New Syntheses and Spectral Properties of Pteridine-related Heterocycles from 2,5-Diamino-3,6-dicyanopyrazine

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The reaction of 2,5-diamino-3,6-dicyanopyrazine (**1**) as a new pyrazine raw material with alkyl isocyanate in the presence of sodium hydride gave novel heptahydroimidazo[4,5-*g*]pteridine-2,6,8-trione (**2**), but with tertiary butyl isocyanate gave trihydroimidazo[4,5-*b*]pyrazine-2-ones (**3**). Similar reaction of **1** with alkyl thioisocyanate followed by alkyl iodide gave tetrahydropyrimido[4,5-*g*]pteridines (**4**). The reaction of **1** with alkylamine gave the amine-adduct of the cyano groups which was further reacted with arylaldehyde to give the pyrimido[4,5-*g*]pteridine (**10**). The products prepared are all of interest as potential pesticides and fluorescent chromophores.

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Pteridine chemistry has been widely studied by Taylor's group [1]. Pyrimido[5,4-*g*]- and pyrimido[4,5-*g*]pteridines were synthesized from 1,3-dimethyl-4,5-diaminouracil [2] or by oxidative self-condensation of diaminopyrimidine in the presence of air [3]. Oxidation of 1,3-dimethyl-6-amino-5-nitrosouracil by lead tetraacetate gave 4,6-dimethyl-5,7-(4*H*,6*H*)-furazano[3,4-*d*]pyrimidinedione together with 1,3,6,8-tetramethyl-2,4,5,7-(1*H*,3*H*,6*H*,8*H*)pyrimido[5,4-*g*]-pteridinetetrone-10-oxide. The structure of it was confirmed by its reduction to give the corresponding pyrimido-[5,4-*g*]pteridinetetrone [4]. Imidazopteridines were also obtained by the alkaline hydrolysis of pyrimidopteridine [4]. General chemistry of pyrimido[5,4-*g*]pteridine and imidazo[4,5-*g*]pteridine systems were reported connected with flavin mimics by Bruice's group [5,6]. Syntheses of 1*H*-imidazo[4,5-*b*]pyrazine derivatives were also known [7].

Recently, we studied pyrazine-based dye chemistry by using three raw materials, *i.e.* diaminomaleonitrile, 2,3-dichloro-5,6-dicyanopyrazine and 2,5-diamino-3,6-dicyanopyrazine [8]. These are available as industrial intermediates and can be widely applied as synthetic raw materials for coloring matters with a variety of chromophoric systems. Some results were recently summarized as a book chapter in title of multifunctional dye materials derived from new dicyanopyrazine chromophores [9]. In particular, newly synthesized 2,5-diamino-3,6-dicyanopyrazine has strong fluorescence and is interesting as new fluorescence materials for various applications such as electroluminescence devices and copy preventing inks [10,11].

In this paper, pteridine-related heterocycles were newly synthesized from the reaction of 2,5-diamino-3,6-dicyanopyrazine with isocyanates or aldehydes, and their absorption and fluorescent properties were correlated with their chemical structures.

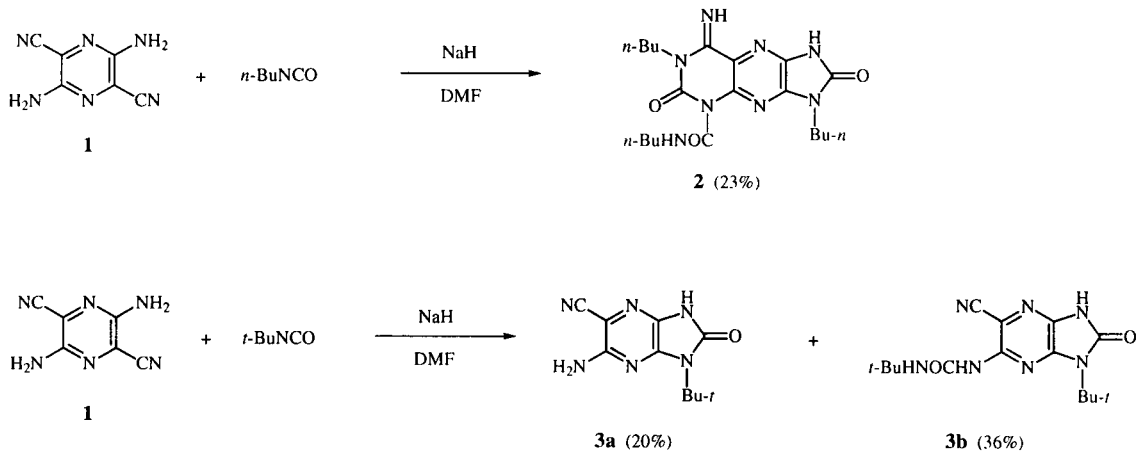
Results and Discussion.

