Syntheses of 1,3,6,8,10,11,14-Heptaazapentaphene-2,4,7,9(14*H*,3*H*,8*H*,-11*H*)-tetrones (Angular Mixed Flavins), 1,3,5,6,8,10,11,14-Octaazapentaphene-2,4,7,9(14*H*,3*H*,8*H*,11*H*)-tetrones (Angular Doubled Flavins), and Their Related Compounds

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Dedicated to Professor Ernest Campaigne on the occasion of his 75th birthday.

Cyclization of *N,N'*-dialkyl-*N*-(3-methyluracil-6-yl)-*N'*-(5-nitro-3-methyluracil-6-yl)-*p*-phenylenediamines with the Vilsmeier reagent gives the corresponding 1,3,6,8,10,11,14-heptaazapentaphene-2,4,7,9-(14*H*,3*H*,8*H*,-11*H*)-tetrones (angular mixed flavins) **2**. Cyclization of *N,N'*-di(5-nitro-3-methyluracil-6-yl)-*p*-phenylenediamines with the Vilsmeier reagent gives the corresponding 1,3,5,6,8,10,11,14-octaazapentaphene-2,4,7,9-(14*H*,3*H*,8*H*,11*H*)-tetrones (angular doubled flavins) **11** along with the angular mixed flavins **2**.

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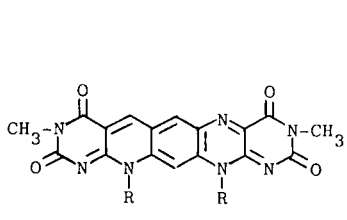
Previously we reported the synthesis of "linear mixed flavins" **1** which contain both a 5-deazaflavin and a flavin moiety with a benzene unit in common in the molecule in expectation of the strong autorecycling oxidizing ability intramolecular co-operation of the 5-deazaflavin and the flavin moiety [1,2]. As expected, they acted as an autorecycling catalyst for the oxidation of cyclopentanol to cyclopentanone under irradiation with a sunlamp. In the present paper, we describe the synthesis of 1,3,6,8,10,11,14-heptaazapentaphene-2,4,7,9(14*H*,3*H*,8*H*,11*H*)-tetrones (angular mixed flavins) **2**. Also we report the synthesis of 1,3,5,6,8,10,11,14-octaazapentaphene-2,4,7,9(14*H*,3*H*,8*H*,-11*H*)-tetrones (angular doubled flavins) **11** and other related polyazapolycyclic compounds.

The requisite starting materials, *N,N'*-dialkyl-*p*-phenylenediamines **3**, were prepared according to the known procedure [3]. Compounds **3** were treated with 6-chloro-3-methyluracil (**4**) to give the corresponding *N,N'*-dialkyl-*N*-(3-methyluracil-6-yl)-*p*-phenylenediamines **5** (Table 1). Compounds **5** were condensed with 6-chloro-5-nitro-3-methyluracil (**6**) to give the corresponding *N,N'*-dialkyl-*N*-(3-methyluracil-6-yl)-*N'*-(5-nitro-3-methyluracil-6-yl)-*p*-phenylenediamines **7**. Cyclization of compounds **7** with the Vilsmeier reagent (DMF:phosphoryl chloride = 5:1 v/v) gave the desired 1,3,6,8,10,11,14-heptaazapentaphene-2,4,7,9(14*H*,3*H*,8*H*,11*H*)-tetrones (angular mixed flavins) **2** along with 1,3,8,10,11,14-hexaazapentaphene-2,4,7,9-(14*H*-3*H*,8*H*,11*H*)-tetrones (angular doubled 5-deazaflavins) **8** [4] (Table 2). The formation of compound **8** would be ascribed to the denitration accompanied by formylation and then cyclization.

The structure of compound **2** was determined by direct ^{1}H nmr examination. The signals of C(12)-H and C(13)-H of **2a** existed as two doublet signals at δ 8.90 ppm (d, J = 10 Hz) and δ 9.00 ppm (d, J = 10 Hz) respectively. Therefore, the structure of **2** turned out to have an angular form (Table 2). Compound **2** showed characteristic C(5)-H signals at low field in the ^{1}H nmr spectra (Table 2). The uv and visible spectra of compound **2c** showed similar absorption pattern with a slight bathochromic shift to that of the corresponding angular doubled 5-deazaflavin **8c** as

