table 1) akin to those of other 5,6-adducts. Aeration for 20 h gave the same final product (0·42 g).

5-*Dimethylamino*-3-*methylpyrimido*[5,4-e]-as-*triazine*.— 1,2-Dihydro-3-methylpyrimidotriazine [5] (0·5 g), pure anhydrous dimethylamine (5 g), barium oxide (5 g), and anhydrous dioxan (200 ml) were stirred by a slow stream of dry air at 25° for 50 h. The mixture was boiled for a few minutes and filtered immediately. The solid was washed with acetone. The filtrate and washings were evaporated to dryness. The residual 5-dimethylamino-3-methylpyrimidotriazine (0·46 g; from ethanol), m.p. 218°, was identified with authentic material [5] by mixed m.p. and i.r. spectra (Found: C, 50·5; H, 5·1; N, 44·5. Calc. for $C_8H_{10}N_6$: C, 50·5; H, 5·3; N, 44·2%).

When diethylamine was used similarly, no homologous product was formed. Instead, the residue from evaporation was acidified with acetic acid to give 3-methylpyrimido-[5,4-*e*]-*as*-triazin-5-one (0·1 g), identified with authentic material [7] by paper chromatography and i.r. spectra; similar use of triethylamine gave the same product (20%).

5-*Propylaminopyrimido*[5,4-e]-as-*triazine*.—(*a*) 1,2-Dihydropyrimidotriazine [5] (0·4 g), propylamine (4 g), barium oxide (10 g), and anhydrous dioxan (150 ml) were aerated for 40 h. The filtered solution was evaporated to give the *5-propylaminopyrimidotriazine* (0·16 g), m.p. 143—145° (Found: C, 50·5; H, 5·2; N, 44·5. $C_8H_{10}N_6$ requires C, 50·5; H, 5·3; N, 44·2%).

(*b*) Similar treatment of 1,2-dihydro-5-methylpyrimidotriazine hydrochloride (0·42 g) for 70 h gave the same product (0·21 g) as in (*a*), identified by mixed m.p. (Found: C, 50·1; H, 5·35; N, 43·8%).

5-*Dimethylaminopyrimido*[5,4-e]-as-*triazine*.—(*a*) 1,2-Dihydropyrimidotriazine [5] (0·3 g), dimethylamine (3 g), barium oxide (5 g), and dioxan (150 ml) were aerated gently for 20 h. Work-up as before gave the *dimethylaminopyrimidotriazine* (0·3 g), m.p. 180—181° (from ethanol) (Found: C, 47·6; H, 4·7; N, 48·2. $C_7H_8N_6$ requires C, 47·7; H, 4·6; N, 47·7%).

(*b*) Similar treatment of 1,2-dihydro-5-methylpyrimidotriazine hydrochloride (0·42 g) for 70 h gave the same proproduct (0·14 g) as in (*a*).

5-*Dimethylamino*-7-*methylpyrimido*[5,4-e]-as-*triazine*.— 1,2-Dihydro-7-methylpyrimidotriazine [5] (0·25 g) was treated like its unmethylated homologue [method (*a*)] for 40 h, giving the 5-*dimethylamino*-7-*methylpyrimidotriazine* (0·27 g), m.p. 179—180° (Found: C, 50·5; H, 5·2; N, 44·5. $C_8H_{10}N_6$ requires C, 50·5; H, 5·3; N, 44·2%).

5-*Dimethylamino*-3,7-*dimethylpyrimido*[5,4-e]-as-*triazine*. —Similar treatment of 1,2-dihydro-3,7-dimethylpyrimidotriazine [5] (0·3 g) for 20 h gave the 5-*dimethylamino*-3,7-*dimethylpyrimidotriazine* (0·28 g), m.p. 222—223° (Found: C, 52·6; H, 6·1; N, 40·9. $C_9H_{12}N_6$ requires C, 52·9; H, 5·9; N, 41·15%).

3,7-*Dimethyl*-5-*propylaminopyrimido*[5,4-e]-as-*triazine*.— Prepared from 1,2-dihydro-3,7-dimethylpyrimidotriazine [5] (0·7 g) as in method (*a*) for its unmethylated homologue, 3,7-*dimethyl*-5-*propylaminopyrimidotriazine* (0·78 g) had m.p. 114—116° (Found: C, 54·9; H, 6·6; N, 38·5. $C_{10}H_{14}N_6$ requires C, 55·0; H, 6·5; N, 38·5%).

3-*methyl*-5-*methylaminopyrimido*[5,4-e]-as-*triazine*.— (*a*) 5-Methoxy-3-methylpyrimidotriazine [5] (0·4 g) and ethanolic 2% methylamine (150 ml) were boiled under reflux for 10 min. Evaporation and recrystallization of the residue from ethanol gave the 3-*methyl*-5-*methylaminopyrimidotriazine* (0·27 g), m.p. 256° (decomp.) (Found: C, 47·9; H, 4·75; N, 48·0. $C_7H_8N_6$ requires C, 47·7; H, 4·6; N, 47·7%).

(*b*) 1,2-Dihydro-3-methyl-5-propylpyrimidotriazine hydrochloride (0·6 g), dimethylamine (6 g; commercial, which later proved to contain *ca.* 3% methylamine),

[14] A. Albert, D. J. Brown, and H. C. S. Wood, *J. Chem. Soc.*, 1954, 3832.

barium oxide (8 g), and tetrahydrofuran (150 ml) were aerated for 40 h. The usual work-up gave the methylamino-derivative (0·24 g), identified by mixed m.p. and i.r. spectra (Found: C, 47·1; H, 4·75; N, 47·4%).

5-Dimethylamino-7-methoxy-3-methylpyrimido[5,4-e]-*as-triazine*.—(*a*) 4-(α-Ethoxyethylidenehydrazino)-2-methoxy-5-nitropyrimidine [9] (5·0 g) was hydrogenated over palladium–carbon (10%; 0·5 g) in methanol (300 ml) at 20° and 720 mmHg for 3 h. Filtration and concentration gave crude 1,2-dihydro-7-methoxy-3-methylpyrimidotriazine (3·0 g), which was dried over phosphorus pentoxide. This material (1·0 g) was stirred with silver oxide (4 g) and barium oxide (10 g) in tetrahydrofuran (100 ml) for 4 h. The filtered solution, dimethylamine (3 g), and manganese dioxide (10 g) were stirred for 30 h. The mixture was filtered and the solid was extracted with ethanol (400 ml). The filtrate and extract were evaporated. Recrystallization of the residue from ethanol gave the *5-dimethylamino-7-methoxy-3-methylpyrimidotriazine* (0·68 g), m.p. 244—245° (decomp.) (Found: C, 48·9; H, 5·9; N, 38·3. $C_9H_{12}N_6O$ requires C, 49·1; H, 5·5; N, 38·2%).

(*b*) *5,7-Dimethoxy-3-methylpyrimidotriazine* [9] (0·6 g) and methanolic 2% dimethylamine (150 ml) were stirred at 25° for 10 h. Evaporation and recrystallization gave the same product (0·55 g) as in (*a*), identified by mixed m.p. and t.l.c. (Found: C, 48·9; H, 5·8; N, 38·4%).

We thank Dr. W. Pendergast for discussions, Dr. J. E. Fildes and her staff for analyses, Mr S. E. Brown for the ^1H n.m.r. spectra, and the Australian National University for supporting T. S. as a Scholar.

[1/1320 *Received, July 29th*, 1971]