The Thermolysis and Photolysis of 6-(Benzylidenehydrazino)uracils. New Syntheses of Pyrazolo[3,4-*d*]pyrimidines. A Method to Convert Aldehydes to Nitriles

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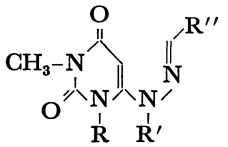
The thermolysis of 6-(benzylidenehydrazino)uracil derivatives generally involves their oxidative cyclization to give the corresponding pyrazolo[3,4-*d*]pyrimidine derivatives. However, the thermolysis of fully methylated 6-(benzylidenehydrazino)uracils gave no pyrazolo[3,4-*d*]pyrimidines, but mixtures of the respective nitriles and 1,3-dimethyl-6-methylaminouracil. The photolysis of the fully methylated 6-(benzylidenehydrazino)uracils give the desired pyrazolo[3,4-*d*]pyrimidines.

Our interest in the pyrazolo[3,4-*d*]pyrimidine ring system,[1] bolstered by the fact that derivatives of pyrazolo[3,4-*d*]pyrimidine possess many kinds of biological activities prompted us to investigate the systematic syntheses of this ring system. Our initial efforts have been directed toward the exploration of a convenient synthesis of derivatives of pyrazolo[3,4-*d*]-pyrimidine-4,6(5*H*,7*H*)-dione, which is isomeric with xanthine. The known synthetic methods for the preparation of pyrazolo[3,4-*d*]pyrimidines have involved the construction of suitably substituted pyrazole precursors, followed by the subsequent annelation of the condensed pyrimidine ring[2,3] and the condensation cyclization of 6-hydrazinopyrimidine derivatives.[4,5] This paper will describe a new, convenient method of synthesizing pyrazolo[3,4-*d*]pyrimidine-4,6(5*H*,7*H*)-dione derivatives, a method which consists of the thermal and photochemical cyclizations of the 6-(benzylidenehydrazino)-uracils, followed by dehydrogenation.[6]

The key intermediates, the 6-(benzylidenehydrazino)-uracil derivatives (**1a**—**w**), were prepared by the treatment of the appropriate 6-hydrazinouracils with several aldehydes in ethanol at room temperature (Table 1).

TABLE 1. 6-(BENZYLIDENEHYDRAZINO)URACILS (**1a**—**w**)



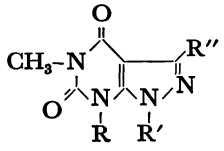
Compd.	R	R′	R″	Mp[a] (°C)	Yield (%)	Analyses % Found (Calcd) C	H	N
1a	CH_3	H	C_6H_5	261[11]	94	60.52 (60.45)	5.78 (5.46)	21.65 (21.70)
1b	CH_3	H	*p*-Cl-C_6H_4	258	100	53.30 (53.34)	4.45 (4.48)	19.08 (19.14)
1c	CH_3	H	3,4-Cl_2-C_6H_3	282	92	47.75 (47.72)	3.72 (3.70)	16.89 (17.13)
1d	CH_3	H	*p*-CH_3O-C_6H_4	261	95	58.43 (58.32)	5.55 (5.59)	19.26 (19.44)
1e	CH_3	H	*p*-$(CH_3)_2N$-C_6H_4	256[11]	95	59.69 (59.78)	6.31 (6.36)	23.05 (23.24)
1f	H	CH_3	C_6H_5	245	96	60.33 (60.45)	5.39 (5.46)	21.42 (21.70)
1g	H	CH_3	*p*-Cl-C_6H_4	194	97	53.42 (53.34)	4.42 (4.48)	19.01 (19.14)
1h	H	CH_3	3,4-Cl_2-C_6H_3	261	71	47.68 (47.72)	3.66 (3.70)	16.92 (17.13)
1i	H	CH_3	*p*-CH_3O-C_6H_4	223	92	58.29 (58.32)	5.40 (5.59)	19.44 (19.44)
1j	H	CH_3	*p*-$(CH_3)_2N$-C_6H_4	244	88	59.64 (59.78)	6.28 (6.36)	23.19 (23.24)
1k	H	H	C_6H_5	298	83	58.74 (59.01)	4.94 (4.95)	22.75 (22.94)
1l	H	H	*p*-Cl-C_6H_4	260	86	51.99 (51.71)	3.78 (3.98)	19.93 (20.15)
1m	H	H	3,4-Cl_2-C_6H_3	262	91	46.30 (46.02)	3.21 (3.22)	17.68 (17.89)
1n	H	H	*p*-CH_3O-C_6H_4	233	76	56.78 (56.93)	5.14 (5.15)	20.26 (20.43)
1o	H	H	*p*-$(CH_3)_2N$-C_6H_4	262	99	58.32 (58.52)	5.93 (5.96)	24.07 (24.38)
1p	CH_3	CH_3	CH_3	131	88	51.55 (51.42)	6.92 (6.71)	26.61 (26.65)
1q	CH_3	CH_3	CH_3CH=CH	151	78	56.23 (55.91)	6.75 (6.83)	23.40 (23.72)
1r	CH_3	CH_3	C_6H_5	151	86	61.90 (61.75)	5.93 (5.92)	20.28 (20.58)
1s	CH_3	CH_3	*p*-Cl-C_6H_4	231	100	55.16 (54.81)	4.85 (4.93)	18.60 (18.27)
1t	CH_3	CH_3	3,4-Cl_2-C_6H_3	225	100	49.51 (49.28)	4.05 (4.14)	16.62 (16.42)
1u	CH_3	CH_3	*p*-CH_3O-C_6H_4	164	90	59.73 (59.59)	6.08 (6.00)	18.60 (18.53)
1v	CH_3	CH_3	*p*-$(CH_3)_2N$-C_6H_4	150	87	60.99 (60.93)	6.90 (6.71)	22.21 (22.21)
1w	CH_3	CH_3	3-Pyridyl	203	94	57.08 (57.13)	5.52 (5.53)	25.34 (25.63)

