PYRIMIDINE REACTIONS*

XV.† SYNTHESES INVOLVING OXIDATION OF HYDRAZINOPYRIMIDINES

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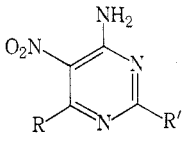
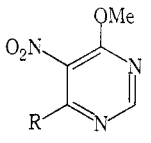
Introduction

Halogeno substituents may be removed conveniently from heterocycles by oxidizing the derived hydrazino compounds.[1] This procedure has been used recently to prepare 5-nitropyrimidine from its 4,6-dichloro derivative.[2] In the present paper the method is applied to other syntheses, which were originally aimed at the formation of pteridines bearing electron-withdrawing substituents, and in which the usual reductive dehalogenations[3] are contraindicated by the presence of a nitro or styryl group.

Results and Discussion

Thus 4-amino-6-chloro-5-nitropyrimidine[4] (I; R = Cl, R′ = H) and hydrazine hydrate gave the 6-hydrazino analogue (I; R = $NHNH_2$, R′ = H) which underwent oxidation by aqueous silver acetate to give 4-amino-5-nitropyrimidine (I; R = R′ = H). The 2-methyl and 2-styryl derivatives (I; R = H, R′ = Me or CH=CHPh)


(I)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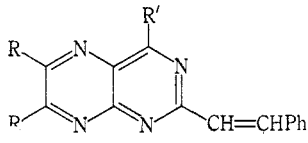
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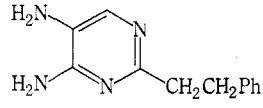
(IV)

were made similarly; in addition, the methyl was converted into the styryl derivative by condensation with benzaldehyde in piperidine. These and other structures were confirmed by the p.m.r. spectra recorded in Table 1.

Attempted aminolysis of 4,6-dimethoxy-5-nitropyrimidine[5] (II; R = OMe) by hydrazine gave only the dihydrazino compound[6] under a variety of conditions, but preferential aminolysis of the chloro substituent in 4-chloro-6-methoxy-5-nitropyrimidine[7] (II; R = Cl) proved possible. The resulting hydrazino compound

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[1] Albert, A., and Catterall, J. G., *J. chem. Soc.* C, 1967, in press.
[2] Biffin, M. E. C., Brown, D. J., and Lee, T.-C., *J. chem. Soc.* C, 1967, in press.
[3] Brown, D. J., "The Pyrimidines." p. 183 *et seq.* (John Wiley: New York 1962.)
[4] Boon, W. R., Jones, W. G. M., and Ramage, G. R., *J. chem. Soc.*, 1951, 96.
[5] Rose, F. L., and Brown, D. J., *J. chem. Soc.*, 1956, 1953.
[6] Krakov, M. H., and Christensen, B. E., *J. org. Chem.*, 1963, **28**, 2677.
[7] Taylor, E. C., Barton, J. W., and Paudler, W. W., *J. org. Chem.*, 1961, **26**, 4961.

(II; R = $NHNH_2$) was oxidized in methanol by silver oxide to give 4-methoxy-5-nitropyrimidine (II; R = H), structurally confirmed by hydrogenation to the known[8] 5-amino-4-methoxypyrimidine and by aminolysis to 4-amino-5-nitro-

