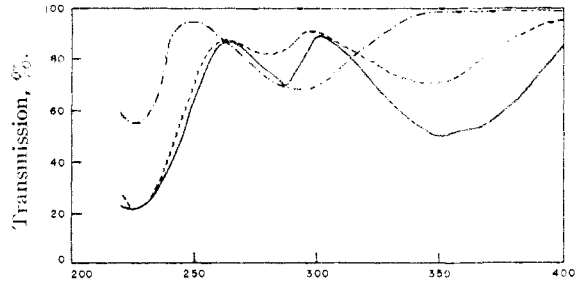
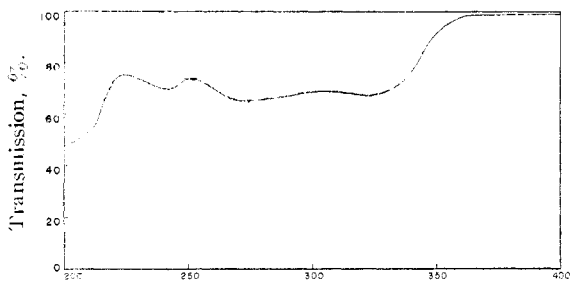


Wave length, millimicrons.

Fig. 1.—Ultraviolet absorption spectra of: ——, (3,3-difluoro-2,4-dioxocyclobutyl)-isoquinolinium betaine, c, 1.66×10^{-5} mole/liter; ----, (3,3-difluoro-2,4-dioxocyclobutyl)-3-methylisoquinolinium betaine, c, 1.12×10^{-5} mole/liter; —·—, 2-[2-heptafluorocyclobutyl)-2,3,3,4,4-pentafluorocyclobutyl]-isoquinolinium carbeniate, c, 2.10×10^{-5} mole/liter.



Wave length, millimicrons.

Fig. 2.—Ultraviolet absorption spectrum of unidentified compound obtained from the reaction of isoquinoline with hexafluorocyclobutene ($C_{22}H_{14}N_2OF_4$), c, 1.01×10^{-5} mole/liter.

lute ethanol. The final product was yellow and had a decomposition point of 240–243°.

Anal. Calcd. for $C_{14}H_9NO_2F_2$: C, 64.37; H, 3.47; N, 5.36; F, 14.6. Found: C, 64.85; H, 3.48; N, 5.46; F, 15.3.

2. Long Reaction Time.—When 40 g. of 3-methylisoquinoline, 85 ml. of ether and 34 g. of hexafluorocyclobutene were allowed to stand together for about one month, the predominant product was a dark solid which was not purified. As before, a small amount of the betaine was isolated.

Ultraviolet Absorption Spectra.—The ultraviolet spectra of the compounds produced were obtained by means of a Beckman model DU spectrophotometer. A quartz prism and a hydrogen discharge lamp were used. The quartz absorption cells were of 1.000 cm. length. The samples were dissolved in absolute ethanol and then diluted to the required concentration. Readings were taken every 5 mμ, except in the regions of maximum absorption, in which case they were taken every 2 mμ. The spectra are recorded in Figs. 1 and 2.

Analyses.[6]—Carbon, hydrogen and nitrogen were determined by combustion. Halogens, with the exception of fluorine, were determined by the Carius tube method. Fluorine was determined by the method of Rickard, Ball and Harris.[7]

(6) Analyses were performed by Clark Microanalytical Laboratory, Urbana, Illinois; Galbraith Laboratories, Knoxville, Tennessee; and Frances Ball and R. R. Rickard of the Microchemical Group of the Analytical Research Section of this Laboratory.

(7) R. R. Rickard, F. L. Ball and W. W. Harris, *Anal. Chem.*, **23**, 919 (1951).

