

**FACILE SYNTHESIS OF 4a-FLUORO-5,10-ETHENOBENZO[f]-QUINAZOLINES THROUGH 1,4-PHOTOCYCLOADDITION OF 5-FLUORO-1,3-DIMETHYLURACIL WITH SUBSTITUTED NAPHTHALENES<sup>1</sup>**

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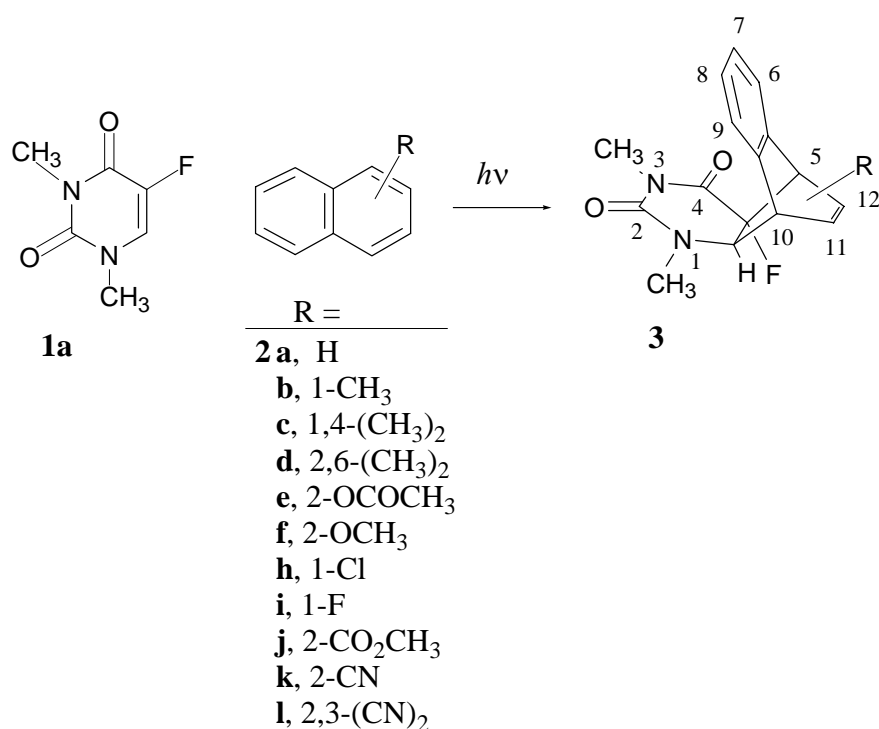
**Abstract**— UV-irradiation of 6-chloro-1,3-dimethyluracil with naphthalenes underwent 1,2-cycloaddition to give naphthocyclobutapyrimidines consisting of a cyclobutene ring. The same reaction of an aprotic solution of 5-fluoro-1,3-dimethyluracil and naphthalenes bearing various substituents underwent 1,4-cycloaddition mode-selectively to give the corresponding ethenobenzoquinazoline derivatives with H and F atoms remaining intact on the newly constructed barrelene moiety. In protic solvents, the reaction preferentially proceeded by way of a substitution reaction to afford 5-(1-naphthyl)uracil.

Photocycloaddition of olefins to aromatic hydrocarbons has been well recognized as a versatile method for constructing a variety of highly strained ring systems.<sup>2</sup> During the course of our continuing studies on the photochemical reaction of uracil derivatives with aromatic compounds, we have found that 6-chloro-1,3-dimethyluracil (6-CIDMU) reacted with benzene at C6 to give the substitution product 6-phenyl-1,3-dimethyluracil DMU in fair yield, whereas in the presence of trifluoroacetic acid (TFA), 6-CIDMU and benzene underwent 1,2-cycloaddition to give cyclooctapyrimidines at room temperature,<sup>3</sup> or pentalenopyrimidines at low temperature.<sup>4</sup> Certain cyclooctapyrimidines were further converted into various novel valence isomers, including bond-switching isomers,<sup>5</sup> and cyclobutaquinazoline derivatives,<sup>6</sup> or pentalenopyrimidines,<sup>7</sup> which were further transformed into highly strained pentacyclic cage compounds by way of variety of electrocyclic processes.

In contrast, photoreaction of a mixture of 5-halo-DMU (5-XDMU; X = Cl, Br, I) and benzene derivatives primarily resulted in the formation of 5-aryl-1,3-dimethyluracils through a conventional aromatic photosubstitution reaction. Addition of TFA to the solution only served to promote the substitution reaction. Similar photoreaction with 5-fluoro-DMU (5-FDMU; **1a**) was found to undergo substitution reaction only upon the addition of TFA,<sup>8,9</sup> however, no cycloadducts were obtained from the reaction with benzenes.<sup>8</sup> Meanwhile, naphthalene and/or its derivatives have been reported to undergo cycloaddition reaction with olefins in various manners including 1,2-,<sup>10,11</sup> 1,4-,<sup>10,11</sup> 1,3-,<sup>12</sup> 1,8-,<sup>13</sup> and/or [4 + 4] cycloadditions<sup>10,14</sup> to give various ring systems. In fact, we have recently demonstrated that UV-irradiation of a solution of 6-CIDMU and naphthalene (**2a**) in a non-polar solvent containing TFA underwent 1,2-cycloaddition (= [2 + 2] cycloaddition) followed by subsequent dehydrochlorination to give cyclobutapyrimidine derivatives in fair yields.<sup>15</sup>

Hence, our attention is focused on the photoreaction of 5-X-1,3-dimethyluracils (**1a**; X = F, **1b**; X = Cl) with naphthalenes (**2**).

In the present paper, we report on the photochemical synthesis of benzopyrimidobarrelene derivatives (**3**) from 5-FDMU (**1a**) and various naphthalenes (**2**).