TABLE 1

PROTON MAGNETIC RESONANCE SPECTRA

Compound	Medium	Signals (τ)
		Pyrimidines
4-Amino-5-nitro	D_2O/DCl	H2: d, 1·01 (J_m 1 c/s); H6: d, 0·39 (J_m 1 c/s)
4-Methoxy-5-nitro	CCl_4	OMe: s, 5·72; H2: s, 1·00; H6: s, 0·78
	$CDCl_3$	5·73; 0·90; 0·66
4-Amino-2-methyl-5-nitro	D_2O/DCl	Me: s, 7·26; H6: s, 0·48
4-Amino-5-nitro-2-styryl	Me_2SO	Hβ: d, 2·81 (J 17 c/s); Ph: m, 2·6–2·04; Hα: d, 1·82 (J 17 c/s); H6: s, 0·7
4-t-Butylamino-5-nitro	$CDCl_3$	Bu^t: s, 8·40; H2: s, 1·14; H6: s, 0·65
4,5-Diamino-2-styryl	Me_2SO	Hβ: d, 2·94 (J 16 c/s); Ph+Hα+H6: m, 2·63–2·18
4,5-Diamino-2-methyl	D_2O/DCl	Me: s, 7·35; H6: s, 1·87
4,5-Diamino	D_2O/DCl	H6: d, 1·91 (J_m 1·5 c/s); H2: d, 1·39 (J_m 1·5 c/s)
4,5-Diamino-2-phenethyl	DCl/D_2O	CH_2CH_2: s(br), 6·86; Ph: s(br), 2·67; H6: s, 1·91
	$(CD_3)_2SO$	CH_2CH_2: m, 7·1; $NH_2$4+$NH_2$5: s(br), 5·45* and 3·73*; Ph: s(br), 2·73; H6: s, 2·38
4-Amino-5-benzylideneamino-2-methyl	$CDCl_3$	Me: s, 7·49; NH_2: s(br), 4·03;* m- and p-H: m, 2·69–2·47; o-H: m, 2·18–2·04; Hα: s, 2·02; H6: s, 1·46
5-Acetamido-4-amino-2-methyl	DCl/D_2O	Ac: s, 7·72; Me: s, 7·36; H6: s, 1·69
		Pteridines
2-Styryl	$CDCl_3$	Ph+Hβ: m, 2·64–2·11; Hα: d, 1·54 (J 17 c/s); H6: d, 0·95 (J 2 c/s); H7: d, 0·73 (J 2 c/s); H4: s, 0·20
6,7-Dimethyl-2-styryl	$CDCl_3$	6-Me+7-Me: s, 7·17+s, 7·23; Ph+Hβ: m, 2·65–2·15; Hα: d, 1·64 (J 16 c/s); H4: s, 0·40
4-Chloro-6,7-dimethyl-2-styryl	$CDCl_3$	6-Me+7-Me: s(br), 7·11; Ph+Hβ: m, 2·67–2·13; Hα: d, 1·61 (J 16 c/s)

* Signal collapses on adding D_2O.

pyrimidine (I; R = R′ = H). The rate of t-butylaminolysis of the methoxy compound by three moles of amine, under the preparative conditions previously used[9] for the isomeric 2-methoxy-5-nitropyrimidine, was measured by change in the

[8] Marchal, L., Promel, R., Martin, R. H., and Cardon, A., *Bull. Soc. chim. Belg.*, 1960, **69**, 177.

[9] Brown, D. J., and Foster, R. V., *Aust. J. Chem.*, 1966, **19**, 1487, 2321.

ultraviolet spectra (Table 2); the apparent first-order rate constants (10^4k; sec^{-1}) were 2·00 (10°), 3·84 (20°), and 6·90 (30°), indicating that 4-methoxy-5-nitropyrimidine was only about 1·2 times more reactive than its 2-methoxy isomer. This figure should be compared with the 1·5 : 1 ratio in the reactivities of 5-bromo-4(and 2)-methoxypyrimidine also towards t-butylamine.[9] 4-Methoxy-5-nitropyrim-

