Pyrimidine Derivatives and Related Compounds. Part 47.[1] A New Synthesis of Xanthines and Pyrrolo[3,2-*d*]pyrimidines by Intramolecular Cyclisation of 6-Substituted 5-Nitrouracil Derivatives[2]

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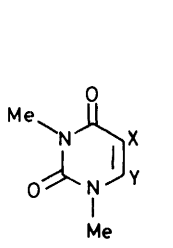
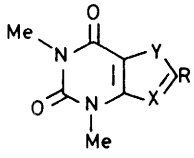
6-Arylalkylamino-1,3-dimethyl-5-nitrouracils (**2a—f**) were prepared by reaction of 6-chloro-1,3-dimethyl-5-nitrouracil (**1**) with arylalkylamines in the presence of triethylamine. Among them, the 6-arylalkylaminouracils (**2a—d**), possessing no substituent at the nitrogen and the benzylic position in the 6-arylalkylamino moiety, were converted into the corresponding 8-aryl-1,3-dimethylxanthines (**3a—d**) when heated under reflux in dimethylformamide (DMF). The reaction of the sodium salt (**7**) of 1,3,6-trimethyl-5-nitrouracil (**6**) with alkyl and arylalkyl halides in dry DMF gave the corresponding 6-(substituted methyl)-1,3-dimethyl-5-nitrouracils (**8a—j**). Among them, 6-(2-arylethyl)uracils (**8b—f**) underwent base-catalysed cyclisation to afford 8-aryl-7-hydroxy-9-deazaxanthines (**9a—e**). On the other hand, treatment of 6-[2-(ethoxycarbonyl, acetyl, and cyano)ethyl]uracil (**8h—j**) with triethylamine led to the formation of the corresponding 6-vinyluracil (**11a—c**). A one-step synthesis of the 7-hydroxy-9-deazaxanthines (**9a—e**) was accomplished by the treatment of the sodium salt (**7**) with arylalkyl chlorides in the presence of potassium carbonate in dry DMF. Deoxygenation of the 7-hydroxy-9-deazaxanthines (**9a—e**) smoothly occurred upon heating them in DMF to give the corresponding 8-aryl-9-deazaxanthines (**10a—e**) in high yield.

Much work has shown that appropriately substituted *ortho*-nitrobenzene derivatives frequently undergo photochemical and thermochemical intramolecular cyclisations as a result of the neighbouring interaction between nitro groups and *ortho*-substituents. These reactions have provided efficient methods for the preparation of various benzoheterocycles.[3] Such a synthetic strategy has been successfully applied to the preparation of biologically active fused pyrimidines. For example, intramolecular cyclisations of 6-azido-, 6-styryl-, 6-anilino-, and 6-(substituted methylthio)-5-nitrouracil gave [1,2,5]oxadiazolo[3,4-*d*]pyrimidine,[4] pyrrolo[3,2-*d*]pyrimidine,[5,6] isoalloxazine,[7] and thiazolo[5,4-*d*]pyrimidine,[8] respectively.

In the course of our investigations on the reaction of 6-chloro- and 6-methyl-5-nitrouracil derivatives, aiming at new synthetic approaches to fused pyrimidines, we found new methods for the preparation of xanthines and pyrrolo[3,2-*d*]pyrimidines (9-deazaxanthines and 7-hydroxy-9-deazaxanthines) which may have biological importance.





(1) X = NO_2, Y = Cl

(2)[a] X = NO_2, Y = N—CH—(C6H4)—R^3 (R^1, R^2)

(6) X = NO_2, Y = Me

(8)[b] X = NO_2, Y = CH_2CH_2R

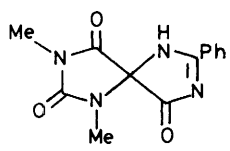
(11)[e] X = H, Y = CH=CHR

(3) a; X = N, Y = NH, R = Ph
b; X = N, Y = NH, R = C_6H_4Me-*p*
c; X = N, Y = NH, R = C_6H_4OMe-*p*
d; X = N, Y = NH, R = C_6H_4Cl-*p*

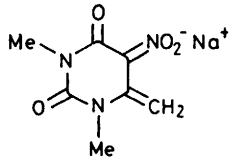
(5) X = N, Y = NOH, R = Ph

(9)[c] X = CH, Y = NOH

(10)[d] X = CH, Y = NH



(4)



(7)

[a] Table 1. [b] Table 2. [c] Table 3. [d] Table 4. [e] Table 5.

