A New, General Synthesis of Purines

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Reactions of 6-amino-5-nitrosouracil derivatives with the 1,1-dimethylhydrazones of a wide variety of aldehydes in dimethylformamide led to the corresponding xanthine derivatives. Alkylation of 9-substituted 1-methylxanthines with an excess of alkyl halide in dimethylformamide in the presence of potassium carbonate gave the corresponding 3,7-dialkyl-1-methylxanthine, with elimination of the 9-substituent. Treatment of 6-amino-4-hydroxy-5-nitroso-2-phenylpyrimidines with aldehyde 1,1-dimethylhydrazones also gave the corresponding purines.

DIRECT syntheses of purines by condensation–cyclization of 6-amino-5-nitrosopyrimidines with several carbon sources, such as alkylamines,[1] benzylideneaniline,[1,2] aromatic aldehydes,[3] quaternized Mannich bases,[4] Vilsmeier reagents,[5] and amide acetals,[6] have been the subject of recent investigations. We now report a new approach to xanthines which is widely applicable and especially convenient for the synthesis of 9-substituted xanthines.[7]

This route consists of treatment of 6-amino-5-nitrosouracils with 1,1-dimethylhydrazones of a wide variety of aldehydes. For example, heating 3-methyl-6-methylamino-5-nitrosouracil (IIa) [1] under reflux with a slight excess of benzaldehyde 1,1-dimethylhydrazone for 5 h in dimethylformamide gave 1,9-dimethyl-8-phenylxanthine (IIId) in good yield. This reaction is equally applicable to other 6-alkylamino-3-methyl-5-nitrosouracils (IIb—e) and to other aldehyde 1,1-dimethylhydrazones, giving the respective 8,9-disubstituted 3-methylxanthines (III)—(VII) (see Table 1).

When 6-benzylamino- (IId) [1] and 6-phenethylamino-3-methyl-5-nitrosouracil (IIe) were used as the starting materials, significant amounts (10—25%) of the intramolecular condensation products, 8-phenyl- (VIIIc) [1] and 8-benzyl-1-methylxanthine (VIIId), were obtained as by-products.

The formation of 8-phenyltheophylline by treatment of 6-amino-1,3-dimethyl-5-nitrosouracil (Ic) with benzaldehyde in dimethylformamide has been reported.[4] However, the reaction of the uracil (IIa) with benzaldehyde in dimethylformamide did not give the purine (IIId); the starting material was recovered. Reactions of the 6-n-propylamino- (IIb) and 6-n-butylamino-uracil (IIc) with benzaldehyde in dimethylformamide did not give the 9-n-propyl- (IVd) or 9-n-butyl-xanthine (Vd), but only the product of intramolecular condensation, 8-ethyl- (VIIIa) or 8-n-propyl-1-methylxanthine (VIIIb), respectively (see later). Furthermore, the uracil (IIa) did not react with 1,1-dimethylhydrazine (which might be liberated from their hydrazones during reaction); starting material was recovered.

From these facts, this new purine synthesis is best rationalized in terms of initial nucleophilic attack of the electron-rich α-carbon atom of the hydrazone on the nitroso-group of the pyrimidine to form a hydroxylamine intermediate, followed by intramolecular cyclization involving addition of the *o*-amino-substituent to the anil carbon atom. Elimination of 1,1-dimethylhydrazine and deoxygenation of the resulting xanthine 7-oxide by the 1,1-dimethylhydrazine (thermal deoxygenation is also conceivable) would then yield the xanthine.

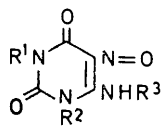
Treatment of 6-amino- (Ia), 6-amino-1-methyl- (Ib), and 6-amino-1,3-dimethyl-5-nitrosouracil (Ic) with aldehyde 1,1-dimethylhydrazones under the same conditions gave, as expected, the corresponding 8-substituted xanthine derivatives (Table 1). The xanthine derivatives (IX), (X), and (XIIIa) thus obtained were all methylated with an excess of methyl iodide in dimethylformamide in the presence of potassium carbonate to give 8-phenylcaffeine (XI).