Scheme 1



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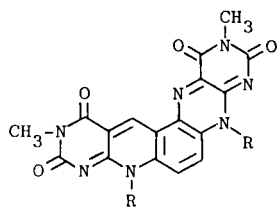
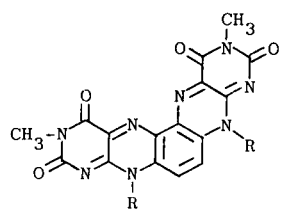
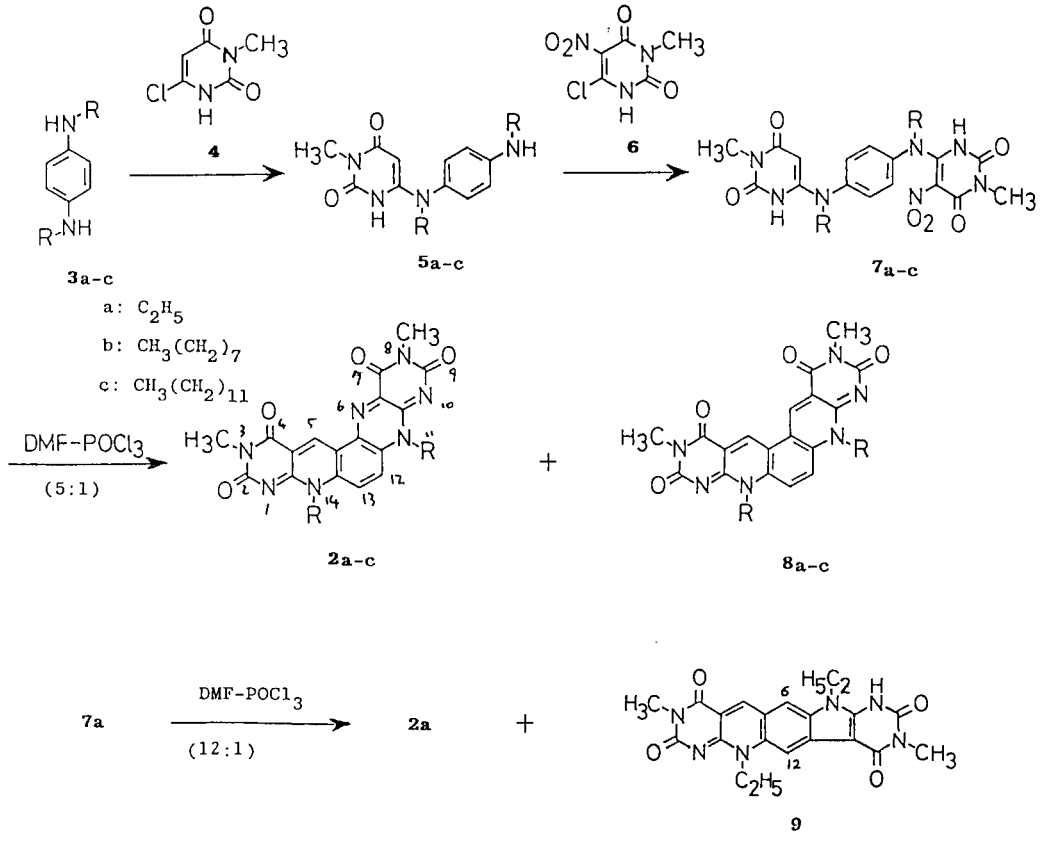


2



11

Scheme 2



Scheme 3

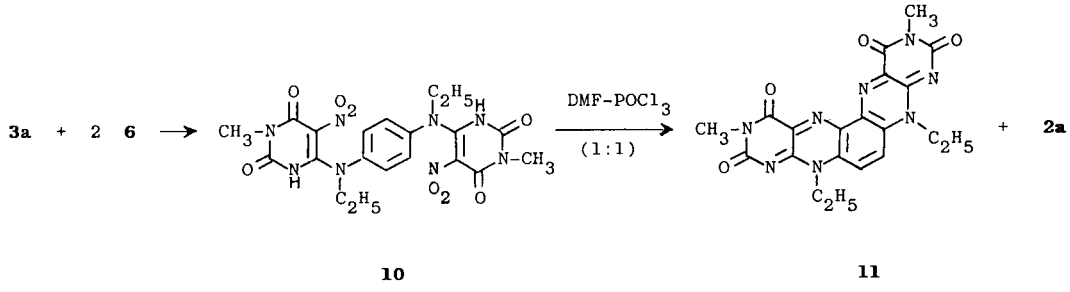


Table 1

Synthesis of *N,N'*-Dialkyl-*N*-(3-methyluracil-6-yl)-*p*-phenylenediamines **5a-c**

Compound	R	Yield (%)	Mp (°C)	Formula	Analysis (%) Calcd./Found C	H	N
5a	C_2H_5	51	216	$C_{15}H_{20}N_4O_2$	62.48 62.41	6.99 7.00	19.43 19.16
5b	$CH_3(CH_2)_7$	57	113	$C_{27}H_{44}N_4O_2$	71.01 71.01	9.71 9.95	12.27 12.30
5c	$CH_3(CH_2)_{11}$	59	89	$C_{35}H_{60}N_4O_2$	73.89 73.84	10.63 10.73	9.85 9.71

Table 2

Synthesis of Angular Mixed Flavins **2a-c** and Angular Doubled 5-Deazaflavins **8a-c**

Compound	R	Yield (%) [a] 2	8	Mp (° C) of 2	Formula of 2	Analysis (%) of 2 Calcd./Found C	H	N	NMR [Deuteriotrifluoroacetuc acid: deuteriochloroform (1:1)] H-13	H-12	H-5
a	C_2H_5	31	3	>330	$C_{21}H_{17}N_7O_4 \cdot H_2O$	55.87 55.91	4.69 4.58	21.72 21.59	8.90 (d, J = 10 Hz)	9.00	10.83 [b]
b	$CH_3(CH_2)_7$	6	2	280	$C_{33}H_{43}N_7O_4$	65.87 65.90	7.20 7.24	16.30 16.22	8.74-9.00 (br)		10.83
c	$CH_3(CH_2)_{11}$	4	1	273	$C_{41}H_{59}N_7O_4$	68.97 69.01	8.33 8.22	13.73 13.57	8.70-9.03 (br)		10.83

[a] Based on compounds **5**. [b] Coupling constant of H-13 and H-12 of **2a**.