Results and Discussion

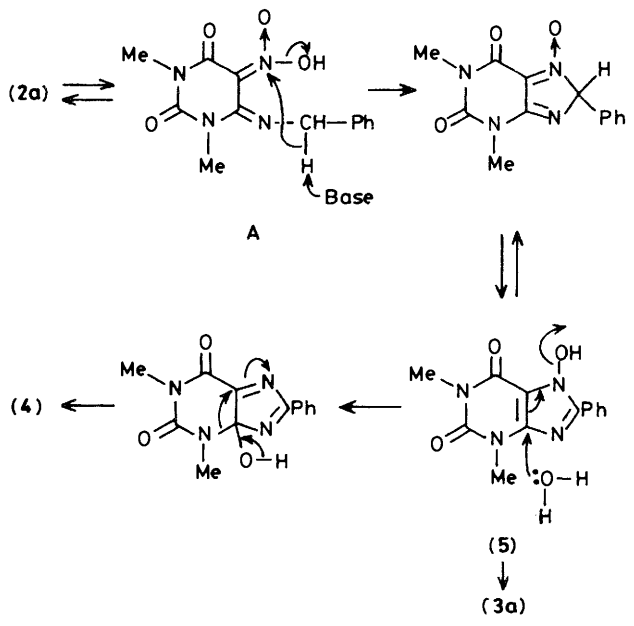
6-(Substituted amino)-1,3-dimethyl-5-nitrouracils (**2a—f**) were readily prepared in high yield by the reaction of 6-chloro-1,3-dimethyl-5-nitrouracil (**1**)[9] with arylalkylamines in the presence of triethylamine (Table 1).

Heating the 6-benzylaminouracil derivative (**2a**) under reflux in DMF led to the formation of two products, 1,3-dimethyl-8-phenylxanthine (**3a**)[10,11] and 1′,3′-dimethyl-2-phenyl-3,5-dihydro-4*H*-imidazole-4-spiro-4′-tetrahydro-4′*H*-imidazole-2′,5,5′-trione (**4**) in 46 and 15% yield, respectively. The structure of the latter product (**4**) was supported by microanalytical and spectral (i.r., ^{1}H n.m.r., and ^{13}C n.m.r.) data. In particular, the i.r. spectrum of the spirohydantoin (**4**) shows three characteristic bands at 1 780, 1 740, and 1 720 cm^{-1}; these absorption bands can be reasonably assigned to the three oxo groups of the strained spirohydantoin system. For example, it has been reported that the i.r. spectra of several 3′,4′-dihydro-1,3,4′,6,7′-pentamethylspiro[imidazolidine-4,2′(1′*H*)-quinoxazaline]-2,5-diones contain two bands in the 1 761—1 770 and 1 709—1 715 cm^{-1} regions.[12a] The two absorption bands are attributable to the 4-oxo and 2-oxo groups in the hydantoin ring.[13] Similar treatment of the uracils (**2b—d**) gave 8-aryl-1,3-dimethylxanthines (**3b—d**) in moderate yield. In these cases, the corresponding spiro compounds could not be isolated, although they were detected in the reaction mixture by t.l.c. and ^{1}H n.m.r. spectroscopy. On the other hand, the uracils (**2e**) and (**2f**) possessing a methyl group at either the nitrogen or benzylic position in the 6-arylalkylamino moiety were not converted into

Table 1. Formation of 6-(substituted amino)uracils (**2a—f**)

Compound	R^1	R^2	R^3	M.p. (°C)	Yield (%)	^{1}H N.m.r. data (δ from $SiMe_4$) 6-NH	6-N–CH_2 or 6-N–CH	Others	Solvent
(**2a**)	H	H	H	141	69	9.35 (br)	4.61 (2 H, s)	3.31 (3 H, s) 3.59 (3 H, s) 7.35 (5 H, s)	$CDCl_3$
(**2b**)	H	H	Me	178—179	86	8.51 (s)	4.30 (2 H, s)	2.30 (3 H, s) 3.15 (3 H, s) 3.45 (3 H, s) 7.20 (4 H, s)	$(CD_3)_2SO$
(**2c**)	H	H	MeO	122	75	9.15 (t)	4.51 (2 H, d)	3.30 (3 H, s) 3.58 (3 H, s) 3.80 (3 H, s) 7.05 (4 H, dd)	$CDCl_3$
(**2d**)	H	H	Cl	175	73	8.50 (br)	4.33 (2 H, s)	3.17 (3 H, s) 3.45 (3 H, s) 7.40 (4 H, s)	$(CD_3)_2SO$
(**2e**)	H	Me	H	168—169	66	9.60 (m)	4.80 (1 H, m)	1.65 (3 H, d) 3.25 (3 H, s) 3.51 (3 H, s) 7.35 (5 H, m)	$CDCl_3$
(**2f**)	Me	H	H	183	74		4.10 (2 H, s)	2.72 (3 H, s) 3.37 (3 H, s) 3.45 (3 H, s) 7.32 (5 H, m)	$CDCl_3$

