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Reaction of 2-aminopyrazine **1** with isothiocyanate, isocyanate or dithioketal reagent furnished pteridines **3,4** in good yield. Thioxo compound **3a** was chlorinated, methylated and subsequently displaced by amines. A simple one-step synthesis of heterocondensed pteridines **8-13** by reaction of 2-aminopyrazine with various imino thioacetals was described **8-13**.

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Tetrahydrobiopterin derivatives and dihydropteridine derivatives are of great interest for their dihydrofolate reductase inhibiting, mental retardation, neurotransmitter and use in treating other neurological problems [1-3]. Recently, 6-pyruvoyltetrahydropterin synthase was found to be deficient in some Japanese patients [4].

In 1992 W. Pfleiderer described in his review paper [5] the synthesis, properties, stereochemistry, reactivities and biological significance of pteridines and their derivatives. The aromatic and heteroaromatic 2-aminoester or 2-aminonitrile compounds undergo readily cyclization which allow convenient preparation of variety of condensed pyrimidines [6]. We have recently reported the synthesis of novel heterocyclic fused pyrimidine systems [7-10] in one-pot annelation by the reaction of 2-aminoester or 2-aminonitrile compounds with the *N*-[bis-(methylthio)methylene]amino (BMMA) or analogs of BMMA reagents.

Although several methods are available for the syntheses of pteridines [11-15], the methodology whereby the pyrazine intermediate requiring the addition of *N*-3 to complete the pteridine ring has not been widely used [12].

Previously we have been interested in the synthesis of substituted heterocycles containing a thienopyrimidine system [7-10,16,17]. The present paper follows that line of research by reporting on a new series of linear fusion of 2-aminopyrazine **1**, in which imidazole, pyrimidine, thiazole, thiazine and pyrazine moieties were annelated, yielding novel tricyclic ring systems. In this paper, we report a simple, one-pot reaction for the synthesis of pteridinone, imidazo[2,1-*b*]pteridine, pyrimido[2,1-*b*]pteridine, thiazolo[2,3-*b*]pteridine, thiazino[2,3-*b*]pteridine and pyrazino[2,1-*b*]pteridine.

The two key intermediates in these syntheses *viz* 3-(2-ethoxycarbonylmethyl)-2-methylthio-4(3*H*)-pteridinone (**4**) and 3-(2-ethoxycarbonylmethyl)-2-chloro-4(3*H*)-pteridinone (**5**) were synthesized by cyclizing the methyl 2-aminopyrazine-3-carboxylate (**1**). As depicted in Scheme 1, the intermediate, **4** can be obtained by one of the following two sequences: 1) preparation of the thioureidopyrazine **2a** by reaction of **1** with ethyl isothiocyanatoacetate and the ensuing cyclization with NaOEt to **3a**, followed by *S*-methylation with methyl iodide, or **2**) by the condensation reaction of ethyl *N*-[bis(methylthio)-methylene]glycinate with **1** in the presence of dry acetic acid.

Utilization of the ethyl isothiocyanatoacetate for the synthesis of 3-(2-ethoxycarbonylmethyl)-2-thioxo-1,2-dihydro-4(3*H*)-pteridinone (**3a**) was advantageous with a simple and useful substitution pattern over a different pathway to thioxopteridine **3a** from methyl 2-aminopyrazine-3-carboxylate (**1**) reported by Urleb *et al*. [13]. The spectroscopical analysis and mp of compound **3a** are also in good agreement with the literature values [13].