Alkylation of the 9-substituted 1-methylxanthines with an excess of alkyl halide in dimethylformamide gave the corresponding 3,7-dialkyl-1-methylxanthines, with elimination of the 9-substituent. For example, treatment of the xanthines (IIId), (IVd), and (VIId) with an excess of methyl iodide in dimethylformamide in the presence (or in the absence) of potassium carbonate in each case gave 8-phenylcaffeine (XI). Treatment of (IIId) with an excess of ethyl iodide in dimethylformamide in the presence of potassium carbonate gave 3,7-diethyl-1-methyl-8-phenylxanthine (XII) in high yield.

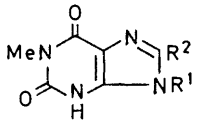
A possible mechanism for 9-dealkylation presumably involves initial full alkylation of the 9-alkyl-1-methyl xanthine. It is possible that quaternization of the imidazole ring then takes place with simultaneous loss of the 9-alkyl group to give the thermodynamically more stable 7-alkylxanthine.

[1] H. Goldner, G. Dietz, and E. Carstens, *Annalen*, 1966, **691**, 142.
[2] G. M. Timmis, J. Cooke, and R. G. W. Spickett, 'Ciba Foundation Symposium on the Chemistry and Biology of Purines,' Churchill, London, 1957, p. 139.
[3] E. C. Taylor and E. E. Garcia, *J. Amer. Chem. Soc.*, 1964, **86**, 4721.
[4] E. C. Taylor and E. E. Garcia, *J. Amer. Chem. Soc.*, 1964, **86**, 4720.
[5] (*a*) F. Yoneda, T. Matsumura, and K. Senga, *J.C.S. Chem. Comm.*, 1972, 606; (*b*) F. Yoneda, M. Higuchi, T. Matsumura, and K. Senga, *Bull. Chem. Soc. Japan*, 1973, **46**, 1836; (*c*) F. Yoneda and M. Higuchi, *Chem. and Pharm. Bull. (Japan)*, 1974, **22**, 1658.
[6] F. Yoneda, M. Higuchi, and A. Hayakawa, *Synthesis*, 1975, 264.
[7] Preliminary report, F. Yoneda, K. Ogiwara, M. Kanahori, and S. Nishigaki, *Chem. Comm.*, 1970, 1068.

The scope of the new purine synthesis has been extended by the following reactions. Treatment of

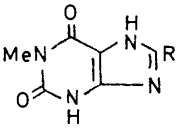


(I) a; $R^1 = R^2 = R^3 = H$
b; $R^1 = R^3 = H$, $R^2 = Me$
c; $R^1 = R^2 = Me$, $R^3 = H$
(II) a; $R^1 = R^3 = Me$, $R^2 = H$
b; $R^1 = Me$, $R^2 = H$, $R^3 = Pr^n$
c; $R^1 = Me$, $R^2 = H$, $R^3 = Bu^n$
d; $R^1 = Me$, $R^2 = H$, $R^3 = CH_2Ph$
e; $R^1 = Me$, $R^2 = H$, $R^3 = [CH_2]_2Ph$