a) All products were recrystallized from ethanol.

Results and Discussion

*Pyrolysis of 6-(Benzylidenehydrazino)uracils (**1a—o**).* The fusion of Compounds **1a—o** at temeratures slightly higher than their melting points for 5 to 30 min, followed by dilution with ethanol, caused a separation of the corresponding pyrazolo[3,4-*d*]pyrimidines (**2a—o**) (Table 2). The fusion of fully methylated 6-(benzylidenehydrazino)uracils (**1p—w**) took a completely different route and gave no detectable amount of pyrazolo[3,4-*d*]-pyrimidines, as will be described below. In the cases of the cyclization of **1a—d** (R=CH_3, R′=H), the

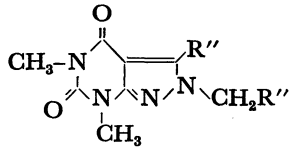
Table 2. Pyrazolo[3,4-*d*]pyrimidine-4,6(5*H*,7*H*)-diones (**2a—o**)



Compd.	R	R′	R″	Reaction condition Temp. (°C)	Time (min)	Mp[a] (°C)	Yield (%)	Analyses % Found (Calcd) C	H	N	IR cm^{-1} (KBr)		
2a	CH_3	H	C_6H_5	280	15	242[5]	35	60.90 (60.93)	4.68 (4.72)	21.59 (21.87)	1703s, 1593s,	1660s, 1572m,	1608m, 1523m
2b	CH_3	H	*p*-Cl-C_6H_4	260	20	>270(sublim.)	45	53.83 (53.71)	3.90 (3.81)	19.04 (19.27)	1706s, 1592s,	1650s, 1520m	1610s,
2c	CH_3	H	3,4-Cl_2-C_6H_3	300	20	>340(sublim.)	42	48.31 (48.02)	3.11 (3.10)	17.20 (17.23)	1707s, 1585s,	1645s, 1516m	1608s,
2d	CH_3	H	*p*-CH_3O-C_6H_4	270	20	267	45	58.79 (58.73)	4.75 (4.93)	19.29 (19.57)	1702s, 1598s,	1660s, 1556m,	1608sh, 1530m
2e	CH_3	H	*p*-$(CH_3)_2N$-C_6H_4	270	20	273	28	60.22 (60.19)	5.66 (5.72)	23.23 (23.40)	1702s, 1610s, 1530m	1668s, 1595s,	1650s, 1560m,
2f	H	CH_3	C_6H_5	300	30	>300(sublim.)	40	60.72 (60.93)	4.76 (4.72)	21.91 (21.87)	1712s, 1600m,	1643s, 1572m	1622s,