the corresponding xanthine and they were recovered unchanged. When a solution of the uracil (**2a**) in ethanol was heated in the presence of potassium carbonate, the 7-hydroxyxanthine (**5**)[11,14] was obtained in 65% yield together with the spiro compound (**4**) (2%). Taylor *et al.* reported that heating the 7-hydroxyxanthine (**5**) in DMF results in the formation of the xanthine (**3a**).[11] Heating the 7-hydroxyxanthine (**5**) in dimethyl sulphoxide (DMSO) in the presence of water, however, gave the xanthine (**3a**) and the spirohydantoin (**4**) in 83 and 10% yield, respectively. These facts indicate clearly that the 7-hydroxyxanthine (**5**) is a common intermediate in the conversion of the uracil (**2a**) into both the xanthine (**3a**) and the spiro compound (**4**).



Scheme 1.

On the basis of the above results, a reaction sequence for the formation of the xanthine (**3a**) and the spirohydantoin (**4**) is proposed (Scheme 1). The 7-hydroxyxanthine intermediate (**5**) could be formed *via* the base-catalysed cyclisation of an *aci*-form **A** of the uracil (**2a**). The deoxygenation of the 7-hydroxyxanthine (**5**) with DMF has been already explained in the literature.[11] The transformation of the 7-hydroxyxanthine (**5**) to the spiro compound (**4**) can be explained in terms of an initial nucleophilic attack of water on the electron-deficient C-4 position in the 7-hydroxyxanthine (**5**) and subsequent ring contraction in the manner shown in Scheme 1. A similar type of ring contraction was demonstrated in the conversion of flavins into spirohydantoins.[12]

Although various synthetic methods of 9-deazaxanthines have been reported,[5,6,15–17] their 7-hydroxy derivatives have hitherto been unknown. In the present work, a further convenient method for the synthesis of 9-deazaxanthines (**10**) involving 7-hydroxy-9-deazaxanthines (**9**) was explored. The present method consists of an alkylation of the 6-methyl group of 1,3,6-trimethyl-5-nitrouracil (**6**) and a subsequent base-catalysed cyclisation.

1,3,6-Trimethyl-5-*aci*-nitrouracil sodium salt (**7**) was used as a starting material. The salt (**7**) was easily prepared by heating 1,3,6-trimethyl-5-nitrouracil (**6**) in ethanolic sodium ethoxide according to Pfleiderer's procedure.[18] The reaction of the sodium salt (**7**) with alkyl iodides and bromides such as methyl iodide, benzyl bromide, and ethoxycarbonylmethyl bromide (ethyl bromoacetate) in dry DMF at 80 °C easily gave the 6-ethyl-, 6-phenethyl-, and 6-ethoxycarbonylethyl-5-nitrouracil (**8a**), (**8b**), and (**8h**), respectively, in good yield. When alkyl chlorides such as benzyl chlorides, chloroacetone, and chloroacetonitrile were employed, no alkylation was observed. Addition of potassium iodide as a catalyst to the reaction mixture, however, overcame this difficulty and gave the corresponding alkylated derivatives (**8b—g**), (**8i**), and (**8j**) in high yield (see Table 2).

Treatment of the uracils (**8b—f**) possessing 6-arylethyl groups with potassium hydroxide in refluxing ethanol led to the forma-

Table 2. Formation of 6-substituted 1,3-dimethyl-5-nitrouracils (**8a—j**)

Compound	R	Alkyl halide X in RCH_2X	M.p. (°C)	Recrystallization solvent	Yield (%)	^{1}H N.m.r. data C-6-$[CH_2]_2$-R	Solvent
(**8a**)	H	I	119—120	Light petroleum[a]	78	1.37 (3 H, t, *J* 7 Hz) 2.72 (2 H, q, *J* 7 Hz)	$CDCl_3$[c]
(**8b**)	Ph	Br	165	EtOH	93 90	2.96 (4 H, s)	$CDCl_3$[c]
(**8c**)	*p*-MeC_6H_4	Cl[b]	152	EtOH	91	2.97 (4 H, s)	$CDCl_3$[c]
(**8d**)	*p*-$MeOC_6H_4$	Cl[b]	157	EtOH	87	2.95 (4 H, s)	$CDCl_3$[c]
(**8e**)	*p*-ClC_6H_4	Cl[b]	185	EtOH	86	3.00 (4 H, s)	$(CD_3)_2SO$[d]
(**8f**)	α-Naphthyl	Cl[b]	235	AcOEt	89	2.80—3.60 (4 H, m)	$(CD_3)_2SO$[d]
(**8g**)	*o*-$NO_2C_6H_4$	Cl[b]	198	AcOEt	92	3.19 (4 H, br s)	$(CD_3)_2SO$[d]
(**8h**)	EtO_2C	Br	81—82	EtOH	44	2.85 (4 H, m)	$CDCl_3$[c]
(**8i**)	MeCO	Cl[b]	123	Light petroleum[a]	51	2.90 (4 H, s)	$(CD_3)_2SO$[d]
(**8j**)	NC	Cl[b]	224—228 (decomp.)	EtOH	47	3.05 (4 H, m)	$CDCl_3$[c]