Scheme 1

A solution of 5-CIDMU (**1b**) and naphthalene (**2a**) in cyclohexane was irradiated with a 500 W

high-pressure mercury lamp in a degassed Pyrex tube ( $\lambda > 300$  nm) for 1 h at ambient temperature to give the conventional substitution product, 1,3-dimethyl-5-(1-naphthyl)pyrimidine-2,4-dione (**4a**), in fair yield. In contrast, irradiation of 5-FDMU (**1a**) and (**2a**) under the analogous conditions gave rise to the formation of a novel 1,4-cycloadduct (= [4 + 2]-cycloadduct), benzopyrimidobarrelene (**3a**), in high yield (91 % based on consumed amounts of **1a**) (Scheme 1, Table 1).

Table 1. Photoreaction (1 h) of 5-FDMU and naphthalene in various solvents<sup>a)</sup>

Solvent	Molar equiv. <b>2a</b>	Yields (%) of		<b>1a</b> consumed (%)
		<b>3a</b>	<b>4a</b>	
Cyclohexane	90	82	0	91
Cyclohexane	10	80	0	90
Cyclohexane	1	82	0	90
Benzene	1	55	0	58
CH <sub>3</sub> CN	1	21	0	28
CH <sub>3</sub> OH	1	0	23	42
Cyclohexane +TFA	1	9	26	65

a) Reaction conditions; an equivalent molar solution of **1a** and **2a** (0.03 mmol) in a solvent (20 mL) was irradiated for 1 h, and the yields of the products were determined by means of <sup>1</sup>H-NMR spectroscopy.

We then investigated the solvent effect on the present photocycloaddition. The 1,4-addition proceeded in various aprotic solvents to give the cycloadduct (**3a**) in similar yields, though the reaction proceeded less effectively as the polarity of the solvent is increased. Contrastingly, substitution reaction proceeded exclusively in the protic solvent methanol to give 5-(1-naphthyl)DMU (**4a**). The substitution reaction was also effected by the addition of TFA to a solution of cyclohexane to afford **4a** together with **3a**.

We then applied the present reaction to various naphthalenes.

First we have examined the photoreaction with naphthalenes having electron-donating groups (**2b**, **2c**).

Photoreaction with 1-methylnaphthalene (**2b**) in cyclohexane for 3 h gave 5-, 10-, 9-, and 6-methyl derivatives of 1,4-cycloadducts (**3b<sub>i</sub>**, **3b<sub>ii</sub>**, **3b<sub>iii</sub>**, and **3b<sub>iv</sub>**) with the *cis*-geometry in 33 %, 30 %, 24 %, and 13 % yields, respectively (Scheme 1, Table 2).

Similar photoreaction with 1,4-dimethylnaphthalene (**2c**) afforded the 5,10-dimethyl (**3c<sub>i</sub>**) and 6,9-dimethyl (**3c<sub>ii</sub>**) derivatives of 1,4-adducts in 50 % and 27 % yields.

Similarly 2,6-dimethylnaphthalene (**2d**) afforded the 8,12-dimethyl (**3d<sub>i</sub>**) and 7,11-dimethyl derivatives (**3d<sub>ii</sub>**) in high yields (65 % and 22 %, respectively).

Photoreaction with 2-acetoxynaphthalene (**2e**) proceeded *via* 1,4-cycloaddition preferentially on the ring bearing the acetoxy group to afford the 12-, 11-, 7-, and 8-acetoxy isomers (**3e<sub>i-iv</sub>**) in 34 %, 31 %, 8 %, and 3 % yield, respectively.

Irradiation of 2-methoxynaphthalene (**2f**) furnished the mixture of 1,4-adducts with a methoxy group at C-12 (**3f<sub>i</sub>**), C-11 (**3f<sub>ii</sub>**), C-8 (**3f<sub>iii</sub>**), and C-7 (**3f<sub>iv</sub>**) in 34, 20, 20, and 12 % yields, respectively.

In the case of 2-*N,N*-dimethylaminonaphthalene (**2g**), no cycloadduct was obtained.

We then carried out the photoreaction with  $\alpha$ -chloro- (**2h**) and  $\alpha$ -fluoronaphthalenes (**2i**) under the similar conditions. UV-irradiation of **2h** for 1 h yielded the 1,4-adduct with a chlorine substituted at the C-10 bridgehead (**3h<sub>i</sub>**) as the major product (27 %), together with the regioisomer with the chlorine atom at the C-9 on the benzene ring (**3h<sub>ii</sub>**) as the minor product (6 %) (at the stage where 40 % of **1a** has been consumed). Photoreaction of 1-fluoronaphthalene (**2i**) (1 h) furnished the 1,4-adduct with a fluorine atom on the olefinic carbon at C-11 (**3i<sub>i</sub>**) (31 % yield) and the regioisomer with the fluorine atom at the C-9 on the benzene ring (**3i<sub>ii</sub>**) (29% yield), respectively.

Similarly photoreaction with naphthalenes having electron-withdrawing groups at the  $\beta$ -position was examined: Photoreaction of methyl 2-naphthoate (**2j**) in cyclohexane gave 1,4-adduct (**3j**, R = 12-CO<sub>2</sub>CH<sub>3</sub>, 49 % yield) in high regio- and stereo-selectivity.<sup>1</sup>

In the case of 2-naphthonitrile (**2k**), 1,4-adduct (**3k<sub>i</sub>**) (12-CN) (34 %) was yielded as the major product, together with the regioisomer (**3k<sub>ii</sub>**) (11-CN) (7%) as a minor component.

The photoreaction of 2,3-dicyanonaphthalene (**2l**)<sup>1</sup> gave the corresponding 1,4-adduct (**3l**) as the sole product, though the reaction proceeded only sluggishly. In this case the photoreaction was performed in benzene or in acetonitrile, since **2l** is sparingly soluble in cyclohexane.

These results are summarized in Table 2.

Table 2. 1,4-Photocycloaddition of 5-FDMU (**1a**) with various naphthalenes (**2**).