2g	H	CH_3	*p*-Cl-C_6H_4	260	5	>320(sublim.)	55	53.88 (53.71)	3.77 (3.81)	19.06 (19.27)	1713s, 1582m,	1645s, 1560m	1619s,
2h	H	CH_3	3,4-Cl_2-C_6H_3	260	5	>320(sublim.)	56	48.22 (48.01)	3.15 (3.10)	17.14 (17.23)	1715s, 1580m,	1643s, 1560m	1619s,
2i	H	CH_3	*p*-CH_3O-C_6H_4	260	20	>330(sublim.)	30	58.66 (58.73)	4.92 (4.93)	19.33 (19.57)	1708s, 1550m,	1650s, 1510w	1610s,
2j	H	CH_3	*p*-$(CH_3)_2N$-C_6H_4	260	20	>350(sublim.)	43	60.24 (60.19)	5.78 (5.72)	23.19 (23.40)	1707s, 1550w,	1650s, 1534m	1605s,
2k	H	H	C_6H_5	300	5	>330(sublim.)	55	59.63 (59.50)	4.09 (4.16)	23.24 (23.13)	1700s, 1530m	1662s,	1620s,
2l	H	H	*p*-Cl-C_6H_4	300	5	>290(sublim.)	51	52.22 (52.09)	3.27 (3.28)	20.11 (20.25)	1706s, 1530m	1669s,	1620m,
2m	H	H	3,4-Cl_2-C_6H_3	300	5	>285(sublim.)	52	46.22 (46.32)	2.58 (2.59)	17.86 (18.01)	1706s, 1527m	1665s,	1622m,
2n	H	H	*p*-CH_3O-C_6H_4	300	5	>295(sublim.)	45	57.22 (57.35)	4.39 (4.44)	20.37 (20.58)	1700s, 1532w,	1664s, 1500s	1611s,
2o	H	H	*p*-$(CH_3)_2N$-C_6H_4	300	5	>360(sublim.)	60	58.79 (58.93)	5.27 (5.30)	24.63 (24.55)	1712s, 1570m,	1664s, 1515m	1613s,

a) All products were recrystallized from ethanol.

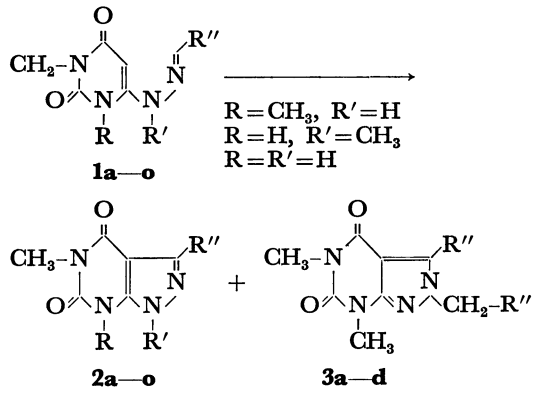
Table 3. 3-Aryl-2-benzylpyrazolo[3,4-*d*]pyrimidines (**3a—d**)



Compd.	R″	Mp[a] (°C)	Yield (%)	Analyses % Found (Calcd) C	H	N
3a	C_6H_5	193	37	69.44 (69.35)	5.30 (5.24)	16.18 (16.18)
3b	*p*-Cl-C_6H_4	177	57	57.75 (57.84)	3.89 (3.88)	13.19 (13.49)
3c	3,4-Cl_2-C_6H_3	194	40	49.70 (49.61)	2.97 (2.91)	11.33 (11.57)
3d	*p*-CH_3O-C_6H_4	160	21	65.00 (65.01)	5.38 (5.46)	13.83 (13.79)

a) All products were recrystallized from ethanol.