[a] Boiling range 75—120 °C. [b] Potassium iodide was added to the reaction mixture as catalyst for the preparation of 6-substituted uracils (**8**). [c] δ From $SiMe_4$. [d] δ From $Me_3Si[CH_2]_3SO_3Na$.

Table 3. Formation of 8-aryl-7-hydroxy-9-deazaxanthines (**9a—e**)

Compound	R	M.p. (°C) (decomp.)	Yield (%) Method A	Yield (%) Method B	^{1}H N.m.r. data [δ from $SiMe_4$; $(CD_3)_2SO$] 9-H	7-OH
(**9a**)	Ph	220—225	93	73	6.25	*a*
(**9b**)	*p*-MeC_6H_4	210—215	92	59	6.28	11.8
(**9c**)	*p*-$MeOC_6H_4$	214—216	87	65	6.25	11.8
(**9d**)	*p*-ClC_6H_4	230—235	80	55	6.40	*a*
(**9e**)	α-Naphthyl	230—235	93	59	6.23	11.6

[a] Could not be detected.

Table 4. Formation of 8-aryl-9-deazaxanthines (**10a—e**)

Compound	R	M.p. (°C)	Yield (%)	I.r. data (KBr) ($\nu_{max.}$/cm^{-1}) (CO)	(NH)
(**10a**)[a]	Ph	>300	85	1 690 1 640	3 180
(**10b**)[a]	*p*-MeC_6H_4	>300	90	1 690 1 640	3 250
(**10c**)[b]	*p*-$MeOC_6H_4$	>300	92	1 690 1 640	3 240
(**10d**)[c]	*p*-ClC_6H_4	>300	95	1 690 1 640	3 180
(**10e**)	α-Naphthyl	>300	84	1 690 1 640	3 180

[a] Ref. 5. [b] Ref. 15. [c] Ref. 17.

tion of 7-hydroxy-9-deazaxanthines (**9a—e**) (Method A). Under analogous conditions, the 6-ethyl-5-nitrouracil (**8a**) was not converted into the corresponding 7-hydroxy-9-deazaxanthine.

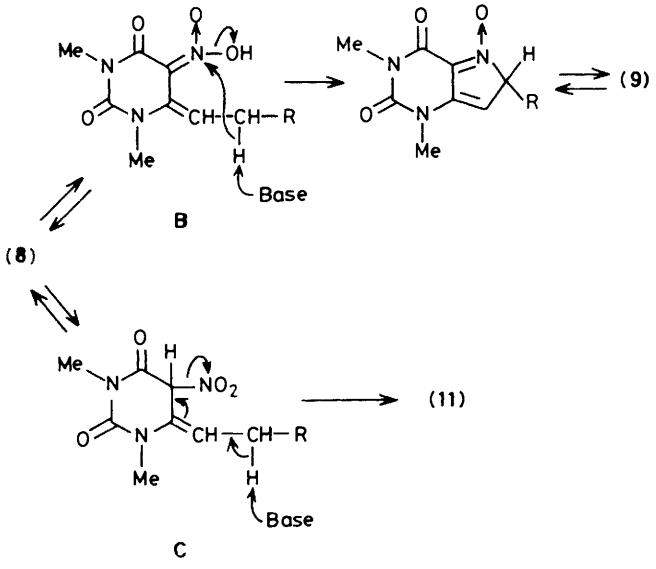
Upon treatment of the salt (**7**) with arylalkyl chlorides in the presence of potassium iodide and potassium carbonate in dry DMF at 120 °C, the 7-hydroxy-9-deazaxanthines (**9a—e**) were directly prepared without isolation of the alkylated compounds (**8**) in about 50—70% yield (Method B). Results of microanalyses and spectral data fully supported the structure of the 7-hydroxy-9-deazaxanthines (**9a—e**) (Table 3). A simple deoxygenation of the 7-hydroxy-9-deazaxanthine (**9a**) to the corresponding 9-deazaxanthine (**10a**) confirmed its structure, *i.e.* heating the 7-hydroxy-9-deazaxanthine (**9a**) in DMF at 150 °C gave 1,3-dimethyl-8-phenyl-9-deazaxanthine (**10a**)[5] in 85% yield. Similar deoxygenation of the 7-hydroxy derivatives (**9b—e**) afforded the corresponding 9-deazaxanthines (**10b—e**) in high yield. The structures of these 9-deazaxanthines (**10a—e**) were fully supported on the basis of microanalytical results and spectral data, *e.g.*, 9-deazaxanthines (**10a—e**) showed the characteristic imidazole NH absorption bands at 3 180—3 250 cm^{-1} in their i.r. spectra (see Table 4).