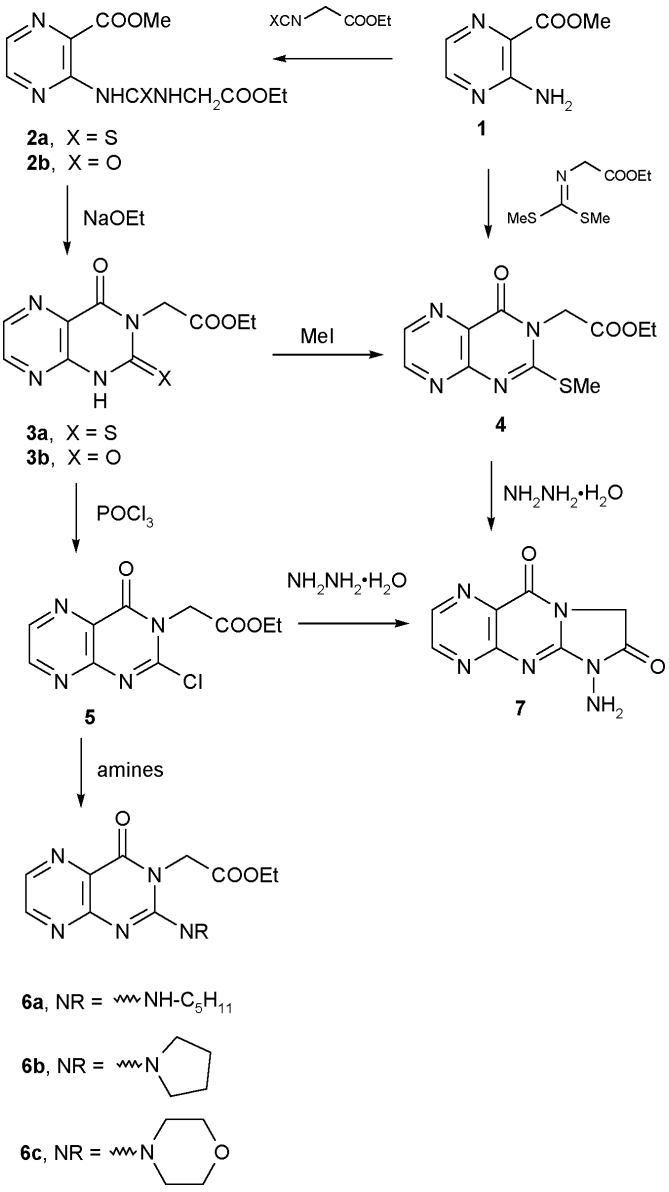
Treatment of 2-aminopyrazine **1** with ethyl isocyanatoacetate in the presence of pyridine gave urethane product **2b** and followed by cyclization with NaOEt to 3-(2-ethoxycarbonylmethyl)-2-oxo-1,2-dihydro-4(3*H*)-pteridinone (**3b**).

Chlorination of thioxopteridine **3a** with phosphorus oxychloride yielded 3-(2-ethoxycarbonylmethyl)-2-chloro-4(3*H*)-pteridinone (**5**), which was used for a further step without analysis.

Chloropyrimidines were the most versatile intermediates for the synthesis of pyrimidine derivatives [17]. Since chloro compound **5** represents an interesting reactive intermediate, we studied some of its transformation with *N*-nucleophiles. The displacement reaction of **5** with amines was an efficient method for the preparation of pteridine derivatives and a product was readily obtained with hydrazine hydrate.

Chloro derivative **5** on heating with pentylamine in triethylamine gave uncyclized pentylaminopteridine derivative **6a** in 53% yield. A substitution reaction of pyrrolidine or morpholine were also afforded 3-(2-ethoxycarbonylmethyl)-2-(1-pyrrolidinyl)-4(3*H*)-pteridinone (**6b**) and 3-(2-ethoxycarbonylmethyl)-2-(4-morpholinyl)-4(3*H*)-pteridinone (**6c**). The reaction of hydrazine hydrate with 3-(2-ethoxycarbonylmethyl)-2-chloro-4(3*H*)-pteridinone (**5**) or the methyl thioester **4** afforded the target linear *N*-aminolactam, 1-aminoimidazo[2,1-*b*]pteridin-2,5(1*H*,3*H*)-dione (**7**) in overall good yield (Scheme 1).

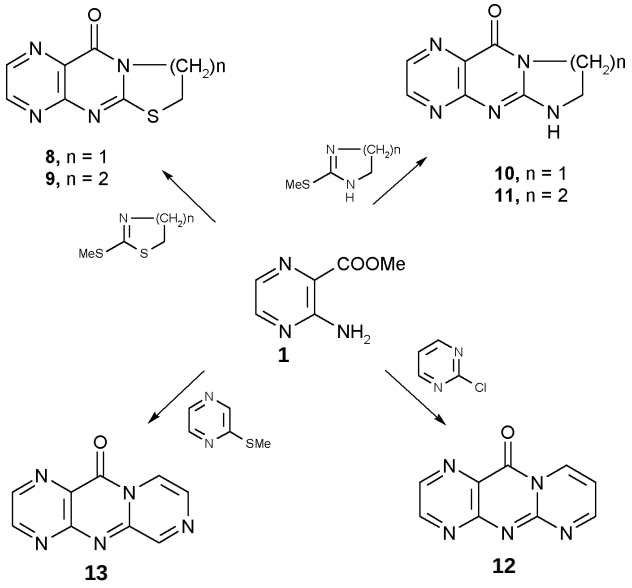
Scheme 1



Furthermore, to extend of our BMMA method to cyclic analogs of BMMA reagents, imino thioacetals were studied to determine their applicability to reactions with 2-aminopyrazine **1**. Displacement reactions have been employed to create the middle ring of tricyclic or tetracyclic systems in one-step as described in the literature [10]. So, the concept of creating our desired tricyclic condensed systems in one-step *via* a double displacement process using the cyclic analogs of BMMA reagents is demonstrated.