OAK RIDGE, TENN. RECEIVED AUGUST 10, 1951

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS, AND THE BAKER LABORATORY OF CHEMISTRY, CORNELL UNIVERSITY]

Pteridines. VII. The Synthesis of 2-Alkylaminopteridines[1,2]

BY E. C. TAYLOR, JR.,[3] AND C. K. CAIN[4]

The synthesis of several 4-amino-2-alkylaminopteridines by reaction of 4-amino-2-mercapto- or 4-amino-2-methylmercaptopteridines with amines is described. The ultraviolet absorption spectra of these compounds are reported, and a brief discussion of the effects of alkyl substitution in the 2-amino group of a 2,4-diaminopteridine on the spectra and physical properties of the compound is given. It has been found that the replacement of the hydrogen atoms of the 2-amino group of 2,4-diamino-6,7-diphenylpteridine by alkyl groups results in a reduction in antifolic acid activity.

Several 2,4-diaminopteridine (Ia) and 4-aminopteroylglutamic acid derivatives (IIb) have been shown to possess marked biological activity, particularly as inhibitors of pteroylglutamic acid (folic acid) (IIa).[5] Most of the compounds of these types so far prepared are not particularly well suited for pharmacological testing, however, because of their toxicity and general insolubility both in water and in organic solvents. Several attempts have been made to modify the structures of the more active antifolic acid compounds so as to decrease their toxicity or increase their solubility. To this end, Cain, Taylor and Daniel[6] prepared and tested a number of derivatives of 2,4-diamino-6,7-diphenylpteridine (Ia, X = Y = —C_6H_5); Elion and Hitchings[7] examined some 2,4-diamino- (Ia) and 2-amino-4-alkylaminopteridine (Ib) derivatives; and Roth, Smith and Hultquist[8] prepared a number of 4-alkylamino-2-aminopteroylglutamic acid derivatives (IIc). All such changes, however, resulted in a marked decrease in antifolic acid activity. It therefore seemed of considerable interest to examine the chemical and biological

(1) For the previous paper in this series, see E. C. Taylor, Jr., and C. K. Cain, THIS JOURNAL, **73**, 4384 (1951).

(2) Presented in part before the Organic Division at the 116th Meeting of the American Chemical Society, Atlantic City, New Jersey, September, 1949.

(3) du Pont Postdoctoral Fellow in Chemistry, University of Illinois, 1950–1951; U. S. Rubber Company Fellow in Chemistry, Cornell University, 1948–1949.

(4) McNeil Laboratories, Inc., Philadelphia, Pa.

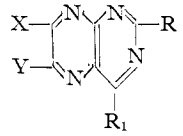
(5) For leading references, see (a) M. F. Mallette, E. C. Taylor, Jr., and C. K. Cain, THIS JOURNAL, **69**, 1814 (1947); (b) L. J. Daniel, L. C. Norris, M. L. Scott and G. F. Heuser, *J. Biol. Chem.*, **169**, 689 (1947); (c) L. J. Daniel and L. C. Norris, *ibid.*, **170**, 747 (1947); (d) D. R. Seeger, J. M. Smith, Jr., and M. E. Hultquist, THIS JOURNAL, **69**, 2567 (1947); (e) D. R. Seeger, D. B. Cosulich, J. M. Smith, Jr., and M. E. Hultquist, *ibid.*, **71**, 1753 (1949); (f) A. L. Franklin, M. Belt, E. L. R. Stokstad and T. H. Jukes, *J. Biol. Chem.*, **177**, 621 (1949).

(6) C. K. Cain, E. C. Taylor, Jr., and L. J. Daniel, THIS JOURNAL, **71**, 892 (1949).

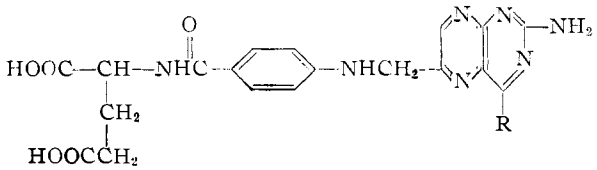
(7) G. B. Elion and G. H. Hitchings, *J. Biol. Chem.*, **188**, 611 (1951).