Reaction of 2,5-Diamino-3,6-dicyanopyrazine (**1**) with Alkyl Isocyanate.

Reaction of **1** with excess of *n*-butyl isocyanate in dimethylformamide in the presence of sodium hydride gave 3,7-di-*n*-butyl-5-*N*-*n*-butylcarbamoyl-1,2,3,5,6,7,8-heptahydroimidazo[4,5-*g*]pteridine-2,6,8-trione (**2**) in 23% yield. In the reaction, two types of intramolecular ring-closure reactions were observed; addition of isocyanate to the amino group in **1** initiates the reaction to give an ureido function. One is the intramolecular ring-closure reaction of the ureido anion to replace the cyano group to form the five-membered imidazolone ring. On the other hand, a second isocyanate additionally reacted to the ureido group to form a six-membered pyrimidinedione ring. As a result, **1** reacted with three equivalent of *n*-butyl isocyanate to give **2** in 23% yield. From these results, the neighboring amino and cyano groups in **1** react with alkyl isocyanate to give different hetero-rings, *i.e.*, imidazolone and pyrimidinedione. On the other hand, reaction of **1** with *tert*-butyl isocyanate gave different kinds of products, 5-amino-3-*tert*-butyl-6-cyano-1*H*-2,3-dihydroimidazo[4,5-*b*]-pyrazin-2-one (**3a**) and 3-*tert*-butyl-5-(1-*N*-*tert*-butylcar-

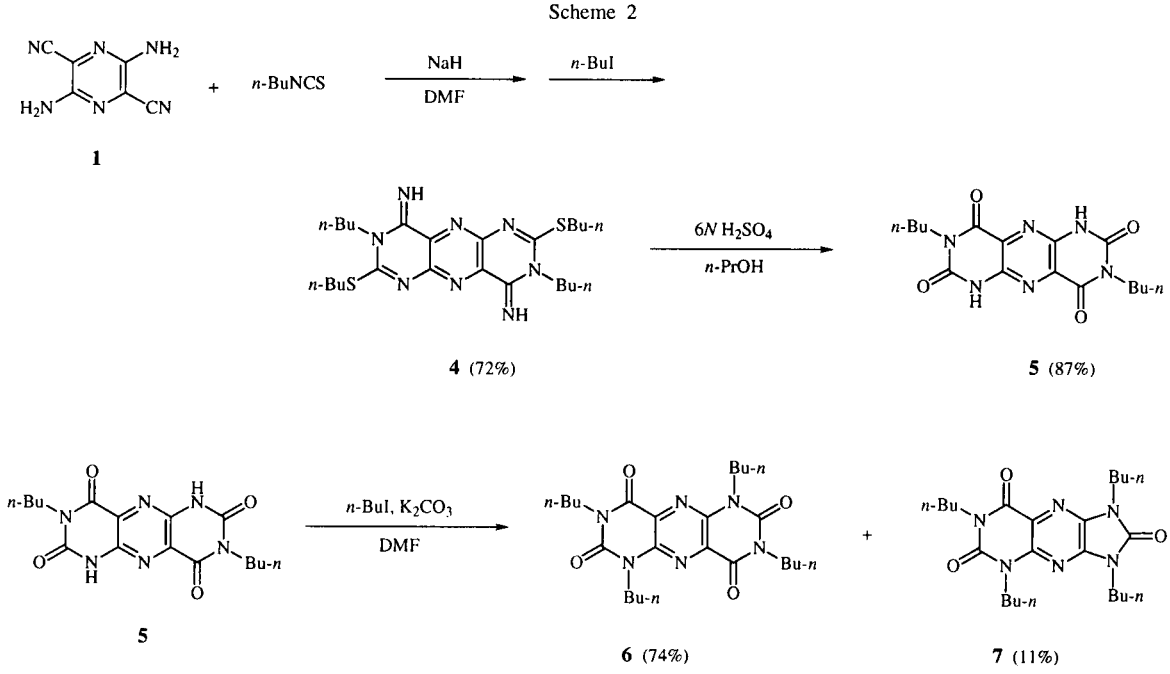
bamoylamino)-6-cyano-1*H*-2,3-dihydroimidazo[4,5-*b*]-pyrazin-2-one (**3b**). Sterically hindered *tert*-butyl isocyanate produced five-membered imidazolone ring but no pyrimidinedione ring as observed in the case of **2** (Scheme 1).