<b>2x/</b> <b>x: R</b>	Reaction time (h)	1,4-adduct ( <b>3</b> )								
		Yield (%) <sup>a)</sup> ( <b>1a</b> consumed)	Isomer ratio (%)							
			<i>site</i>							
			5	10	11	12	7	8	6	9
<b>a: H</b>	1	91 (90)								
<b>b: 1-CH<sub>3</sub></b>	3	100 (91)	33	30					13	24
<b>c: 1,4-(CH<sub>3</sub>)<sub>2</sub></b>	3	77 (66)	65						35	
<b>d: 2,6-(CH<sub>3</sub>)<sub>2</sub></b>	3	87 (84)			25 <sup>b)</sup>	75 <sup>c)</sup>	/	/		
<b>e: 2-OAc</b>	0.5	76 (41)			41	45	11	4		
<b>f: 2-OCH<sub>3</sub></b>	1	86 (50)			23	40	14	23		
<b>g: 2-N(CH<sub>3</sub>)<sub>2</sub></b>	2	42 (70)								
<b>h: 1-Cl</b>	1	33 (40)		83						17
<b>i: 1-F</b>	1	60 (50)			52					48
<b>j: 2-CO<sub>2</sub>CH<sub>3</sub></b>	5	49 (96)				100				
<b>k: 2-CN</b>	1	45 (92)			17	83				
<b>l: 2,3-(CN)<sub>2</sub></b>	12	80 (30)			100					

a) Yields and the isomer ratios were determined by means of <sup>1</sup>H-NMR spectroscopy. b) 8,12-dimethyl isomer (**3d<sub>i</sub>**). c) 7,11-dimethyl derivative (**3d<sub>ii</sub>**).

Structural assignments, including the stereochemistry of **3a**<sup>1</sup> were made on the basis of detailed MS and <sup>1</sup>H-NMR spectroscopic studies.

The nuclear Overhauser effect (NOE) observed for the H-11 vinyl proton upon irradiation of the H-10a proton revealed the stereochemistry to be *cis*.

The structures of the other adducts (**3**) were determined on the basis of the similarity in their <sup>1</sup>H chemical shifts and the <sup>1</sup>H-<sup>1</sup>H coupling constants as listed in Tables 3 and 4, respectively.

We have previously reported that the photoreaction of **1a** with naphthalenes with an electron-withdrawing group, acetyl (**2m**) and cyano (**2n**), at the  $\alpha$ -position gave exceptional results; **2m** gave rise to the predominant formation of the unexpected *trans* 1,4-adduct as the major product, while **2n** preferentially furnished the 1,4-adduct having the cyano group on the benzene ring.<sup>16</sup> These results were explained as follows: In the case of acetonephthone, *cis*-oriented 1,4-adducts with the acetyl group at the bridgehead were initially formed as the major reaction components. However, these compounds are fragile in the dark at ambient temperature, and rapidly undergo cycloreversion back to the starting materials, resulting in the accumulation of the minor but thermochemically more stable component in the reaction mixture

upon continuing irradiation. Thus, prolonged irradiation of 1-acetonaphthone (**2m**) gave rise to the formation of the *trans*-isomer as the predominant product. In the case of 1-naphthonitrile (**2n**), the *cis*-oriented 1,4-adduct having the cyano group on the benzene moiety was accumulated as the thermodynamically controlled product through a similar mechanism.

Table3. <sup>1</sup>H-NMR Chemical Shifts,  $\delta$ (ppm), for Fluoroethenobenzoquinazolines (**3a-l**).

Compd.	N <sup>1</sup> -CH <sub>3</sub>	N <sup>3</sup> -CH <sub>3</sub>	5	10	10a	11	12	Aromatics	Others (CH <sub>3</sub> )
<b>3a</b> <sup>a)</sup>	3.10	2.71	4.64	4.29	3.58	6.74	6.68	7.11-7.23	
<b>3b</b> <sup>i,a)</sup>	3.10	2.65	--	4.28	3.68	6.77	6.34	7.18-7.40	1.94
<b>3b</b> <sup>ii,a)</sup>	3.10	2.56	4.53	--	3.44	6.46	6.67	7.10-7.27	1.83
<b>3b</b> <sup>iii,a)</sup>	3.13	2.68	4.60	4.51	3.54	6.72	6.66	6.97-7.01	2.32
<b>3b</b> <sup>iv,b)</sup>	3.08	2.72	4.88	4.23	3.52	6.72	6.66	6.94-7.24	2.29
<b>3c</b> <sup>a)</sup>	3.15	2.42	--	--	3.46	6.45	6.25	7.18-7.27	1.83, 1.93
<b>3c</b> <sup>i,a)</sup>	3.12	2.84	4.87	4.48	3.54	6.74	6.67	6.84	2.26, 2.30
<b>3d</b> <sup>i,a)</sup>	3.07	2.73	4.87	4.01	3.58	6.24	--	6.74-7.02	2.00, 2.26
<b>3d</b> <sup>ii,a)</sup>	3.07	2.72	4.44	3.91	3.53	--	6.22	6.93-7.08	2.00, 2.26
<b>3e</b> <sup>a)</sup>	3.09	2.72	4.51	4.23	3.73	6.53	--	7.1-7.3	2.19
<b>3e</b> <sup>i,a)</sup>	3.10	2.73	4.60	4.15	4.25	--	6.15	7.1-7.3	2.24
<b>3e</b> <sup>ii,a)</sup>	3.10	2.79	4.62	4.28	3.58	6.70	6.70	6.85-7.20	2.25
<b>3e</b> <sup>iv,a)</sup>	3.05	2.70	4.59	4.22	3.53	6.66	6.66	6.82-7.10	2.26
<b>3f</b> <sup>c)</sup>	3.10	2.61	4.26	4.41	3.79	5.37	--	7.11-7.39	3.59
<b>3f</b> <sup>ii,a)</sup>	3.10	2.71	4.49	4.01	3.76	--	5.23	7.11-7.15	3.62
<b>3f</b> <sup>iii,a)</sup>	3.10	2.78	4.56	4.22	3.57	6.66-6.74		6.78-7.06	3.75
<b>3f</b> <sup>iv,c)</sup>	3.09	2.77	4.56	4.21	3.56	6.75	6.66	6.63-6.77	3.74
<b>3h</b> <sup>i,a)</sup>	3.33	2.57	4.57	--	3.85	6.74	6.67	7.1-7.6	
<b>3h</b> <sup>ii,a)</sup>	3.19	2.76	4.69	4.83	3.60	6.73		7.0-7.2	
<b>3i</b> <sup>a)</sup>	3.21	2.67	4.58	--	3.85	6.77	6.62	7.1-7.4	
<b>3i</b> <sup>b)</sup>	2.61	2.70	4.56	4.19	3.06	6.07	6.25	6.4-6.7	
<b>3j</b> <sup>a)</sup>	3.11	2.74	5.21	4.44	3.68	7.66	--	7.15-7.29	3.82
<b>3k</b> <sup>b)</sup>	2.34	2.59	4.77	3.18	2.75	6.31	--	6.54-6.75	
<b>3k</b> <sup>ii,b)</sup>	2.26	2.57	4.40	3.70	3.00	--	6.39	6.53-6.71	
<b>3l</b> <sup>b)</sup>	2.22	2.47	4.70	3.64	2.83	--	--	6.45-6.65	

