A New, General, and Convenient Synthesis of 5-Deazaflavins (5-Deazaisoalloxazines) and Bis-(5-deazaflavin-10-yl)alkanes

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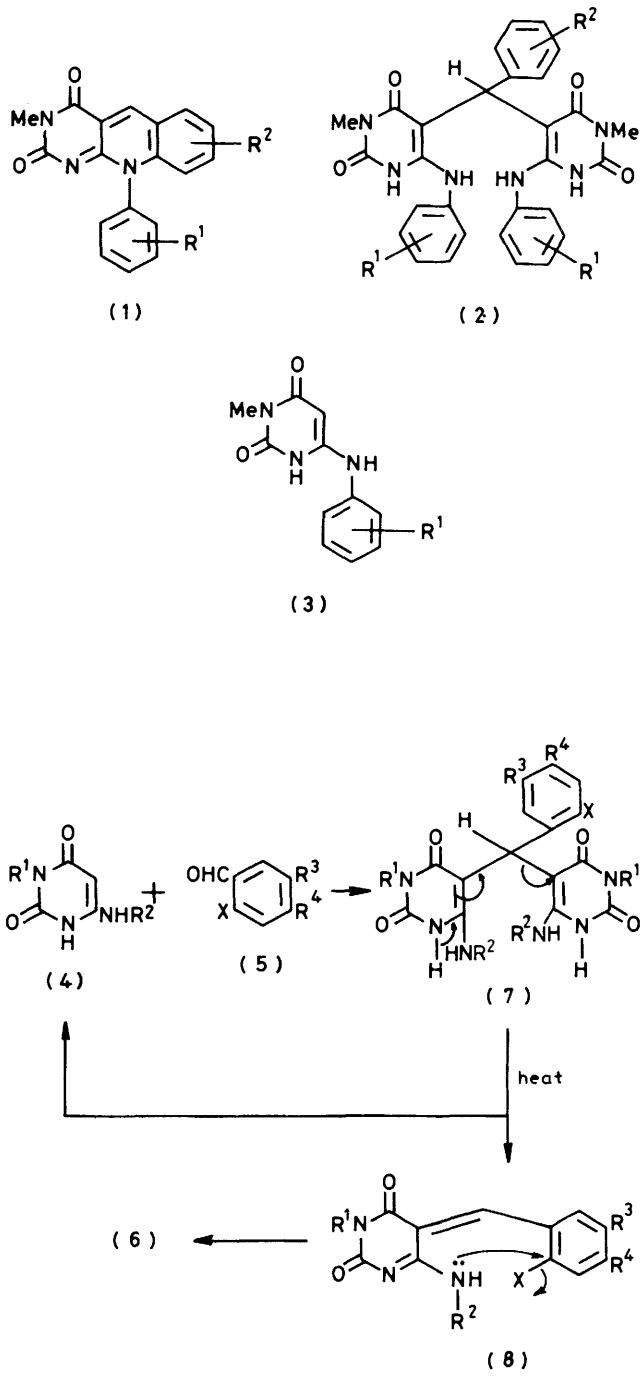
The condensation of 6-substituted aminouracils or bis(uracil-6-ylamino)alkanes with *o*-halogenobenzaldehydes in dimethylformamide led to the formation of the corresponding 5-deazaflavins or bis-(5-deazaflavin-10-yl)alkanes in a single step.

Since the synthesis of 5-deazariboflavin by Cheng and his co-workers [1] 5-deazaflavins (5-deazaisoalloxazines) have been studied extensively in both enzymatic [2] and model systems [3] to provide mechanistic insight into flavin-catalysed reactions. They have aroused further interest because of the recent discovery that coenzyme F_{420} from methanogenic bacteria possesses the 8-hydroxy-5-deazaflavin moiety.[4] Moreover, our findings that the oxidation of alcohols under alkaline conditions by 5-deazaflavins yields the corresponding carbonyl compounds [5] and that the reduction of carbonyl compounds by 1,5-dihydro-5-deazaflavins yields the corresponding alcohols in the presence of strong proton sources [6] have prompted us to prepare a great variety of 5-deazaflavins in order to ascertain the more efficient oxidizing or reducing agents.