Scheme 1



Similar reaction of **1** with *n*-butyl thioisocyanate followed by *n*-butyl iodide gave 3,8-di-*n*-butyl-2,7-di-*n*-butylthio-4,9-diimino-3,4,8,9-tetrahydropyrimido[4,5-*g*]-pteridine (**4**) in 72% yield. In this reaction, the higher reactivity of the thioisocyanate compared with the isocyanate gave the bis(six-membered pyrimidine) ring and subsequent *n*-butylation of the thiocarbonyl groups to give **4**. Hydrolysis of **4** in the presence of sulfuric acid proceeded smoothly to give 3,8-di-*n*-butyl-1,2,3,4,6,7,8,9-octahydropyrimido[4,5-*g*]pteridine-2,3,7,9-tetrone (**5**) in 87% yield. Alkylation of **5** with *n*-butyl iodide in the presence of potassium carbonate in dimethylformamide gave 1,3,6,8-tetra-*n*-butyl-1,2,3,4,6,7,8,9-octahydropyrimido-[4,5-*g*]pteridine-2,4,7,9-tetrone (**6**) in 73% yield together with 1,3,5,7-tetra-*n*-butyl-1*H*-2,3,5,6,7,8-hexahydroimidazo[4,5-*g*]pteridine-2,6,8-trione (**7**) in 11% yield (Scheme 2). In the reaction, alkaline hydrolysis of **6**

Scheme 2



accompanying decarboxylation gave **7**. Similar alkaline hydrolysis of 10-oxide of the methyl derivative of **6** had been reported [4]. These ring-size transformation reactions from the six-membered pyrimidinedione to the five-membered imidazolone ring are very interesting and will be a better synthetic method for **7** compared with that from **2**.

Reaction of **1** with Alkylamine Followed by Carbonyl Compounds.

Mild reaction of **1** with alkylamines in dimethylformamide proceeded by addition to the cyano groups forming the amidines, **8a** and **8b**. The reaction of **8b** with benzaldehyde gave 2,7-diphenyl-4,9-bis(*n*-propylamino)-pyrimido[4,5-*g*]pteridine (**10**) in 12% yield which is the oxidized product of 2,7-diphenyl-4,9-bis(*n*-propylamino)-1,2,6,7-tetrahydropyrimido[4,5-*g*]pteridine (**9**) which has not been isolated (Scheme 3).

From these results, it was found that **1** was a valuable starting material for the synthesis of polycyclic nitrogen heterocycles such as pyrimidopteridines and imidazopteridines.

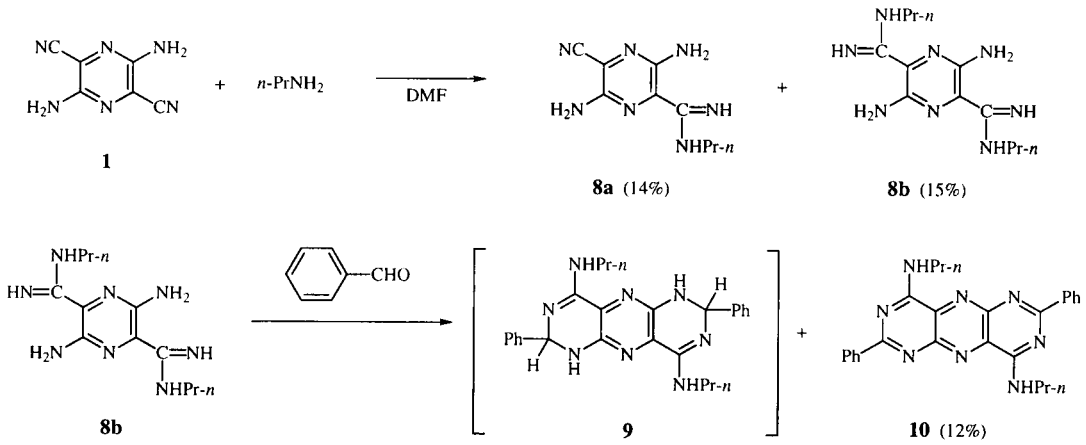
Identification of the products were conducted by ms, nmr and elemental analyses. Those results were summarized in the Experimental. Some of the related compounds have been patented from Nippon Soda Co., Ltd. [12].

Visible and Fluorescence Spectra.

Visible spectra in long wavelength and fluorescence spectra of dyes **2-11** are compared with those of 2,5-diamino-3,6-dicyanopyrazine (**1**) from their structural characterization (Table 1).

Dye **1** absorbs at 445 nm and emits at 528 nm in chloroform, both of which are abnormally observed in the longer wavelength region in spite of its small molecular size. It is due to the strong intramolecular charge-transfer

Scheme 3



Furthermore, reaction of **1** with methylamine followed by the reaction with cyclohexanone in dimethylformamide gave 4,9-bis(methylamino)bisspiro[1,2,6,7-tetrahydropyrimido[4,5-*g*]pteridine[2,1':8,1"]biscyclohexane (**11**) in 43% yield. In this reaction, the bis-adduct of methylamine to the cyano groups in **1** was proposed to be an intermediate for **11**. Further oxidation of **11** to **12** was not observed under the reaction conditions (Scheme 4).