Thus, a series of imino thioacetals: 2-(methylthio)-2-thiazoline, 5,6-dihydro-2-(methylthio)-4*H*-1,3-thiazine, 2-(methylthio)-2-imidazoline, 2-(methylthio)-1,4,5,6-tetrahydropyrimidine and 2-(methylthio)-2-pyrazine, reacted readily with *2*-aminopyrazine **1** to give the desired tricyclic fusion products, thiazolo[2,3-*b*]pteridine derivative (**8**), thiazino[2,3-*b*]pteridine derivative (**9**), imidazo[2,1-*b*]pteridine derivative (**10**), pyrimido[2,1-*b*]pteridine derivative (**11**) and pyrazino[2,1-*b*]pteridine derivative (**13**) respectively by one-step reaction. The thiazolo[2,3-*b*]pteridine (**8**) and thiazino[2,3-*b*]pteridine (**9**) systems have already been synthesized earlier in different research groups [14,15] utilizing multi-step approaches different from the method reported in this paper. 2-Aminopyrazine **1** with 2-(methylthio)-1,4,5,6-tetrahydropyrimidine at 150° furnished identical product **11** in a neat reaction or in hexamethylphosphoric triamide (HMPTA). Solvent played an important role in the reaction medium. In the preparation of compounds **8,9** dry acetic acid [18] was optimal and for **10,11** it was HMPTA. 2-Chloropyrimidine was heated with aminopyrazine **1** at 150° under nitrogen in a one-pot reaction to afford 6*H*-pyrimido[2,1-*b*]pteridin-6-one (**12**) in only 42% yield. (Scheme 2).

Scheme 2



EXPERIMENTAL

Melting points were determined on a Yanaco hot stage apparatus and are uncorrected. Thin layer chromatography (tlc) was performed on silica gel F_{254} precoated plastic sheets (layer thickness 0.2 mM) and spots were detected by UV lamp (Model UVGL 58). Column chromatography was carried out at room temperature with silica gel G_{60}. All evaporations were conducted under reduced pressure with a bath temperature below 40 °C. The nmr spectra (^{1}H and ^{13}C) were recorded on a JNM-ALPHA 500 (500 MHz) spectrometer in deuteriochloroform or dimethyl-d_6 sulfoxide using tetramethylsilane (TMS) as an internal standard and the chemical

shifts are expressed in δ ppm. Elemental analyses were performed on an EA 1108 (Fisons Instruments) Elemental Analyzer.

Ethyl isothiocyanatoacetate [17] and ethyl *N*-[bis(methylthio)-methylene]glycinate [19] were prepared using the method reported by Sauter *et al*. both as a syrup. *Via* a two-step procedure 2-(methylthio)-2-thiazoline [20,21] and 5,6-dihydro-2-(methylthio)-4*H*-1,3-thiazine [20,22] were synthesized from 2-aminoethanol or 3-aminopropanol and CS_2 and subsequent methylation with methyl iodide. 2-(Methylthio)-2-imidazoline and 2-(methylthio)-1,4,5,6-tetrahydropyrimidine were obtained according to literature procedures [23,24]. Methyl 2-aminopyrazine-3-carboxylate (**1**) was purchased from TCI (Tokyo Chemical Industry Co., Ltd.). Ethyl isocyanatoacetate, 2-chloropyrimidine and 2-(methylthio)-2-pyrazine were purchased from Aldrich.

For the preparation of dry acetic acid, technically pure acetic acid was purchased from Merck (Art. No. 63), slowly crystallized at 4° and separated from the remaining liquid by decanting or quickly filtering in the cold. Finally, it was dried over phosphorous pentoxide and distilled. To maintain dryness it was kept over molecular sieve.

Methyl 2-(3-Ethoxycarbonylmethylthioureido)pyrazine-3-carboxylate (**2a**).

A solution of methyl 2-aminopyrazine-3-carboxylate (**1**, 0.61 g, 4 mmol) and ethyl isothiocyanatoacetate (0.58 g, 4 mmol) in pyridine (7 ml) was refluxed for 2 hours. The reaction mixture was diluted with ethanol and cooled. The resulting crystals were collected by filtration and recrystallized from ethanol to give **2a** as brown needles, 0.78 g (66%), mp 126-128°; ^{1}H nmr (deuteriochloroform): δ_H 1.25-1.29 (t, *J* = 7.2 Hz, 3H, Me), 3.96 (s, 3H, Me), 4.21-4.25 (q, *J* = 7.2 Hz, 2H, OCH_2), 4.35 (s, 2H, CH_2), 7.84 (s, 1H, NH), 8.68 (d, *J* = 2.4 Hz, 1H, 5-H), 8.82 (d, *J* = 2.4 Hz, 1H, 6-H); ^{13}C nmr (deuteriochloroform): δ_C 14.05 (q, Me), 48.03 (t, CH_2), 52.76 (q, Me), 61.93 (t, OCH_2), 127.90 (d, C-5), 133.51 (d, C-6), 142.68 (s, C-3), 149.04 (s, C-2), 157.96 (s, C=O), 166.63 (s, C=O), 176.24 (s, C=S).