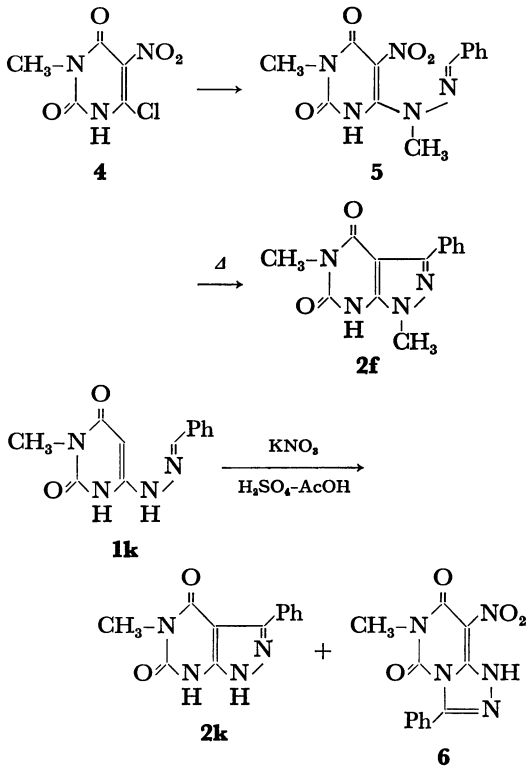
formation of 3-aryl-2-benzylpyrazolo[3,4-*d*]pyrimidine derivatives (**3a—d**) in addition to **2a—d** (see Table 3) was observed; their structures were established by unequivocal synthesis by the benzylation of **2a—d** with the corresponding benzyl halides. The mechanism of the formation of these compounds is currently under investigation.



Scheme 1.

Structural Elucidation of (2a—o) Products. The structures of **2a—o** were established by microanalyses and by the use of mass and other spectral data. Furthermore, representatives of these compounds were identified by comparison with authentic samples prepared by the following alternative routes. Some of the **2a—o** compounds were identified with the products prepared by the cyclization of the corresponding 6-benzylidenehydrazino-1,3-dimethyl-5-nitrouracils[5] in dimethylformamide. Compound **2f** was alternatively synthesized as follows: the treatment of 6-chloro-3-methyl-5-nitrouracil (**4**)[7] with benzaldehyde methylhydrazone gave 6-(benzylidene-1'-methylhydrazino)-3-methyl-5-nitrouracil (**5**); it was then converted into **2f** in 40 and 42% yields by fusion and by refluxing in dimethylformamide respectively.

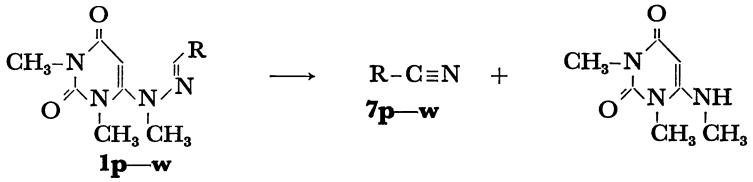
The nitration of **1k** with potassium nitrate in acetic acid in the presence of sulfuric acid gave a mixture of **2k** (32%) and 5,7-dioxo-6-methyl-8-nitro-3-phenyl-1,5,6,7-tetrahydro-*s*-triazolo[4,3-*c*]pyrimidine (**6**) (15.3 %). The latter belongs to a type of compound observed previously.[7-9]



Scheme 2.

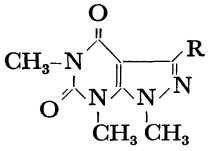
Pyrolysis of 6-(Benzylidene-1'-methylhydrazino)-1,3-dimethyluracils (1p—w). Formation of Nitriles (7p—w): As has been stated above, the thermolysis of 6-(benzylidenehydrazino)uracils constituted a convenient synthetic route to pyrazolo[3,4-*d*]pyrimidines. The reaction, however, appeared to be dependent on the presence of protons at the 1-position and/or the 1'-position of the 6-substituent. The thermolysis of fully substituted 6-benzylidenehydrazinouracils (**1p—w**) gave no pyrazolo[3,4-*d*]pyrimidines, but mixtures of the respective

Table 4. Pyrolysis of 6-(benzylidene-1'-methylhydrazino)-1,3-dimethyluracils (**1p—w**)



Starting materials No.	Reaction condition		No.	Products		
	Temp. (°C)	Time (min)		Nitriles R	Yield (%)	1,3-Dimethyl-6-methylamino-uracil Yield (%)
1p	200	10	**7p**	CH_3	59	85
1q	190	30	**7q**	CH_3-CH=CH	not identified	70
1r	250	30	**7r**	C_6H_5	83	85
1s	260	30	**7s**	*p*-Cl-C_6H_4	87	91
1t	280	15	**7t**	3,4-Cl_2-C_6H_3	86	90
1u	220	30	**7u**	*p*-CH_3O-C_6H_4	75	82
1v	220	40	**7v**	*p*-$(CH_3)_2N$-C_6H_4	73	80
1w	240	30	**7w**	3-Pyridyl	69	75