(CT) chromophoric system of **1**. Dye **1** shows a fluorescence quantum yield of 0.3 and is a good candidate for fluorescence chromophore [10]. Dyes **2** and **3** absorb at 360-400 nm and produce a large hypsochromic shift from **1** which are mainly due to their lack of strong intramolecular charge-transfer chromophoric system, but their molar absorbance (ε_{max}) increase 6 to 9 times compared with that of **1** induced by the enlargement of the π-system.

Scheme 4

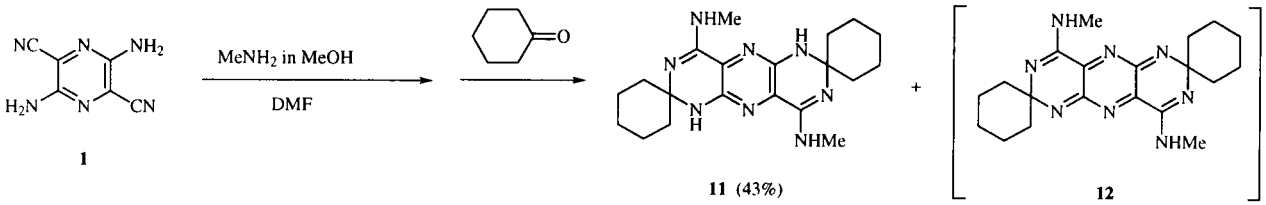


Table 1
The Absorption and Fluorescence Spectra of **1-11**

Dye No.	λ_{max} [a] (nm)	ε	F_{max} [a] (nm)	SS [b] (nm)	F_{max} [c] (nm)	RI [d]
1	445	2200	528	83	[e]	
2	396	20400	427	31	477	300
3a	365	14200	421	56	451	1900
3b	363	15300	416	53	431	1500
4	444	18100	483	39		
5	407	9900	455	48	490	600
6	438	8500	456	18	502	8200
7	379	13000	409	30	420	4700
8a	434	8800	536	102	[e]	
8b	429	10300	520	91	[e]	
10	494	23100	519	25	570	600
11	493	8400	577	84	605	1300

[a] Measured in chloroform; [b] Stokes shift, F_{max} - λ_{max}; [c] In the powder state; [d] Relative intensity of fluorescence in the powder state excited at maximum fluorescence intensity obtained; [e] Not detectable, because of strong intermolecular interactions [11].

Dyes **4**, **5** and **6** absorb at 410-440 nm and emit blue fluorescence at 450-480 nm along with increment of the ε_{max} values compared with that of **1**. These results are in accordance with enlargement of their π-system and lack of the CT chromophoric system. The difference in λ_{max} of 31 nm between **5** and **6** is due to the difference in donor property of the butylamido group (stronger donor) of **6** and the amido group (weaker donor) of **5**. Their ε_{max} values are similar because both possess the same chromophoric system.

Dye **7** absorbs at 379 nm and emits at 409 nm indicating a decrease in electron withdrawing ability in the chromophoric system compared with the two cyano groups in **1**. Similar hypsochromic shifts of absorption bands were observed in dyes **8a** and **8b** in which the cyano groups in **1** were substituted with alkylamine to decrease electron withdrawing ability. On the same way, ε_{max} values increased along with enlargement of the π-system.

Dyes **10** and **11** absorb at longer wavelength than **1** due to enlargement of the π-conjugation system with increment of ε_{max} value. Dyes **10** and **11** showed almost same long wavelength absorption maximum in chloroform in spite of their different ring-conjugation systems, but their short wavelength λ_{max} were quite different (see Experimental). A distinguished difference was observed in their ε_{max} value; conjugated **10** has large ε_{max} value of 23100 but less conjugated **11** has smaller value of 8400. Their fluorescence spectra and the Stokes shift were generally affected by the chromophoric system. In general, the stronger the intramolecular charge-transfer character, the bigger the Stokes shift value [11]. Dyes **2**, **6**, **7** and **10** showed smaller Stokes shift values, and dyes **1**, **3** and **8** showed larger ones. Relative intensity of fluorescence in the solid state were largely affected by their chemical structure and then the stronger the intermolecular π-π interactions, the stronger the fluorescence quenching [11]. Fluorescence maximum in the solid state produces a bathochromic shift of 11-51 nm from those in the solution, and their relative intensity of fluorescence changed from 300 to 8200 depending on the chromophoric system.