Anal. Calcd. for $C_{11}H_{14}N_4O_4S$: C, 44.28; H, 4.72; N, 18.78. Found: C, 44.41; H, 4.83; N, 18.94.

Methyl 2-(3-ethoxycarbonylmethylureido)pyrazine-3-carboxylate (**2b**).

The title compound was prepared in the same manner as **2a** from methyl 2-aminopyrazine-3-carboxylate (**1**, 0.61 g, 4 mmol) and ethyl isocyanatoacetate (0.51 g, 4 mmol), reaction time 2 hours and recrystallized from ethanol to give **2b** as yellow needles, 0.64 g (57%), mp 135-137°; ^{1}H nmr (deuteriochloroform): δ_H 1.25-1.28 (t, *J* = 7.2 Hz, 3H, Me), 3.95 (s, 3H, Me), 4.20-4.24 (q, *J* = 7.2 Hz, 2H, OCH_2), 4.40 (s, 2H, CH_2), 7.99 (s, 1H, NH), 8.61 (d, *J* = 2.4 Hz, 1H, 5-H), 8.76 (d, *J* = 2.4 Hz, 1H, 6-H), 11.00 (s, 1H, NH); ^{13}C nmr (deuteriochloroform): δ_C 14.01 (q, Me), 48.40 (t, CH_2), 52.70 (q, Me), 61.65 (t, OCH_2), 127.45 (d, C-5), 133.37 (d, C-6), 141.59 (s, C-3), 148.09 (s, C-2), 159.77 (s, C=O), 167.18 (s, C=O), 169.16 (s, C=O).

Anal. Calcd. for $C_{11}H_{14}N_4O_5$: C, 46.80; H, 4.99; N, 19.85. Found: C, 46.95; H, 5.07; N, 19.62.

3-(2-Ethoxycarbonylmethyl)-2-thioxo-1,2-dihydro-4(3*H*)-pteridinone (**3a**).

A solution of thiourea derivative **2a** (0.59 g, 2 mmol) and NaOEt (0.14 g, 2 mmol) in 10 ml of absolute ethanol was stirred for 2 hours at room temperature. The solvent was removed *in vacuo* and the obtained solid was recrystallized from ethanol to give **3a** as pale red crystals, 0.43 g (82%), mp 240-242° (Lit. [13] 238-241°); ^{1}H nmr (deuteriochloroform): δ_H 1.20-1.23 (t, *J* = 7.1 Hz, 3H, Me), 4.18-4.23 (q, *J* = 7.1 Hz, 2H, OCH_2), 5.15 (s, 2H, CH_2), 8.71 (d, *J* = 2.4 Hz, 1H, 6-H), 8.86 (d, *J* = 2.4 Hz, 1H, 7-H), 9.91 (s, 1H, NH); ^{13}C nmr (deuteriochloroform): δ_C 14.14 (q, Me), 48.21 (t, CH_2), 61.70 (t, OCH_2), 127.93 (s, C-4a), 142.42 (d, C-6), 147.56 (s, C-8a), 150.24 (d, C-7), 159.15 (s, C=O), 167.35 (s, C=O), 176.39 (s, C=S).

Anal. Calcd. for $C_{10}H_{10}N_4O_3S$: C, 45.10; H, 3.78; N, 21.04. Found: C, 45.23; H, 3.87; N, 21.14.

3-(2-Ethoxycarbonylmethyl)-2-oxo-1,2-dihydro-4(3*H*)-pteridinone (**3b**).

The title compound was obtained in 70 % yield using a procedure similar to that which afforded **3a** as red crystals from urea derivative **2b**, mp 251-253 °; ^{1}H nmr (deuteriochloroform): δ_H 1.20-1.23 (t, *J* = 7.1 Hz, 3H, Me), 4.18-4.22 (q, 2H, *J* = 7.1 Hz, OCH_2), 5.20 (s, 2H, CH_2), 8.58 (d, *J* = 2.4 Hz, 1H, 6-H), 8.75 (d, *J* = 2.4 Hz, 1H, 7-H), 10.01 (s, 1H, NH); ^{13}C nmr (deuteriochloroform): δ_C 14.04 (q, Me), 48.02 (t, CH_2), 61.56 (t, OCH_2), 127.29 (s, C-4a), 141.53 (d, C-6), 147.53 (s, C-8a), 150.61 (d, C-7), 154.58 (s, C=O), 166.15 (s, C=O), 169.15 (s, C=O).