Table 3

Synthesis of Linear Doubled Flavins **14a,b**

Compound	R	Yield (%) [a]	Mp (° C)	Formula	Analysis (%) of 2 Calcd./Found C	H	N	NMR [Deuteriotrifluoroacetic acid:deuteriochloroform (1:1)] H-6 and H-13
14a	C_2H_5	75	>330	$C_{20}H_{18}N_8O_4$	55.29 54.94	4.18 3.81	25.80 25.47	9.15
14b	$CH_3(CH_2)_7$	20	>330	$C_{32}H_{42}N_8O_4$	63.76 63.62	7.02 6.90	18.59 18.61	9.02

[a] Based on compounds **12**.

Table 4

Synthesis of 10-Alkyl-7-[*N*-alkyl-*N*-(3-methyluracil-6-yl)]amino-3-methyl-5-deazaflavins **18a-c**

Compound	R	Yield (%)	Mp (° C)	Formula	Analysis (%) Calcd./Found C	H	N
18a	C_2H_5	10	312	$C_{21}H_{22}N_6O_4$	59.70 59.61	5.25 5.30	19.90 19.78
18b	$CH_3(CH_2)_7$	20	224	$C_{33}H_{46}N_6O_4$	67.09 66.99	7.85 7.91	14.23 14.01
18c	$CH_3(CH_2)_{11}$	28	207	$C_{41}H_{62}N_6O_4$	70.05 70.03	8.89 8.97	11.96 11.65

seen in Figure 1. This implies that compound **2** have the same conjugated system as that of compound **8**.

When compound **7a** was treated with the DMF rich Vilsmeier reagent (DMF:phosphoryl chloride = 12: v/v) in chloroform, a linear type 1,3,7,8,10,13-hexaazaindeno-[2,3-*h*]anthracene-2,4,9,11(13*H*,3*H*,8*H*,10*H*)-tetrone **9** was obtained along with an angular mixed flavin **2a** (Scheme 2). The structure of compound **9** was determined by direct ^{1}H nmr examination. The signals of C(6)-H and C(12)-H of **9** existed as two sharp singlets at δ 8.49 ppm and δ 8.90 ppm respectively. Therefore, the structure of **9** turned out to have a linear form.

Next, we planned to synthesize "angular doubled flavins", which contain two flavin moieties with a benzene unit in common in the molecule, according to the same synthetic methodology as above.

The starting material, compound **3a** was treated with 2 molar amounts of 6-chloro-5-nitro-3-methyluracil (**6**) to give *N,N'*-diethyl-*N,N'*-di(5-nitro-3-methyluracil-6-yl)-*p*-phenylenediamine (**10**). Cyclization of **10** with the Vilsmeier reagent (DMF:phosphoryl chloride = 1:1 v/v) gave 1,3,5,6,8,10,11,14-octaazapentaphene-2,4,7,9(14*H*,-3*H*,8*H*,11*H*)-tetrone (angular doubled flavin) **11** along with angular mixed flavin **2a** (Scheme 3).

The uv and visible spectra of compound **11** showed a similar absorption pattern with a slight bathochromic shift to that of the corresponding angular mixed flavin **2c**. This suggested that compound **11** has the same conjugated system as that of compound **2** (Figure 1). In order to determine definitely the structure of **11** in comparison with that of "linear doubled flavins" **14**, we synthesized compounds **14** according to the known procedure [5].