EXPERIMENTAL

The pmr and cmr spectra were taken on a Jeol FX 270 (270 MHz) spectrometer using TMS as internal reference. The ms spectra were recorded on a Shimadzu GCMS-QP5000 spectrometer. The UV/visible spectra were measured on a Hitachi 220A spectrophotometer. Fluorescence spectra were measured on a Hitachi F-4500 fluorescence spectrophotomator and those in the solid state on a Hamamatsu Photonic Multi-channel Analyzer PMA-11 using a Jasco SM-3 type monochromator as a light source. Melting points were determined on a Yamato melting point apparatus (MP-21) without correction. Microanalyses were conducted with a Yanaco CHN MT-3 recorder. Wako gel C-200 (silica gel) was used for column chromatography.

2,5-Diamino-3,6-dicyanopyrazine (**1**) was synthesized and identified previously [10].

Synthesis of 3,7-Di-*n*-butyl-5-*N*-*n*-butylcarbamoyl-1,2,3,5,6,7,8-heptahydroimidazo[4,5-*g*]pteridine-2,6,8-trione (**2**).

Compound **1** (0.48 g, 3.0 mmoles) and *n*-butyl isocyanate (0.81 ml, 7.2 mmoles) were dissolved in distilled dimethylformamide (5 ml), and sodium hydride (60% in oil) (0.50 g, 12.5 mmoles) was gradually added cooling with ice, and then the mixture was stirred at room temperature for 2 hours. After quenching with water, diluted hydrochloric acid was added to the reaction mixture. The separated product was extracted with dichloromethane and the extract was washed with water, dried over anhydrous magnesium sulfate, and was evaporated under reduced pressure. The product was isolated by column chromatography on silica gel using benzene/ethyl acetate (v/v = 1/1) as eluent to give the crude product. The crude product was recrystallized from ethyl acetate to give **2** as a pale yellow solid in 23% yield, mp (dec) 284-285°; ms: m/z 430 (M^+); pmr (deuteriochloroform): δ 11.2 (broad, 1H, NH), 9.59 (t, 1H, NH, J = 6.7 Hz), 8.67 (s, 1H, NH), 4.37 (t, 2H, CH_2, J = 7.3 Hz), 4.02 (t, 2H, CH_2, J = 7.3 Hz), 3.44 (q, 2H, CH_2, J = 6.7 Hz), 1.87-1.73 (m, 4H, $2CH_2$), 1.63 (quin, 2H, CH_2, J = 7.3 Hz), 1.48-1.37 (m, 6H, $3CH_2$), 0.99 (t+t, 6H, $2CH_3$, J = 7.3 Hz), 0.94 (t, 3H, CH_3, J = 7.3 Hz) ppm; cmr (deuteriochloroform): δ 157.3, 154.3, 153.6, 146.5, 144.3, 135.2, 111.7, 42.65, 40.28, 40.21, 31.79, 30.04, 29.98, 20.17, 19.97, 13.82, 13.78, 13.54 ppm; uv/vis (chloroform) λ_{max} 239 (ε 13100), 265 (ε 16600), 376 (ε 23600), 386 (ε 20400) and 396 nm (ε 20400).

Anal. Calcd. for $C_{20}H_{30}N_8O_3$: C, 55.80; H, 7.02; N, 26.03. Found: C, 55.94; H, 6.90; N, 26.08.

Syntheses of **3a** and **3b**.

Reaction was carried out under a nitrogen atmosphere. *tert*-Butyl isocyanate (1.05 ml, 9.2 mmoles) was added to a solution of **1** (0.48 g, 3.0 mmoles) in distilled dimethylformamide (5 ml), and

sodium hydride (60% in oil) (0.51 g, 12.8 mmoles) was added gradually cooling with ice, and then the mixture was stirred at room temperature for 2 hours. The reaction was quenched with water and diluted hydrochloric acid was added and the *p*H was adjusted to *p*H 4. The product was extracted with ethyl acetate (240 ml) and the extract was washed with water, dried over anhydrous magnesium sulfate, and was evaporated under reduced pressure. The products were isolated by column chromatography on silica gel using benzene/ethyl acetate (v/v = 5/1) as eluent to give the crude products **3a** and **3b**.

5-Amino-3-*tert*-butyl-6-cyano-1*H*-2,3-dihydroimidazo[4,5-*b*]-pyrazin-2-one (**3a**).

The crude product was recrystallized from dichloromethane to give **3a** as a pale yellow solid in 20% yield, mp 269-270°; ms: m/z 232 (M^+); pmr (deuteriochloroform): δ 8.80 (broad, 1H, NH), 4.88 (s, 2H, NH_2), 1.75 (s, 9H, $3CH_3$) ppm; cmr (deuteriochloroform): δ 153.3, 142.5, 131.0, 125.4, 116.9, 98.72, 60.26, 28.94 ppm; uv/vis (chloroform) λ_{max} 267 (ε 9200), 244 (ε 13000) and 365 nm (ε 14200).