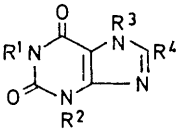


(III) a; $R^1 = Me$, $R^2 = H$
b; $R^1 = R^2 = Me$
c; $R^1 = Me$, $R^2 = Pr^n$
d; $R^1 = Me$, $R^2 = Ph$
e; $R^1 = Me$, $R^2 = 4\text{-}ClC_6H_4$
f; $R^1 = Me$, $R^2 = 4\text{-}MeO\cdot C_6H_4$
g; $R^1 = Me$, $R^2 = 3,4\text{-}(CH_2O_2)C_6H_3$
(IV) a; $R^1 = Pr^n$, $R^2 = H$
b; $R^1 = Pr^n$, $R^2 = Me$
c; $R^1 = R^2 = Pr^n$
d; $R^1 = Pr^n$, $R^2 = Ph$
e; $R^1 = Pr^n$, $R^2 = 4\text{-}ClC_6H_4$
f; $R^1 = Pr^n$, $R^2 = 4\text{-}MeO\cdot C_6H_4$
g; $R^1 = Pr^n$, $R^2 = 3,4\text{-}(CH_2O_2)C_6H_3$
(V) a; $R^1 = Bu^n$, $R^2 = H$
b; $R^1 = Bu^n$, $R^2 = Me$
c; $R^1 = Bu^n$, $R^2 = Pr^n$
d; $R^1 = Bu^n$, $R^2 = Ph$
e; $R^1 = Bu^n$, $R^2 = 4\text{-}ClC_6H_4$
f; $R^1 = Bu^n$, $R^2 = 4\text{-}MeO\cdot C_6H_4$
g; $R^1 = Bu^n$, $R^2 = 3,4\text{-}(CH_2O_2)C_6H_3$
(VI) a; $R^1 = CH_2Ph$, $R^2 = H$
b; $R^1 = CH_2Ph$, $R^2 = Me$
c; $R^1 = CH_2Ph$, $R^2 = Pr^n$
d; $R^1 = CH_2Ph$, $R^2 = Ph$
e; $R^1 = CH_2Ph$, $R^2 = 4\text{-}ClC_6H_4$
f; $R^1 = CH_2Ph$, $R^2 = 4\text{-}MeO\cdot C_6H_4$
g, $R^1 = CH_2Ph$, $R^2 = 3,4\text{-}(CH_2O_2)C_6H_3$
(VII) a; $R^1 = [CH_2]_2Ph$, $R^2 = H$
b; $R^1 = [CH_2]_2Ph$, $R^2 = Me$
c; $R^1 = [CH_2]_2Ph$, $R^2 = Pr^n$
d; $R^1 = [CH_2]_2Ph$, $R^2 = Ph$
e; $R^1 = [CH_2]_2Ph$, $R^2 = 4\text{-}ClC_6H_4$
f; $R^1 = [CH_2]_2Ph$, $R^2 = 4\text{-}MeO\cdot C_6H_4$
g; $R^1 = [CH_2]_2Ph$, $R^2 = 3,4\text{-}(CH_2O_2)C_6H_3$

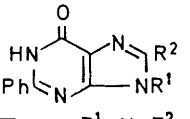
6-amino-4-hydroxy-5-nitroso-2-phenylpyrimidine (XIV) with benzaldehyde 1,1-dimethylhydrazone in dimethylformamide gave 6-hydroxy-2,8-diphenylpurine (XVI).[8] Similarly, treatment of 4-hydroxy-6-methylamino-5-nitroso-2-phenylpyrimidine (XV) with 1,1-dimethylhydrazones of benzaldehyde and *p*-chlorobenzaldehyde gave the corresponding 8-substituted 6-hydroxy-9-methyl-2-phenylpurines (XVIIa and b).



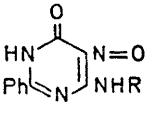
(VIII) a; R = Et
b; R = Pr^n
c; R = Ph
d; R = CH_2Ph



(IX) $R^1 = R^2 = R^3 = H$, $R^4 = Ph$
(X) $R^1 = R^3 = H$, $R^2 = Me$, $R^4 = Ph$
(XI) $R^1 = R^2 = R^3 = Me$, $R^4 = Ph$
(XII) $R^1 = Me$, $R^2 = R^3 = Et$, $R^4 = Ph$
(XIII a) $R^1 = R^2 = Me$, $R^3 = H$, $R^4 = Ph$
(XIII b) $R^1 = R^2 = Me$, $R^3 = H$, $R^4 = 4\text{-}ClC_6H_4$
(XIII c) $R^1 = R^2 = Me$, $R^3 = H$, $R^4 = 3,4\text{-}Cl_2C_6H_3$
(XIII d) $R^1 = R^2 = Me$, $R^3 = H$, $R^4 = 4\text{-}MeO\cdot C_6H_4$