(8) B. Roth, J. M. Smith, Jr., and M. E. Hultquist, THIS JOURNAL, **72**, 1914 (1950).

properties of pteridines having a substituted amino group in the 2- rather than in the 4-position, and this paper reports the preparation and properties of some 4-amino-2-alkylaminopteridines (Ic).[9]



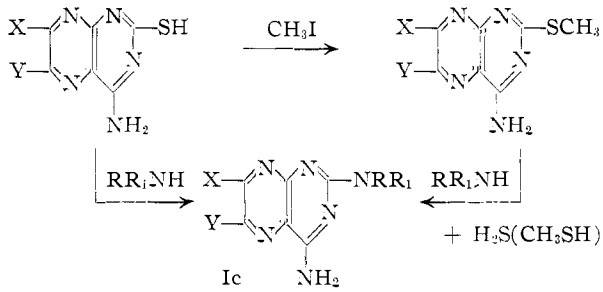
Ia, R = R_1 = $-NH_2$
Ib, R = $-NH_2$, R_1 = —NH alkyl, —N (alkyl)$_2$
Ic, R = —NH alkyl, —N (alkyl)$_2$ R_1 = $-NH_2$



IIa, R = —OH
IIb, R = $-NH_2$
IIc, R = —NH alkyl, —N (alkyl)$_2$

An examination of the literature revealed that a number of alkyl- and arylamino derivatives of various heterocyclic compounds have been prepared by conversion of a thioamide or S-alkylisothioamide to an amidine by the action of an amine. The reaction has been utilized successfully, for example, in the conversion of 2,4-dithiobarbituric acids to 4-imino-2-thiobarbituric acids,[10] 2,4-dimercaptohydantoins to 4-imino (or substituted imino)-2-mercaptohydantoins,[11] 2,4-dimercaptopyrimidines to 4-alkylamino- and 4-arylamino-2-mercaptopyrimidines,[12] 2-methylmercapto-4,5-dihydroimidazoles to 2-alkylamino-4,5-dihydroimidazoles[13] and 4-mercapto- or 4-methylmercaptoquinazolines to 4-alkylaminoquinazolines.[14,15] The application of this method to the preparation of 2-alkylaminopteridines seemed particularly attractive because the synthesis of pteridines having a mercapto or methylmercapto group in the 2-position may be readily carried out. Polonovski and co-workers[16,17] described the preparation of several 4-hydroxy-2-mercaptopteridines by the condensation of 5,6-diamino-4-hydroxy-2-mercaptopyrimidine with α,-β-diketones, and the preparation of 2-ethylmercaptopteridines by an analogous procedure. Likewise, Elion and Hitchings[18] reported the synthesis of 4,6,7-trihydroxy-2-mercaptopteridine, and Wieland and Liebig[19] reported the synthesis of 4-amino-6,7-dihydroxy-2-mercaptopteridine. More recently Gal[20] described the preparation of several 4-amino-2-mercapto- and 4-hydroxy-2-mercaptopteridines. We have found that 4,5,6-triamino-2-mercaptopyrimidine sulfate condenses smoothly with biacetyl and with benzil to give 4-amino-6,7-dimethyl-2-mercaptopteridine[21] and 4-amino-2-mercapto-6,7-diphenylpteridine, respectively. The corresponding 2-methylmercapto derivatives were prepared either from 4,5,6-triamino-2-methylmercaptopyrimidine sulfate or, more conveniently, by methylation of the 4-amino-2-mercaptopteridine with methyl iodide.