Anal. Calcd. for $C_{10}H_{12}N_6O$: C, 51.71; H, 5.21; N, 36.19. Found: C, 51.76; H, 5.15; N, 36.12.

3-*tert*-Butyl-5-(1-*N*-*tert*-butylcarbamoylamino)-6-cyano-1*H*-2,3-dihydroimidazo[4,5-*b*]pyrazin-2-one (**3b**).

The crude product was recrystallized from dichloromethane/-ethyl acetate to give **3b** as a colorless solid in 36% yield, mp (dec) 216-217°; ms: m/z 331 (M^+); pmr (deuteriochloroform): δ 8.91 (broad, 1H, NH), 7.27 (s, 1H, NH), 7.20 (s, 1H, NH), 1.84 (s, 9H, $3CH_3$), 1.44 (s, 9H, $3CH_3$) ppm; cmr (deuteriochloroform): δ 152.8, 151.6, 147.1, 140.1, 132.1, 115.1, 103.0, 60.28, 51.72, 29.31, 29.26 ppm; uv/vis (chloroform) λ_{max} 277 (ε 13700), 247 (ε 13800) and 363 nm (ε 15300).

Anal. Calcd. for $C_{15}H_{21}N_7O_2$: C, 54.37; H, 6.39; N, 29.59. Found: C, 54.39; H, 6.39; N, 29.30.

Synthesis of 3,8-Di-*n*-butyl-2,7-di-*n*-butylthio-4,9-diimino-3,4,8,9-tetrahydropyrimido[4,5-*g*]pteridine (**4**).

The reaction was carried out under a nitrogen atmosphere. Compound **1** (0.96 g, 6.0 mmoles) and *n*-butyl isothiocyanate (1.70 ml, 14.1 mmoles) were dissolved in distilled dimethylformamide (20 ml), and *n*-butyl iodide (2.10 ml, 18.5 mmoles) and then sodium hydride (60% in oil) (0.72 g, 18.0 mmoles) was added gradually cooling with ice. After ten minutes, dichloromethane (250 ml) and water (100 ml) were added into the reaction mixture. Dichloromethane layer was washed with water, dried over anhydrous magnesium sulfate, and was evaporated under reduced pressure to give the crude product. The crude product was recrystallized from *n*-hexane to give **4** as a yellow solid in 72% yield, mp 189-190°; pmr (deuteriochloroform): δ 9.32 (s, 2H, 2NH), 4.22 (t, 4H, $2CH_2$, J = 7.3 Hz), 3.37 (t, 4H, $2CH_2$, J = 7.3 Hz), 1.81-1.76 (m, 8H, $4CH_2$), 1.58-1.45 (m, 8H, $4CH_2$), 1.00 (t, 12H, $4CH_3$, J = 7.3 Hz) ppm; cmr (deuteriochloroform): δ 162.6, 156.6, 147.5, 133.0, 46.07, 32.20, 30.40, 28.63, 22.06, 20.16, 13.78, 13.72 ppm; uv/vis (chloroform) λ_{max} 285 (ε 11100), 328 (ε 19100), 346 nm (ε 19300), 419 (ε 16300) and 444 (ε 18100).

Synthesis of 3,8-Di-*n*-butyl-1,2,3,4,6,7,8,9-octahydropyrimido-[4,5-*g*]pteridine-2,3,7,9-tetrone (**5**).

Compound **4** (0.92 g, 1.83 mmoles) in *n*-propanol (40 ml) and 6*N* sulfuric acid (40 ml) was stirred under reflux for 24 hours. After standing at room temperature, the reaction mixture was cooled with ice water. The separated precipitate was collected by filtration, washed with water, methanol and ether, and was dried *in vacuo* to give the crude product. The crude product was recrystallized from dichloromethane/*n*-hexane to give **5** as a yellow solid in 87% yield, mp >300°; ms: m/z 360 (M^+, 100%); pmr (deuteriochloroform): δ 12.16 (s, 2H, 2NH), 3.92 (t, 4H, $2CH_2$, J = 7.3 Hz), 1.60 (quin, 4H, $2CH_2$, J = 7.3 Hz), 1.34 (sextet, 4H, $2CH_2$, J = 7.3 Hz), 0.92 (t, 6H, $2CH_3$, J = 7.3 Hz) ppm; cmr (deuteriochloroform): δ 159.3, 149.3, 144.1, 128.9, 40.79, 29.27, 19.52, 13.44 ppm; uv/vis (chloroform) λ_{max} 256 (ε 28700), 292 (ε 2200) and 407 nm (ε 9900).

Anal. Calcd. for $C_{16}H_{20}N_6O_4$: C, 53.33; H, 5.59; N, 23.32. Found: C, 53.26; H, 5.46; N, 23.09.