On the other hand, treatment of the 6-(2-ethoxycarbonylethyl)-

Table 5. Formation of 6-(2-substituted vinyl)uracils (11a—c)

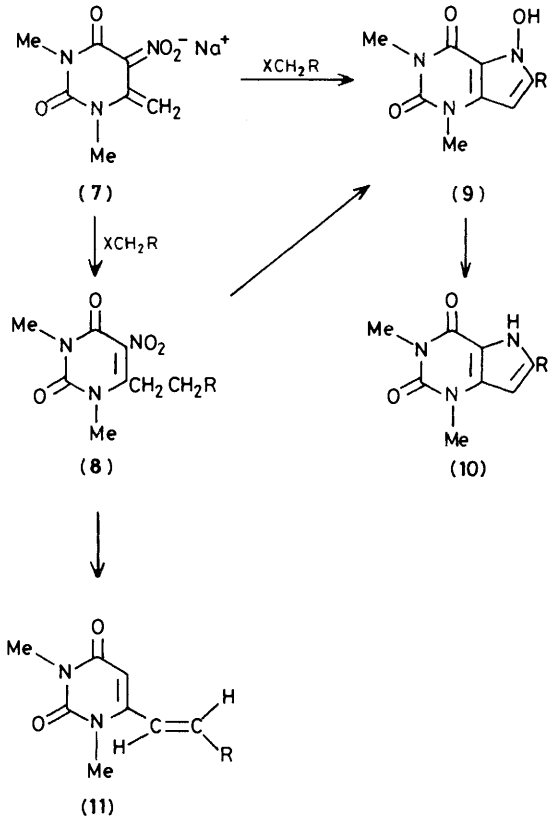
Compound	R	M.p. (°C)	Yield (%)	^{1}H N.m.r. data (δ from $SiMe_4$; $CDCl_3$) C-6-CH_a=CH_b-R H_a	H_b	5-H
(11a)	EtO_2C	127	90	7.50 (d) ($J_{a,b}$ 16 Hz)	6.40(d)	5.90 (s)
(11b)	MeCO	135	85	7.30 (d) ($J_{a,b}$ 16 Hz)	6.68 (d)	5.91 (s)
(11c)	NC	144	89	7.27 (d) ($J_{a,b}$ 16 Hz)	6.05 (d)	5.90 (s)

uracil (**8h**) with triethylamine did not afford the expected 9-deazaxanthine but gave (*E*)-6-(2-ethoxycarbonylvinyl)-1,3-dimethyluracil (**11a**) in 90% yield with loss of the nitro group. The vinyl moiety of the uracil (**11a**) has a coupling constant, *J* 16 Hz, clearly indicating it to be the (*E*)-isomer (see Table 5). The reaction of the uracils (**8i**) and (**8j**) under analogous conditions also afforded the denitrated 6-vinyluracils (**11b**) and (**11c**) in 85 and 89% yield, respectively. The results indicate that the 5-nitrouracils (**8h—j**) which possess a stronger electron-withdrawing group than an aryl group at the β-position of the 6-ethyl group undergo predominantly denitration rather than intramolecular cyclisation.



Scheme 2.

A reaction sequence for the formation of the 9-deazaxanthines (**9a—e**)and the 6-vinyluracils (**11a—c**) is outlined in Scheme 2. The base-catalysed dehydration of an intermediate *aci*-form **B** could form the corresponding 9-deazaxanthines (**9a—e**) and the base-catalysed denitration of a tautomer **C** appears to form the 6-vinyluracils (**11a—c**) as described previously.[19] Scheme 3 shows the reaction sequence from the *aci*-nitrouracil salt (**7**) to the final products (**10**) and (**11**).



Scheme 3.

Experimental

M.p.s were determined on a Yanagimoto melting-point apparatus and are uncorrected. I.r. spectra were recorded with an Hitachi Model 215 spectrophotometer, using KBr pellets; ^{1}H n.m.r. spectra were determined with an Hitachi–Perkin-Elmer R-20B 60 MHz instrument, using tetramethylsilane as internal standard; ^{13}C n.m.r. spectra were determined with a JEOL JNM-FX-100 Fourier transform spectrometer operating at 25.00 MHz, with tetramethylsilane as internal standard; mass spectra were taken on a JEOL JMS-D300 machine operating at 70 eV. Elemental analyses were carried out at the Microanalytical Laboratory of our college—the results are given in Table 6.

