Aza-analogues of Pteridine. Part VI.[1] Some 3-Alkyl-5(and 7)-aminopyrimido[5,4-*e*]-*as*-triazines and Related Compounds

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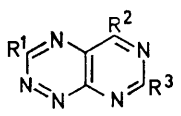
4-[*N'*-(1-Ethoxypropylidene)hydrazino]-2-methoxy-5-nitropyrimidine (3; R = Et) was converted into 3-ethyl-5,7-dimethoxy[5,4-*e*]-*as*-triazine (1a), which underwent ammonolysis to 5-amino-3-ethyl-7-methoxypyrimidotriazine (1b) and its 5,7-diamino-analogue (1c). Hydrolysis of the same dimethoxypyrimidotriazine gave 3-ethyl-7-methoxypyrimidotriazin-5(6*H*)-one (2b), which on ammonolysis gave its 7-amino-analogue (2e). Homologous compounds were made similarly.

In boiling toluene, the pyrimidine intermediate (3; R = Et) isomerized to 3-ethoxy-3-ethyl-2,3-dihydro-5-methoxy-8-nitro-*s*-triazolo[4,3-*c*]pyrimidine (4; R = Et).

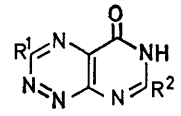
5-Amino-3-methylthio-*as*-triazine-6-carboxamide (6; R^1 = SMe, R^2 = R^3 = NH_2) was converted by Vilsmeier reagents into 8-chloro-6-dimethylamino-5,6-dihydro-3-methylthiopyrimido[4,5-*e*]-*as*-triazine (7) or by triethyl orthoformate into 3-methylthiopyrimido[4,5-*e*]-*as*-triazin-8(7*H*)-one (5; R = SMe). Assigned structures were consistent with ionization constants and with the u.v., i.r., ^{1}H n.m.r., and mass spectra recorded.

SEVERAL 5,7-diaminopyrimido[5,4-*e*]-*as*-triazines and related compounds have been prepared recently by routes involving the covalent 5,6-addition of appropriate amines or other reagents to 5-unsubstituted- or 5-alkylpyrimidotriazines, followed by an oxidative step.[1,2] However, more conventional aminolytic methods[3,4] are sometimes preferable. In this paper we describe the preparation of some methoxypyrimido[5,4-*e*]-*as*-triazines



(1)

	R^1	R^2	R^3
a:	Et	OMe	OMe
b:	Et	NH_2	OMe
c:	Et	NH_2	NH_2
d:	Me	NH_2	OMe
e:	Me	NH_2	NH_2
f:	Ph	OMe	OMe
g:	Ph	NH_2	NH_2
h:	H	OMe	OMe
i:	Me	OMe	OMe

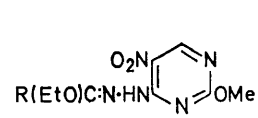


(2)

	R^1	R^2
a:	H	OMe
b:	Et	OMe
c:	Ph	OMe
d:	Me	OMe
e:	Et	NH_2
f:	Ph	NH_2
g:	Me	NH_2
h:	H	NH_2

[(1; R^2 = R^3 = OMe), (2; R^2 = OMe)]; their ammonolysis to give 3-alkyl-5-amino-7-methoxypyrimidotriazines (1; R^2 = NH_2, R^3 = OMe), the 5,7-diamino-analogues (1; R^2 = R^3 = NH_2), and some 3-alkyl-7-aminopyrimidotriazin-5(6*H*)-ones (2; R^2 = NH_2) required for antileukaemia testing; the thermal isomerization of the intermediate 4-[*N'*-(1-ethoxyalkylidene)-hydrazino]pyrimidines (3) into 3-alkyl-3-ethoxy-2,3-dihydro-*s*-triazolo[4,3-*c*]pyrimidines (4); and an attempt to produce 3-aminopyrimido[4,5-*e*]-*as*-triazin-8(7*H*)-one (5; R = NH_3) by ammonolysis of its 3-methylthio-analogue (5; R = SMe).