Syntheses of **6** and **7**.

To the solution of compound **5** (2.16 g, 6.0 mmoles) in distilled dimethylformamide (80 ml), anhydrous potassium carbonate (6.63 g, 48.0 mmoles) and *n*-butyl iodide (3.41 ml, 30.0 mmoles) were added, and the mixture was stirred under reflux for 2 hours. After cooling at room temperature, the solid was separated by filtration, and the filtrate was extracted with dichloromethane. Dichloromethane layer was washed with water and evaporated under reduced pressure. The residue was dried *in vacuo*. The product was isolated by column chromatography on silica gel using benzene/ethyl acetate (v/v = 5/1) as eluent to give the crude products **6** and **7**.

1,3,6,8-Tetra-*n*-butyl-1,2,3,4,6,7,8,9-octahydropyrimido[4,5-*g*]-pteridine-2,4,7,9-tetrone (**6**).

The crude product was recrystallized from dichloromethane/-*n*-hexane to give **6** as a yellow powder in 74% yield, mp 153-154°; ms: m/z 472 (M^+); pmr (deuteriochloroform): δ 4.41 (t, 4H, $2CH_2$, J = 7.4 Hz), 4.14 (t, 4H, $2CH_2$, J = 7.6 Hz), 1.82-1.67 (m, 8H, $4CH_2$), 1.44 (sextet, 8H, $4CH_2$, J = 7.3 Hz), 0.99 (t, 6H, $2CH_3$, J = 7.3 Hz), 0.98 (t, 6H, $2CH_3$, J = 7.3 Hz) ppm; cmr (deuteriochloroform): δ 158.4, 149.6, 144.0, 129.2, 43.08, 42.74, 29.79, 29.73, 20.26, 20.01, 13.72 ppm; uv/vis (chloroform) λ_{max} 264 (ε 31700), 416 (ε 9800) and 438 nm (ε 8500).

Anal. Calcd. for $C_{24}H_{36}N_6O_4$: C, 61.00; H, 7.68; N, 17.78. Found: C, 61.30; H, 7.68; N, 17.63.

1,3,5,7-Tetra-*n*-butyl-1*H*-2,3,5,6,7,8-hexahydroimidazo[4,5-*g*]-pteridine-2,6,8-trione (**7**).

The product was recrystallized from *n*-hexane to give **7** as a colorless solid in 11% yield, mp 83-84°; ms: m/z 444 (M^+); pmr (deuteriochloroform): δ 12.10 (broad, 2H, 2NH), 4.33 (t, 2H, CH_2), 4.15-4.00 (m, 6H, $3CH_2$), 1.90-1.80 (m, 4H, $2CH_2$), 1.80-1.66 (m, 4H, $2CH_2$), 1.48-1.36 (m, 8H, $4CH_2$), 1.01-0.93 (m, 12H, $4CH_3$) ppm; uv/vis (chloroform) λ_{max} 254 (ε 19800), 275 (ε 8100), 361 (ε 17400), 371 (ε 15600) and 379 nm (ε 13000).

Anal. Calcd. for $C_{23}H_{36}N_6O_3$: C, 62.14; H, 8.16; N, 18.90. Found: C, 62.01; H, 8.06; N, 18.65.

Synthesis of **8a** and **8b**.

To the solution of compound **1** (0.64 g, 4.0 mmoles) in dimethylacetamide (10 ml), *n*-propylamine (3.3 ml, 40 mmoles) was added and stirred at room temperature for 9 hours. The reaction was quenched with water and the separated precipitate was filtered and dried *in vacuo*. The product was isolated by column chromatography on silica gel using ethyl acetate as eluent to give the crude products **8a** and **8b**.

2,5-Diamino-6-cyanopyrazine-3-(*N*-*n*-propylamino)carboxamidine (**8a**).

The crude product was recrystallized from chloroform to give **8a** as an orange solid in 14% yield, mp 160-161°; ms: m/z 219 (M^+); pmr (deuteriochloroform): δ 3.14 (t, 2H, CH_2, J = 7.2 Hz), 1.75 (sex, 2H, CH_2, J = 7.2 Hz), 1.58 (broad, 5H, $2NH_2$ + NH), 1.03 (t, 3H, CH_3, J = 7.2 Hz) ppm; uv/vis (chloroform) λ_{max} 434 (ε 8800), 270 nm (ε 17000).

Anal. Calcd. for $C_9H_{13}N_7$: C, 49.30; H, 5.98; N, 44.72. Found: C, 49.26; H, 6.00; N, 44.32.

2,5-Diaminopyrazine-3,6-bis[(*N*-*n*-propylamino)carboxamidine] (**8b**).