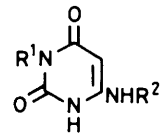
5-Deazaflavins have previously been prepared by (*a*) the condensation of anthranilaldehydes with barbituric acid,[1] (*b*) the cyclization of 6-(*N*-alkylanilino)uracils with one-carbon reagents including the Vilsmeier reagent,[7] (*c*) the condensation of 6-chloro-5-formylpyrimidines with *N*-alkylanilines,[7] and (*d*) the oxidative cyclization of arylbis-(6-substituted amino-3-methyluracil-5-yl)methanes with diethyl azodicarboxylate (DAD).[8,9] However, we encountered difficulties when attempting to prepare the 10-aryl-5-deazaflavin derivatives (1) by methods (*b*) and (*c*), because the intermediate 6-(*N*-arylanilino)uracils were not available by the usual condensation of 6-chlorouracils with diphenylamines and because the 6-chloro-5-formylpyrimidines and diphenylamines were unreactive under conventional conditions. Furthermore, synthetic method (*d*), consisting of the oxidative coupling of arylbis-(6-anilinouracil-5-yl)methanes (2), gave the corresponding 5-deazaflavins (1) in low overall yield based on the starting 6-anilinouracils (3).

In our previous communication,[10] we reported a new, general, and convenient synthesis of the 5-deazaflavin derivatives (6), which consists of the condensation of (6-substituted amino)uracils (4) with *o*-halogenobenzaldehydes (5). In this report, we present full experimental details and the reaction mechanism for the synthesis of 5-deazaflavins (6). Furthermore, we report the synthesis of bis-(5-deazaflavin-10-yl)alkanes (11) which consists of the condensation of bis-(uracil-6-ylamino)alkanes (10) with *o*-halogenobenzaldehydes (5). This method is noteworthy owing to the availability of all kinds of 5-deazaflavins, the simplicity of the procedure, and the very high yield of products.

The requisite starting materials, 6-*N*-alkyl- or 6-*N*-aryl-aminouracils (4) were prepared by the condensation of 6-chlorouracils with alkyl- or aryl-amines in the usual way.[11] Heating the 6-*N*-alkyl- or 6-*N*-aryl-aminouracils (4) thus obtained with the appropriate *o*-chloro- or *o*-bromo-benzaldehyde (5) in dimethylformamide (DMF) gave the corresponding 5-deazaflavins (6) *via* dehydration and dehydrochlorination or dehydrobromination in very high yield as indicated in Table 1. The structures of the products (6) were

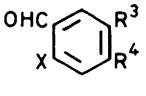


Scheme.



(4)

a; R^1 = H, R^2 = Bu^n
b; R^1 = H, R^2 = $CH_3[CH_2]_7$
c; R^1 = H, R^2 = $CH_3[CH_2]_{11}$
d; R^1 = H, R^2 = Ph
e; R^1 = H, R^2 = 2,4-$Me_2C_6H_3$
f; R^1 = H, R^2 = 3,4-$Me_2C_6H_3$
g; R^1 = H, R^2 = 4-ClC_6H_4
h; R^1 = R^2 = Me
i; R^1 = Me, R^2 = Pr^n
j; R^1 = Me, R^2 = Bu^n
k; R^1 = Me, R^2 = C_6H_{11}
l; R^1 = Me, R^2 = $PhCH_2$
m; R^1 = Me, R^2 = Ph
n; R^1 = Me, R^2 = 3-MeC_6H_4
o; R^1 = Me, R^2 = 4-MeC_6H_4
p; R^1 = Me, R^2 = 3,4-$Me_2C_6H_3$
q; R^1 = Me, R^2 = 4-ClC_6H_4
r; R^1 = Ph, R^2 = Me
s; R^1 = Ph, R^2 = Bu^n
t; R^1 = Ph, R^2 = $CH_3[CH_2]_7$
u; R^1 = Ph, R^2 = $CH_3[CH_2]_{11}$
v; R^1 = R^2 = Ph
w; R^1 = Ph, R^2 = 3,4-$Me_2C_6H_3$
x; R^1 = Ph, R^2 = 4-ClC_6H_4



X = halogen

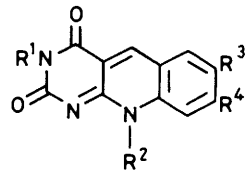
(5)

a; R^3 = R^4 = H
b; R^3 = NO_2, R^4 = H
c; R^3 = H, R^4 = Cl
d; R^3 = H, R^4 = OH

established from satisfactory analytical and spectral data and, in particular, by the presence of the characteristic C-5 proton resonance at δ 9.6—10.1 in the ^1H n.m.r. spectra for compounds (6) (see Table 1).