4-Hydrazino-2-methoxy-5-nitropyrimidine[5] was converted by triethyl orthopropionate into its *N'*-ethoxypropylidene derivative (3; R = Et). On catalytic hydrogenation in methanol followed by shaking with silver oxide, this underwent several sequential reactions (*cf.* ref. 5) to give 3-ethyl-5,7-dimethoxypyrimidotriazine (1a) which reacted with methanolic ammonia to yield the monoamine (1b) or the diamine (1c) according to



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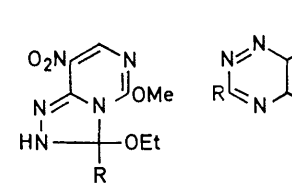

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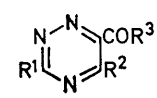

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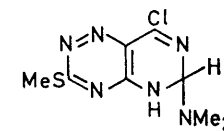

(7)

conditions. The lower homologues (1d and e) were made similarly and the ethoxybenzylidene compound (3; R = Ph) furnished the pyrimidotriazines (1f and g). Just as 5,7-dimethoxypyrimidotriazine (1h) gave only 7-methoxypyrimidotriazin-5(6*H*)-one (2a) on cold alkaline hydrolysis,[5] so the homologues (1a, f, and i) gave the products (2b—d) which underwent ammonolysis to yield the amines (2e—g) respectively; the structures (2b—g) were confirmed by comparison of the pK_a values and spectra (see Experimental section) with those[2,5] of the appropriately related compounds, *e.g.* (2a), (2h), and 5-aminopyrimidotriazin-7(6*H*)-one.

When the aforementioned 4-[N'-(1-ethoxyalkylidene)-hydrazino]pyrimidines (3; R = Me or Et) were boiled in toluene for 2 h, isomerization to the respective bicyclic triazolopyrimidines (4; R = Me or Et) occurred to the extent of 70—80% (as judged by ^{1}H n.m.r. spectra, which also confirmed the structures); in neither case

[1] Part V, D. J. Brown and T. Sugimoto, *J.C.S. Perkin I*, 1972, 237.

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

[3] C. Temple, C. L. Kussner, and J. A. Montgomery, *J. Org. Chem.*, 1969, **34**, 2102.

[4] D. J. Brown and T. Sugimoto, *Austral. J. Chem.*, 1971, **24**, 633.

[5] D. J. Brown and T. Sugimoto, *J. Chem. Soc.* (*C*), 1970, 2661.

did the proportion of bicyclic isomer increase on prolonged boiling, an observation suggesting equilibration. The addition of a little trifluoroacetic acid to the toluene led to as yet unidentified products, each lacking an ethoxy-group but retaining alkyl, methoxy, and H-7 n.m.r. signals at appreciably higher δ values. The ethoxybenzylidene homologue (3; R = Ph) underwent no isomerization, perhaps on account of steric hindrance by the phenyl group.

In our first approach to aminopyrimido[4,5-*e*]-*as*-triazinones analogous to those of the [5,4-*e*] series, the carboxytriazinone (6; R^1 = SMe, $R^2 = R^3$ = OH) [6] was converted (*cf.* ref. 7) into the acid chloride (6; R^1 = SMe, $R^2 = R^3$ = Cl) and thence into the amide (6; R^1 = SMe, $R^2 = R^3 = NH_2$). On boiling with triethyl orthoformate in acetic anhydride this gave the methylthiopyrimidotriazinone (5; R = SMe), but when triethyl orthoacetate was used, no reaction occurred. The ring system of the thioether (5; R = SMe) proved unstable: attempts to prepare the amino-analogue (5; $R = NH_2$) by ammonolysis gave only the known diaminotriazine [8] (6; $R^1 = R^2 = R^3 = NH_2$), and even prolonged boiling in water or ethanol gave the triazine amide (6; R^1 = SMe, $R^2 = R^3 = NH_2$). When this amide was treated in dimethylformamide with phosphoryl or thionyl chloride (with a view to nitrile formation), the dimethylformamide was involved in the formation of a product formulated as the dihydropyrimido[4,5-*e*]-*as*-triazine (7) on analytical and spectral evidence (see Experimental section); elimination of dimethylamine occurred in acidic media, probably to give initially the unstable 8-chloro-3-methylthiopyrimidotriazine.