The crude product was recrystallized from chloroform to give **8b** as a yellowish-orange solid in 15% yield, mp 190-191°; ms: m/z 278 (M^+); pmr (deuteriochloroform): δ 6.51 (broad, 2H, 2NH), 3.15 (t, 4H, $2CH_2$, J = 7.2 Hz), 1.74 (sex, 4H, $2CH_2$, J = 7.2 Hz), 1.63 (broad, 6H, $2NH_2$ + 2NH), 1.03 (t, 6H, $2CH_3$, J = 7.2 Hz) ppm; uv/vis (chloroform) λ_{max} 429 (ε 10300), 274 nm (ε 13100).

Anal. Calcd. for $C_{12}H_{22}N_8$: C, 51.78; H, 7.97; N, 40.26. Found: C, 51.67; H, 8.13; N, 39.78.

Synthesis of 2,7-Diphenyl-4,9-bis(*n*-propylamino)pyrimido[4,5-*g*]-pteridine (**10**).

Compound **1** (1.28 g, 8.0 mmoles) and *n*-propylamine (6.60 ml, 80.0 mmoles) were dissolved in distilled dimethylformamide (20 ml) at room temperature and the mixture was stirred for 6 days. Ethyl acetate was added to the mixture and excess of amine was evaporated together with ethyl acetate. Benzaldehyde (2.50 ml, 25.0 mmoles) was then added to the residue and refluxed for 1 hour. The mixture was evaporated under reduced pressure at 100°. Chloroform was added to the residue and standing for 1 day, and the separated precipitate was filtered and dried to give the crude product. The crude product was recrystallized from ethyl acetate/*n*-hexane to give **10** as an orange solid in 12% yield, mp 257-258°; ms: m/z 450 (M^+); pmr (deuteriochloroform): δ 8.67-8.64 (m, 4H, phenyl protons), 7.73 (t, 2H, 2NH, J = 6.9 Hz), 7.53-7.49 (m, 6H, phenyl protons), 3.83 (q, 4H, $2CH_2$, J = 6.8 Hz), 1.87 (sextet, 4H, $2CH_2$, J = 7.3 Hz), 1.11 (t, 6H, $2CH_3$, J = 7.3 Hz) ppm; cmr (deuteriochloroform): δ 164.9, 160.3, 151.1, 137.8, 131.4, 129.3, 128.3, 77.21, 43.36, 22.50, 11.65 ppm; uv/vis (chloroform) λ_{max} 263 (ε 10200), 322 (ε 52900), 465 (ε 20400) and 494 nm (ε 23100), (dimethoxyethane) λ_{max} 320, 463 and 493 nm.

Anal. Calcd. for $C_{26}H_{26}N_8$: C, 69.31; H, 5.82; N, 24.87. Found: C, 69.11; H, 6.16; N, 24.61.

Synthesis of 4,9-Bis(methylamino)bisspiro[1,2,6,7-tetrahydro-pyrimido[4,5-*g*]pteridine[2,1':8,1"]biscyclohexane (**11**).

Compound **1** (1.28 g, 8.0 mmoles) in 40% alcoholic methylamine (6.30 ml, 65.0 mmoles) and distilled dimethylformamide (20 ml) were stirred at room temperature for 6 days. Dichloromethane was added to the mixture and excess of methylamine was evaporated together with dichloromethane, and then cyclohexanone (10 ml, 96.4 mmoles) was added to the residue. The mixture was refluxed with stirring for 30 minutes and was evaporated under reduced pressure at 100°. Dichloromethane was added and the separated precipitate was filtered and dried *in vacuo*. The product was isolated by column chromatography on silica gel using benzene/ethyl acetate (v/v = 5/1) as eluent to give the crude product. The crude product was recrystallized from dichloromethane/ethyl acetate/methanol (v/v/v = 1/2/1) to give **11** as an orange solid in 43% yield, mp 225-226°; ms: m/z 382 (M^+); pmr (deuteriochloroform): δ 5.85 (q, 2H, 2NH), 5.57 (s, 2H, 2NH), 2.84 (d, 6H, $2CH_3$, J = 4.3 Hz), 1.80-1.70 (m, 8H, $4CH_2$), 1.61-1.58 (m, 4H, $2CH_2$), 1.52-1.39 (m, 8H, $4CH_2$) ppm; cmr (deuteriochloroform): δ 149.9, 144.4, 125.1, 69.72, 40.20, 26.88, 24.96, 21.51 ppm; uv/vis (chloroform) λ_{max} 239 (ε 7600), 298 (ε 10200) and 493 nm (ε 8400), (dimethoxyethane) λ_{max} 226, 299 and 500 nm.

Anal. Calcd. for $C_{20}H_{30}N_8$: C, 62.80; H, 7.91; N, 29.30. Found: C, 62.50; H, 7.97; N, 28.87.

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