This reaction presumably involves initial formation of arylbis-(6-substituted aminouracil-5-yl)methanes (7), followed by the elimination of 6-substituted aminouracils (4) from the intermediates (7), to yield the reactive intermediates (8) (see Scheme). Then, ring-closure of the intermediates (8) with concomitant dehydrochlorination or dehydrobromination gives the final products, 5-deazaflavins (6). Moreover, the eliminated 6-substituted aminouracils (4) may react again with more *o*-halogenobenzaldehyde (5) to afford further quantities of the methanes (7) which are converted into the deazaflavins (6) in the same way as above. This process would be repeated until exhaustion of the starting materials, to give the high yields of the final products. In fact, an intermediate, *o*-bromophenylbis-(6-anilino-3-methyluracil-5-yl)methane (7bb; X = Br), was isolated by treatment of 6-anilino-3-methyluracil (4 m) with *o*-bromobenzaldehyde (5a) in DMF at 140 °C for 1.5 h or by treatment of them in n-butanol under reflux for 3 h. This intermediate was easily converted into 3-methyl-10-phenyl-5-deazaflavin (6bb) on being heated in DMF under reflux for 3 h. The structure of this intermediate was established by analytical and spectral data, particularly by the presence of the characteristic proton resonance of the trisubstituted methane at δ 5.97 in the ^1H n.m.r. spectrum (trifluoroacetic acid).

Similarly, bis-(5-deazaflavin-10-yl)alkanes (11) were prepared by the above method. The precursors of compounds (11), bis(uracil-6-yl-amino)alkanes (10), were synthesized by heating 6-chlorouracils (9) and α,ω-diaminoalkanes in n-butanol (Table 2). Refluxing the bis(uracil-6-yl-amino)alkanes



(6)