TABLE 2

IONIZATION CONSTANTS AND ULTRAVIOLET SPECTRA

Compound	pK_a*	λ_{max} (log ε)†	pH or H_0
	Pyrimidines		
4-Amino-5-benzylideneamino-2-methyl	—	343(3·96), 276(4·10), 248(4·17)	E†
4-Amino-6-chloro-5-nitro-2-styryl	—	*355(4·08)*, 320(4·22), *258(3·96)*, 232(4·30)	E
4-Amino-6-hydrazino-2-methyl-5-nitro	4·08±0·03 (272)	338(3·88), *232(4·12)*, 210(4·33)	7·0
Cation		331(3·82), *292(3·62)*, 237(4·26)	1·0
4-Amino-6-hydrazino-5-nitro	3·70±0·04 (370)	337(3·91), *229(4·18)*	6·0
Cation		333(3·80), *296(3·58)*, 235(4·25)	1·0
4-Amino-6-hydrazino-5-nitro-2-styryl	—	353(4·41), *323(4·31)*, 231(4·28)	E
4-Amino-2-methyl-5-nitro	2·72±0·02 (350)	341(3·79), *257(3·70)*, 250(3·78), 216(4·29)	6·0
Cation		317(3·63), *255(3·89)*, 248(3·98), 215(4·25)	1·0
4-Amino-5-nitro	1·98±0·03 (355)	341(3·74), *256(3·66)*, 248(3·79)	6·0
Cation		319(3·63), *256*(3·93), 249(4·04), 210(4·14)	−2·0
4-Amino-5-nitro-2-styryl	2·35±0·05 (390)	365(4·24), *330(4·17)*, *256(4·05)*, 232(4·23)	E
2-Benzyl-4,6-dihydrazino-5-nitro[2]	4·11±0·04 (400)	361(3·84), 215(4·34)	7·0
Cation		320(3·80), *230(4·16)*	1·0
2-Benzyl-4,6-dihydroxy[2]	5·78±0·05 (300)	253(4·04)	3·0
Anion		253(3·92)	9·0
2-Benzyl-4,6-dihydroxy-5-nitro[2]	3·49±0·05 (310)	325(3·80), *244(3·63)*, 214(4·47)	1·0
Anion		334(3·75), *224(4·16)*	7·0
4-t-Butylamino-5-nitro	2·60±0·04 (400)	374(3·68), *262(3·82)*, 255(3·89), 222(4·26)	6·0
Cation		340(3·49), 259(4·08), 216(4·03)	−1·0
4,5-Diamino-6-chloro-2-styryl	2·85±0·04 (386)	328(4·27), 300(4·25), 222(4·21)	6·0
Cation		350(4·30), 298(4·20), *220(4·09)*	0·0
4,5-Diamino-2-phenethyl	6·65±0·04 (270)	291(3·80), 247(3·86)	9·0
Cation		278(3·92)	1·0
4,6-Dichloro-5-nitro-2-styryl	—	331(4·30), *240(3·90)*	E
4,6-Dihydrazino-2-methyl-5-nitro[2]	4·45±0·05 (380)	359(3·95), *234(4·23)*, 217(4·32)	7·0‡
Cation		327(3·81), *244(4·11)*, 230(4·19)	1·0
4-Hydrazino-6-methoxy-5-nitro	2·77±0·05 (400)	360(3·86), 280(3·81), 231(4·46)	6·0
Cation		320(3·89), *284(3·85)*, 224(4·50)	−1·0‡
4-Methoxy-5-nitro	—	277(3·58), 233(3·73)	E
	Pteridines		
4-Chloro-6,7-dimethyl-2-styryl	—	353(4·27), 312(4·39), *268(4·04)*, 216(4·39)	E
6,7-Dimethyl-2-styryl	—	345(4·04), 304(4·10), *280(4·05)*, 217(4·34)	E
2-Styryl	—	350(3·97), 304(4·11), 280(4·05), 220(4·24)	E

* Measured at 20° spectrometrically by the methods of Albert, A. and Serjeant, E. P., "Ionization Constants of Acids and Bases." (Methuen: London 1962.) Analytical wavelength in parentheses.

† In aqueous buffer of given pH or H_0, or in ethanol (E); inflexions in italics.

‡ Peaks measured rapidly because of instability in aqueous buffer.

idine was unstable in aqueous acid or alkali. Thus in 2N DCl/D_2O or in 0·1N $NaOD/D_2O$, the p.m.r. spectra indicated completed ring fission at 33° within 2 min. Changes in ultraviolet spectra were similarly rapid at room temperature.