EXPERIMENTAL

Ionization constants were measured spectrometrically at 20° in buffers [9] of 10^{-2}M ionic strength by methods outlined by Albert and Sergeant,[10] without thermodynamic corrections. ^{1}H N.m.r. spectra were recorded at 33° (tetramethylsilane or sodium 3-trimethylsilylpropane-1-sulphonate standard) with a Perkin-Elmer R10 60 MHz instrument; i.r. spectra ($\nu_{max.}$ in cm^{-1} for Nujol mulls) were obtained with a Unicam SP 200 instrument and u.v. spectra ($\lambda_{max.}$ in nm; inflections in italics) with a Shimadzu RS27 instrument (peak data checked on an Optica manual instrument).

5,7-*Diamino*-(*and* 5-*Amino*-7-*methoxy*-)3-*methylpyrimido*-[5,4-e]-as-*triazine* (1e and d).—5,7-Dimethoxy-3-methylpyrimidotriazine [5] (1·0 g) and saturated methanolic ammonia (50 ml) were heated in a sealed tube at 100° for 16 h. On cooling, the mixture deposited the yellow *diaminomethylpyrimidotriazine* (47%), m.p. ≮320° (from water) (Found: C, 41·1; H, 4·0; N, 54·9. $C_6H_7N_7$ requires C, 40·7; H, 4·0; N, 55·3%); $\nu_{max.}$ 3320 (NH), 3220 (NH), 3100 (NH), and 1642 (C:N); pK_a 5·36 ± 0·02; $\lambda_{max.}$ (log ε) at pH 8: 400 (3·62), 313 (3·25), 261 (4·32), *216* (4·19); δ (CF_3·CO_2H) 3·12 p.p.m. (s, 3-Me).

The residue from evaporation of the filtrate gave the light yellow *aminomethoxymethylpyrimidotriazine* (38%), m.p. 200° (from ethanol) (Found: C, 43·8; H, 4·4; N, 43·6. $C_7H_8N_6O$ requires C, 43·7; H, 4·2; N, 43·7%); $\nu_{max.}$ 3340 (NH) and 1630 (C:N); δ [$(CD_3)_2SO$] 8·91br (s, NH_2), 4·09 (s, OMe), and 3·02 p.p.m. (s, 3-Me). Further treatment as before with ammonia gave more diamine.

3-*Ethyl*-5,7-*dimethoxypyrimido*[5,4-e]-as-*triazine* (1a).—4-Hydrazino-2-methoxy-5-nitropyrimidine [5] (3·5 g), triethyl orthopropionate (10 ml), and ethanol (40 ml) were boiled under reflux for 1 h. Concentration and refrigeration gave yellow 4-[N′-(1-*ethoxypropylidene*)*hydrazino*]-2-*methoxy*-5-*nitropyrimidine* (3; R = Et) (47%), m.p. 137—138° (from ethanol) (Found: C, 44·7; H, 5·7; N, 26·0. $C_{10}H_{15}N_5O_4$ requires C, 44·6; H, 5·6; N, 26·0%); $\nu_{max.}$ 3330 (NH) and 1603 (C:N); δ ($CDCl_3$) 9·35 (s, H-6), 4·34 (q, O·CH_2Me), 4·17 (s, OMe), 2·62 (q, C·CH_2Me), 1·48 (t, O·CH_2·CH_3), and 1·32 p.p.m. (t, C·CH_2·CH_3) [*cf.* ethoxymethylenehydrazino-homologue [5] in $CDCl_3$: 9·35 (s, H-6), 7·06 (s, CH_2), 4·38 (q, O·CH_2), 4·18 (s, OMe), and 1·46 (O·CH_2·CH_3)]. This pyrimidine (2·0 g) was hydrogenated (20°; 760 mmHg) in methanol (150 ml) over palladium–carbon (10%; 0·3 g) during 1·5 h. The filtered solution was stirred with anhydrous sodium sulphate (20 g) for 2 h. Then the mixture was stirred and boiled under reflux with silver oxide (5·0 g) for 2·5 h. The filtered solution was evaporated. The residual yellow *ethyldimethoxypyrimidotriazine* (26%) had m.p. 142—143° (from ethanol) (Found: C, 48·9; H, 5·2; N, 31·7. $C_9H_{11}N_5O_2$ requires C, 48·9; H, 5·0; N, 31·7%); $\nu_{max.}$ 1602 (C:N); δ [$(CD_3)_2SO$] 4·40 (s, OMe), 4·32 (s, OMe), 3·42 (q, CH_2), and 1·48 p.p.m. (t, CH_3).