a; R^1 = R^3 = R^4 = H, R^2 = Bu^n
b; R^1 = R^4 = H, R^2 = Bu^n, R^3 = NO_2
c; R^1 = R^3 = H, R^2 = Bu^n, R^4 = Cl
d; R^1 = R^3 = R^4 = H, R^2 = $CH_3[CH_2]_7$
e; R^1 = R^4 = H, R^2 = $CH_3[CH_2]_7$, R^3 = NO_2
f; R^1 = R^3 = H, R^2 = $CH_3[CH_2]_7$, R^4 = Cl
g; R^1 = R^3 = R^4 = H, R^2 = $CH_3[CH_2]_{11}$
h; R^1 = R^4 = H, R^2 = $CH_3[CH_2]_{11}$, R^3 = NO_2
i; R^1 = R^3 = H, R^2 = $CH_3[CH_2]_{11}$, R^4 = Cl
j; R^1 = R^3 = R^4 = H, R^2 = Ph
k; R^1 = R^4 = H, R^2 = Ph, R^3 = NO_2
l; R^1 = R^3 = H, R^2 = Ph, R^4 = Cl
m; R^1 = R^3 = H, R^2 = Ph, R^4 = OH
n; R^1 = R^3 = R^4 = H, R^2 = 2,4-$Me_2C_6H_3$
o; R^1 = R^4 = H, R^2 = 2,4-$Me_2C_6H_3$, R^3 = NO_2
p; R^1 = R^3 = H, R^2 = 2,4-$Me_2C_6H_3$, R^4 = Cl
q; R^1 = R^3 = R^4 = H, R^2 = 3,4-$Me_2C_6H_3$
r; R^1 = R^4 = H, R^2 = 3,4-$Me_2C_6H_3$, R^3 = NO_2
s; R^1 = R^3 = H, R^2 = 3,4-$Me_2C_6H_3$, R^4 = Cl
t; R^1 = R^3 = R^4 = H, R^2 = 4-ClC_6H_4
u; R^1 = R^3 = H, R^2 = 4-ClC_6H_4, R^4 = Cl
v; R^1 = R^2 = Me, R^3 = H, R^4 = OH
w; R^1 = Me, R^2 = Pr^n, R^3 = R^4 = H
x; R^1 = Me, R^2 = Bu^n, R^3 = R^4 = H
y; R^1 = Me, R^2 = Bu^n, R^3 = H, R^4 = OH
z; R^1 = Me, R^2 = C_6H_{11}, R^3 = H, R^4 = Cl
aa; R^1 = Me, R^2 = $PhCH_2$, R^3 = R^4 = H
bb; R^1 = Me, R^2 = Ph, R^3 = R^4 = H
cc; R^1 = Me, R^2 = Ph, R^3 = H, R^4 = Cl
dd; R^1 = Me, R^2 = 3-MeC_6H_4, R^3 = R^4 = H
ee; R^1 = Me, R^2 = 4-MeC_6H_4, R^3 = R^4 = H
ff; R^1 = Me, R^2 = 3,4-$Me_2C_6H_3$, R^3 = NO_2, R^4 = H
gg; R^1 = Me, R^2 = 4-ClC_6H_4, R^3 = R^4 = H
hh; R^1 = Me, R^2 = 4-ClC_6H_4, R^3 = H, R^4 = Cl
ii; R^1 = Ph, R^2 = Me, R^3 = H, R^4 = OH
jj; R^1 = Ph, R^2 = Bu^n, R^3 = R^4 = H
kk; R^1 = Ph, R^2 = Bu^n, R^3 = NO_2, R^4 = H
ll; R^1 = Ph, R^2 = Bu^n, R^3 = H, R^4 = Cl
mm; R^1 = Ph, R^2 = $CH_3[CH_2]_7$, R^3 = R^4 = H
nn; R^1 = Ph, R^2 = $CH_3[CH_2]_7$, R^3 = H, R^4 = Cl
oo; R^1 = Ph, R^2 = $CH_3[CH_2]_{11}$, R^3 = R^4 = H
pp; R^1 = Ph, R^2 = $CH_3[CH_2]_{11}$, R^3 = H, R^4 = Cl
qq; R^1 = R^2 = Ph, R^3 = R^4 = H
rr; R^1 = R^2 = Ph, R^3 = H, R^4 = Cl
ss; R^1 = Ph, R^2 = 3,4-$Me_2C_6H_3$, R^3 = R^4 = H
tt; R^1 = Ph, R^2 = 3,4-$Me_2C_6H_3$, R^3 = H, R^4 = Cl
uu; R^1 = Ph, R^2 = 4-ClC_6H_4, R^3 = R^4 = H
vv; R^1 = Ph, R^2 = 4-ClC_6H_4, R^3 = H, R^4 = Cl

(10) thus obtained with *o*-halogenobenzaldehydes (5) in DMF afforded the corresponding bis-(5-deazaflavin-10-yl)alkanes (11) (Table 3). The structures of the products (11) were confirmed on the basis of elemental analyses and, in particular, by the presence of the equivalent C-5 proton and C′-5 proton resonance at δ 9.75—9.84 in the ^1H n.m.r. spectra.

Experimental

M.p.s were determined on a Yanagimoto hot-stage apparatus and are uncorrected. ^1H N.m.r. spectra were obtained in CF_3CO_2H with a Hitachi R-24B spectrometer with $SiMe_4$ as internal standard and chemical shifts are expressed as δ values.