The above styrylpyrimidine (I; R = H; R′ = CH=CHPh) provided an ideal intermediate for the synthesis of simple 2-styrylpteridines (III), hitherto unavailable because simple 2-methylpteridines were decomposed by treatment with benzal-

dehyde.[10] The nitro group in the intermediate underwent selective reduction by stannous chloride and the resulting diamine condensed with ethanolic glyoxal or biacetyl to give 2-styrylpteridine (III; R = R′ = H), and its 6,7-dimethyl derivative (III; R = Me, R′ = H) respectively. Similar reduction of 4-amino-6-chloro-5-nitro-2-styrylpyrimidine (I; R = Cl, R′ = CH=CHPh), followed by condensation with biacetyl, gave 4-chloro-6,7-dimethyl-2-styrylpteridine (III; R = Me, R′ = Cl); treatment of the same pyrimidine with hydrazine, sodium hydroxide, and palladized strontium carbonate in ethanol caused complete reduction to 4,5-diamino-2-phenethylpyrimidine (IV). Two additional related pyrimidines are described below. Neither the 2-styryl- nor the 2-methyl-pteridines could be successfully oxidized to 2-formyl- or 2-carboxyl-pteridines.

Experimental

Analyses were done by Dr J. E. Fildes and her staff; ultraviolet spectra by Mr A. Arandjelovic; pK_a values by Mr D. Light; and p.m.r. spectra by Mr S. E. Brown.

4-Amino-6-hydrazino-5-nitropyrimidine

4-Amino-6-chloro-5-nitropyrimidine[4] (5·0 g) and 98% hydrazine hydrate (3·0 ml) in ethanol (200 ml) were heated under reflux for 2 hr. The resulting solid was washed with ethanol and recrystallized from water to give the *hydrazinopyrimidine* (3·5 g) as yellow needles, m.p. 199° (Found: C, 28·1; H, 3·6; N, 49·3. $C_4H_6N_6O_2$ requires C, 28·25; H, 3·6; N, 49·4%). Treatment with aqueous ethanolic hydrogen chloride gave the *hydrochloride* hydrate, m.p. ≮ 300° (Found: C, 21·7; H, 3·8; N, 36·7. $C_4H_9ClN_6O_3$ requires C, 21·4; H, 4·0; N, 37·4%).

4-Amino-5-nitropyrimidine

(i) The above hydrazinopyrimidine (2·0 g) was heated and stirred under reflux with silver acetate (8·8 g) in water (100 ml) for 2 hr. Nitrogen was evolved and silver was precipitated. The mixture was filtered while hot and the filtrate and aqueous washings were made alkaline with ammonium hydroxide. Evaporation under reduced pressure to *c.* 20 ml and subsequent refrigeration gave the *aminonitropyrimidine* (68%), m.p. 212–214°, after sublimation (98°/0·05 mm) or recrystallization from ethanol (Found: C, 34·0; H, 3·15; N, 39·6. $C_4H_4N_4O_2$ requires C, 34·3; H, 2·9; N, 40·0%).

(ii) Oxidation on the same scale with hot aqueous 10% cupric sulphate pentahydrate (50 ml), and subsequent removal of copper ion as sulphide, gave a 5% yield of aminonitropyrimidine.

(iii) 4-Methoxy-5-nitropyrimidine (see below; 0·10 g) and concentrated ammonium hydroxide (10 ml) were warmed on the steam-bath for a few minutes and evaporated to dryness. The residual aminonitropyrimidine (0·03 g) was identified with the above material by mixed m.p. and infrared spectra.

4-Amino-6-hydrazino-2-methyl-5-nitropyrimidine

4-Amino-6-chloro-2-methyl-5-nitropyrimidine[4] (2·0 g) was converted as above into the *hydrazinomethylpyrimidine* (1·4 g), m.p. 252° (from methoxyethanol) (Found: C, 32·4; H, 4·35; N, 45·5. $C_5H_8N_6O_2$ requires C, 32·6; H, 4·4; N, 45·6%).

4-Amino-2-methyl-5-nitropyrimidine

The hydrazino derivative (2·0 g) was stirred under reflux with silver acetate (10·6 g) in boiling water (100 ml) for 2 hr. The filtrate was treated with hydrochloric acid until no further silver chloride precipitated, and then refiltered. Addition of ammonium hydroxide and finishing

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

as above gave the *pyrimidine* (20%), m.p. 277–278°, after sublimation (98°/0·05 mm) or recrystallization from ethanol (Found: C, 38·65; H, 4·0; N, 36·05. $C_5H_6N_4O_2$ requires C, 38·95; H, 3·9; N, 36·4%). Cupric sulphate oxidation gave 16% yield.