TABLE 5. 1,5,7-TRIMETHYLPYRAZOLO[3,4-*d*]PYRIMIDINE-4,6(5*H*,7*H*)-DIONES (**2p—w**)

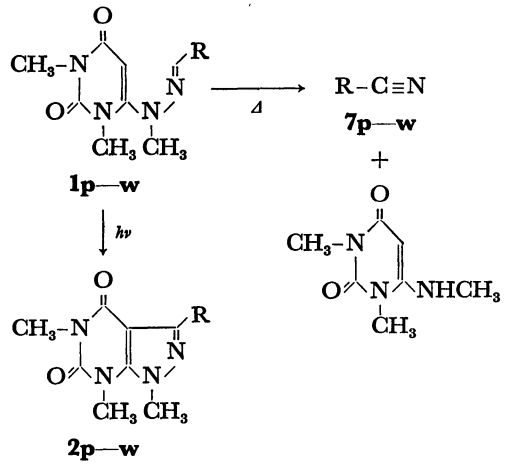


Compd.	R	Irradiation time hr	Mp (°C)	Yield (%)	Recrystn solvent	Analyses % Found (Calcd) C	H	N	IR cm^{-1} (KBr)
2p	CH_3	35	251	78	ethanol	51.61 (51.91)	5.92 (5.81)	26.87 (26.91)	1693s, 1651s, 1583s, 1555s
2q	CH_3-CH=CH	35	215	81	ethanol	56.69 (56.40)	6.10 (6.02)	23.90 (23.92)	1693s, 1645s, 1581s, 1550s
2r	C_6H_5	43	192[5]	82	ethanol	62.40 (62.21)	5.12 (5.22)	20.60 (20.73)	1690s, 1659s, 1640sh, 1578s, 1538s
2s	*p*-Cl-C_6H_4	26	257	78	dioxane	55.13 (55.18)	4.14 (4.30)	18.27 (18.39)	1695s, 1645s, 1578s, 1527m
2t	3,4-Cl_2-C_6H_3	30	242	82	dioxane	49.42 (49.57)	3.57 (3.57)	16.37 (16.52)	1698s, 1650s, 1576s, 1527m
2u	*p*-CH_3O-C_6H_4	34	214	90	ethanol	60.01 (59.99)	5.07 (5.37)	18.69 (18.66)	1695s, 1647s, 1575s, 1534m 1515m
2v	*p*-$(CH_3)_2N$-C_6H_4	35	193	85	ethanol	61.21 (61.32)	6.00 (6.11)	22.75 (22.35)	1689s, 1648s, 1601m, 1578s, 1558s, 1527s
2w	3-Pyridyl	38	211	75	ethanol	57.26 (57.56)	4.49 (4.83)	25.65 (25.82)	1691s, 1645s, 1572s, 1532s

nitriles (**7p—w**) and 1,3-dimethyl-6-methylaminouracil[4] in high yields and in a state of high purity. The reaction can be performed merely by heating the starting materials at temperatures slightly higher than their melting points for 10—40 min, followed by distillation, sublimation, or extraction using the ether of the reaction mixtures to give the respective nitriles (**7p—w**). The residue includes 1,3-dimethyl-6-methylaminouracil[4] exclusively (Table 4). We consider this nitrile formation as possessing a potential synthetic utility because of the good yields obtained and the neutral condition employed.

Photolysis of Compounds ***1p—w***. For the purpose of exploiting the preparative method of fully substituted pyrazolo[3,4-*d*]pyrimidine-4,6(5*H*,7*H*)-diones, photolysis of Compounds **1p—w** was carried out. The irradiation of solution of **1p—w** in benzene under aerobic condition, with a 100 W high-pressure mercury lamp at room temperature resulted in the formation of the respective pyrazolo[3,4-*d*]pyrimidines (**2p—w**) as the sole products in excellent yields (Table 5). Thus, the photolysis of fully methylated 6-(benzylidenehydrazino)uracils (**1p—w**) has been proved to offer a new method of synthesizing 1,5,7-trimethylpyrazolo[3,4-*d*]pyrimidine-4,6(5*H*,7*H*)diones (**2p—w**).