Table 1. Formation of 5-deazaflavins (6) and their C-5 proton chemical shifts

Starting materials	Product (Formula)	Yield (%)	M.P.[a] (°C)	Recrystallization solvent	δ (CF_3CO_2H)	Found (%) (Required) C	H	N
(4a) + (5a)	(6a)[7]	79	302	EtOH	9.77	66.7	5.6	15.5
	($C_{15}H_{15}N_3O_2$)					(66.9	5.6	15.6)
(4a) + (5b)	(6b)	80	290	EtOH	9.96	57.2	4.2	17.6
	($C_{15}H_{14}N_4O_4$)					(57.3	4.5	17.8)
(4a) + (5c)	(6c)	88	>300	DMF	9.75	59.2	4.5	13.7
	($C_{15}H_{14}ClN_3O_2$)					(59.3	4.65	13.8)
(4b) + (5a)	(6d)	73	246	EtOH	9.77	70.4	6.9	12.8
	($C_{19}H_{23}N_3O_2$)					(70.1	7.1	12.9)
(4b) + (5b)	(6e)	82	282	DMF–EtOH	9.99	61.7	6.1	15.2
	($C_{19}H_{22}N_4O_4$)					(61.6	6.0	15.1)
(4b) + (5c)	(6f)	81	295	DMF	9.74	63.6	6.1	13.4
	($C_{19}H_{22}ClN_3O_2$)					(63.4	6.2	13.3)
(4c) + (5a)	(6g)	74	211	DMF	9.78	72.5	8.0	10.9
	($C_{23}H_{31}N_3O_2$)					(72.4	8.2	11.0)
(4c) + (5b)	(6h)	89	242	DMF–EtOH	9.93	64.9	6.9	13.0
	($C_{23}H_{30}N_4O_4$)					(64.8	7.1	13.1)
(4c) + (5c)	(6i)	74	274	DMF	9.75	66.7	7.2	9.9
	($C_{23}H_{30}ClN_3O_2$)					(66.4	7.3	10.1)
(4d) + (5a)	(6j)	82	>330	DMF	9.91	70.7	4.0	14.4
	($C_{17}H_{11}N_3O_2$)					(70.6	3.8	14.5)
(4d) + (5b)	(6k)	90	>330	DMF–EtOH	10.05	61.0	3.2	16.8
	($C_{17}H_{10}N_4O_4$)					(61.1	3.0	16.8)
(4d) + (5c)	(6l)	95	>330	DMF	9.87	63.3	3.2	12.8
	($C_{17}H_{10}ClN_3O_2$)					(63.1	3.1	13.0)
(4d) + (5d)	(6m)	79	>330	EtOH	9.66	67.0	3.6	13.8
	($C_{17}H_{11}N_3O_3$)					(66.9	3.6	13.8)
(4e) + (5a)	(6n)	82	>310	DMF	9.96	71.7	4.6	13.2
	($C_{19}H_{15}N_3O_2$)					(71.9	4.8	13.2)
(4e) + (5b)	(6o)	94	>300	DMF	9.47	62.8	3.7	15.5
	($C_{19}H_{14}N_4O_4$)					(63.0	3.9	15.5)
(4e) + (5c)	(6p)	77	>300	DMF–EtOH	9.93	65.0	3.9	11.9
	($C_{19}H_{14}ClN_3O_2$)					(64.9	4.0	11.9)
(4f) + (5a)	(6q)	80	>330	EtOH	9.86	72.1	4.6	13.2
	($C_{19}H_{15}N_3O_2$)					(71.9	4.8	13.2)
(4f) + (5b)	(6r)	99	>300	DMF	10.08	62.9	3.9	15.3
	($C_{19}H_{14}N_4O_4$)					(63.0	3.9	15.5)
(4f) + (5c)	(6s)	67	>300	DMF	9.85	65.1	4.2	11.9
	($C_{19}H_{14}ClN_3O_2$)					(64.9	4.0	11.9)
(4g) + (5a)	(6t)	95	>300	DMF	9.94	62.8	3.4	13.1
	($C_{17}H_{10}ClN_3O_2$)					(63.1	3.1	13.0)
(4g) + (5c)	(6u)	98	>300	DMF	9.90	56.9	2.4	11.6
	($C_{17}H_9Cl_2N_3O_2$)					(57.0	2.5	11.7)
(4h) + (5d)	(6v)[5]	83	>330	AcOH	9.56	60.8	4.3	16.4
	($C_{13}H_{11}N_3O_3$)					(60.7	4.3	16.3)
(4i) + (5a)	(6w)[7]	78	267	EtOH	9.80	67.0	5.7	15.6
	($C_{15}H_{15}N_3O_2$)					(66.9	5.6	15.6)
(4j) + (5a)	(6x)[5]	56	252	EtOH	9.87	67.9	6.1	14.8
	($C_{16}H_{17}N_3O_2$)					(67.8	6.05	14.8)
(4j) + (5d)	(6y)	92	>330	DMF	9.61	64.4	5.8	14.1
	($C_{16}H_{17}N_3O_3$)					(64.2	5.7	14.0)
(4k) + (5c)	(6z)	54	266	EtOH	9.74	63.1	5.1	12.2
	($C_{18}H_{18}ClN_3O_2$)					(62.9	5.3	12.2)
(4l) + (5a)	(6aa)[5]	73	>330	EtOH	9.94	72.2	4.6	13.2
	($C_{19}H_{15}N_3O_2$)					(71.9	4.8	13.2)
(4m) + (5a)	(6bb)[9]	95	>330	DMF	9.92	71.0	4.3	13.9
	($C_{18}H_{13}N_3O_2$)					(71.3	4.3	13.9)
(4m) + (5c)	(6cc)[9]	92	>330	DMF	9.93	64.3	3.4	12.4
	($C_{18}H_{12}ClN_3O_2$)					(64.0	3.6	12.4)
(4n) + (5a)	(6dd)	82	>330	EtOH	9.96	72.2	4.9	13.1
	($C_{19}H_{15}N_3O_2$)					(71.9	4.8	13.2)
(4o) + (5a)	(6ee)[9]	89	>330	DMF	9.97	71.8	4.6	13.2
	($C_{19}H_{15}N_3O_2$)					(71.9	4.8	13.2)
(4p) + (5b)	(6ff)	73	>330	DMF–EtOH	9.97	63.7	4.3	14.8
	($C_{20}H_{16}N_4O_4$)					(63.8	4.3	14.9)
(4q) + (5a)	(6gg)[9]	86	>300	DMF	9.97	63.9	3.6	12.5
	($C_{18}H_{12}ClN_3O_2$)					(64.0	3.6	12.4)
(4q) + (5c)	(6hh)	96	>310	DMF	9.97	58.0	2.9	11.3
	($C_{18}H_{11}Cl_2N_3O_2$)					(58.1	3.0	11.3)