6-(*Substituted amino*)-1,3-*dimethyl*-5-*nitrouracils* (**2a—f**).—*General procedure.* An appropriate benzylamine derivative (11 mmol) was added dropwise to a cooled, stirred solution of the uracil (**1**)[9] (2.20 g, 10 mmol) and triethylamine (1.10 g, 11 mmol) in ethyl acetate (20 ml). The resulting mixture was stirred at room temperature for 6 h. The precipitate was filtered off and washed with water. Recrystallization from ethanol gave the corresponding *uracil* (**2a—f**) (physical and analytical data are given in Tables 1 and 6).

Preparation of 1,3-*Dimethyl*-8-*phenylxanthine* (**3a**) *and* 1′,3′-*Dimethyl*-2-*phenyl*-3,5-*dihydro*-4H-*imidazole*-4-*spiro*-4′-*tetrahydro*-4′H-*imidazole*-2′,5,5′-*trione* (**4**).—(a) A solution of the

uracil (**2a**) (1.45 g, 5 mmol) in DMF (10 ml) was refluxed for 24 h. After the mixture had cooled, the precipitate was filtered off and washed with diethyl ether to give the analytically pure xanthine (**3a**)[11] (0.588 g, 46%) (see Table 6). The filtrate was evaporated to dryness and the residue was subjected to column chromatography (silica gel; chloroform) to afford the *spirohydantoin* (**4**) (0.204 g, 15%), m.p. 219—220 °C (Found: C, 57.5; H, 4.45; N, 20.4. $C_{13}H_{12}N_4O_3$ requires C, 57.35; H, 4.45; N, 20.6%); *m/z* 272 (M^+); $\nu_{max.}$ 1 780, 1 740, and 1 720 cm^{-1}; δ_H[$(CD_3)_2SO$] 2.75 (3 H, s), 3.00 (3 H, s), 7.25—8.30 (5 H, m), and 12.30 (1 H, br); δ_C[$(CD_3)_2SO$] 25.3 (q), 25.9 (q), 85.2 (br), 127.1 (s), 127.9 (d), 129.1 (d), 133.6 (d), 155.7 (s), 166.2 (s), 167.6 (s), and 177.4 p.p.m. (s).

(b) A mixture of the 7-hydroxyxanthine (**5**) (0.5 g, 1.8 mmol), water (2 ml), and DMSO (10 ml) was refluxed for 5 h. The solvent was removed under reduced pressure and the residue was treated with methanol. The precipitate was filtered off and washed with diethyl ether to give the xanthine (**3a**) (0.38 g, 83%). The methanolic mixture was evaporated to dryness and the residue was treated with chloroform. The precipitate was filtered off to give the spirohydantoin (**4**) (0.05 g, 10%) which was identical with the sample obtained by procedure (a).

8-*Aryl*-1,3-*dimethylxanthines* (**3b—d**).—*General procedure.* A solution of a uracil (**2b—d**) (5 mmol) in DMF (10 ml) was refluxed for 24 h. After the mixture had cooled, the precipitate was filtered off and washed with diethyl ether to give the respective analytically pure xanthine (**3b**)[20] (40%), (**3c**)[21] (47%), and (**3d**)[20] (39%) (see Table 6).

Preparation of 7-*Hydroxy*-1,3-*dimethyl*-8-*phenylxanthine* (**5**) *and the Spirohydantoin* (**4**).—A suspension of the uracil (**2a**) (1.0 g, 3.4 mmol) and anhydrous potassium carbonate (0.5 g, 3.6 mmol) in ethanol (20 ml) was refluxed for 20 h. The solvent was removed under reduced pressure and the residue was treated with water (10 ml). The solution was neutralized with acetic acid. The precipitate was filtered off and washed with water. Recrystallization from n-butanol gave analytically pure 7-hydroxy-1,3-dimethyl-8-phenylxanthine (**5**) (0.61 g, 65%), identical with a sample prepared by the reaction of 6-anilino-1,3-dimethyl-5-nitrosouracil with benzylideneaniline.[14] The aqueous filtrate was evaporated to dryness and the residue was subjected to column chromatography (silica gel; chloroform) to afford the spirohydantoin (**4**) (0.02 g, 2%), which was identical with the sample obtained above.