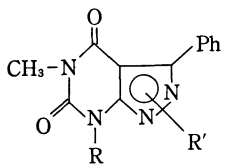
On the other hand, the photolysis of **1a—o** under the same conditions did not give **2a—o**; rather the starting materials were completely recovered.



Scheme 3.

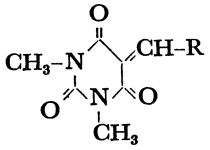
Structural Elucidation of (2p—w) Products. The structures of **2p—w** were established by microanalyses, by molecular-weight determination by means of mass spectrometry, and by comparison with authentic samples prepared by the methylation of the corresponding 1,5-dimethylpyrazolo[3,4-*d*]pyrimidine-4,6(5*H*,7*H*)-diones (**2f—j**). The methylation of **2k** with methyl iodide gave **2r** (15.4%) and its isomeric 2,5,7-trimethylpyrazolo[3,4-*d*]pyrimidine-4,6(5*H*,7*H*)-dione (**8**) (51.3 %). Table 6 gives the ultraviolet absorption data for a series of 3-phenylpyrazolo[3,4-*d*]pyrimidine-4,6-

TABLE 6. UV ABSORPTIONS OF PYRAZOLO-[3,4-*d*]PYRIMIDINES



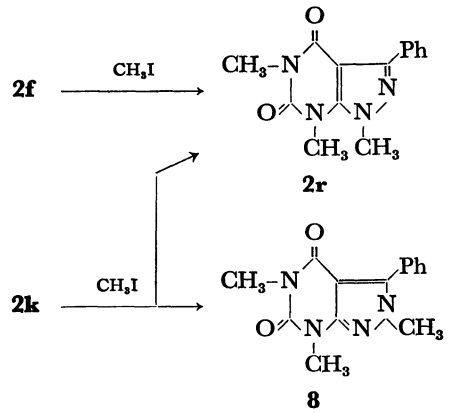
Compd.	R	R′	λ_{max}^{EtOH} nm	log ε
2a	CH_3	2-H	267.5	4.10
2k	H	2-H	267	4.13
8	CH_3	2-CH_3	261	4.12
2f	H	1-CH_3	231.5, 244(sh), 263(sh)	4.26, 4.21 4.09
2r	CH_3	1-CH_3	232, 261	4.32, 4.13

TABLE 7. 5-BENZYLIDENE-1,3-DIMETHYLBARBITURIC ACIDS (**9r—v**)



Compd.	R	Mp[a] (°C)	Yield (%)	Analyses % Found (Calcd) C	H	N
9r	C_6H_5	164	53	63.81 (63.92)	4.77 (4.95)	11.27 (11.47)
9s	p-Cl-C_6H_4	155	82	55.79 (56.00)	3.83 (3.98)	9.92 (10.05)
9t	3,4-Cl_2-C_6H_3	200	81	49.73 (49.86)	3.07 (3.22)	9.09 (9.27)
9u	p-CH_3O-C_6H_4	151	84	61.82 (61.31)	5.02 (5.15)	10.55 (10.21)
9v	p-$(CH_3)_2N$-C_6H_4	242	77	63.01 (62.70)	5.80 (5.96)	14.14 (14.63)

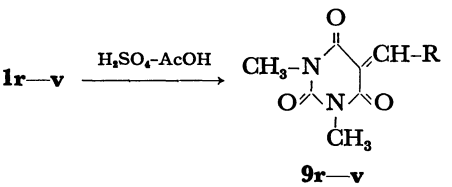
a) All products were recrystallized from ethanol.



Scheme 4.

(5*H*,7*H*)-diones. The 1,5,7-trimethyl derivative (**2r**) exhibited spectra with two intense peaks at *ca.* 230 and 260 nm, while the 2,5,7-trimethyl derivative (**8**) exhibited spectra with only one peak in the 260-nm region. It is noticeable that both **2a** and **2k** have the 2*H*-pyrazole tautomeric form in alcoholic solutions.