Anal. Calcd. for $C_{10}H_{10}N_4O_4$: C, 48.00; H, 4.02; N, 22.39. Found: C, 48.17; H, 4.13; N, 22.56.

3-(2-Ethoxycarbonylmethyl)-2-methylthio-4(3*H*)-pteridinone (**4**).

Method A.

To a solution of sodium methoxide (0.53 g, 10 mmol) in dry methanol (75 ml) was added thioxo compound **3a** (2.66 g, 10 mmol) and the mixture was stirred as the temperature raised to 60°. Methyl iodide (1.42 g, 10 mmol) was added while the mixture was refluxed under nitrogen for 2 hours and then cooled to give a solid. The solid was collected and recrystallized from ethanol, 1.82 g (65%).

Method B.

A solution of methyl 2-aminopyrazine-3-carboxylate (**1**, 0.61 g, 4 mmol) and ethyl *N*-[bis(methylthio)methylene]glycinate (C_1-reagent) (0.82 g, 4 mmol) in 8 ml of dry acetic acid was heated under reflux for 8 hours. The solution was then poured into ice - water. The mixture was stirred for 1 hour and the precipitate was collected by filtration and recrystallized from ethanol, 0.63 g (57%). The compound is identical with the compound obtained by method A. mp 194-196°; ^{1}H nmr (deuteriochloroform): δ_H 1.15-1.18 (t, *J* = 7.1 Hz, 3H, Me), 2.60 (s, 3H, SMe), 4.25-4.28 (q, *J* = 7.1 Hz, 2H, OCH_2), 4.90 (s, 2H, CH_2), 8.62 (d, *J* = 2.4 Hz, 1H, 6-H), 8.76 (d, *J* = 2.4 Hz, 1H, 7-H); ^{13}C nmr (deuteriochloroform): δ_C 14.03 (q, SMe), 14.91 (q, Me), 44.25 (t, CH_2), 61.73 (t, OCH_2), 128.26 (s, C-4a), 142.48 (d, C-6), 147.60 (s, C-8a), 150.30 (d, C-7), 159.20 (s, C-2), 162.32 (s, C=O), 166.46 (s, C=O).

Anal. Calcd. for $C_{11}H_{12}N_4O_3S$: C, 47.13; H, 4.31; N, 19.98. Found: C, 46.98; H, 4.34; N, 19.87.

3-(2-Ethoxycarbonylmethyl)-2-chloro-4(3*H*)-pteridinone (**5**).

A suspension of the thioxo product **3a** (4.26 g, 16 mmol) in phosphoryl chloride (100 ml) was refluxed at 120° for 22 hours. Excess phosphoryl chloride was removed by distillation under vacuum. Ether (150 ml) was added and the mixture stirred for 2 hours. The solid was collected by filtration and washed with ether to afford

chloro product **5**, 2.92 g (68%), mp 140-142°. This compound, without further purification and analysis, was used in the next step.

3-(2-Ethoxycarbonylmethyl)-2-pentylamino-4(3*H*)-pteridinone (**6a**).

A solution of the chloro product **5** (0.54 g, 2 mmol) and pentylamine (0.26 g, 3 mmol) in triethylamine (5 ml) was refluxed for 8 hours. The solvent was evaporated *in vacuo*. The obtained solid was recrystallized from ethyl acetate to give **6a** as white crystals, 0.34 g (53%), mp 213-215°; ^{1}H nmr (deuteriochloroform): δ_H 1.10 (t, *J* = 7.0 Hz, 3H, Me), 1.20 (t, *J* = 7.1 Hz, 3H, Me), 1.30-1.70 (m, 6H, -CH_2-CH_2-CH_2-), 3.30 (m, 2H, N-CH_2), 4.25-4.28 (q, *J* = 7.1 Hz, 2H, OCH_2), 4.84 (s, 2H, CH_2), 6.00 (s, 1H, NH), 8.59 (d, *J* = 2.4 Hz, 1H, 6-H), 8.74 (d, *J* = 2.4 Hz, 1H, 7-H); ^{13}C nmr (deuteriochloroform): δ_C 13.63 (q, Me), 13.79 (q, Me), 22.12 (t, CH_2), 28.80 (t, CH_2), 28.91 (t, CH_2), 39.56 (t, N-CH_2), 46.94 (t, CH_2), 61.80 (t, OCH_2), 128.70 (s, C-4a), 142.80 (d, C-6), 147.65 (s, C-8a), 149.95 (d, C-7), 160.40 (s, C-2), 162.44 (s, C=O), 165.95 (s, C=O).