a) CDCl<sub>3</sub>. b) C<sub>6</sub>D<sub>6</sub>. c) Acetone-*d*<sub>6</sub>.

Thus, photoreaction of **1a** essentially underwent stereoselective [4 + 2] cycloaddition with naphthalenes bearing either electron-withdrawing groups or electron-donating groups to give the corresponding *cis*-formed 4a-fluoro-5,10-ethenobenzo[*f*]quinazolines (benzopyrimidobarrelenes) (**3**) in fair yields with 10a-H and 4a-F remaining intact at the original position of the pyrimidine ring. 5-FDMU (**1a**) adds to naphthalene more preferentially at the ring possessing a substituent rather than the unsubstituted ring. The highly electron-rich *N,N*-dimethylaminonaphthalene (**2g**) preferentially underwent substitution reaction,

while significantly electron-deficient dicyanonaphthalene (**2l**) underwent sparing 1,4-cycloaddition under prolonged irradiation.

Table 4. Spin-Spin Coupling Constants ( $J$ =Hz) for Fluoroethenobenzoquinazolines (**3a-l**)

Compd.	$^1\text{H}$ - $^1\text{H}$ and $^1\text{H}$ - $^{19}\text{F}$ Coupling constants ( $J$ =Hz)							
	5-4aF	5-11	5-12	10-10a	10-11	10-12	10a-4aF	11-12
<b>3a</b>	5.4	1.7	5.4	2.6	6.2	1.5	31.3	7.2
<b>3b<sub>i</sub></b>	--	--	--	2.7	7.0	1.3	30.8	7.7
<b>3b<sub>ii</sub></b>	5.9	1.7	5.9	--	--	--	30.6	7.5
<b>3b<sub>iii</sub></b>	5.3	1.7	5.8	2.7	5.8	1.5	31.4	7.2
<b>3b<sub>iv</sub></b>	5.5	1.7	5.7	2.7	6.1	1.7	31.4	7.6
<b>3c<sub>i</sub></b>	--	--	--	--	--	--	30.0	7.5
<b>3c<sub>ii</sub></b>	5.9	1.7	5.9	2.6	6.2	1.5	31.7	7.3
<b>3d<sub>i</sub></b>	4.9	1.8	--	2.8	6.8	--	31.9	--
<b>3d<sub>ii</sub></b>	5.6	--	5.6	2.6	--	1.9	31.1	--
<b>3e<sub>i</sub></b>	4.9	2.4	--	2.3	7.1	--	31.5	--
<b>3e<sub>ii</sub></b>	5.1	--	6.5	2.6	--	2.2	31.3	--
<b>3e<sub>iii</sub></b>	5.5	1.5	5.5	2.7	6.2	-- a)	31.3	-- a)
<b>3e<sub>iv</sub></b>	5.5	1.7	5.5	2.9	-- a)	-- a)	31.5	-- a)
<b>3f<sub>i</sub></b>	5.1	2.6	--	2.7	7.1	--	32.6	--
<b>3f<sub>ii</sub></b>	5.5	--	6.4	2.5	--	2.2	30.0	--
<b>3f<sub>iii</sub></b>	5.0	2.4	5.0	2.8	-- a)	2.0	31.3	-- a)
<b>3h<sub>i</sub></b>	5.9	1.8	5.9	1.8			29.1	7.9
<b>3h<sub>ii</sub></b>	5.1	1.7	5.1	2.7	-- a)	-- a)	31.5	-- a)
<b>3i<sub>i</sub></b>	5.1 b)	-- a)	5.1	2.8 b)	9.7 b)	5.2 b)	30.6	8.0
<b>3j</b>	5.1	1.8	--	2.4	6.7	--	31.5	--
<b>3k<sub>i</sub></b>	4.9	2.0	--	2.6	6.6	--	31.1	--
<b>3k<sub>ii</sub></b>	5.0	--	6.0	2.8	--	1.3	31.0	--
<b>3l</b>	4.8	--	--	2.4	--	--	30.8	--

a) Not determined. b) Coupling constants due to  $^1\text{H}$  and 10-F.

Addition of the triplet quencher piperylene to a solution of **1a** and **2a** in cyclohexane suppressed the formation of **3a** significantly, suggesting that the present 1,4-cycloaddition may be initiated *via* the excited triplet states of naphthalene. In view of the fact that the present 1,4-addition proceeds more efficiently as the polarity of the solvent decreases and excess amounts of **2a** over **1a** do not improve the efficiency of the 1,4-addition, the involvement of an exciplex or diradical intermediates are presumably an important factor.<sup>17</sup> The substituents may partially serve to stabilize the intermediate radicals thereby

affecting the regioselectivities that cycloaddition occurred more preferentially at the ring having a substituent rather than the other unsubstituted ring of the naphthalene moiety.