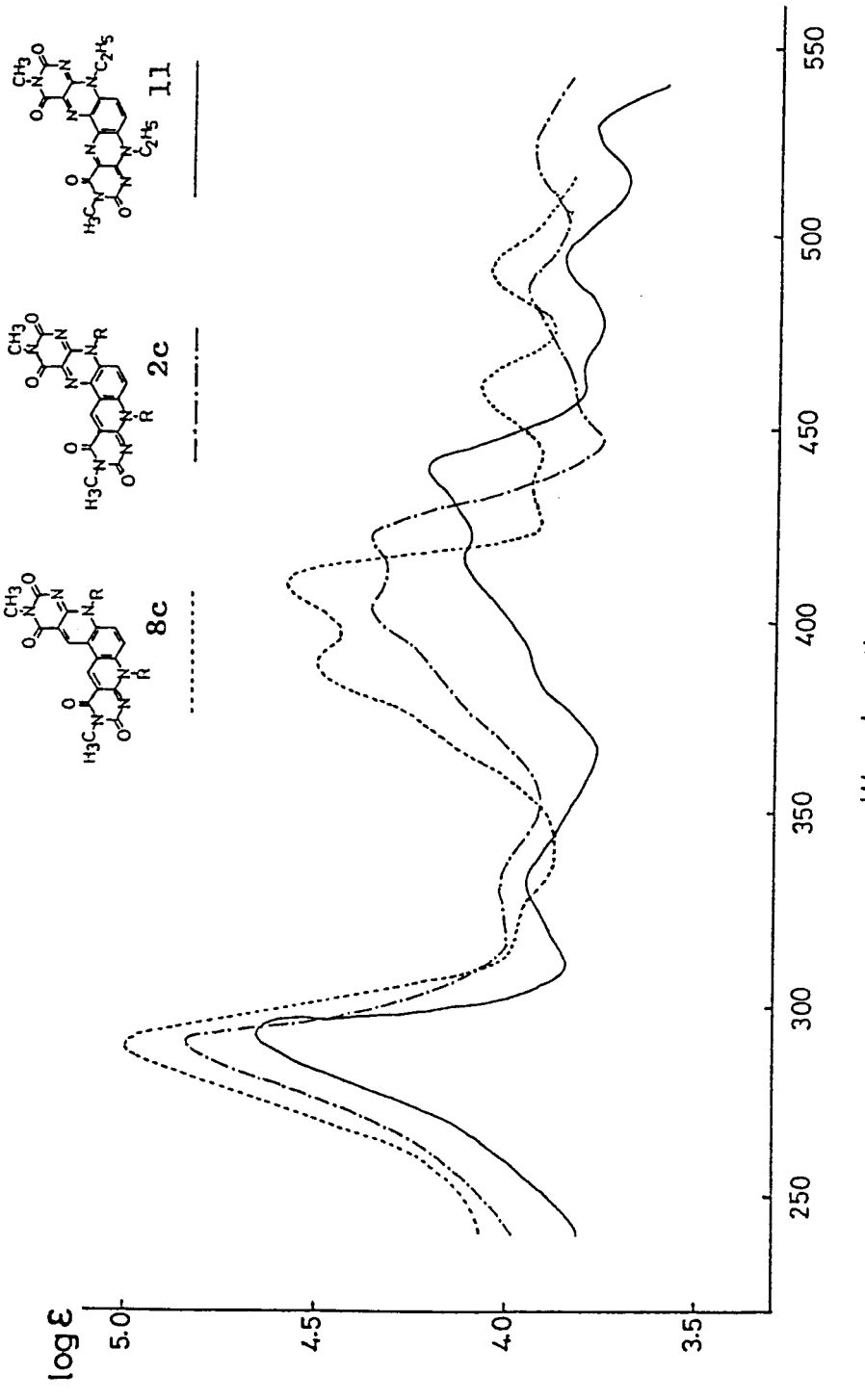

11
2c
8c
log ε
5.0
4.5
4.0
3.5
250
300
350
400
450
500
550
Wavelength, nm

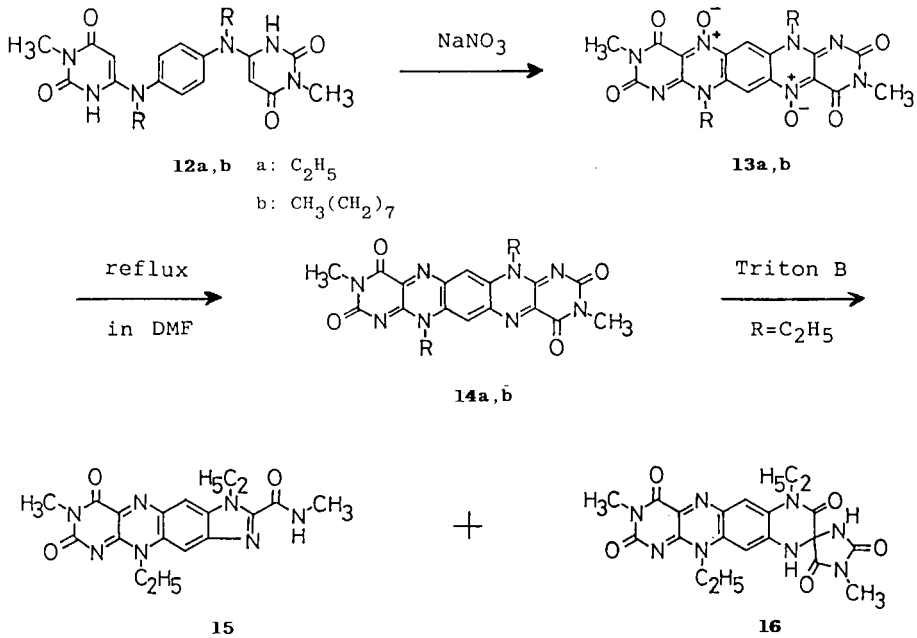
Figure 1

Thus, *N,N'*-dialkyl-*N'*-di(3-methyluracil-6-yl)-*p*-phenylenediamines **12a,b** [4] were treated with sodium nitrate and sulfuric acid in acetic acid to give the corresponding linear doubled flavin 5,12-di-*N*-oxide **13a,b**. This ring closure is an application of the flavin *N*-oxide synthesis by nitrative cyclization [6]. Compounds **13a,b** were refluxed in DMF to eliminate the *N*-oxide group to give the linear doubled flavins **14a,b** (Table 3). Furthermore, compound **14a** was treated with Triton B to give rise to 7,11-diethyl-3-methyl-1,3,5,7,9,11-hexaazaimidazo[5,4-*h*]anthracene-2,4(11*H*,3*H*)-dione-8-*N*-methylcarboxamide (**15**) and a spiro compound **16** (Scheme 4).