4,6-Dichloro-5-nitro-2-styrylpyrimidine

4,6-Dihydroxy-5-nitro-2-styrylpyrimidine[11] (2·4 g), phosphoryl chloride (10·0 ml), and *NN*-diethylaniline (4·0 ml) were refluxed for 1 hr. The cooled mixture was added to crushed ice and the solid product was removed. The filtrate was extracted with ether and the extract evaporated to give more product. The combined crude material recrystallized from ether to give yellow needles of the *dichloropyrimidine*, (2·4 g), m.p. 169–170° (Found: C, 48·7; H, 2·4; N, 14·2. $C_{12}H_7Cl_2N_3O_2$ requires C, 48·7; H, 2·4; N, 14·2%).

4-Amino-6-chloro-5-nitro-2-styrylpyrimidine

Methanolic ammonia (2·0 ml, saturated at 25°, and subsequently diluted to 5·0 ml) was added in drops to a stirred suspension of the above dichloropyrimidine (1·7 g) in ether (20 ml) at room temperature. After 2 hr the solid was removed and washed with ethyl acetate and then ether. The filtrate and washings were evaporated to dryness, giving the *aminochloropyrimidine* (1·3 g), m.p. 196–198° (from ether) (Found: C, 52·1; H, 3·1; N, 20·2. $C_{12}H_9ClN_4O_2$ requires C, 52·1; H, 3·25; N, 20·3%).

4-Amino-6-hydrazino-5-nitro-2-styrylpyrimidine

The above aminochloropyrimidine (1·0 g) and 98% hydrazine hydrate (1·0 g) were stirred in refluxing ethanol (100 ml) for 1 hr. The resulting *hydrazinostyrylpyrimidine* (0·53 g) had m.p. 212–214° (from ethanol) (Found: C, 52·95; H, 4·4; N, 30·75. $C_{12}H_{12}N_6O_2$ requires C, 52·9; H, 4·4; N, 30·9%). The *hydrochloride hydrate* formed pale yellow needles (from dilute hydrochloric acid), m.p. 194–197° (Found: C, 44·2; H, 4·6; N, 25·2. $C_{12}H_{15}ClN_6O_3$ requires C, 44·1; H, 4·6; N, 25·7%).

4-Amino-5-nitro-2-styrylpyrimidine

(i) The above hydrazino derivative (1·0 g) and silver acetate (3·8 g) were stirred in boiling water (50 ml) for 2 hr. The solid was extracted by ethanol in a Soxhlet apparatus. Evaporation of the extract, and subsequent recrystallization of the residue from methanol, gave a product (21%) identical with the styrylpyrimidine below in melting point, i.r. spectrum, and paper chromatography.

(ii) 4-Amino-2-methyl-5-nitropyrimidine (0·44 g), benzaldehyde (4·0 ml), and piperidine (2·0 ml) were heated at 95° for 90 min and then at 150° for 15 min. The cooled mixture was diluted with methanol (10 ml) and ether (10 ml). Refrigeration gave the *styrylpyrimidine* (0·48 g), m.p. 227° (from methanol) (Found: C, 59·4; H, 4·25; N, 23·15. $C_{12}H_{10}N_4O_2$ requires C, 59·55; H, 4·1; N, 23·1%).

4-Hydrazino-6-methoxy-5-nitropyrimidine

A solution of 98% hydrazine hydrate (2·7 ml) in 95% ethanol (50 ml) was added dropwise to a stirred solution of 4-chloro-6-methoxy-5-nitropyrimidine[7] (5·0 g) in 95% ethanol (200 ml) maintained at −8°. After 30 min, the yellow *hydrazinopyrimidine* (3·6 g) was filtered off and recrystallized from 95% ethanol. It decomposed at about 154–155° when the bath was preheated to 140° (Found: C, 32·3; H, 4·0; N, 37·8. $C_5H_7N_5O_3$ requires C, 32·4; H, 3·8; N, 37·8%).