Anal. Calcd. for $C_{15}H_{21}N_5O_3$: C, 56.41; H, 6.62; N, 21.92. Found: C, 56.60; H, 6.80; N, 21.75.

3-(2-Ethoxycarbonylmethyl)-2-(1-pyrrolidinyl)-4(3*H*)-pteridinone (**6b**).

A solution of the chloro product **5** (0.54 g, 1 mmol) and pyrrolidine (0.98 g, 3 mmol) in triethylamine (5 ml) was refluxed for 6 hours. The solvent was evaporated *in vacuo*. The obtained solid was recrystallized from ethanol to give **6b** as white crystals, 0.35 g (57%), mp 225-227°; ^{1}H nmr (deuteriochloroform): δ_H 1.22 (t, *J* = 7.1 Hz, 3H, Me), 1.75-1.95 (m, 4H, -CH_2-CH_2-), 3.34-3.51 (m, 4H, -H_2C-N-CH_2-), 4.30 (q, *J* = 7.1 Hz, 2H, CH_2O), 4.76 (s, 2H, CH_2), 8.65 (d, *J* = 2.4 Hz, 1H, 6-H), 8.79 (d, *J* = 2.4 Hz, 1H, 7-H); ^{13}C nmr (dimethyl-d_6 sulfoxide): δ_C 14.20 (q, Me), 25.40 (t, -CH_2-CH_2-), 47.20 (t, CH_2), 50.50 (t, -H_2C-N-CH_2-), 61.88 (t, OCH_2), 128.65 (s, C-4a), 142.48 (d, C-6), 147.52 (s, C-8a), 150.20 (d, C-7), 160.25 (s, C-2), 162.14 (s, C=O), 165.89 (s, C=O).

Anal. Calcd. for $C_{14}H_{17}N_5O_3$: C, 55.44; H, 5.64; N, 23.08. Found: C, 55.60; H, 5.49; N, 23.26.

3-(2-Ethoxycarbonylmethyl)-2-(4-morpholinyl)-4(3*H*)-pteridinone (**6c**).

The title compound was prepared in the same manner as **6a** from chloro product **5** (0.54 g, 2 mmol) and morpholine (0.26 g, 3 mmol), reaction time 8 hours and recrystallized from ethanol to give **6c** as white crystals, 0.36 g (56%), mp 163-165°; ^{1}H nmr (deuteriochloroform): δ_H 1.25 (t, *J* = 7.1 Hz, 3H, Me), 3.15 (m, 4H, -H_2C-N-CH_2-), 3.80 (m, 4H, -H_2C-O-CH_2-), 4.30 (q, 2H, CH_2O), 4.65 (s, 2H, CH_2), 8.58 (d, *J* = 2.4 Hz, 1H, 6-H), 8.76 (d, *J* = 2.4 Hz, 1H, 7-H); ^{13}C nmr (deuteriochloroform): δ_C 14.04 (q, Me), 26.65 (t, C-8), 50.47 (t, -H_2C-N-CH_2-), 61.60 (t, OCH_2), 66.20 (t, -H_2C-O-CH_2-), 128.15 (s, C-4a), 142.35 (d, C-6), 147.48 (s, C-8a), 150.13 (d, C-7), 160.01 (s, C-2), 162.09 (s, C=O), 165.46 (s, C=O).

Anal. Calcd for $C_{14}H_{17}N_5O_4$: C, 52.66; H, 5.36; N, 21.93. Found: C, 52.53; H, 5.27; N, 21.76.

1-Aminoimidazo[2,1-*b*]pteridin-2,5(1*H*,3*H*)-dione (**7**).

Method A.

A solution of the chloro product **5** (0.54 g, 2 mmol) and 99% of hydrazine hydrate (0.10 g, 3 mmol) in triethylamine (5 ml) was refluxed for 5 hours. The solvent was evaporated *in vacuo*. The obtained solid was recrystallized from ethanol to give **7** as pale red crystals, 0.27 g (61%).

Method B.

A solution of the methylthio derivative **4** (0.56 g, 2 mmol) and 99% of hydrazine hydrate (5 ml) in absolute ethanol (8 ml) was stirred and heated under reflux for 8 hours. The solvent was evaporated under reduced pressure. The solid was washed with water and recrystallized from isopropanol to give pale red crystals, 0.22 g (51%), mp 294-296 °; ^{1}H nmr (deuteriochloroform): δ_H 4.45 (s, 2H, 3-H), 5.30 (s, 2H, NH_2) 8.68 (d, *J* = 2.4 Hz, 1H, 7-H), 8.87 (d, *J* = 2.4 Hz, 1H, 8-H); ^{13}C nmr (dimethyl-d_6 sulfoxide): δ_C 46.40 (t, C-3), 128.90 (s, C-5a), 142.75 (d, C-7), 147.98 (s, C-9a), 150.84 (d, C-8), 154.75 (s, C-10a), 162.90 (s, C=O), 166.35 (s, C=O).