5,7-*Diamino*-3-*ethyl*-(*and* 5-*Amino*-3-*ethyl*-7-*methoxy*-)-*pyrimido*[5,4-e]-as-*triazine* (1c and b).—Like its methyl homologue, the foregoing ethyldimethoxypyrimidotriazine underwent ammonolysis to give the *diaminoethylpyrimidotriazine* (60%), m.p. ≮320° (from water) (Found: C, 43·4; H, 4·6; N, 51·6. $C_7H_9N_7$ requires C, 44·0; H, 4·7; N, 51·3%); $\nu_{max.}$ 3300 (NH), 3230 (NH), 3100 (NH), and 1642 (C:N); δ (CF_3·CO_2H) 3·46 (q, CH_2) and 1·54 p.p.m. (t, CH_3); pK_a 4·09 ± 0·02; $\lambda_{max.}$ (log ε) at pH 8: 398 (3·66), 312 (3·30), 262 (4·34), and *218* (4·13). The mother liquors gave the *aminoethylmethoxypyrimidotriazine* (32%), m.p. 205° (from ethanol) (Found: C, 46·3; H, 5·2; N, 40·9. $C_8H_{10}N_6O$ requires C, 46·6; H, 4·9; N, 40·8%); $\nu_{max.}$ 3340 (NH) and 1636 (C:N); δ [$(CD_3)_2SO$] 4·08 (s, OMe), 3·31 (q, CH_2), and 1·49 p.p.m. (t, CH_3).

5,7-*Dimethoxy*-3-*phenylpyrimido*[5,4-e]-as-*triazine* (1f).—Using triethyl orthobenzoate in place of the orthopropionate in the foregoing condensation gave 4-[N′-(α-*ethoxybenzylidene*)*hydrazino*]-2-*methoxy*-5-*nitropyrimidine* (3; R = Ph) (74%), m.p. 170° (from ethanol) (Found: C, 52·5; H, 4·7; N, 22·3. $C_{14}H_{15}N_5O_4$ requires C, 53·0; H, 4·8; N, 22·1%); $\nu_{max.}$ 3330 (NH) and 1610 (C:N); δ ($CDCl_3$) 9·36 (s, H-6), 7·84 (m: 2′-, 6′-H), 7·63 (m, 3′-, 4′-, 5′-H), 4·30 (q, CH_2), 4·20 (s, OMe), and 1·47 p.p.m. (t, CH_3). Hydrogenation followed by oxidation with silver oxide (as for the propylidene analogue) gave the *dimethoxyphenylpyrimidotriazine* (40%), m.p. 188° (decomp.) (from ethanol) (Found: C, 58·2; H, 4·3; N, 26·0. $C_{13}H_{11}N_5O_2$ requires C, 58·0; H, 4·1; N, 26·0%); $\nu_{max.}$ 1604 (C:N); δ [$(CD_3)_2SO$] 8·74 (m,

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[8] E. C. Taylor and R. W. Morrison, *J. Amer. Chem. Soc.*, 1965, **87**, 1976.
[9] D. D. Perrin, *Austral. J. Chem.*, 1963, **16**, 572.
[10] A. Albert and E. P. Serjeant, 'The Determination of Ionization Constants,' Chapman and Hall, London, 1971.

2′-, 6′-H), 7·85 (m, 3′-, 4′-, 5′-H), 4·34 (s, OMe), and 4·25 p.p.m. (s, OMe).