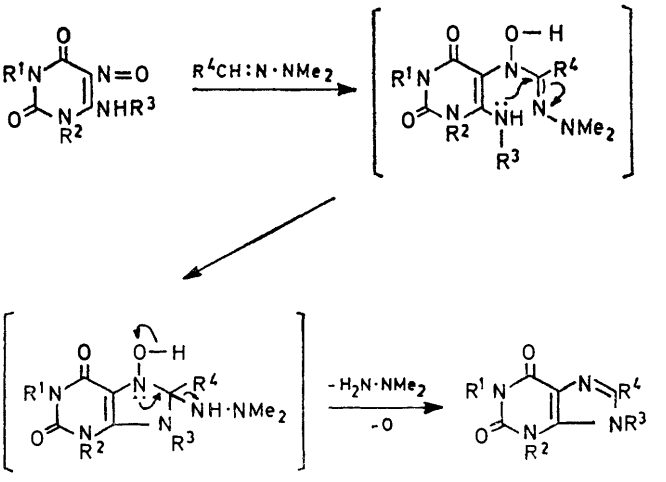


(XVI) $R^1 = H$, $R^2 = Ph$
(XVII) a; $R^1 = Me$, $R^2 = Ph$
b; $R^1 = Me$, $R^2 = 4\text{-}ClC_6H_4$



(XIV) R = H
(XV) R = Me

These products were sometimes accompanied by small amounts of intramolecular condensation products, as described above. Some of the latter were synthesized for identification purposes. Refluxing the uracils (IIb,



[8] F. Yoneda, M. Higuchi, and T. Nagamatsu, *J. Amer. Chem. Soc.*, 1974, **96**, 5607.

c, and e) in dimethylformamide for 4 h gave 8-ethyl- (VIIIa), 8-n-propyl- (VIIIb), and 8-benzyl-1-methylxanthine (VIIId), respectively.

The structures of the purines obtained were established by elemental analyses and molecular weight determinations (by mass spectrometry), and confirmed by n.m.r. spectra [available as Supplementary Publication No. SUP 21769 (3 pp.)].†

EXPERIMENTAL

M.p.s were determined with a Yanagimoto microapparatus. N.m.r. spectra were determined with a JEOL JNM 3H-60 spectrometer, with tetramethylsilane as internal standard.

3-*Methyl*-5-*nitroso*-6-*n-propylaminouracil* (IIb).—A mixture of 6-chloro-3-methyluracil (15 g, 0.09 mol) and n-propylamine (11 g, 0.185 mol) in n-butyl alcohol (100 ml) was refluxed for 4 h. After cooling, the crystalline material was collected, washed with water, and recrystallized from ethanol to give needles of 3-*methyl*-6-*n-propylaminouracil* (73%), m.p. 243° (Found: C, 52.3; H, 7.3; N, 22.75. $C_8H_{13}N_3O_2$ requires C, 52.45; H, 7.15; N, 22.95%). This material (8 g, 0.044 mol) was dissolved in acetic acid (150 ml) and saturated aqueous sodium nitrite (4.4 g, 0.064 mol) was added drop by drop with cooling at 10 °C. The crystals were collected, washed with water and recrystallized from ethanol to give the *nitroso-derivative* as a pale orange powder (86%), m.p. 242° (Found: C, 45.35; H, 5.75; N, 26.55. $C_8H_{12}N_4O_3$ requires C, 45.3; H, 5.7; N, 26.4%).

Similarly, 6-chloro-3-methyluracil and phenethylamine gave 3-*methyl*-6-*phenethylaminouracil* (87%), m.p. 238° (Found: C, 63.45; H, 6.3; N, 17.05. $C_{13}H_{15}N_3O_2$ requires C, 63.65; H, 6.15; N, 17.2%), which was nitrosated to give 3-*methyl*-5-*nitroso*-6-*phenethylaminouracil* (IIe), pale violet crystals (90%), m.p. 225° (Found: C, 56.8; H, 5.25; N, 20.2. $C_{13}H_{14}N_4O_3$ requires C, 56.95; H, 5.15; N, 20.45%).

Xanthine Derivatives (III)—(VII). *General Procedure.*—A mixture of a 6-amino-5-nitrosouracil (0.005 mol), an aldehyde (0.007 mol), and 1,1-dimethylhydrazine (0.007 mol) in dimethylformamide (30 ml) was refluxed for 5—7 h. The solution was evaporated under reduced pressure and the residue was diluted with ethanol and set aside overnight or for several days. The *product* which separated was filtered off, washed with a small amount of ethanol, and recrystallized (Table 1).