Anal. Calcd. for $C_8H_6N_6O_2$: C, 44.04; H, 2.77; N, 38.51. Found: C, 44.13; H, 2.89; N, 38.37.

2,3-Dihydro-5*H*-thiazolo[2,3-*b*]pteridin-5-one (**8**).

A solution of methyl 2-aminopyrazine-3-carboxylate (**1**, 0.61 g, 4 mmol) and 2-(methylthio)-2-thiazoline (0.66 g, 5 mmol) in dry acetic acid (6 ml) was heated to 100° for 10 hours. After cooling to room temperature, crushed ice (100 g) was added and the mixture stirred for 1 hour. The separated product was collected and recrystallized from methanol to give **8** as yellow crystals, 0.43 g, (53%), mp 292-293° (decomposed) (Lit. [14,15] >300°); ^{1}H nmr (deuteriochloroform): δ_H 3.50 (t, *J* = 7.8 Hz, 2H, 2-H), 4.50 (t, *J* = 7.8 Hz, 2H, 3-H), 8.77 (d, *J* = 1.9 Hz, 1H, 7-H), 8.88 (d, *J* = 1.9 Hz, 1H, 8-H); ^{13}C nmr (deuteriochloroform): δ_C 26.72 (t, C-2), 48.10 (t, C-3), 132.55 (s, C-5a), 138.08 (d, C-7), 147.16 (s, C-9a), 147.90 (d, C-8), 150.01 (s, C-10a), 162.45 (s, C=O).

Anal. Calcd. for $C_8H_6N_4OS$: C, 46.59; H, 2.93; N, 27.16. Found: C, 46.68; H, 3.06; N, 27.31.

3,4-Dihydro-2*H*,6*H*-[1,3]thiazino[2,3-*b*]pteridin-6-one (**9**).

The title compound was prepared in the same manner as **8** from methyl 2-aminopyrazine-3-carboxylate (**1**, 0.61 g, 4 mmol) and 5,6-dihydro-2-(methylthio)-4*H*-1,3-thiazine (0.73 g, 5 mmol), reaction time 5 hours and recrystallized from ethanol to afford **9** as colourless crystals, 0.37 g (42%), mp 283-285° (Lit. [14] 285-287°); ^{1}H nmr (deuteriochloroform): δ_H 2.30 (m, 2H, 3-H), 3.20 (t, *J* = 7.5 Hz, 2H, 2-H), 4.20 (t, *J* = 6.5 Hz, 2H, 4-H), 8.77 (d, *J* = 2.1 Hz, 1H, 8-H), 8.81 (d, *J* = 2.1 Hz, 1H, 9-H); ^{13}C nmr (deuteriochloroform): δ_C 22.95 (t, C-3), 27.86 (s, C-2), 40.95 (t, C-4), 132.20 (s, C-6a), 138.41 (d, C-8), 147.32 (C-9), 147.85 (s, C-10a), 153.52 (s, C-11a), 161.85 (s, C=O).

Anal. Calcd. for $C_9H_8N_4OS$: C, 49.07; H, 3.65; N, 25.43. Found: C, 49.27; H, 3.77; N, 25.14.

2,3-Dihydroimidazo[2,1-*b*]pteridin-5(1*H*)-one (**10**).

A solution of methyl 2-aminopyrazine-3-carboxylate **1**, (0.61 g, 4 mmol) and 2-(methylthio)-2-imidazoline (0.69 g, 6 mmol) in hexamethylphosphoric triamide (HMPTA, 5 ml) was heated to 150° for 3 hours. After cooling to room temperature, crushed ice (70 g) was added and the mixture stirred for 1 hour. The separated product was collected and crystallized from ethyl acetate to give **10** as pale red crystals, 0.40 g (53%), mp 295-297° (decomposed); ^{1}H nmr (deuteriochloroform): δ_H 3.70 (t, *J* = 6.7 Hz, 2H, 2-H), 4.09 (t, *J* = 6.7 Hz, 2H, 3-H), 8.62 (d, *J* = 1.9 Hz, 1H, 7-H), 8.86 (d, *J* = 1.9 Hz, 1H, 8-H), 9.65 (s, 1H, NH); ^{13}C nmr (deuteriochloroform): δ_C 40.69 (t, C-2), 45.13 (t, C-3), 128.80 (s, C-5a), 141.84 (d, C-7), 146.80 (s, C-9a), 148.94 (C-8), 153.72 (d, C-10a), 165.07 (s, C=O).