5,7-*Diamino*-3-*phenylpyrimido*[5,4-e]-as-*triazine* (1g).—5,7-Dimethoxy-3-phenylpyrimidotriazine underwent ammonolysis as did its 3-methyl analogue to give the *diamino-phenylpyrimidotriazine* (62%), m.p. ≮320° (Found: C, 55·0; H, 3·5; N, 40·4. $C_{11}H_9N_7$ requires C, 55·2; H, 3·8; N, 40·8%); $\nu_{max.}$ 3420 (NH), 3350 (NH), 3160 (NH), and 1642 (C:N); δ (CF_3·CO_2H) 8·61 (m, 2′-, 6′-H) and 7·82 p.p.m. (m, 3′-, 4′-, 5′-H).

7-*Methoxy*-(*and* 7-*Amino*-)3-*methylpyrimido*[5,4-e]-as-*triazin*-5(6H)-*one* (2d and g).—5,7-Dimethoxy-3-methylpyrimidotriazine [5] (0·3 g) was stirred in 0·3N-sodium hydroxide (10 ml) at 20° for 24 h. The solution was adjusted to pH 2 to yield the yellow *methoxymethylpyrimidotriazinone* (71%), m.p. 176—178° (decomp.) (from ethanol) (Found: C, 43·4; H, 3·9; N, 36·0. $C_7H_7N_5O_2$ requires C, 43·5; H, 3·7; N, 36·3%); $\nu_{max.}$ 1716 (C:O) and 1616 (C:N); δ [$(CD_3)_2SO$] 4·10 (s, OMe) and 2·92 p.p.m. (s, Me). This methoxy-compound (0·05 g) and saturated methanolic ammonia (10 ml) were heated at 95° for 15 h. Concentration and subsequent refrigeration gave the yellow *aminomethylpyrimidotriazinone* (62%), m.p. ≮320° (Found: C, 40·8; H, 3·4; N, 47·3. $C_6H_6N_6O$ requires C, 40·5; H, 3·4; N, 47·3%); $\nu_{max.}$ 3320 (NH), 3100 (NH), and 1703 (C:O); δ [$(CD_3)_2SO$] 2·86 p.p.m. (s, Me); pK_a 1·14 ± 0·06 and 6·95 ± 0·01; $\lambda_{max.}$ (log ε) at pH 9: 392 (3·57), 311 (3·95), 259 (4·35), and *212* (4·14); and at pH 4: 379 (3·46), *268* (4·10), and 252 (4·14).

3-*Ethyl*-7-*methoxy*-(*and* 7-*Amino*-3-*ethyl*-)*pyrimido*[5,4-e]-as-*triazin*-5(6H)-*one* (2b and e).—Like its 3-methyl homologue, 3-ethyl-5,7-dimethoxypyrimidotriazine was converted first into the *ethylmethoxypyrimidotriazinone* (68%), m.p. 154—156° (decomp.) (from ethanol) (Found: C, 46·2; H, 4·2; N, 33·3. $C_8H_9N_5O_2$ requires C, 46·4; H, 4·4; N, 33·8%); $\nu_{max.}$ 1721 (C:O) and 1610 (C:N); δ [$(CD_3)_2SO$] 4·15 (s, OMe), 3·30 (q, CH_2), and 1·40 p.p.m. (t, CH_3). Ammonolysis of this gave the *aminoethylpyrimidotriazinone* (44%), m.p. ≮320° (Found: C, 44·3; H, 4·1; N, 43·3. $C_7H_8N_6O$ requires C, 43·7; H, 4·2; N, 43·7%); $\nu_{max.}$ 3320 (NH), 3100 (NH), and 1704 (C:N); δ [$(CD_3)_2SO$] 3·32 (q, CH_2) and 1·38 p.p.m. (t, CH_3); pK_a 1·15 ± 0·04 and 7·00 ± 0·02; $\lambda_{max.}$ (log ε) at pH 9: 390 (3·54), 310 (3·06), 259 (4·32), and *211* (4·14); and at pH 4: 378 (3·41), *270* (4·07), and 252 (4·10).