When 4,6-dimethoxy-5-nitropyrimidine was treated similarly at 25° with only 1 mole of hydrazine hydrate in ethanol or tetrahydrofuran, the only isolatable product was 4,6-dihydrazino-5-nitropyrimidine, m.p. 200° (lit.[6] 203°).

4-Methoxy-5-nitropyrimidine

The above hydrazino derivative (1·55 g), silver oxide (6·0 g), and anhydrous methanol (350 ml) were stirred at *c.* 25° for 2 hr. The oily residue from evaporation under reduced pressure

[11] Brown, D. J., England, B. T., and Lyall, J. M., *J. chem. Soc.* C, 1966, 226.

was extracted with boiling light petroleum (b.p. 60–80°, 4 × 100 ml) and concentration gave colourless *methoxynitropyrimidine* (62%), m.p. 39–40° (from light petroleum) (Found: C, 38·9; H, 3·4; N, 26·7. $C_5H_5N_3O_3$ requires C, 38·7; H, 3·25; N, 27·1%).

5-Amino-4-methoxypyrimidine

The above nitropyrimidine (0·13 g) was hydrogenated at atmospheric pressure in methanol over Raney nickel. The filtered solution was evaporated to dryness and the residue was recrystallized from light petroleum (b.p. 40–60°) to give the 5-amino derivative (67%), m.p. 71–73° (cf. lit.[8] m.p. 61–63°) (Found: C, 47·6; H, 5·6; N, 33·4. Calc. for $C_5H_7N_3O$: C, 48·0; H, 5·6; N, 33·6%).

4-t-Butylamino-5-nitropyrimidine

4-Methoxy-5-nitropyrimidine (1·90 g), t-butylamine (2·0 ml), and methanol (50 ml) were refluxed for 3 hr. The residue from evaporating the methanol *in vacuo* gave some crystalline material on refrigeration. This was removed and distillation of the filtrate gave the *t-butylaminopyrimidine* (90%), b.p. 80–83°/0·2 mm and m.p. 34° (Found: C, 48·8; H, 6·2; N, 28·2. $C_8H_{12}N_4O_2$ requires C, 49·0; H, 6·2; N, 28·55%). The *picrate* had m.p. 132–134° (from 95% ethanol) (Found: C, 39·5; H, 3·55; N, 23·05. $C_{14}H_{15}N_7O_9$ requires C, 39·85; H, 3·7; N, 22·6%).

4,5-Diamino-2-styrylpyrimidine

4-Amino-5-nitro-2-styrylpyrimidine (0·26 g) was shaken with a mixture of concentrated hydrochloric acid (2·0 ml) and stannous chloride dihydrate (2·0 g), first for 10 min at 25°, and then at 95–100° for 10 min. Addition of an excess of 2N sodium hydroxide gave a solid product which was purified by dissolution in hot dilute hydrochloric acid and addition of 10N sodium hydroxide until alkaline. The rather hygroscopic *diamine* (0·12 g) had m.p. 191–193° (Found: C, 66·35; H, 5·7; N, 25·55. $C_{12}H_{12}N_4$,0·25H_2O requires C, 66·5; H, 5·8; N, 25·85%).

2-Styrylpteridine

4,5-Diamino-2-styrylpyrimidine (0·23 g) and glyoxal monohydrate (0·08 g) were shaken in ethanol (40 ml) at 25° for 2·5 hr. The sticky residue from evaporation in vacuum was chromatographed on alumina and elution with benzene gave the pteridine (0·01 g), m.p. 136° (Found: C, 69·0; H, 4·4; N, 22·7. $C_{14}H_{10}N_4$,0·5H_2O requires C, 69·1; H, 4·6; N, 23·0%).

6,7-Dimethyl-2-styrylpteridine

The same diamine (0·09 g) and biacetyl (0·25 ml) were heated under reflux for 1 hr in ethanol (25 ml). The filtered solution was evaporated to dryness and the residue recrystallized from ethanol to give the *dimethylpteridine* (0·075 g), m.p. 183° (Found: C, 71·0; H, 5·55; N, 20·8. $C_{16}H_{14}N_4$,0·5H_2O requires C, 70·85; H, 5·6; N, 20·65%).