Reaction of ***1r—v*** *with Sulfuric Acid in Acetic Acid.* In order to find another method of cyclizing Compounds **1r—v**, we tried the reaction of **1r—v** with sulfuric acid in acetic acid. However, the products obtained were 5-benzylidene-1,3-dimethylbarbituric acid (**9r—v**) (Table 7), whose structures were established by comparison with authentic samples prepared by the condensation of 1,3-dimethylbarbituric acid with the corresponding aryl aldehydes.



Scheme 5.

Experimental

All the melting points are corrected and were determined on a Mettler FP-1 apparatus.

1,3-Dimethyl-6-hydrazinouracil,[4] *3-methyl-6-(1′-methylhydrazino)uracil,*[10] and *3-methyl-6-hydrazinouracil.*[7] These were prepared by the known procedures.

1,3-Dimethyl-6-(1′-methylhydrazino)uracil. To a solution of 6-chloro-1,3-dimethyluracil (5 g, 0.029 mol) in EtOH (60 ml), we added methylhydrazine (5.25 g, 0.114 mol), after which the mixture was stirred for 2 hr at room temperature. The crystals which separated were collected by filtration. The filtrate was evaporated *in vacuo* to give more crystals. The combined crystals were recrystallized from EtOH to give 4.47 g (84.7%) of colorless needles; mp 135—137 °C. Found: C, 45.50; H, 6.59; N, 30.23%. Calcd. for $C_7H_{12}N_4O_2$: C, 45.64; H, 6.57; N, 30.42%.

*6-(Benzylidenehydrazino)uracils (**1a—w**): General Procedure.* To a stirred solution or suspension of a 6-hydrazinouracil (0.01 mol) in 50—200 ml of EtOH, we added an aldehyde (0.015—0.02 mol) at room temperature. After stirring had been continued for 2 hr at room temperature, the product which separated was collected by filtration and recrystallized from EtOH.

*Pyrazolo[3,4-d]pyrimidine-4,6(5H,7H)-dione Derivatives (**2a—o**): General Procedure.* A 6-(benzylidenehydrazino)uracil (**1a—o**) (0.005 mol) was fused as has been described in Table 2. The reaction mixture was then dissolved in 100—200 ml of EtOH with warming. After cooling, the precipitated crystals were collected by filtration and recrystallized from EtOH.

*2-Benzyl Derivatives of **2a—d** (**3a—d**).* When Compounds **1a—d** were used as the starting materials in the above reaction, the 2-benzyl derivatives of **2a—d** (**3a—d**) were obtained by the evaporation of the filtrate, followed by the recrystallization of the residue from EtOH.

6-(Benzylidene-1′-methylhydrazino)-3-methyl-5-nitrouracil (**5**). To a stirred solution of 6-chloro-3-methyl-5-nitrouracil (**4**) (5 g, 0.024 mol) in EtOH (70 ml), we added methylhydrazine (1.12 g, 0.024 mol) and benzaldehyde (2.58 g, 0.024 mol) at room temperature. After stirring for 2 hr, the crystals thus precipitated were collected by filtration and recrystallized from EtOH to give 6.53 g (85.8%) of **5** as yellow prisms; mp 226—227 °C. Found: C, 51.32; H, 4.29; N, 22.84%. Calcd for $C_{13}H_{13}N_5O_4$: C, 51.48; H, 4.32; N, 23.09%.

*5-Mehtyl-3-phenylpyrazolo[3,4-d]pyrimidine-4,6(5H,7H)-dione (**2k**)* and *5,7-Dioxo-6-methyl-8-nitro-3-phenyl-1,5,6,7-tetrahydro-s-triazolo[4,3-c]pyrimidine (**6**).* A mixture of **1k** (0.5 g, 0.002 mol), potassium nitrate (0.415 g, 0.0041 mol), and sulfuric acid (0.3 g) in acetic acid (20 ml) was heated at 90—95 °C for 2 hr. After removing the undissolved inorganic substances by filtration, the filtrate was evaporated to dryness and the residue was diluted with water to precipitate crystals, which were then collected by filtration and recrystallized from

EtOH to give 0.16 g (32%) of **2k**. After the filtrate had been kept in the refrigerator, the crystals separated were collected by filtration and recrystallized from EtOH to give 0.09 g (15.3%) of **6** as pale yellow plates; mp 148—149 °C. Mass: 287 (M^+). UV λ_{max}^{EtOH} nm (log ε): 219sh (4.21), 264.5 (4.05), and 356 (3.87). IR cm^{-1} (KBr): 3470, 3375, 1733s, 1659s, 1608s, and 1340 (NO_2). Found: C, 50.08; H, 3.12; N, 24.07%. Calcd for $C_{12}H_9N_5O_4$: C, 50.18; H, 3.16; N, 24.38%.