Because of high yields, high stereoselectivity, no presence of acid needed and no excess amounts of naphthalene to **1a** required, the present work represents a simple and useful method for the skeletal modification of the pyrimidine ring.

## EXPERIMENTAL

NMR spectra were measured with a JEOL JNM-EX400 (400 MHz) spectrometer and JEOL JNM-ECA500 (500 MHz). Chemical shifts are given on the  $\delta$  (ppm) scale based on the residual deuterated solvent signals as reference;  $\text{CDCl}_3$  ( $\delta$ 7.26),  $\text{C}_6\text{D}_6$  ( $\delta$ 7.15). MS spectra and high-resolution EIMS and FABMS (HRMS) spectra were recorded with a JEOL FABmate and a JEOL JMS-HX110, respectively. HPLC was conducted on a Shim-pac PREP-Sil (H) (25 cm x 20 mm *i. d.*) (silica gel), using a LC-6A apparatus (Shimadzu, Kyoto) with monitoring at 254 nm. UV-Irradiation was carried out externally with a 500 W high-pressure mercury (h.p. Hg) lamp (Eiko-sha, Osaka) in a degassed Pyrex tube (> 300 nm) on a merry-go-round apparatus. Yields are determined by means of  $^1\text{H}$ -NMR spectroscopy with *p*-dinitrobenzene as an internal standard, and are given as average values obtained from the reaction performed repeatedly at least three times.

**Photoreaction of 5-FDMU with naphthalenes (2a-1)** — An equivalent molar solution (1.5 mM) of 5-FDMU and a naphthalene in cyclohexane (benzene in the case of **2l**) (160 mL) was introduced portion-wise (5 mL each) into 32 degassed Pyrex tubes, and irradiated externally at rt. The reaction mixture was concentrated *in vacuo*, and the residual oil was submitted to HPLC with 25-30% ethyl acetate in hexane.

### **4a-Fluoro-4a,5,10,10a-tetrahydro-1,3,5-trimethyl-cis-5,10-ethenobenzo[*f*]quinazoline-2,4-dione (3b<sub>i</sub>):**

Colorless crystals (hexane); mp 125-126°C. NOE: H-10a with  $\text{N}^1\text{-CH}_3$  (4.9%), H-11 (1.9%), H-10 (5.8%); H-10 with H-10a (8.2%), H-11 (10.8%),  $\text{N}^1\text{-CH}_3$  (8.2%); H-12 with H-11 (13.1%),  $\text{C}^5\text{-CH}_3$  (4.6%); H-11 with H-12 (7%), H-10 (8.7%), H-10a (3.1%);  $\text{N}^1\text{-CH}_3$  with H-10a (3%), H-10 (3.4%). FABMS *m/z*: 301 ( $\text{M}+\text{H}$ )<sup>+</sup>. HRFABMS: Calcd for  $\text{C}_{17}\text{H}_{18}\text{N}_2\text{O}_2\text{F}$ : 301.1352. Found: 301.1370.

### **4a-Fluoro-4a,5,10,10a-tetrahydro-1,3,10-trimethyl-cis-5,10-ethenobenzo[*f*]quinazoline-2,4-dione (3b<sub>ii</sub>):**

Colorless crystals (methanol); mp 158-159°C. NOE: H-10a with  $\text{N}^1\text{-CH}_3$  (6.9%), H-11 (2.3%); H-5 with H-12 (5.7%); H-11 with H-12 (7.3%), H-10a (1.5%),  $\text{C}^{10}\text{-CH}_3$  (4.9%); H-12 with H-11 (4.9%), H-5 (5.9%);  $\text{C}^{10}\text{-CH}_3$  with  $\text{N}^1\text{-CH}_3$  (12.4%), H-10a (3.7%), H-11 (8.6%);  $\text{N}^1\text{-CH}_3$  with H-10a (5.2%), H-11 (9.7 %). FABMS *m/z*:



301 (M+H)<sup>+</sup>. HRFABMS: Calcd for C<sub>17</sub>H<sub>18</sub>N<sub>2</sub>O<sub>2</sub>F: 301.1352. Found: 301.1331.

**4a-Fluoro-4a,5,10,10a-tetrahydro-1,3,9-trimethyl-cis-5,10-ethenobenzo[f]quinazoline-2,4-dione (3b<sub>iii</sub>):**

Colorless oil. NOE: H-10a with N<sup>1</sup>-CH<sub>3</sub> (6.5%), H-11 (2.9%), H-10 (5.4%); H-10 with H-10a (8.2%), H-11 (8.1%), N<sup>1</sup>-CH<sub>3</sub> (8.2%), C<sup>9</sup>-CH<sub>3</sub> (9.4%); H-5 with H-12 (8.7%); C<sup>9</sup>-CH<sub>3</sub> with H-10 (4%), N<sup>1</sup>-CH<sub>3</sub> (1.8%); N<sup>1</sup>-CH<sub>3</sub> with H-10a (15.6%), H-10 (8.9%), C<sup>9</sup>-CH<sub>3</sub> (4.1%). FABMS *m/z*: 301 (M+H)<sup>+</sup>. HRFABMS: Calcd for C<sub>17</sub>H<sub>18</sub>N<sub>2</sub>O<sub>2</sub>F: 301.1352. Found: 301.1353.