Xanthine derivatives

Compound	M.p. (°C)	Yield (%)	Found (%) C	Found (%) H	Found (%) N	Formula	Required (%) C	Required (%) H	Required (%) N	Recryst. solvent *
(IIIa) [a]	352	51	45.7	4.4	15.5	$C_7H_8N_4O_2$	45.65	4.4	15.25	DMF–EtOH
(IIIb)	340	47	49.65	5.3	28.7	$C_8H_{10}N_4O_2$	49.5	5.2	28.85	DMF–EtOH
(IIIc)	340	54	54.1	6.35	25.0	$C_{10}H_{14}N_4O_2$	54.05	6.35	25.2	DMF
(IIId)	375	71	61.05	4.6	21.85	$C_{13}H_{12}N_4O_2$	60.95	4.7	21.85	DMF
(IIIe)	362	76	53.75	3.6	19.35	$C_{13}H_{11}ClN_4O_2$	53.7	3.8	19.25	DMF
(IIIf)	>360	68	58.65	4.9	19.3	$C_{14}H_{14}N_4O_3$	58.75	4.95	19.55	DMF
(IIIg)	356	67	55.9	4.1	18.35	$C_{14}H_{12}N_4O_4$	56.0	4.05	18.65	DMF
(IVa)	285	26	51.95	5.9	26.75	$C_9H_{12}N_4O_2$	51.9	5.8	26.9	EtOH
(IVb)	315	40	54.2	6.35	25.05	$C_{10}H_{14}N_4O_2$	54.05	6.35	25.2	EtOH
(IVc)	231	42	57.7	7.3	22.2	$C_{12}H_{18}N_4O_2$	57.6	7.25	22.4	EtOH
(IVd)	335	43	63.5	5.55	19.55	$C_{15}H_{16}N_4O_2$	63.35	5.65	19.7	DMF
(IVe)	363	46	56.5	4.7	17.7	$C_{15}H_{15}ClN_4O_2$	56.5	4.75	17.6	DMF
(IVf)	319	54	60.95	5.7	17.8	$C_{16}H_{18}N_4O_3$	61.15	5.75	17.85	DMF
(IVg)	335	50	58.6	4.9	17.2	$C_{16}H_{16}N_4O_4$	58.55	4.9	17.05	DMF
(Va)	257	28	54.0	6.4	25.35	$C_{10}H_{14}N_4O_2$	54.05	6.35	25.2	EtOH
(Vb)	282	40	55.9	6.75	23.6	$C_{11}H_{16}N_4O_2$	55.9	6.85	23.7	EtOH
(Vc)	202	36	57.1	8.2	22.0	$C_{13}H_{20}N_4O_2$	57.1	8.0	22.2	EtOH
(Vd)	295	40	64.3	6.3	18.8	$C_{16}H_{18}N_4O_2$	64.4	6.1	18.75	DMF
(Ve)	370	45	57.7	5.15	16.8	$C_{16}H_{17}ClN_4O_2$	57.75	5.15	16.85	DMF
(Vf)	332	53	62.3	5.95	17.0	$C_{17}H_{20}N_4O_3$	62.2	6.15	17.05	DMF
(Vg)	330	47	59.5	5.4	16.2	$C_{17}H_{18}N_4O_4$	59.65	5.3	16.35	DMF
(VIa)	325	21	60.85	4.6	21.65	$C_{13}H_{12}N_4O_2$	60.95	4.7	21.85	EtOH
(VIb)	337	22	62.2	5.3	20.85	$C_{14}H_{14}N_4O_2$	62.2	5.2	20.75	EtOH
(VIc)	293	31	64.4	6.2	18.65	$C_{16}H_{18}N_4O_2$	64.4	6.1	18.75	DMF
(VId)	356	37	68.65	4.8	16.6	$C_{19}H_{16}N_4O_2$	68.65	4.85	16.85	DMF
(VIe)	287	34	62.1	4.15	15.0	$C_{19}H_{15}ClN_4O_2$	62.2	4.1	15.3	DMF
(VIf)	288	28	66.1	5.1	15.4	$C_{20}H_{18}N_4O_3$	66.3	5.0	15.45	DMF
(VIg)	296	31	63.6	4.4	14.85	$C_{20}H_{16}N_4O_4$	63.8	4.3	14.9	DMF
(VIIa)	242	30	62.2	5.3	20.8	$C_{14}H_{14}N_4O_2$	62.2	5.2	20.75	EtOH
(VIIb)	241	33	63.35	5.4	19.85	$C_{15}H_{16}N_4O_2$	63.35	5.65	19.7	EtOH
(VIIc)	229	36	65.5	6.25	17.85	$C_{17}H_{20}N_4O_2$	65.35	6.45	17.95	EtOH
(VIId)	331	31	69.2	5.05	16.35	$C_{20}H_{18}N_4O_2$	69.35	5.25	16.2	DMF
(VIIe)	357	35	63.2	4.4	14.95	$C_{20}H_{17}ClN_4O_2$	63.05	4.5	14.7	DMF
(VIIf)	326	36	67.0	5.1	14.6	$C_{21}H_{20}N_4O_3$	67.0	5.35	14.9	DMF
(VIIg)	304	39	64.3	4.7	14.5	$C_{21}H_{18}N_4O_4$	64.6	4.65	14.35	DMF
(IX)	>360	65	57.75	3.4	24.4	$C_{11}H_8N_4O_2$	57.9	3.55	24.55	DMF
(X)	>360	63	59.6	4.2	23.4	$C_{12}H_{10}N_4O_2$	59.5	4.15	23.15	DMF
(XIIIa) [b]	>360	61				$C_{13}H_{12}N_4O_2$	60.95	4.7	21.85	DMF
(XIIIb)	>360	58	53.7	3.7	19.1	$C_{13}H_{11}ClN_4O_2$	53.7	3.8	19.25	DMF
(XIIIc)	>360	66	48.3	3.15	17.05	$C_{13}H_{10}Cl_2N_4O_2$	48.0	3.1	17.25	DMF
(XIIId)	>360	70	58.6	4.85	19.35	$C_{14}H_{14}N_4O_3$	58.75	4.95	19.55	DMF

