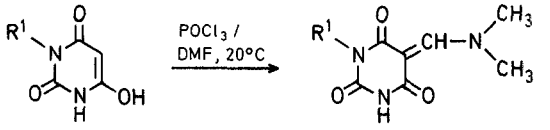
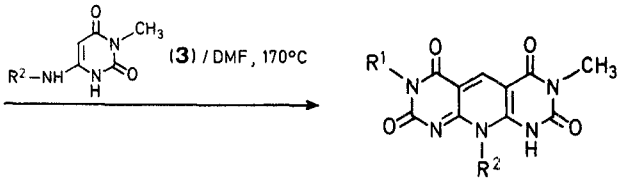


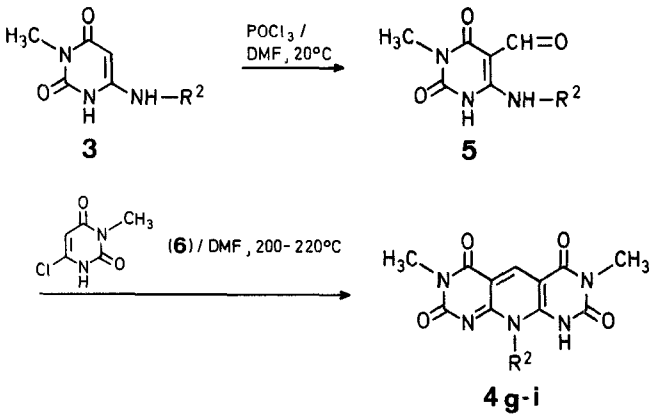
1a R^1 = H
b R^1 = CH_3

2 a,b



4 a-k

Alternatively, compounds **4** can be obtained starting from 6-alkylamino-3-methyluracils **(3)**. Vilsmeier formylation of **3** furnishes 6-alkylamino-5-formyl-3-methyluracils **(5)** (Table 2) which, by condensation with 6-chloro-3-methyluracil **(6)**, are converted to compounds **4** (Method B, Table 1).



3 **5** **4 g-i**

The microanalytical and spectral data are in agreement with the structure of compounds **4**. The protons at C-5 exhibit significant signals at $\delta = 9.5$-9.9 ppm in the ^{1}H-N.M.R. spectra (Table 1).

5-Dimethylaminomethylenebarbituric Acid (2a):
To a mixture of phosphoryl chloride (2.3 g, 0.015 mol) and dimethylformamide (5 ml) at room temperature, barbituric acid (**1a**; 1.92 g, 0.015 mol) is added with stirring. After stirring for 3 h, the precipitated crystals are collected and recrystallized from 95% ethanol to give pale yellow needles; yield: 2.4 g (88%); m.p. 250–252°C.

$C_7H_9N_3O_3$	calc.	C 45.90	H 4.95	N 22.94
(183.2)	found	45.98	4.81	22.69

^{1}H-N.M.R. (CF_3COOH/TMS): $\delta = 3.58$ (s, 3H); 3.71 (s, 3H); 8.47 ppm (s, 1H).

3-Methyl-5-dimethylaminomethylenebarbituric Acid (2b):
From 1-methylbarbituric acid, compound **2b** is obtained by the same procedure; yield: 2.1 g (71%); m.p. 208–209°C.

$C_8H_{11}N_3O_3$	calc.	C 48.72	H 5.62	H 21.31
(197.2)	found	48.59	5.81	21.28

^{1}H-N.M.R. (CF_3COOH/TMS): $\delta = 3.42$ (s, 3H); 3.51 (s, 3H); 3.67 (s, 3H); 8.44 ppm (s, 1H).

Pyrido[2,3-*d*:6,5-*d'*]dipyrimidine-2,4,6,8(3*H*,10*H*,7*H*,9*H*)-tetrones (4a-k); General Procedure for Method A:
Heating of 5-dimethylaminomethylenebarbituric acid (**2**; 1.3 mmol) and the appropriate 6-alkylamino-3-methyluracil **3** (1.3 mmol) in dimethylformamide (4 ml) under reflux at 170°C for 2 h, followed by cooling and diluting with 95% ethanol gives the corresponding pyridodipyrimidines **(4a-k)** (Table 1).

A New and Facile Synthesis of Pyrido[2,3-*d*:6,5-*d'*]dipyrimidine Derivatives

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5-Deazaflavins[1], their analogues[1], and pyridodipyrimidines[2] are of interest as $NAD[P]^+$ model compounds which mediate biomimetic oxidation. For further studies on $NAD[P]^+$ model compounds, we have developed a facile synthesis of pyrido[2,3-*d*:6,5-*d'*]dipyrimidine-2,4,6,8(3*H*,10*H*,7*H*,9*H*)-tetrone derivatives **(4)**.