**4a-Fluoro-4a,5,10,10a-tetrahydro-1,3,6-trimethyl-cis-5,10-ethenobenzo[f]quinazoline-2,4-dione (3b<sub>iv</sub>):**

Colorless oil. NOE: H-10a with N<sup>1</sup>-CH<sub>3</sub> (4.3%), H-11 (1.9%), H-10 (5.3%); H-10 with H-10a (5.4%), H-11 (7.3%), N<sup>1</sup>-CH<sub>3</sub> (8.2%); H-5 with H-12 (6.8%), C<sup>6</sup>-CH<sub>3</sub> (7.6%); C<sup>6</sup>-CH<sub>3</sub> with H-5 (3%); N<sup>1</sup>-CH<sub>3</sub> with H-10a (2.2%), H-10 (2.7%). FABMS *m/z*: 301 (M+H)<sup>+</sup>. HRFABMS: Calcd for C<sub>17</sub>H<sub>18</sub>N<sub>2</sub>O<sub>2</sub>F: 301.1352. Found: 301.1370

**4a-Fluoro-4a,5,10,10a-tetrahydro-1,3,5,10-tetramethyl-cis-5,10-ethenobenzo[f]quinazoline-2,4-dione**

**(3c<sub>i</sub>):** Colorless crystals (hexane); mp 93-96°C. NOE: H-10a with N<sup>1</sup>-CH<sub>3</sub> (8.9%), H-11 (5.2%), C<sup>10</sup>-CH<sub>3</sub> (2.7%); H-12 with H-11 (8.8%), C<sup>5</sup>-CH<sub>3</sub> (2.8%); H-11 with H-12 (7.2%), H-10a (2%), C<sup>10</sup>-CH<sub>3</sub> (2.6%); C<sup>5</sup>-CH<sub>3</sub> with H-12 (4.4%), N<sup>3</sup>-CH<sub>3</sub> (1.3%); N<sup>1</sup>-CH<sub>3</sub> with H-10a (7.8%), C<sup>10</sup>-CH<sub>3</sub> (3.6%). FABMS *m/z*: 315 (M+H)<sup>+</sup>. HRFABMS: Calcd for C<sub>18</sub>H<sub>20</sub>N<sub>2</sub>O<sub>2</sub>F: 315.1523. Found: 315.1520

**4a-Fluoro-4a,5,10,10a-tetrahydro-1,3,6,9-tetramethyl-cis-5,10-ethenobenzo[f]quinazoline-2,4-dione**

**(3c<sub>ii</sub>):** Colorless crystals (methanol); mp 165-167°C. NOE: H-10a with N<sup>1</sup>-CH<sub>3</sub> (8.8%), H-11 (5.7%); H-10 with H-10a (3.0%), H-11 (7.6%), N<sup>1</sup>-CH<sub>3</sub> (5.2%), C<sup>9</sup>-CH<sub>3</sub> (5.2%); H-5 with H-12 (6.0%), C<sup>6</sup>-CH<sub>3</sub> (6.4%); H-12 with H-5 (6.1%); C<sup>9</sup>-CH<sub>3</sub> with H-10 (4.4%). FABMS *m/z*: 315 (M+H)<sup>+</sup>. HRFABMS: Calcd for C<sub>18</sub>H<sub>20</sub>N<sub>2</sub>O<sub>2</sub>F: 315.1523. Found: 315.1516.

**4a-Fluoro-4a,5,10,10a-tetrahydro-1,3,8,12-tetramethyl-cis-5,10-ethenobenzo[f]quinazoline-2,4-dione**

**(3d<sub>i</sub>):** Colorless crystals (hexane); mp 151-152°C. NOE: H-10a with N<sup>1</sup>-CH<sub>3</sub> (9.3%), H-11 (5.7%); H-10 with H-10a (14.4%), H-11 (13.3%), N<sup>1</sup>-CH<sub>3</sub> (10.2%), H-9 (12.7%); H-5 with H-6 (10.8%), C<sup>12</sup>-CH<sub>3</sub> (6%); H-11 with H-10a (1.2%), C<sup>12</sup>-CH<sub>3</sub> (1.7%), H-10 (7.7%); C<sup>12</sup>-CH<sub>3</sub> with H-5 (6.3%), H-11 (4.9%); C<sup>8</sup>-CH<sub>3</sub> with H-7 (5.1%), H-9 (5%); N<sup>1</sup>-CH<sub>3</sub> with H-10a (22%), H-10 (21%). FABMS *m/z*: 315 (M+H)<sup>+</sup>. HRFABMS: Calcd for C<sub>18</sub>H<sub>20</sub>N<sub>2</sub>O<sub>2</sub>F: 315.1523. Found: 315.1536.

**4a-Fluoro-4a,5,10,10a-tetrahydro-1,3,7,11-tetramethyl-cis-5,10-ethenobenzo[f]quinazoline-2,4-dione**

**(3d<sub>ii</sub>):** Colorless crystals; mp 157-159°C (hexane). NOE: H-10a with N<sup>1</sup>-CH<sub>3</sub> (6.7%), H-10 (6.3%); H-10 with

H-10a (7.1%), H-9 (8%), N<sup>1</sup>-CH<sub>3</sub> (4.2%); H-5 with H-12 (10%), H-6 (8.6%); H-12 with H-5 (9.3%), C<sup>11</sup>-CH<sub>3</sub> (4.3%); C<sup>11</sup>-CH<sub>3</sub> with H-10a (16%), H-10 (9.4%), H-12 (8.2%); N<sup>1</sup>-CH<sub>3</sub> with H-10a (2.9%), H-10 (3.3%). FABMS *m/z*: 315 (M+H)<sup>+</sup>. HRFABMS: Calcd for C<sub>18</sub>H<sub>20</sub>N<sub>2</sub>O<sub>2</sub>F: 315.1523. Found: 315.1533.

**12-Acetoxy-4a-fluoro-4a,5,10,10a-tetrahydro-1,3-dimethyl-cis-5,10-ethenobenzof[*f*]quinazoline-2,4-dione (3e<sub>i</sub>):** Colorless crystals; mp 142.5-143.5°C (dichloromethane). NOE: N<sup>1</sup>-CH<sub>3</sub> with H-10a (10.3%), H-10 (6.3%), H-9 (6.1%); H-10a with N<sup>1</sup>-CH<sub>3</sub> (3.3%), H-10 (6.5%), H-11 (1.7%); H-10 with N<sup>1</sup>-CH<sub>3</sub> (10.3%), H-10a (4.3%), H-11 (4.2%); H-5 with H-6 (4.5%); H-11 with H-10 (6.2%), H-10a (3.7%). FABMS *m/z*: 345 (M+H)<sup>+</sup>. HRFABMS: Calcd for C<sub>18</sub>H<sub>18</sub>N<sub>2</sub>O<sub>4</sub>F: 345.1172. Found: 345.1258.