[a] W. Pfleiderer and G. Nübel, *Annalen*, 1961, **647**, 155. [b] Ref. 3.

* DMF = dimethylformamide.

† For details of Supplementary Publications, see Notice to Authors No. 7 in *J.C.S. Perkin I*, 1975, Index issue.

In the preparations of 8-unsubstituted or 8-methyl derivatives, an excess of 37% formaldehyde or acetaldehyde (0.015 mol) and 1,1-dimethylhydrazine (0.015 mol) were used.

8-Phenylcaffeine (XI).—*Method A*. A mixture of 3-methyl-8-phenylxanthine (X) (0.5 g, 0.002 mol), methyl iodide (2.8 g, 0.02 mol), and potassium carbonate (0.5 g) in dimethylformamide (20 ml) was refluxed for 2 h. The solution was evaporated to dryness and the residue was diluted with water to precipitate *crystals* (65%), m.p. 185° (from ethanol), M^+ 270 (Found: C, 62.4; H, 5.25; N, 20.6. $C_{14}H_{14}N_4O_2$ requires C, 62.2; H, 5.2; N, 20.75%).

Method B. A mixture of 1-methyl-9-n-propyl-8-phenylxanthine (IVd) (0.25 g, 0.0009 mol), methyl iodide (1.24 g, 0.009 mol), and potassium carbonate (0.5 g) in dimethylformamide (20 ml) was refluxed for 2 h, then evaporated under reduced pressure to dryness. The residue was diluted with water to precipitate crystals (71%).

3,7-Diethyl-1-methyl-8-phenylxanthine (XII).—A mixture of the purine (IIId) (0.4 g, 0.0016 mol), ethyl iodide (1 g, 0.0064 mol), and potassium carbonate (1 g) in dimethylformamide (30 ml) was treated as above to give *needles* (68%), m.p. 150°, M^+ 298 (Found: C, 64.35; H, 6.2; N, 18.85. $C_{16}H_{18}N_4O_2$ requires C, 64.4; H, 6.1; N, 18.8%).

8-Ethyl-1-methylxanthine (VIIIa).—A solution of 3-methyl-5-nitroso-6-n-propylaminouracil (IIb) (0.7 g, 0.0033 mol) in dimethylformamide (20 ml) was refluxed for 6 h. After cooling, the *crystals* were filtered off, washed with ethanol, and recrystallized from dimethylformamide; yield 71%; m.p. >370°; M^+ 194 (Found: C, 49.2; H, 5.2; N 29.0. $C_8H_{10}N_4O_2$ requires C, 49.5; H, 5.2; N, 28.85%).