4,5-Diamino-6-chloro-2-styrylpyrimidine

4-Amino-6-chloro-5-nitro-2-styrylpyrimidine (5·0 g) was reduced as above with 10N hydrochloric acid (20 ml) and stannous chloride dihydrate (4·3 g). The *diamine* (4·3 g) formed deep yellow crystals, m.p. 232–234°, from methanol (Found: C, 59·0; H, 4·6; N, 22·35. $C_{12}H_{11}ClN_4$ requires C, 58·4; H, 4·5; N, 22·7%). Dissolution in warm methanol containing a little hydrochloric acid gave the *hydrochloride*, m.p. 277–279° (Found: C, 50·8; H, 4·2; N, 19·8. $C_{12}H_{12}Cl_2N_4$ requires C, 50·8; H, 4·25; N, 19·8%).

4-Chloro-6,7-dimethyl-2-styrylpteridine

The above diamine (0·25 g) was refluxed with biacetyl (0·5 ml) in ethanol (50 ml) for 1 hr. Refrigeration of the filtered solution gave the *chloropteridine* (0·15 g), m.p. 208° (dec.) (Found: C, 64·25; H, 4·4; N, 18·9. $C_{16}H_{13}ClN_4$ requires C, 64·75; H, 4·4; N, 18·9%).

4,5-Diamino-2-phenethylpyrimidine

4,5-Diamino-6-chloro-2-styrylpyrimidine (0·5 g), 98% hydrazine hydrate (1·0 ml), 10% palladized strontium carbonate (1·0 g), potassium hydroxide (5·0 g), and ethanol (150 ml) were

refluxed for 30 min. The solid was filtered off and washed with water (100 ml) and ethanol. The filtrate and washings were concentrated under reduced pressure and a stream of carbon dioxide was introduced into the warm solution to neutralize the alkali. Gummy material was removed at once, and on chilling, the yellow *phenethylpyrimidine* (0·24 g) crystallized. It had m.p. 164–165° (Found: C, 67·0; H, 6·9; N, 25·6. $C_{12}H_{14}N_4$ requires C, 67·25; H, 6·6; N, 26·1%). The same starting material was unaffected by refluxing with palladized charcoal and ethanolic hydrazine for 30 min.

4(5)-Amino-5(4)-benzylideneamino-2-methylpyrimidine

4,5-Diamino-2-methylpyrimidine[10] (0·3 g), benzaldehyde (2·0 ml), and piperidine (1·0 ml) were heated at 95° for 1·5 hr and then at 150° for 10 min. The cooled mass was recrystallized from light petroleum and then chromatographed on alumina. Elution with benzene/chloroform (1 : 1) gave the *benzylideneamine*, m.p. 187–189° (from benzene) (Found: C, 67·7; H, 5·9; N, 26·8. $C_{12}H_{12}N_4$ requires C, 67·9; H, 5·7; N, 26·4%).

5-Acetamido-4-amino-2-methylpyrimidine

In an attempted bromination, 4,5-diamino-2-methylpyrimidine[10] (0·49 g), anhydrous sodium acetate (0·6 g), acetic acid (10 ml), and acetic anhydride (2·0 ml) were heated at 55° while bromine (0·3 ml) in acetic acid was added. After 1 hr, the mixture was concentrated, treated with crushed ice, and made alkaline with sodium hydroxide. After further concentration, refrigeration gave the *5-acetamido* derivative (0·28 g), crystallizing from water as the dihydrate (Found: C, 41·9; H, 6·9; N, 28·0. $C_7H_{14}N_4O_2$ requires C, 41·7; H, 7·0; N, 27·7%) with ultraviolet absorption maxima in pH 7 buffer at 278 and 232 mμ (cf. 4-amino-5-formamidopyrimidine:[12] 279, 233).

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[12] Brown, D. J., Ford, P. W., and Tratt, K. H., *J. chem. Soc.* C, 1967, in press.