Table 1 (*continued*)

Starting materials	Product (Formula)	Yield (%)	M.P.[a] (°C)	Recrystallization solvent	δ (CF_3CO_2H)	Found (%) (Required) C	H	N
(4r) + (5d)	(6ii) ($C_{18}H_{13}N_3O_3$)	74	>330	DMF	9.60	67.9 (67.7)	4.1 4.1	13.2 13.2)
(4s) + (5a)	(6jj) [b] ($C_{21}H_{19}N_3O_2$)	41	294	EtOH	9.83	73.3 (73.0)	5.8 5.55	12.1 12.2)
(4s) + (5b)	(6kk) ($C_{21}H_{18}N_4O_4$)	48	178	EtOH	10.00	64.9 (64.6)	4.5 4.65	14.2 14.35)
(4s) + (5c)	(6ll) ($C_{21}H_{18}ClN_3O_2$)	44	281	EtOH	9.80	66.7 (66.4)	5.1 4.8	11.0 11.1)
(4t) + (5a)	(6mm) [c] ($C_{25}H_{27}N_3O_2$)	66	171	EtOH	9.82	75.1 (74.8)	7.0 6.8	10.3 10.5)
(4t) + (5c)	(6nn) ($C_{25}H_{26}ClN_3O_2$)	74	201	EtOH	9.75	68.6 (68.9)	6.1 6.0	9.7 9.6)
(4u) + (5a)	(6oo) [c] ($C_{29}H_{35}N_3O_2$)	42	169	EtOH	9.85	76.4 (76.1)	8.0 7.7	9.0 9.2)
(4u) + (5c)	(6pp) ($C_{29}H_{34}ClN_3O_2$)	67	152	EtOH	9.80	71.0 (70.8)	7.1 7.0	8.4 8.5)
(4v) + (5a)	(6qq) ($C_{23}H_{15}N_3O_2$)	81	>330	DMF	10.00	75.9 (75.6)	4.0 4.1	11.6 11.5)
(4v) + (5c)	(6rr) ($C_{23}H_{14}ClN_3O_2$)	87	>330	DMF–EtOH	9.90	68.8 (69.1)	3.4 3.5	10.7 10.5)
(4w) + (5a)	(6ss) ($C_{25}H_{19}N_3O_2$)	63	>310	EtOH	9.95	76.0 (76.3)	5.0 4.9	11.0 10.7)
(4w) + (5c)	(6tt) ($C_{25}H_{18}ClN_3O_2$)	25	>300	DMF–EtOH	9.91	70.3 (70.2)	4.1 4.2	9.7 9.8)
(4x) + (5a)	(6uu) ($C_{23}H_{14}ClN_3O_2$)	80	>300	DMF	9.97	69.4 (69.1)	3.7 3.5	10.4 10.5)
(4x) + (5c)	(6vv) ($C_{23}H_{13}Cl_2N_3O_2$)	77	>300	DMF–EtOH	9.92	63.5 (63.6)	3.3 3.0	9.4 9.7)