7-*Methoxy*-(*and* 7-*Amino*)3-*phenylpyrimido*[5,4-e]-as-*triazin*-5(6H)-*one* (2c and f).—5,7-Dimethoxy-3-phenylpyrimidotriazine underwent alkaline hydrolysis similarly to give the *methoxyphenylpyrimidotriazinone* (74%), m.p. 216° (decomp.) (from ethanol) (Found: C, 56·2; H, 3·6; N, 27·3. $C_{12}H_9N_5O_2$ requires C, 56·5; H, 3·6; N, 27·4%); $\nu_{max.}$ 1712 (C:O) and 1616 (C:N); δ [$(CD_3)_2SO$] 8·55 (m, 2′-, 6′-H), 7·67 (m, 3′-, 4′-, 5′-H), and 4·12 p.p.m. (s, OMe). Ammonolysis then gave the *aminophenylpyrimidotriazinone* (60%), m.p. ≮320° (Found: C, 54·6; H, 3·7; N, 34·6. $C_{11}H_8N_6O$ requires C, 55·0; H, 3·4; N, 35·0%); $\nu_{max.}$ 3300 (NH), 3150 (NH), and 1708 (C:O); δ [$(CD_3)_2SO$] 8·51 (m, 2′-, 6′-H) and 7·62 p.p.m. (m, 3′-, 4′-, 5′-H); pK_a 1·00 ± 0·03 and 6·77 ± 0·03; $\lambda_{max.}$ (log ε) at pH 9: 407 (3·24), *311* (3·84), 285 (4·18), and 210 (4·04); and at pH 4: 396 (3·38), 296 (4·18), and 260 (3·87).

Cyclization of 4-[N′-(1-*Ethoxyalkylidene*)*hydrazino*]-2-*methoxy*-5-*nitropyrimidines* (3).—4-[N′-(1-Ethoxyethylidene)hydrazino]2-methoxy-5-nitropyrimidine [5] (0·2 g) and anhydrous toluene (5 ml) were boiled under reflux for 2 h. The residue from evaporation was recrystallized twice from ethanol to give yellow 3-*ethoxy*-2,3-*dihydro*-5-*methoxy*-3-*methyl*-8-*nitro*-s-*triazolo*[4,3-c]*pyrimidine* (4; R = Me) (70%), m.p. 134—136° (Found: C, 41·6; H, 5·0; N, 27·1. $C_9H_{13}N_5O_4$ requires C, 42·3; H, 5·1; N, 27·4%); δ ($CDCl_3$) 93·0 (s, H-7), 4·32 (q, O·CH_2), 4·08 (s, OMe), 2·13 (s, 3-Me), and 1·37 p.p.m. (t, O·CH_2·CH_3) [*cf.* starting material in $CDCl_3$: 9·30 (s, H-6), 4·25 (q, O·CH_2), 4·12 (s, OMe), 2·27 (s, N:C·CH_3), and 1·47 p.p.m. (O·CH_2·CH_3)].

Similarly, the *N*′-(1-ethoxypropylidene)hydrazino]-homologue gave 3-*ethoxy*-3-*ethyl*-2,3-*dihydro*-5-*methoxy*-8-*nitro*-s-*triazolo*[4,3-c]*pyrimidine* (4; R = Et), m.p. 150—153° (from ethanol) (Found: C, 44·3; H, 5·6; N, 26·4. $C_{10}H_{15}N_5O_4$ requires C, 44·6; H, 5·6; N, 26·0%); δ ($CDCl_3$) 9·35 (s, H-7), 4·41 (q, O·CH_2), 4·15 (s, OMe), 2·53 (q, C·CH_2), 1·37 (t, O·CH_2·CH_3), and 1·22 p.p.m. (t, C·CH_2·CH_3).

The 4-[*N*′-(α-ethoxybenzylidene)hydrazino]-homologue was unchanged after being boiled in toluene for 4 h.