6-*Ethyl*-1,3-*dimethyl*-5-*nitrouracil* (**8a**).—A suspension of the sodium salt (**7**)[18] (2.0 g, 9 mmol) and methyl iodide (6.4 g, 45 mmol) in dry DMF (10 ml) was heated at 80 °C for 1.5 h. The solvent was removed under reduced pressure and the residue was treated with water (10 ml) to give 6-*ethyl*-1,3-*dimethyl*-5-*nitrouracil* (**8a**) (1.5 g, 78%), m.p. 110 °C. Recrystallization from light petroleum (boiling range 75—120 °C) gave analytically pure (**8a**), m.p. 119—120 °C (physical and analytical data are given in Tables 2 and 6).

1,3-*Dimethyl*-5-*nitro*-6-*phenethyluracil* (**8b**).—A suspension of the sodium salt (**7**)[18] (1.1 g, 5 mmol) and benzyl bromide (1.03 g, 6 mmol) in dry DMF (10 ml) under nitrogen was heated at 80 °C for 2 h. The solvent was removed under reduced pressure and the residue was treated with water (10 ml). The precipitate was filtered off. Recrystallization from ethanol gave analytically pure 1,3-*dimethyl*-5-*nitro*-6-*phenethyluracil* (**8b**) (1.34 g, 93%), m.p 165 °C (physical and analytical data are given in Tables 2 and 6).

6-(*Substituted methyl*)-1,3-*dimethyl*-5-*nitrouracils* (**8b—j**).—*General procedure.* A suspension of the sodium salt (**7**)[18] (1.1 g, 5 mmol), potassium iodide (0.3 g, 1.8 mmol), and an appropriate chloride (6 mmol) (Table 2) in dry DMF (10 ml) under nitrogen was heated at 80 °C for 2 h. The solvent was removed under reduced pressure and the residue was treated with water (10 ml). The precipitate was filtered off. Recrystallization from an appropriate solvent (Table 2) gave the corresponding 6-(*substituted methyl*)*uracils* (**8b—g**) (physical and analytical data are given in Tables 2 and 6). In cases where there was no precipitate (**7h—j**), the aqueous solution was extracted with chloroform. The extract was dried ($MgSO_4$) and evaporated to dryness. Recrystallization from an appropriate solvent (Table 2) gave the corresponding 6-(*substituted methyl*)*uracil* (**8h—j**) (physical and analytical data are given in Tables 2 and 6). Preparation of the uracil (**8h**) was performed using ethoxycarbonylmethyl bromide (ethyl bromoacetate) without use of potassium iodide.

8-*Aryl*-7-*hydroxy*-1,3-*dimethyl*-9-*deazaxanthines* (**9a—e**).—*General procedures. Method A.* To a suspension of potassium hydroxide (0.12 g, 2.2 mmol) in ethanol (30 ml) was added a uracil (**8a—e**) (2 mmol) and the mixture was refluxed for 1—2 h. The solvent was removed under reduced pressure and the residue was dissolved in water (10 ml). The solution was neutralized with acetic acid. The precipitate was filtered off and washed with water. Recrystallization from ethanol gave the corresponding analytically pure 7-hydroxy-9-deazaxanthine (**9a—e**) (physical and analytical data are given in Tables 3 and 6).

Method B. A suspension of the sodium salt (**7**)[8] (1.10 g, 5 mmol), an arylalkyl chloride (6 mmol), potassium iodide (0.3 g, 1.8 mmol), and anhydrous potassium carbonate (0.76 g, 5.5 mmol) in dry DMF (10 ml) under nitrogen was heated at 120 °C for 2—3 h. The solvent was removed under reduced pressure and the residue was treated as described above to give the corresponding 7-*hydroxy*-9-*deazaxanthine* (**9a—e**) (yields are given in Table 3.)

8-*Aryl*-1,3-*dimethyl*-9-*deazaxanthines* (**10a—e**).—*General procedure.* A solution of a 7-hydroxy-9-deazaxanthine (**9a—e**) (1 mmol) in DMF (10 ml) was refluxed for 2 h. The solvent was removed under reduced pressure and the residue was recrystallized from ethanol to give the corresponding analytically pure 9-deazaxanthine (**10a—e**) (physical and analytical data are given in Tables 4 and 6).

1,3-*Dimethyl*-6-[(E)-2-*substituted vinyl*]*uracils* (**11a—c**).—*General procedure.* A mixture of the uracils (**8i—k**) (20 mmol) and triethylamine (0.4 g, 40 mmol) in ethanol (20 ml) was heated at 60 °C for 10 h. The solvent was removed under reduced pressure and the residue was recrystallized from light petroleum (boiling range 75—120 °C) to give the corresponding pure *uracil* (**11a—c**) (physical and analytical data are given in Tables 5 and 6).