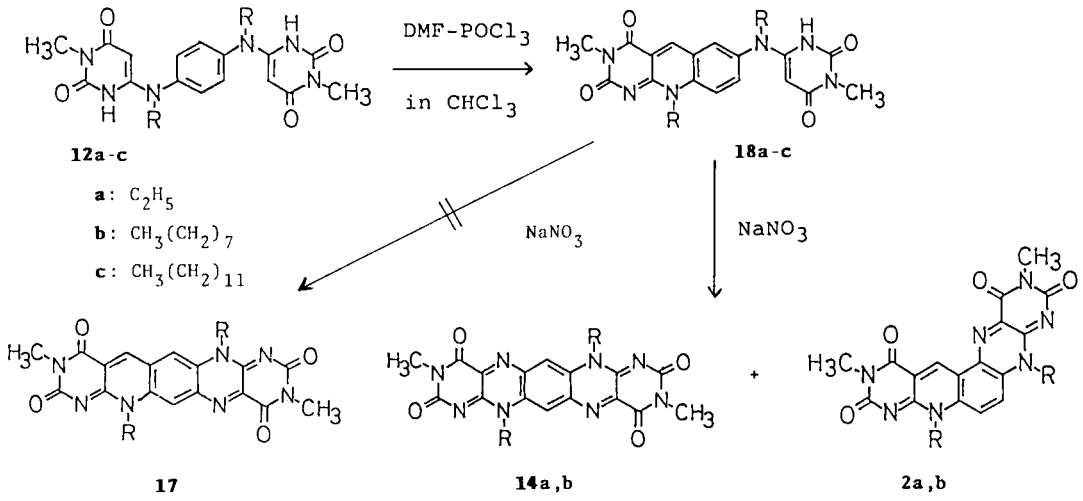
In the ^{1}H nmr spectrum, the equivalent signal of C(6)-H and C(13)-H of compound **14** at δ 9.15 ppm (in deuteriotrifluoroacetic acid:deuteriochloroform = 1:1) was split into δ 8.76 ppm (s) and δ 8.91 ppm (s) in that of the spiro compound **16** respectively, because of disappearance of the symmetry of compound **14**. Therefore, the structure of **14** turned out to have a linear form. Namely, the structure of **11** turned out to have an angular form.

As mentioned above, the cyclization of compound **10** with Vilsmeier reagent gave the angular compounds such as compounds **11**, while the cyclization of compounds **12** by nitration gave the linear compounds such as compound

Scheme 4



Scheme 5



14. Therefore, for the purpose of synthesizing the linear type mixed flavins, 1,3,7,8,10,12,14-heptaazapentacene-2,-4,9,11(14*H*,3*H*,7*H*,10*H*)-tetrones **17**, we have examined the nitrative cyclization of the initially formed 10-alkyl-7-[*N*-alkyl-*N*-(3-methyluracil-6-yl)-amino-3-methyl-5-deazaflavins **18**.

Thus, *N,N'*-dialkyl-*N,N'*-di(3-methyluracil-6-yl)-*p*-phenylenediamines **12** was treated with the Vilsmeier reagent (DMF:phosphoryl chloride = 7:1 v/v) in chloroform to give the partially cyclized 5-deazaflavins **18** (Table 4). Subsequently compounds **18** were treated with sodium nitrate and sulfuric acid in acetic acid at 90° to give no target linear mixed flavins **17** but the corresponding angular mixed flavins **2** and surprisingly linear doubled flavins **14** in moderate yields. (Scheme 5). This result shows that the 5-deazaflavin ring changed into the flavin ring under nitrative conditions. Although the mechanism is not clear at the moment, it may be assumed that the partially cyclized 5-deazaflavins **18** suffer ring opening by the nitrative oxidation followed by ring closure again with nitration to give linear doubled flavins **14**. Such a ring conversion of 5-deazaflavin to flavin would be interesting from the viewpoint of chemical evolution.

EXPERIMENTAL

All melting points were determined on a Yanagimoto hot-stage apparatus, and are uncorrected. The ir spectra were obtained on a Shimazu IR-400 spectrometer and the ^{1}H nmr spectra on a JEOL FX 200 spectrometer. Mass spectra were taken on a JEOL JMS OISG-2 instrument by direct insertion at 70 eV. The uv and visible spectra were obtained on a Hitachi model 200-20 spectrophotometer. Column chromatography was carried out with Silica gel 60 (E. M. Merk, 230 mesh) and Wakogel-200 and Wakogel-300. Preparative tlc was run on 20 x 20 cm plates coated with a 0.25-0.5 mm layer of Merk silica gel GF 254 and PF 254.

Synthesis of *N,N'*-Dialkyl-*N*-(3-methyluracil-6-yl)-*p*-phenylenediamines **5a-c**.

General Procedure.