Similarly, compound (IIc) gave *1-methyl-8-n-propylxanthine* (VIIIb) (70%), m.p. 362°, M^+ 208 (Found: C 51.75; H, 5.8; N, 26.65. $C_9H_{12}N_4O_2$ requires C, 51.9; H, 5.8; N, 26.9%). Compound (IIe) gave *8-benzyl-1-methylxanthine* (VIIId) (85%), m.p. 374°, M^+ 256 (Found: C 60.95; H, 4.75; N, 21.95. $C_{13}H_{12}N_4O_2$ requires C, 60.95; H, 4.7; N, 21.85%).

4-Hydroxy-6-methylamino-5-nitroso-2-phenylpyrimidine (XV).—To a mixture of concentrated hydrochloric acid (30 ml) and n-butyl alcohol (50 ml) was added 4,6-dichloro-2-phenylpyrimidine (5.8 g, 0.026 mol), and the mixture was refluxed for 3 h. After cooling, the crystals were filtered off, washed with water, and dried. Recrystallization from ethanol gave needles of 6-chloro-4-hydroxy-2-phenylpyrimidine [9] (64%), m.p. 226° (Found: C, 57.9; H, 3.4; N, 13.4. Calc. for $C_{10}H_7ClN_2O$: C, 58.1; H, 3.4; N, 13.55%).

This material (3.77 g, 0.018 mol) and 40% aqueous methylamine (20 ml) were heated in an autoclave at 150 °C for 5 h. The mixture was evaporated to dryness and the residue was crushed in hot water to give crystals. Recrystallization from ethanol gave *4-hydroxy-6-methylamino-2-phenylpyrimidine* (73%), m.p. 270° (Found: C, 65.55; H, 5.4; N, 20.9. $C_{11}H_{11}N_3O$ requires C, 65.65; H, 5.5; N, 20.9%).

A mixture of the 6-methylaminopyrimidine (2.3 g, 0.01 mol) and sodium nitrite (1.6 g, 0.02 mol) in water (20 ml) was heated at 95 °C for 10 min with stirring. The mixture was then acidified with acetic acid and the green crystals which separated were filtered off, washed with water, and recrystallized from ethanol to give a pale green *powder* (XV) (95.5%), m.p. 253° (Found: C, 57.45; H, 4.6; N, 24.2. $C_{11}H_{10}N_4O_2$ requires C, 57.4; H, 4.4; N, 24.35%).

9-Methyl-2,8-diphenyl-6-hydroxypurine (XVIIa).—A mixture of the 5-nitrosopyrimidine (XV) (1 g, 0.0044 mol), benzaldehyde (0.64 g, 0.006 mol), and 1,1-dimethylhydrazine (0.45 g, 0.0075 mol) in dimethylformamide (30 ml) was refluxed for 8 h. The solution was evaporated to dryness and the residue was diluted with ethanol. The *crystals* which separated were filtered off and recrystallized from dimethylformamide–ethanol; yield 29%; m.p. 240° (decomp.); M^+ 302 (Found: C, 71.4; H, 4.8; N, 18.4. $C_{18}H_{14}N_4O$ requires C, 71.5; H, 4.65; N, 18.55%).

6-Hydroxy-2,8-diphenylpurine (XVI) was prepared similarly from 6-amino-5-nitroso-2-phenylpyrimidine and benzaldehyde 1,1-dimethylhydrazone. Recrystallization from dimethylformamide–ethanol gave prisms (49%), m.p. >360°, M^+ 288 (Found: C, 70.55; H, 4.3; N, 19.55. $C_{17}H_{12}N_4O$ requires C. 70.8; H 4.2; N, 19.45%).

8-(4-Chlorophenyl)-6-hydroxy-9-methyl-2-phenylpurine (XVIIb) was prepared as above and recrystallized from dimethylformamide; yield 35%; m.p. 320°; M^+ 336 (Found: C, 64.35; H, 3.75; N, 16.7. $C_{18}H_{13}ClNO_4$ requires C, 64.2; H, 3.9; H, 16.65%).

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[9] H. C. Carrington, F. H. S. Curd, and D. N. Richardson, *J. Chem. Soc.*, 1955, 1858.