Anal. Calcd. for $C_8H_7N_5O$: C, 50.79; H, 3.73; N, 37.01. Found: C, 50.67; H, 3.85; N, 36.67.

1,2,3,4-Tetrahydro-6*H*-pyrimido[2,1-*b*]pteridin-6-one (**11**).

Method A.

This compound was prepared in the same manner as **10** from 2-aminopyrazine **1** (0.61 g, 4 mmol) and reagent 2-(methylthio)-1,4,5,6-tetrahydropyrimidine (0.65 g, 5 mmol) with a reaction time of 3 hours, followed by recrystallized from ethanol to give **11** as pale red crystals, 0.46 g (57%).

Method B.

A mixture of 2-aminopyrazine **1** (0.92 g, 6 mmol) and 2-(methylthio)-1,4,5,6-tetrahydropyrimidine (1.17 g, 9 mmol) was heated to 150° under nitrogen for 2 hours. The solid mass was recrystallized from water-ethanol to give **11** as pale red crystals, 0.54 g, (44%), mp 283-285° (decomposed); ^{1}H nmr (deuteriochloroform): δ_H 1.95 (m, 2H, 3-H), 3.30 (t, *J* = 5.5 Hz, 2H, 2-H), 3.98 (t, *J* = 5.5 Hz, 2H, 4-H), 8.62 (d, *J* = 1.9 Hz, 1H, 8-H), 8.86 (d, *J* = 1.9 Hz, 1H, 9-H), 9.65 (s, 1H, NH); ^{13}C nmr (deuteriochloroform): δ_C 21.82 (s, C-3), 37.95 (s, C-2), 38.60 (s, C-4), 132.06 (s, C-6a), 139.42 (d, C-8), 147.95 (d, C-9), 150.38 (s, C-10a), 156.15 (s, C-11a), 165.40 (s, C=O).

Anal. Calcd. for $C_9H_9N_5O$: C, 53.19; H, 4.46; N, 34.46. Found: C, 53.05; H, 4.40; N, 34.12.

6*H*-Pyrimido[2,1-*b*]pteridin-6-one (**12**).

A mixture of 2-aminopyrazine **1** (0.92 g, 6 mmol) and 2-chloropyrimidine (0.91g, 8 mmol) was heated to 150° under nitrogen for 2 hours. The solid mass was recrystallized from water-ethanol to give **12** as pale red crystals, 0.50 g (42%), mp 291-293°; ^{1}H nmr (deuteriochloroform): δ_H 8.30-8.45 (m, 3H, 2-H, 3-H and 4-H), 8.65 (d, *J* = 1.9 Hz, 1H, 8-H), 8.87 (d, *J* = 1.9 Hz, 1H, 9-H); ^{13}C nmr (deuteriochloroform): δ_C 131.46 (s, C-6a), 132.9 (s, C-3), 138.35 (s, C-2), 138.62 (d, C-8), 142.18 (s, C-4), 148.21 (d, C-9), 156.35 (s, C-10a), 156.44 (s, C-11a), 162.50 (s, C=O).

Anal. Calcd. for $C_9H_5N_5O$: C, 54.27; H, 2.53; N, 35.16. Found: C, 54.46; H, 2.65; N, 35.39.

11*H*-Pyrazino[2,1-*b*]pteridin-11-one (**13**).

A mixture of 2-aminopyrazine **1** (1.37 g, 9 mmol) and 2-(methylthio)-2-pyrazine (1.51 g, 12 mmol) was heated to 150° under nitrogen for 2 hours. The solid mass was chromatographed on silica gel (chloroform/acetone 9:2) to give **13** as pale red crystals, 0.44 g (25%), mp >300 °; ^{1}H nmr (deuteriochloroform): δ_H 8.30 (d, *J* = 1.9 Hz, 1H, 8-H), 8.65 (d, *J* = 1.9 Hz, 1H, 2-H), 8.72 (d, *J* = 1.9 Hz, 1H, 3-H), 8.86 (s, 1H, 6-H), 9.05 (d, *J* = 1.9 Hz, 1H, 9-H); ^{13}C nmr (deuteriochloroform): δ_C 130.65 (s, C-11a), 138.08 (d, C-2), 145.81 (s, C-8), 147.90 (d, C-3), 148.30 (s, C-9), 150.25 (s, C-6), 156.30 (s, C-4a), 156.50 (s, C-5a), 162.96 (s, C=O).

Anal. Calcd. for $C_9H_5N_5O$: C, 54.27; H, 2.53; N, 35.16. Found: C, 54.10; H, 2.69; N, 34.89.

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