**11-Acetoxy-4a-fluoro-4a,5,10,10a-tetrahydro-1,3-dimethyl-cis-5,10-ethenobenzof[*f*]quinazoline-2,4-dione (3e<sub>ii</sub>):** Colorless crystals; mp 170.5-172°C (methanol). NOE: N<sup>1</sup>-CH<sub>3</sub> with H-10a (13.8%), H-10 (20.1%); H-10a with N<sup>1</sup>-CH<sub>3</sub> (5.7%), H-10 (6.5%); H-10 with N<sup>1</sup>-CH<sub>3</sub> (6.4%), H-10a (6.3%), H-9 (5.1%); H-5 with H-6 (6.6%), H-12 (9.5%); H-12 with H-5 (7.4%), H-10a (1.0%). FABMS *m/z*: 345 (M+H)<sup>+</sup>. HRFABMS: Calcd for C<sub>18</sub>H<sub>18</sub>N<sub>2</sub>O<sub>4</sub>F: 345.1172. Found: 345.1239.

**7-Acetoxy-4a-fluoro-4a,5,10,10a-tetrahydro-1,3-dimethyl-cis-5,10-ethenobenzof[*f*]quinazoline-2,4-dione (3e<sub>iii</sub>):** Colorless crystals (ethyl acetate-hexane); mp 129-130.5°C. NOE: H-10a with N<sup>1</sup>-CH<sub>3</sub> (1.5%), H-10 (8.5%), H-11 (1.6%); H-5 with H-6 (7.3%), H-12 (9.7%). FABMS *m/z*: 345 (M+H)<sup>+</sup>. HRFABMS: Calcd for C<sub>18</sub>H<sub>18</sub>N<sub>2</sub>O<sub>4</sub>F: 345.1172. Found: 345.1265.

**8-Acetoxy-4a-fluoro-4a,5,10,10a-tetrahydro-1,3-dimethyl-cis-5,10-ethenobenzof[*f*]quinazoline-2,4-dione (3e<sub>iv</sub>):** NOE: H-10a with N<sup>1</sup>-CH<sub>3</sub> (1%), H-10 (4.6%), H-11 (5.5%); H-5 with H-6 (24.6%), H-12 (5.0%). FABMS *m/z*: 345 (M+H)<sup>+</sup>. HRFABMS: Calcd for C<sub>18</sub>H<sub>18</sub>N<sub>2</sub>O<sub>4</sub>F: 345.1172. Found: 345.1239.

**4a-Fluoro-4a,5,10,10a-tetrahydro-12-methoxy-1,3-dimethyl-cis-5,10-ethenobenzof[*f*]quinazoline-2,4-dione (3f<sub>i</sub>):** Colorless crystals (ethyl acetate-hexane); mp 161-163°C. NOE : H-10a with N<sup>1</sup>-CH<sub>3</sub> (4.8 %), H-10 (8.9%), H-11 (1.4%); H-5 with H-6; H-10 with N<sup>1</sup>-CH<sub>3</sub>, H-10a, H-9, H-11; C<sup>12</sup>-OCH<sub>3</sub> with H-11. FABMS *m/z*: 317 (M+H)<sup>+</sup>. HRFABMS: Calcd for C<sub>17</sub>H<sub>18</sub>N<sub>2</sub>O<sub>3</sub>F: 317.1301. Found: 317.1280.

**4a-Fluoro-4a,5,10,10a-tetrahydro-11-methoxy-1,3-dimethyl-cis-5,10-ethenobenzof[*f*]quinazoline-2,4-dione (3f<sub>ii</sub>):** Colorless crystals (ethyl acetate-hexane); mp 165-167°C. NOE : H-10a with N<sup>1</sup>-CH<sub>3</sub> (6.9%), H-10 (7.3%), H-12 (2.0%); H-12 with H-5, C<sup>11</sup>-OCH<sub>3</sub>; H-10 with N<sup>1</sup>-CH<sub>3</sub>, H-10a, H-9. FABMS *m/z*: 317 (M+H)<sup>+</sup>. HRFABMS: Calcd for C<sub>17</sub>H<sub>18</sub>N<sub>2</sub>O<sub>3</sub>F: 317.1301. Found: 317.1272.

**4a-Fluoro-4a,5,10,10a-tetrahydro-8-methoxy-1,3-dimethyl-cis-5,10-ethenobenzof[*f*]quinazoline-2,4-dione**

(**3f<sub>iii</sub>**): Colorless crystals (ethyl acetate-hexane); mp 171-173°C. FABMS *m/z*: 317 (M+H)<sup>+</sup>. HRFABMS: Calcd for C<sub>17</sub>H<sub>18</sub>N<sub>2</sub>O<sub>3</sub>F: 317.1301. Found: 317.1313.

**4a-Fluoro-4a,5,10,10a-tetrahydro-7-methoxy-1,3-dimethyl-cis-5,10-ethenobenzo[f]quinazoline-2,4-dione**

(**3f<sub>iv</sub>**): NOE: H-10a with N<sup>1</sup>-CH<sub>3</sub> (6.6%), H-10 (6.1%), H-11 (2.9%). FABMS *m/z*: 317 (M+H)<sup>+</sup>. HRFABMS: Calcd for C<sub>17</sub>H<sub>18</sub>N<sub>2</sub>O<sub>3</sub>F: 317.1301. Found: 317.1309.