A mixture of *N,N'*-dialkyl-*p*-phenylenediamines **3a-c** (9.1 mmoles) and 6-chloro-3-methyluracil (**4**) (11.0 mmoles) and triethylamine (5 ml) of *N,N*-diethylaniline (5 ml) in *n*-butanol (50 ml) was refluxed for 5-10 hours under an argon atmosphere. The reaction mixture was evaporated to dryness under reduced pressure and the residue was diluted with methanol. The precipitate was filtered off and recrystallized from methanol, or purified by column chromatography (chloroform) and recrystallized from methanol to give the corresponding *N,N'*-dialkyl-*N*-(3-methyluracil-6-yl)-*p*-phenylenediamines **5a-c** as colorless powders (Table 1).

Synthesis of *N,N'*-Diethyl-*N*-(3-methyluracil-6-yl)-*N'*-(5-nitro-3-methyluracil-6-yl)-*p*-phenylenediamine (**7a**).

A mixture of compound **5a** (1.2 g, 4.2 mmoles) and 6-chloro-5-nitro-3-methyluracil (**6**) (7.4 mmoles) and *N,N*-diethylaniline (2.4 ml) in chloroform (5 ml) and ethanol (5 ml) was refluxed for 3 hours under an argon atmosphere. The reaction mixture was evaporated to dryness under reduced pressure and the residue was diluted with methanol. The precipitate was filtered off and washed with boiling methanol and then ether to give *N,N'*-diethyl-*N'*-(3-methyluracil-6-yl)-*N'*-(5-nitro-3-methyluracil-6-yl)-*p*-phenylenediamine (**7a**) (1.7 g, 90% yield based on **5a**) as a pale yellow powder, mp 310°; ir (Nujol): 1710, 1700, 1600 cm^{-1}; ^{1}H nmr [200 MHz, deuteriotrifluoroacetic acid:deuteriochloroform (1:1)]: δ 3.45 (s, 3H, 3''-NCH$_3$), 3.49 (s, 3H, 3'-NCH$_3$), 3.90 (q, J = 7 Hz, 2H, N'-CH$_2$), 4.11 (q, J = 7 Hz, 2H, N-CH$_2$), 7.33 (d, J = 9 Hz, 2H, H-2 and H-6), 7.44 (d, J = 9 Hz, 2H, H-3 and H-5).

Anal. Calcd. for $C_{10}H_{28}N_7O_6$: C, 52.51; H, 5.07; N, 21.43. Found: C, 52.22; H, 4.97; N, 21.15.

Synthesis of *N,N'*-Dialkyl-*N*-(3-methyluracil-6-yl)-*N'*-(5-nitro-3-methyluracil-6-yl)-*p*-phenylenediamines **7b,c**.

A mixture of compounds **5b,c** (0.35 mmole) and compound **6** (0.97 mmole) in chloroform (15 ml) was refluxed for 24 hours under an argon atmosphere. The reaction mixture was evaporated to dryness under reduced pressure and the residue was diluted with methanol. The precipitate was filtered off and washed with methanol to give the corresponding *N,N'*-dialkyl-*N*-(3-methyluracil-6-yl)-*N'*-(5-nitro-3-methyluracil-6-yl)-*p*-phenylenediamines **7b,c** as pale yellow powder. Compounds **7b,c** were unstable in air and so we used them for the next step without purification.

Synthesis of 1,3,6,8,10,11,14-Heptaazapentaphene-2,4,7,9(14*H*,-3*H*,8*H*,11*H*)-tetrones (Angular Mixed Flavins) **2a-c**.

General Procedure.

A mixture of compounds **7a-c** (0.22 mmole) and Vilsmeier reagent (DMF:phosphoryl chloride = 5:1 v/v) (6 ml) was heated at 100° for 5 hours under argon atmosphere. The reaction mixture was cooled and diluted with methanol. The precipitate was filtered off, washed with methanol and ether, and then chromatographed. The first fraction eluted with chloroform-acetone was recrystallized from chloroform-methanol to give the corresponding angular doubled 5-deazaflavins **8a-c** as yellow powder. The next fraction was recrystallized from chloroform-methanol to give the corresponding angular mixed flavins **2a-c** as orange powder (Table 2).

Synthesis of 1,3,7,8,10,13-hexaazaindeno[2,3-*h*]anthracene-2,4,-9,11(13*H*,3*H*,8*H*,10*H*)-tetrone **9**.

A mixture of compound **7a** (300 mg, 0.66 mmole) and Vilsmeier reagent (DMF:phosphoryl chloride = 12:1 v/v) (16.5 ml) in chloroform (15 ml) was stirred for 20 hours under argon atmosphere. The reaction mixture was evaporated to dryness under reduced pressure and the residue was diluted with methanol. The precipitate was filtered off, washed with methanol and ether, and further refluxed in DMF (60 ml) for 5 hours. The reaction mixture was evaporated to dryness under reduced pressure and chromatographed. The first fraction eluted with chloroform-methanol (10:1) was recrystallized from chloroform-methanol to give the 1,3,7,8,-10,13-hexaazaindeno[2,3-*h*]anthracene-2,4,9,11(13*H*,3*H*,8*H*,-10*H*)-tetrone **9** (21 mg, 7% yield based on **7a**) as yellow powder, mp >330°; ir (Nujol): 1720, 1690, 1670, 1600 cm^{-1}; nmr [200 MHz, deuteriotrifluoroacetic acid:deuteriochloroform (1:1)]: δ 3.63 (s, 3H, 10-NCH$_3$), 3.64 (s, 3H, 3-NCH$_3$), 4.56 (q, J = 7 Hz, 2H, 7-NCH$_2$), 5.12 (q, J = 7 Hz, 2H, 13-NCH$_2$), 8.49 (s, 1H, H-12), 8.90 (s, 1H, H-6), 9.84 (s, 1H, H-5).