Alkoxy- and aminopyrimidines are known to yield the corresponding formyl derivatives when treated with the Vilsmeier reagent (dimethylformamide/phosphoryl chloride)[3]. In hydroxy-substituted pyrimidines, the formylation is usually accompanied by replacement of the hydroxy group with a chlorine atom[4]. However, in the reaction of barbituric acids **(1)** with equimolar amounts of the Vilsmeier reagent, 5-dimethylaminomethylene barbituric acids **(2)** are obtained. Heating of compounds **2** with 6-alkylamino-3-methyluracils **(3)** in dimethylformamide at reflux temperature results in the formation of pyrido[2,3-*d*:6,5-*d'*]dipyrimidine-2,4,6,8(3*H*,10*H*,7*H*,9*H*)-tetrones **(4)** in good yields (Method A, Table 1).

Table 1. Pyrido[2,3-*d*:6,5-*d'*]dipyrimidine-2,4,6,8(3*H*,10*H*,7*H*,9*H*)-tetrones **(4a–k)** prepared

Product No.	R^1	R^2	Yield [%] by Method A	Method B	m.p. [°C][a]	Molecular Formula[b]	^{1}H-N.M.R. (CF_3COOH/TMS) δ (C-5—H) [ppm]
4a	H	CH_3	84	—	>300°	$C_{11}H_6N_5O_4$ (275.2)	9.58
4b	H	C_2H_5	72	—	>300°	$C_{12}H_{11}N_5O_4$ (289.3)	9.60
4c	H	*n*-C_4H_9	64	—	>300°	$C_{14}H_{15}N_5O_4$ (317.3)	9.60
4d	H	*n*-C_8H_{17}	65	—	294–295°	$C_{18}H_{23}N_5O_4$ (373.4)	9.50
4e	H	*n*-$C_{12}H_{25}$	60	—	285–287°	$C_{22}H_{31}N_5O_4$ (429.5)	9.68
4f	H	$C_6H_5(CH_2)_2$	72	—	252–254°	$C_{18}H_{15}N_5O_4$ (365.3)	9.90
4g	CH_3	CH_3	87	81	>300°	$C_{12}H_{11}N_5O_4$ (289.3)	9.76
4h	CH_3	*n*-C_3H_7	76	77	>300°	$C_{14}H_{15}N_5O_4$ (317.3)	9.72
4i	CH_3	*n*-C_4H_9	71	68	>300°	$C_{15}H_{17}N_5O_4$ (331.3)	9.72
4j	CH_3	*n*-C_8H_{17}	67	64	219–220°	$C_{19}H_{25}N_5O_4$ (387.4)	9.74
4k	CH_3	*n*-$C_{12}H_{25}$	64	—	205–206°	$C_{23}H_{33}N_5O_4$ (443.5)	9.72

[a] m.p. not corrected. All compounds were recrystallized from dimethylformamide or glacial acetic acid.

[b] Satisfactory microanalyses obtained: C ±0.31, H ±0.23, H ±0.29.

Table 2. 6-Alkylamino-5-formyl-3-methyluracils **(5a–d)** prepared

Product No.	R^2	Yield [%]	m.p. [°C][a]	Molecular formula[b]	^{1}H-N.M.R. (CF_3COOH/TMS) δ (C-5—H) [ppm]
5a	CH_3	85	>300°	$C_7H_9N_3O_3$ (183.2)	9.76
5b	*n*-C_3H_7	75	194–195°	$C_9H_{13}N_3O_3$ (211.2)	9.76
5c	*n*-C_4H_9	65	189–191°	$C_{10}H_{15}N_3O_3$ (237.3)	9.77
5d	*n*-C_8H_{17}	57	163–164°	$C_{14}H_{23}N_3O_3$ (281.4)	9.79

[a] m.p. not corrected. All compounds were recrystallized from 95% ethanol.

[b] Satisfactory microanalyses obtained: C ±0.19, H ±0.21, N ±0.23.

6-Alkylamino-5-formyl-3-methyluracils (5a–d); General Procedure:
To a mixture of phosphoryl chloride (3.1 g, 0.02 mol) and dimethylformamide (4 ml) at room temperature, the 6-alkylamino-3-methyluracil **3a, c–e** (6 mmol) is added. The mixture is then heated with stirring at 90°C for 6 h followed by cooling and addition of ice/water to give the corresponding 6-alkylamino-5-formyl-3-methyluracils **(5a–d)** (Table 2).

Pyrido[2,3-*d*:6,5-*d'*]dipyrimidine-2,4,6,8(3*H*,10*H*,7*H*,9*H*)-tetrones (4g–j); General Procedure for Method B:
Heating of 6-alkylamino-5-formyl-3-methyluracils **5a–d** (2 mmol) and 6-chloro-3-methyluracil (**6**; 2 mmol) in dimethylformamide (5 ml) under reflux at 200–220°C (oil bath temperature) for 7 h, followed by concentration yields, after dilution with 95% ethanol, the corresponding pyridodipyrimidines **(4g–j)** which are identical with the compounds prepared by Method A (Table 1).

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