Table 6. Analytical data (%)

Compound	Formula	Found (Required) C	H	N
(**2a**)	$C_{13}H_{14}N_4O_4$	53.7 (53.8)	4.75 (4.85)	19.4 (19.3)
(**2b**)	$C_{14}H_{16}N_4O_4$	55.1 (55.25)	5.45 (5.3)	18.35 (18.4)
(**2c**)	$C_{14}H_{16}N_4O_5$	52.55 (52.5)	4.9 (5.05)	17.6 (17.5)
(**2d**)	$C_{13}H_{13}ClN_4O_4$	47.85 (48.1)	3.95 (4.05)	17.15 (17.25)
(**2e**)	$C_{14}H_{16}N_4O_4$	55.45 (55.25	5.35 (5.3)	18.6 (18.4)
(**2f**)	$C_{14}H_{16}N_4O_4$	55.2 (55.25)	5.35 (5.3)	18.55 (18.4)

Table 6. (*cont.*)

Compound	Formula	Found (Required) C	H	N
(3a)	$C_{13}H_{12}N_4O_2$	60.65 (60.95)	4.75 (4.7)	21.85 (21.85)[a]
(3b)	$C_{14}H_{14}N_4O_2$	62.35 (62.2)	5.2 (5.2)	20.8 (20.75)
(3c)	$C_{14}H_{14}N_4O_3$	58.55 (58.75)	4.85 (4.95)	20.75 (19.55)[a]
(3d)	$C_{13}H_{11}ClN_4O_2$	53.7 (53.7)	3.7 (3.8)	19.3 (19.25)[a]
(8a)	$C_8H_{11}N_3O_4$	45.25 (45.05)	5.2 (5.2)	19.85 (19.7)
(8b)	$C_{14}H_{15}N_3O_4$	58.0 (58.1)	5.1 (5.25)	14.25 (14.55)
(8c)	$C_{15}H_{17}N_3O_4$	59.5 (59.4)	5.6 (5.65)	13.8 (13.85)
(8d)	$C_{15}H_{17}N_3O_5$	56.4 (56.4)	5.25 (5.35)	13.1 (13.15)
(8e)	$C_{14}H_{14}ClN_3O_4$	51.7 (51.95)	4.3 (4.35)	12.85 (12.95)
(8f)	$C_{18}H_{17}N_3O_4$	63.45 (63.7)	5.1 (5.05)	12.4 (12.4)
(8g)	$C_{14}H_{14}N_4O_6$	50.15 (50.3)	4.1 (4.2)	16.75 (16.75)
(8h)	$C_{11}H_{15}N_3O_6$	46.3 (46.3)	5.2 (5.3)	14.7 (14.75)
(8i)	$C_{10}H_{13}N_3O_4$	46.85 (47.05)	5.1 (5.15)	16.35 (16.45)
(8j)	$C_9H_{10}N_4O_4$	45.2 (45.4)	4.15 (4.25)	23.25 (23.5)
(9a)	$C_{14}H_{13}N_3O_3$	61.75 (62.0)	4.7 (4.85)	15.4 (15.5)
(9b)	$C_{15}H_{15}N_3O_3$	63.1 (63.15)	5.25 (5.3)	14.75 (14.7)
(9c)	$C_{15}H_{15}N_3O_4$	59.65 (59.8)	4.95 (5.0)	13.9 (13.95)
(9d)	$C_{14}H_{12}ClN_3O_3$	55.0 (55.0)	3.8 (3.95)	13.7 (13.75)
(9e)	$C_{18}H_{15}N_3O_4$	67.3 (67.3)	4.8 (4.7)	12.9 (13.1)
(10a)	$C_{14}H_{13}N_3O_2$	60.65 (60.95)	4.75 (4.7)	21.85 (21.85)[a]
(10b)	$C_{15}H_{15}N_3O_2$	66.65 (66.9)	5.55 (5.6)	15.5 (15.6)[a]
(10c)	$C_{15}H_{15}N_3O_3$	63.0 (63.15)	5.4 (5.3)	14.55 14.55)[a]
(10d)	$C_{14}H_{12}ClN_3O_2$	57.85 (58.05)	4.05 (4.2)	14.45 (14.5)[a]
(10e)	$C_{18}H_{15}N_3O_2$	70.55 (70.8)	5.05 (4.95)	13.5 (13.75)
(11a)	$C_{11}H_{14}N_2O_4$	55.55 (55.45)	5.95 (5.9)	11.75 (11.75)
(11b)	$C_{10}H_{12}N_2O_3$	57.5 (57.7)	5.9 (5.8)	13.5 (13.45)
(11c)	$C_9H_9N_3O_2$	56.25 (56.55)	4.8 (4.75)	21.75 (22.0)

[a] Calculated values (known compound).

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