[a] All compounds were obtained as yellow needles, prisms, or plates. [b] F. Yoneda, K. Kuroda, and M. Kamishimoto, *J. Chem. Soc., Chem. Commun.*, 1981, 1160. [c] K. Kuroda, T. Nagamatsu, Y. Sakuma, and F. Yoneda, *J. Heterocycl. Chem.*, 1982, **19**, 929.

Table 2. Analytical data for the bis(uracil-6-ylamino)alkanes (10)

Compound (Formula)	Yield (%)	M.p.[a] (°C)	Found (%) (Required) C	H	N
(10a) ($C_{16}H_{24}N_6O_4$)	80	>330	53.0 (52.7)	6.5 6.6	22.9 23.1)
(10b) ($C_{18}H_{28}N_6O_4$)	100	>330	54.7 (55.1)	7.4 7.2	21.2 21.4)
(10c) ($C_{16}H_{24}N_6O_4$)	58	>330	52.5 (52.7)	6.5 6.6	23.3 23.1)
(10d) ($C_{18}H_{28}N_6O_4$)	58	>330	54.9 (55.1)	7.4 7.2	21.3 21.4)
(10e) ($C_{20}H_{32}N_6O_4$)	32	315	57.3 (57.1)	7.7 7.7	19.7 20.0)
(10f) ($C_{22}H_{36}N_6O_4$)	64	305	58.8 (58.9)	8.3 8.1	18.6 18.7)

[a] All compounds were recrystallized from glacial acetic acid and were obtained as colourless powders.

The identity of the compounds was confirmed by comparison of i.r. spectra determined in Nujol with a JASCO IRA-1 i.r. spectrophotometer. Molecular weights were determined by mass spectrometry with a JEOL-01SG instrument.

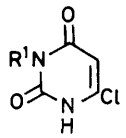
Compounds (4a—x) were prepared according to the known procedure.[11]

5-Deazaflavins (6a—vv). *General Procedure.*—A mixture of a 6-*N*-alkyl- or 6-*N*-aryl-aminouracil (4) (2.5 mmol) and the appropriate *o*-chloro- or *o*-bromo-benzaldehyde (5) (3.0 mmol) in DMF (20 ml) was heated under reflux for 3—5 h. Concentration of the solution under reduced pressure and recrystallization of the residue from appropriate solvents (indicated in Table 1) gave the corresponding *5-deazaflavin* (6a—vv).

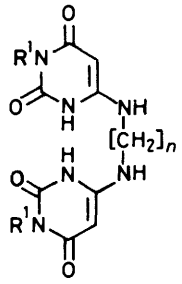
o-Bromophenylbis-(6-anilino-3-methyluracil-5-yl)methane (7bb; X = Br).—When a mixture of 6-anilino-3-methyluracil (4 m) (2.5 mmol) and *o*-bromobenzaldehyde (5a; X = Br) (3.0 mmol) was heated either in DMF (20 ml) at 140 °C for 1.5 h or in n-butanol (30 ml) under reflux for 3 h, and the mixture was cooled, the *bisuracil-5-ylmethane* (7bb; X = Br) was obtained in 75—90% yield, m.p. 258—261 °C (dedomp.) (from n-butanol) (Found: C, 57.7; H, 4.2; N, 13.9. $C_{29}H_{25}BrN_6O_4$ requires C, 57.9; H, 4.2; N, 14.0%); δ_H (60 MHz) 3.53 (6 H, s, 2 × Me), 5.97 (1 H, s, methine), and 6.95—7.70 (14 H, m, ArH); *m/z* 601. This intermediate (0.5 g, 0.83 mmol) was converted into *3-methyl-10-phenyl-5-deazaflavin* (6bb) (98% yield) by being heated in DMF (20 ml) under reflux for 3 h.