**1,3-Dimethyl-5-(2-dimethylamino)naphth-1-yluracil (4g)**. Oil, <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 2.69 (6H, s, C<sup>2'</sup>-N(CH<sub>3</sub>)<sub>2</sub>), 3.45 (3H, s, N<sup>1</sup>-CH<sub>3</sub>), 3.47 (3H, s, N<sup>3</sup>-CH<sub>3</sub>), 7.12 (1H, s, H-6), 7.31 (1H, t, *J* = 8.6 Hz, H-6'), 7.37 (2H, m, H-3' and 7'), 7.45 (1H, d, *J* = 8.0 Hz, H-8'), 7.74 (1H, d, *J* = 8.6 Hz, H-5'), 7.81 (1H, d, *J* = 9.2 Hz, H-4'). NOE: H-6 with N<sup>1</sup>-CH<sub>3</sub> (7.1%), C<sup>2'</sup>-N(CH<sub>3</sub>)<sub>2</sub> (1%), H-8' (3.8%), H-4' with H-3' (7.6%), H-5' (1.2%). EIMS *m/z*: 309 (M<sup>+</sup>), 294, 153. HRMS: Calcd for C<sub>18</sub>H<sub>19</sub>N<sub>3</sub>O<sub>2</sub>: 309.1477. Found: 309.1484.

**10-Chloro-4a-fluoro-4a,5,10,10a-tetrahydro-1,3-dimethyl-cis-5,10-ethenobenzo[f]quinazoline-2,4-dione**

(**3h<sub>i</sub>**): Colorless crystals (ethyl acetate-hexane); mp 106-107.5°C. <sup>1</sup>H-NMR (CDCl<sub>3</sub>) NOE: N<sup>1</sup>-CH<sub>3</sub> with H-10a (3.2%); H-10a with N<sup>1</sup>-CH<sub>3</sub> (6.3%), H-11 (0.9%); H-5 with H-6 (7.1%), H-12 (6.9%); H-12 with H-5 (8.8%); H-11 with H-10a (4.2%), H-5 (0.6%). FABMS *m/z*: 321 (M+H)<sup>+</sup>, 323 (M+H)<sup>+</sup>. HRFABMS: Calcd for C<sub>16</sub>H<sub>15</sub>N<sub>2</sub>O<sub>2</sub>FCl: 321.0728. Found: 321.0788.

**9-Chloro-4a-fluoro-4a,5,10,10a-tetrahydro-1,3-dimethyl-cis-5,10-ethenobenzo[f]quinazoline-2,4-dione**

(**3h<sub>ii</sub>**): Colorless crystals (ethyl acetate-hexane); mp 146-148°C. NOE: N<sup>1</sup>-CH<sub>3</sub> with H-10a (2.5%), H-10a (8.4%), H-11 (5.7%); H-5 with H-6 (6.7%), H-12 (8.0%). FABMS *m/z*: 321 (M+H)<sup>+</sup>, 323 (M+H)<sup>+</sup>. HRFABMS: Calcd for C<sub>16</sub>H<sub>15</sub>N<sub>2</sub>O<sub>2</sub>FCl: 321.0728. Found: 321.0832.

**4a,11-Difluoro-4a,5,10,10a-tetrahydro-1,3-dimethyl-cis-5,10-ethenobenzo[f]quinazoline-2,4-dione (3i<sub>i</sub>):**

Colorless crystals (benzene-hexane); mp 137-138°C. NOE: N<sup>1</sup>-CH<sub>3</sub> with H-10a (7.5%); H-10a with N<sup>1</sup>-CH<sub>3</sub> (3.1%); H-5 with H-12 (11.1%), H-6 (9.6%); H-12 with H-5 (11.8%), H-11 (24.9%); H-11 with H-12 (17.6%). FABMS *m/z*: 321 (M+H)<sup>+</sup>. HRFABMS: Calcd for C<sub>16</sub>H<sub>15</sub>N<sub>2</sub>O<sub>2</sub>F<sub>2</sub>: 305.1023. Found: 305.1074.

**4a,9-Difluoro-4a,5,10,10a-tetrahydro-1,3-dimethyl-cis-5,10-ethenobenzo[f]quinazoline-2,4-dione (3i<sub>ii</sub>):**

Colorless crystals (ethyl acetate-hexane); mp 131-132°C. <sup>1</sup>H-NMR (C<sub>6</sub>D<sub>6</sub>) δ: 2.61 (3H, s, N<sup>1</sup>-CH<sub>3</sub>), 2.70 (3H, s, N<sup>3</sup>-CH<sub>3</sub>), 3.06 (1H, dd, *J* = 31.3, 2.8 Hz, H-10a), 4.19 (1H, m, H-10), 4.56 (1H, m, H-5), 6.07 (1H, m, H-11), 6.25 (1H, m, H-12), 6.4-6.7 (3H, m, H-6, 7, and 8). NOE: N<sup>1</sup>-CH<sub>3</sub> with H-10a, H-10, H-10a with H-10, H-11, H-10 with H-10a, H-11, N<sup>1</sup>-CH<sub>3</sub>, H-5 with H-12, H-6. FABMS *m/z*: 321 (M+H)<sup>+</sup>. HRFABMS: Calcd for C<sub>16</sub>H<sub>15</sub>N<sub>2</sub>O<sub>2</sub>F<sub>2</sub>: 305.1023. Found: 305.1101.

**4a-Fluoro-4a,5,10,10a-tetrahydro-1,3-dimethyl-2,4-dioxo-cis-5,10-ethenobenzo[f]quinazoline-11,12-dicarbonitrile (3l):** Colorless crystals (ethanol); mp (dec.) 170-180°C. NOE: H-10a with N<sup>1</sup>-CH<sub>3</sub> (10.0%), H-10 (10.2%); H-10 with H-9 (11.5%), H-10a (8.7%), N<sup>1</sup>-CH<sub>3</sub> (10.2%); H-5 with H-6 (9.8%); H-7 and H-8 with H-6 and H-9 (13.8%). FABMS *m/z*: 337 (M+H)<sup>+</sup>. HRFABMS: Calcd for C<sub>18</sub>H<sub>14</sub>N<sub>4</sub>O<sub>2</sub>F: 337.1023. Found: 337.1101.

**Photoreaction of 5-FDMU (1a) with naphthalene (2a) in the presence of piperylene-----** An equivalent molar solution (1.5 mM) of **1a** and **2a** in cyclohexane containing *trans*-piperylene (1.5 mM) was irradiated for 1h to give **3a** in 20 % yield together with recovery of **1a** in 76 % yield.

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