By heating the appropriate 4-amino-2-mercapto-(or methylmercapto)-pteridine with an amine under the necessary conditions, the following compounds have been prepared: 2,4-diamino-6,7-diphenylpteridine, 4-amino-2-methylamino-6,7-diphenylpteridine, 4-amino-2-dimethylamino-6,7-diphenylpteridine, 4-amino-2-morpholino-6,7-diphenylpteridine, 4-amino-2-piperidino-6,7-diphenylpteridine and 4-amino-2-dimethylamino-6,7-dimethylpteridine. The general reactions involved are



In those cases where the reaction was carried out both with the 2-mercapto- and 2-methylmercaptopteridines, the former were found to give consistently better yields of the 2-alkylamino derivatives. Leonard and Curtin[14] reported the same observation in their experiments with substituted quinazolines. No pure products could be isolated from the reaction between the 2-mercaptopteridines and isopropylamine, cyclohexylamine or aniline, although evolution of hydrogen sulfide was noted in each case. The action of high boiling, strongly basic amines on such pteridines to give 2,4-bis-(alkylamino)-pteridines and the mechanism for all these transformations have already been reported.[1]

Marked differences in the physical properties of the pteridines were observed upon replacement of the hydrogen atoms of the 2-amino group by alkyl groups.[22] The 2-alkylamino derivatives have lower melting points than the parent amino compounds and are much more soluble in water and in organic solvents. With both hydrogen atoms replaced by alkyl groups as in 4-amino-2-dimethylamino-6,7-diphenylpteridine, these differences become even more pronounced; the melting point is lowered almost 50° and the compound is soluble even in

(9) A recent paper by B. Roth, J. M. Smith, Jr., and M. E. Hultquist, *ibid.*, **73**, 2864 (1951), describes the preparation by a different method of several 4-amino-2-alkylaminopteridine and pteroylglutamic acid derivatives.

(10) H. C. Carrington, *J. Chem. Soc.*, 124 (1944).

(11) H. C. Carrington, *ibid.*, 684 (1947).

(12) P. B. Russell, G. B. Elion, E. A. Falco and G. H. Hitchings, THIS JOURNAL, **71**, 2279 (1949).

(13) S. R. Aspinall and E. J. Bianco, *ibid.*, **73**, 602 (1951).

(14) N. J. Leonard and D. Y. Curtin, *J. Org. Chem.*, **11**, 349 (1946).

(15) A. J. Tomisek and B. E. Christensen, THIS JOURNAL, **70**, 2423 (1948).

(16) M. Polonovski, R. Viellefosse and M. Pesson, *Bull. soc. chim.* [5] **12**, 78 (1945).

(17) M. Polonovski, M. Pesson and R. Viellefosse, *Compt. rend.*, **218**, 796 (1944).

(18) G. B. Elion and G. H. Hitchings, THIS JOURNAL, **69**, 2553 (1947).

(19) H. Wieland and R. Liebig, *Ann.*, **555**, 146 (1944).

(20) E. M. Gal, THIS JOURNAL, **72**, 3532 (1950).

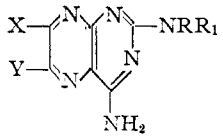
(21) This compound was also prepared by Gal (Ref. 20). However, since our yield was appreciably higher and since the work herein described was presented (Ref. 2) before submittal of the above paper for publication, we have included the preparation of this compound in this paper.

(22) See also A. Albert, D. J. Brown and G. Cheeseman, *J. Chem. Soc.*, 474 (1951).

ether. Several interesting features of the ultraviolet absorption spectra data (Table I) may be noted for the compounds 1–5. No marked change in the shape of the curves occurs, although there is a progressive shift of the entire curve to longer wave lengths in ethanol solution as loading increases on the 2-amino group. The spectra of the alkyl-substituted 6,7-diphenyl derivatives in acidic ethanol are almost identical. There is a marked hypsochromic effect upon acidification. If one considers compounds 1, 2 and 3, it is evident that this hypsochromic effect increases progressively with increasing substitution on the 2-amino group. The effect of a 2-piperidino (compound 4) or 2-morpholino (compound 5) group is approximately the same in this respect as that of a 2-dimethylamino group.