5-*Amino*-3-*methylthio*-as-*triazine*-6-*carboxamide* (6; R^1 = SMe, R^2 = R^3 = NH_2).—4,5-Dihydro-3-methylthio-5-oxo-*as*-triazin-6-carboxylic acid [6] (2·0 g), thionyl chloride (7 ml), dimethylformamide (0·1 g), and chloroform (15 ml) were boiled under reflux for 2 h. Removal of volatile material under reduced pressure left the crude acid chloride [$\nu_{max.}$ 1770 (C:O), δ ($CDCl_3$) 2·70 p.p.m. (s, SMe)], which was immediately diluted with methanol (5 ml) and then added to saturated methanolic ammonia (15 ml). The mixture was stirred at 20° for 16 h, then the solid was recrystallized from water to give the *aminomethylthiotriazinecarboxamide* (60%), m.p. 242° (Found: C, 32·4; H, 3·8; N, 37·3; S, 17·0. $C_5H_7N_5OS$ requires C, 32·4; H, 3·8; N, 37·8; S, 17·3%); $\nu_{max.}$ 3380 (NH), 3280 (NH), 3180 (NH), 1679 (C:O), and 1620 (C:N); δ [$(CD_3)_2SO$] 8·40br (s, NH_2), 7·80br (s, NH_2), and 2·53 p.p.m. (s, SMe) (NH_2 signals disappear on addition of D_2O).

3-*Methylthiopyrimido*[4,5-e]-as-*triazin*-8(7H)-*one* (5; R = SMe).—The foregoing amino-amide (0·55 g), triethyl orthoformate (3 ml), and acetic anhydride (10 ml) were heated under reflux for 1 h. Evaporation under reduced pressure followed by sublimation (200° at 0·1 mmHg) of the residue gave the colourless *methylthiopyrimidotriazinone* (57%), m.p. ≮300° (Found: C, 37·1; H, 3·0; N, 36·0; S, 16·1. $C_6H_5N_5OS$ requires C, 36·9; H, 2·6; N, 35·9; S, 16·3%); $\nu_{max.}$ 1720 (C:O); δ [$(CD_3)_2SO$] 3·53 (s, H-6) and 2·69 p.p.m. (s, SMe). When triethyl orthoacetate replaced the orthoformate, no cyclization occurred.

Attempted aminolysis (methanolic ammonia at 100° for 10 h) gave, on concentration, 3,5-diamino-*as*-triazine-6-carboxamide, m.p. ≮320° (lit.,[8] >350°) (Found: C, 31·4; H, 3·7. Calc. for $C_4H_6N_6O$: C, 31·2; H, 3·9%); $\nu_{max.}$ 3440 (NH), 3340 (NH), 3220 (NH), and 1690 (C:O).

Boiling the pyrimidotriazinone under reflux in water for 1 h or in ethanol for 60 h gave back the triazine precursor in high yield.

8-*Chloro*-6-*dimethylamino*-5,6-*dihydro*-3-*methylthiopyrimido*[4,5-e]-as-*triazine* (7).—Thionyl chloride or phosphoryl chloride (1·0 ml) was added to a stirred suspension of 5-amino-3-methylthio-*as*-triazine-6-carboxamide (0·5 g) in dimethylformamide (2 ml) at 0°. After the vigorous reaction, the mixture was heated at 70° for 10 min, cooled to 20°, diluted with water (5 ml), and refrigerated to give the cream-coloured *chloropyrimidotriazine* (62%, 51%), m.p. 240—241° (Found: C, 37·2; H, 4·5; Cl, 13·6; H, 32·4; S, 12·4. $C_8H_{11}ClN_6S$ requires C, 37·2; H, 4·4; Cl, 13·7; N, 32·5; S, 12·4%), which contained no ionic halogen; $\nu_{max.}$ 3470 (NH), 3300 (NH), and 1640 (C:N); *m/e* 258 (^{35}Cl), 260

(^{37}Cl), 211 (^{35}Cl, M — SMe), and 213 (^{37}Cl, M — SMe); δ ($CDCl_3$) 6·13 (s, H-6), 3·09 (s, NMe_2), and 2·41 p.p.m. (s, SMe); δ (6N-DCl–D_2O) 3·50 (s, free HN^+Me_2, ?) and 2·54 p.p.m. (s, SMe); $\lambda_{max.}$ (log ε) (MeOH) 257 (3·92) and *225* (3·66); $\lambda_{max.}$ (MeOH–HCl) (after 20 min) 360 (3·12), *312* (3·25), 275 (2·75), and 229 (3·83).

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