*Pyrolysis of 6-(Benzylidene-1'-methylhydrazino)-1,3-dimethyluracils (**1p—w**). Formation of Nitriles (**7p—w**): General Procedure.* One gram of Compound **1p—w** was fused under the conditions indicated in Table 4. During the reaction, the respective nitriles (**8p—w**) were sublimed or distilled; they were then collected. After the reaction, the mixtures were extracted with ether, and the ether extracts were evaporated to give more nitriles. The residue was almost pure 1,3-dimethyl-6-methylaminouracil.[4]

*Photolysis of **1p—w**. Synthesis of 1,5,7-Trimethylpyrazolo[3,4-d]pyrimidine-4,6(5H,7H)-diones (**2p—w**).* A solution of **1p—w** (0.5 g) in benzene (600 ml) was irradiated with a 100 W high-pressure mercury lamp surrounded by a water-cooled Pyrex filter, as is shown in Table 5. The completion of the reaction was judged by tlc, using silica gel G and the appropriate mixtures of benzene, acetone, EtOH, and chloroform as the developing solvents. The removal of the solvent, followed by recrystallization from EtOH or dioxane, gave the respective pyrazolo[3,4-*d*]pyrimidines (**2p—w**).

*Methylation of 3-Substituted 1,5-Dimethylpyrazolo[3,4-d]pyrimidine-4,6(5H,7H)-diones (**2f—j**): General Procedure.* To a solution of **2f—j** (0.001 mol) in dimethylformamide (5 ml), we added methyl iodide (0.21 g, 0.015 mol) and potassium carbonate (0.2 g), after which the mixture was refluxed for 3 hr. After the reaction mixture had then been evaporated *in vacuo*, the residue was diluted with water to precipitate crystals; these crystals were collected by filtration and recrystallized from EtOH to afford **2r—v** in 50—65% yields.

*Methylation of 5-Methyl-3-phenylpyrazolo[3,4-d]pyrimidine-4,6(5H,7H)-dione (**2k**). 3-Phenyl-1,5,7-trimethylpyrazolo[3,4-d]pyrimidine-4,6(5H,7H)-dione (**2r**) and 3-Phenyl-2,5,7-trimethylpyrazolo[3,4-d]pyrimidine-4,6(5H,7H)-dione (**8**).* To a solution of **2k** (0.35 g, 0.0015 mol) in dimethylformamide (10 ml), we added methyl iodide (2.1 g, 0.015 mol) and potassium carbonate (0.7 g), after which the mixture was refluxed for 1 hr. After the reaction mixture had then been evaporated under reduced pressure, the residue was recrystallized from EtOH to give 0.2 g (51.3%) of **8** as colorless prisms; mp 204—206 °C. Mass: 270 (M^+). IR cm^{-1} (KBr): 1699s, 1662s, 1600m, 1580s, 1539m, and 1512m. Found: C, 62.01; H, 5.40; N, 20.78%. Calcd for $C_{14}H_{14}N_4O_2$: C, 62.21; H, 5.22; N, 20.73%.

The filtrate was evaporated to dryness, and the residue was diluted with H_2O to separate 0.06 g (15.4%) of **2r**.

*5-Benzylidene-1,3-dimethylbarbituric Acids (**9r—v**): General Procedure.* *A)* To a solution of **1r—v** (0.5 g) in acetic acid (10 ml), sulfuric acid (0.25 g) was added. After the mixture had been heated under stirring at 90—95 °C for 2 hr, the reaction mixture was diluted with H_2O to precipitate crystals; these crystals were then collected by filtration and recrystallized from EtOH.

B) A mixture of 1,3-dimethylbarbituric acid (1.5 g, 0.0096 mol) and aryl aldehyde (0.014 mol) in EtOH (40 ml) was refluxed for 1 hr. After cooling, the crystals which separated were collected by filtration. The filtrate was evaporated to dryness to give more crystals. The combined crystals were recrystallized from EtOH to give **9r—v**.

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