Bis(uracil-6-ylamino)alkanes (10a—f). *General Procedure.*—A mixture of a 6-chlorouracil (9a or b) (6.8 mmol) and an α,ω-diaminoalkane (3.4 mmol) in n-butanol (20 ml) was heated under reflux for 8 h, and then cooled, to afford the corresponding *bisuracil-6-ylalkane* (10) as indicated in Table 2. Evaporation of the mother liquid to dryness under reduced pressure and recrystallization of the residue from glacial acetic acid afforded a second crop of *compound* (10).

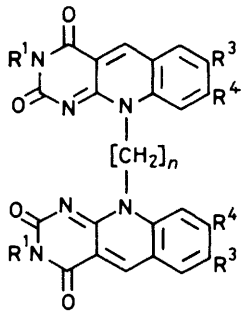
Bis-(5-deazaflavin-10-yl)alkanes (11a—i). *General Procedure.*—A mixture of a compound (10) (1.4 mmol) and a *o*-halogenobenzaldehyde (5) (3.4 mmol) in DMF (20 ml) was heated under reflux for 6—8 h, and then the mixture was cooled to afford the corresponding *bis(deazaflavin)alkane* (11) as indicated in Table 3. Evaporation of the mother liquid to dryness under reduced pressure and recrystallization of the



(9)
a; R^1 = H
b; R^1 = Me



(10)
a; R^1 = H, n = 8
b; R^1 = H, n = 10
c; R^1 = Me, n = 6
d; R^1 = Me, n = 8
e; R^1 = Me, n = 10
f; R^1 = Me, n = 12



(11)
a; R^1 = R^3 = H, R^4 = Cl, n = 8
b; R^1 = R^3 = H, R^4 = Cl, n = 10
c; R^1 = Me, R^3 = R^4 = H, n = 6
d; R^1 = Me, R^3 = R^4 = H, n = 8
e; R^1 = Me, R^3 = H, R^4 = Cl, n = 8
f; R^1 = Me, R^3 = R^4 = H, n = 10
g; R^1 = Me, R^3 = H, R^4 = Cl, n = 10
h; R^1 = Me, R^3 = R^4 = H, n = 12
i; R^1 = Me, R^3 = H, R^4 = Cl, n = 12

Table 3. Formation of bis-(5-deazaflavin-10-yl)alkanes (11) and their equivalent C-5 and C′-5 proton chemical shifts

Starting materials	Product (Formula)	Yield (%)	M.p.[a] (°C)	δ (CF_3CO_2H)	Found (%) (Required) C	H	N
(10a) + (5c)	(11a) ($C_{30}H_{26}Cl_2N_6O_4$)	52	>330	9.75	59.7 (59.5	4.2 4.3	13.5 13.9)
(10b) + (5c)	(11b) ($C_{32}H_{30}Cl_2N_6O_4$)	70	285 (decomp.)	9.77	60.4 (60.7	4.9 4.8	13.3 13.3)
(10c) + (5a)	(11c) ($C_{30}H_{28}N_6O_4$)	46	>300	9.81	66.9 (67.15	5.0 5.3	15.45 15.7)
(10d) + (5a)	(11d) ($C_{32}H_{32}N_6O_4$)	35	>300	9.84	68.3 (68.1	5.8 5.7	14.7 14.9)
(10d) + (5c)	(11e) ($C_{32}H_{30}Cl_2N_6O_4$)	64	>300	9.81	60.5 (60.7	4.9 4.8	13.1 13.3)
(10e) + (5a)	(11f) ($C_{34}H_{36}N_6O_4$)	49	308	9.83	68.6 (68.9	6.0 6.1	14.25 14.2)
(10e) + (5c)	(11g) ($C_{34}H_{34}Cl_2N_6O_4$)	44	282	9.76	61.9 (61.7	5.1 5.2	12.6 12.7)
(10f) + (5a)	(11h) ($C_{36}H_{40}N_6O_4$)	34	>300	9.81	69.9 (69.65	6.8 6.5	13.4 13.5)
(10f) + (5c)	(11i) ($C_{36}H_{38}Cl_2N_6O_4$)	60	233	9.80	62.9 (62.7	5.4 5.55	12.1 12.2)

[a] All compounds were recrystallized from DMF and were obtained as yellow powders.

residue from DMF afforded a second crop of the *compound* (11).

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Received 10*th August* 1983; *Paper* 3/1406