Anal. Calcd. for $C_{21}H_{20}N_6O_4$: C, 59.99; H, 4.80; N, 19.99. Found: C, 59.68; H, 4.60; N, 19.48.

The next fraction was recrystallized from chloroform-methanol to give 3,8-dimethyl-11,14-diethyl-angular mixed flavin (**2a**) (41 mg, 14% yield based on **7a**) as an orange powder.

Synthesis of *N,N'*-Diethyl-*N,N'*-di(5-nitro-3-methyluracil-6-yl)-*p*-phenylenediamine (**10**).

A mixture of *N,N'*-diethyl-*p*-phenylenediamine (**3a**) (409 mg, 2.5 mmoles) and 6-chloro-5-nitro-3-methyluracil (**6**) (1231 mg, 6.0 mmoles) in diethylaniline (2 ml) was heated at 100° for 2.5 hours under an argon atmosphere. The reaction mixture was cooled and diluted with methanol. The precipitate was filtered off and washed with methanol and ether to give *N,N'*-diethyl-*N,N'*-di(5-nitro-3-methyluracil-6-yl)-*p*-phenylenediamine (**10**) (965 mg, 77% yield based on **3a**) as a pale yellow powder, mp >300°; ir (Nujol): 1720, 1700, 1660, 1590 cm^{-1}; nmr [200 MHz, deuteriotrifluoroacetic acid:deuteriochloroform (1:1)]: δ 3.44 (s, 6H, 3'-NCH_3 and 3''-NCH_3), 4.06 (q, J = 7 Hz, 4H, N-CH_2 and N'-CH_2), 7.28 (s, 4H, H-2, H-3, H-5, and H-6).

Anal. Calcd. for $C_{20}H_{22}N_8O_8$: C, 47.81; H, 4.41; N, 22.30. Found: C, 47.55; H, 4.42; N, 22.55.

Synthesis of 3,8-Dimethyl-11,14-diethyl-1,3,5,6,8,10,11,14-octaazapentaphene-2,4,7,9(14*H*,3*H*,8*H*,11*H*)-tetrone (3,8-Dimethyl-11,14-diethyl-Angular Doubled Flavin) (**11**).

A mixture of *N,N'*-diethyl-*N,N'*-di(5-nitro-3-methyluracil-6-yl)-*p*-phenylenediamine (**10**) (500 mg, 1.0 mmole) and the Vilsmeier reagent (DMF:phosphoryl chloride = 1:1 v/v) was heated at 100-110° for 2 hours under an argon atmosphere. The reaction mixture was cooled, diluted with methanol and evaporated to dryness under reduced pressure. The residue was chromatographed [chloroform-acetone (4:1)] and purified by preparative tlc [chloroform-actone (3:1)]. The first fraction was recrystallized from chloroform-methanol to give 3,8-dimethyl-11,14-diethyl-angular mixed flavin (**2a**) (10 mg, 2% yield based on **10**) as an orange powder. The next fraction was recrystallized from chloroform-methanol to give 3,8-dimethyl-11,14-diethyl-angular doubled flavin (**11**) (30 mg, 7% yield based on **10**) as a red powder, mp >330°; ir (Nujol): 1710, 1660, 1600, 1590 cm^{-1}; nmr [200 MHz, deuteriotrifluoroacetic acid:deuteriochloroform (1:1)]: δ 3.64 (s, 6H, 3-NCH_3 and 8-NCH_3), 4.84-5.33 (br, 4H, 11-NCH_2 and 14-NCH_2), 8.87 (s, 2H, H-12 and H-13).

Anal. Calcd. for $C_{20}H_{16}N_8O_4$: C, 55.29; H, 4.18; N, 25.80. Found: C, 55.37; H, 4.20; N, 25.66.

Synthesis of 7,14-Dialkyl-3,10-dimethyl-1,3,5,7,8,10,12,14-octaazapentacene-2,4,9,11(14*H*,3*H*,7*H*,10*H*)-tetrones (7,14-Dialkyl-3,10-dimethyl-Linear Doubled Flavins) **14a,b**.

General Procedure.

A mixture of *N,N'*-dialkyl-*N,N'*-di(3-methyluracil-6-yl)-*p*-phenylenediamines **12** (1.47 mmoles), sodium nitrate (8.81 mmoles), and sulfuric acid (1.5 mmoles) in acetic acid (9.1 ml) was heated at 90° for 8 hours under argon atmosphere. The reaction mixture was cooled and diluted with methanol. The precipitate was filtered off and washed with methanol to give the corresponding 7,14-dialkyl-3,10-dimethyl-linear doubled flavin 5,7-di-*N*-oxide **13** as purple powder. Compounds **13** were refluxed for 4 hours in DMF (300 ml) to eliminate oxygens from the *N*-oxide groups. The reaction mixture was evaporated to dryness under reduced pressure and the residue was diluted with methanol. The precipitate was filtered off, washed with methanol, and recrystallized from chloroform-methanol to give the corresponding 7,14-dialkyl-3,10-dimethyl-linear doubled flavins **14** as dark red powder (Table 3).

Structure Determination of 7,14-Diethyl-3,10-dimethyl-Linear Doubled Flavin (**14a**) by Partial Hydrolysis.

A mixture of compound **14a** (200 mg, 0.5 mmole) and 40% methanol solution of Triton B (0.7 mmole) in DMF (40 ml) was heated at 120-130° for 50 hours under an argon atmosphere in the dark. The reaction mixture was cooled, neutralized with acetic acid, evaporated to dryness under reduced pressure, and the residue was chromatographed. The fraction eluted with chloroform-acetone (10:1) was recrystallized from methanol to give 7,11-diethyl-1,3,5,7,9,11-hexaazaimidazo[5,4-*i*]anthracene-2,4-(11*H*,3*H*)-dione-8-*N*-methylcarboxamide (**15**) (11 mg, 6% yield based on **14a**) as red powder, mp >330°; ir (Nujol): 1715, 1685, 1670 cm^{-1}; nmr [200 MHz, deuteriotrifluoroacetic acid:deuteriochloroform (1:1)]: δ 3.22 (s, 3H, N-CH_3), 3.69 (s, 3H, 3-NCH_3), 4.89-5.23 (m, 4H, 7-NCH_2 and 11-NCH_2), 8.76 (s, 1H, H-10), 8.92 (s, 1H, H-6); Calcd. Mass for $C_{16}H_{19}N_7O_3$: 381.15493. Found: m/z 381.15520.

Anal. Calcd. for $C_{16}H_{19}N_7O_3$: C, 56.69; H, 5.02; N, 25.71. Found: C, 56.29; H, 4.80; N, 25.61.

The fraction eluted with chloroform-acetone (10:2) was recrystallized from chloroform-methanol-acetone-ether to give spiro compound, 7',12'-diethyl-3'-methyl-1-methylspiro[imidazolidine-4,9'(10'*H*)-1',3',5',7',10',12'-hexaazanaphthacene]-2,2',4',5,8'-(3*H*,12'*H*,3'*H*,1*H*,7'*H*)-pentone (**16**) (3 mg, 1% yield based on **14a**) as an orange powder, mp ∇330°; ir (Nujol): 1790, 1730, 1680, 1620 cm^{-1}; ^1H nmr [200 MHz, deuteriotrifluoroacetic acid:deuteriochloroform (1:1)]: δ 3.20 (s, 3H, 1-NCH_3), 3.63 (s, 3H, 3'-NCH_3), 4.20-4.38 (m, 2H, 7'-NCH_2), 4.67-4.98 (m, 2H, 12'-NCH_2), 7.50 (br, 1H, H-11'), 7.93 (s, 1H, H-6'); Calcd. Mass for $C_{20}H_{20}N_8O_5$: 452.15565. Found: m/z 452.15512.

Anal. Calcd. for $C_{20}H_{20}N_8O_5 \cdot H_2O$: C, 51.06; H, 4.71; O, 23.82. Found: C, 51.26; H, 4.38; N, 23.52.

Synthesis of 10-Alkyl-7-[*N*-alkyl-*N*-(3-methyluracil-6-yl)]amino-3-methyl-5-deazaflavins **8a-c**.

General Procedure.

A mixture of *N,N'*-dialkyl-*N,N'*-di(3-methyluracil-6-yl)-*p*-phenylenediamines **12a-c** (0.73 mmole) and the Vilsmeier reagent (DMF:phosphoryl chloride = 7:1 v/v) (23 ml) in chloroform (20 ml) was stirred for 17 hours under argon atmosphere. The reaction mixture was cooled, diluted with methanol, and evaporated to dryness under reduced pressure, and then the residue was chromatographed. The fraction eluted with chloroform-acetone was recrystallized from chloroform-methanol to give the corresponding 10-alkyl-7-[*N*-alkyl-*N*-(3-methyluracil-6-yl)]-amino-3-methyl-5-deazaflavins **18a-c** as a yellow powder (Table 4).

Nitrative Cyclization of 10-Alkyl-7-[*N*-alkyl-*N*-(3-methyluracil-6-yl)]amino-3-methyl-5-deazaflavins **18a,b**.

General Procedure.

A mixture of **18a,b** (0.12 mmole), sodium nitrate (0.48 mmole), and sulfuric acid (0.6 mmole) in acetic acid (0.8 ml) was heated at

90° for 10 hours under argon atmosphere. The reaction mixture was cooled and chromatographed. The fraction eluted with chloroform-acetone was recyrstallized from chloroform-methanol to give the corresponding angular mixed flavins **2a,b** as orange powder in 15 and 6% yield respectively. The next fraction eluted was recrystallized from chloroform-methanol to give the corresponding linear doubled flavins **14a,b** as a dark red powder in 12 and 19% yield respectively.

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