TABLE I

ULTRAVIOLET ABSORPTION SPECTRA OF 2-ALKYLAMINOPTERIDINES



Compound	R	R_1	X	Y	Maxima mμ	log ε
1	H–	H–	C_6H_5–	C_6H_5–	[a]225	4.36
					277	4.36
					388	4.08
					[b]267	4.25
					370	4.19
2	H–	CH_3–	C_6H_5–	C_6H_5–	[a]220–230[c]	4.36
					228	4.42
					402	4.11
					[b]277	4.33
					380	4.26
3	CH_3–	CH_3–	C_6H_5–	C_6H_5–	[a]220–230[c]	4.38
					292	4.40
					412	4.10
					[b]277	4.36
					380	4.28
4	—N(CH₂—CH₂)(CH₂—CH₂)CH₂		C_6H_5–	C_6H_5	[a]233	4.34
					295	4.48
					418	4.12
					[b]276	4.36
					376	4.27
5	—N(CH₂—CH₂)(CH₂—CH₂)O		C_6H_5–	C_6H_5–	[a]230	4.35
					292	4.48
					406	4.12
					[b]277	4.37
					375	4.27
6	CH_3–	CH_3–	CH_3–	CH_3–	[a]243	4.17
					272	4.35
					387	3.89
					[b]250	4.20
					294	3.83
					341	4.10

[a] Solvent is absolute ethanol. [b] Solvent is absolute ethanol made 0.1 *N* in hydrochloric acid. [c] Shoulder.

There is also a marked decrease in the antifolic acid activity of these compounds tested *in vitro* against *S. faecalis* (Table II); the decrease is considerably greater for the 2-dimethylamino derivative than for the 2-methylamino derivative. These results are in line with the preliminary observations of Roth, Smith and Hultquist[8,9] on the antifolic acid activity of 4-alkylamino- and 2-alkylaminopteroylglutamic acid derivatives, and with the results of Elion and Hitchings[7] on the activity of 4-alkylaminopteridines.

TABLE II

INHIBITORY INDICES OF 2-ALKYLAMINOPTERIDINES

Compound	Inhibitory index *vs. S. faecalis*
1	10
2	250
3	11,000

Experimental[23]

4,6-Diamino-2-methylmercaptopyrimidine.—The following procedure is a modification of that described by Wheeler and Jamieson.[24] It leads to slightly improved yields and a purer product and greatly facilitates the preparation of large amounts.

A mixture of 30 g. (0.21 mole) of 4,6-diamino-2-mercaptopyrimidine,[25] 36 g. (0.25 mole) of methyl iodide and 150 ml. of absolute ethanol was heated under reflux on a water-bath for one hour. The clear red solution was treated with 4 g. of Norit and the filtrate evaporated to dryness under reduced pressure. The solid residue (consisting mainly of the hydroiodide of 4,6-diamino-2-methylmercaptopyrimidine) was dissolved in 100 ml. of hot water and the *p*H adjusted to 9 with ammonium hydroxide. Cooling caused the separation of a heavy solid in the form of long colorless prisms. This solid, consisting of 4,6-diamino-2-methylmercaptopyrimidine contaminated with a small amount of unreacted starting material, was collected by filtration, washed with a generous amount of ice-cold water, suspended in 200 ml. of acetone and heated to boiling. Filtration removed the unreacted 4,6-diamino-2-mercaptopyrimidine (0.5 g.). The acetone was removed by distillation under reduced pressure, the crystalline residue dissolved in 200 ml. of boiling water and cooled rapidly to give a heavy colorless solid in the form of small rectangular prisms; yield 27.5 g. (83.5%); m.p. 188–189°.

4,6-Diamino-2-methylmercapto-5-nitrosopyrimidine.—This compound was prepared essentially by the method of Baddiley, *et al.*[26]

4,5,6-Triamino-2-methylmercaptopyrimidine Sulfate.—Reduction of the 5-nitroso derivative with sodium dithionite was found to be more convenient than with ammonium sulfide as previously reported.[26] A suspension of 10.0 g. (0.054 mole) of 4,6-diamino-2-methylmercapto-5-nitrosopyrimidine in 180 ml. of boiling water was stirred mechanically and 27.1 g. (0.155 mole) of sodium dithionite added slowly in small portions. The blue color of the nitrosopyrimidine was shortly completely bleached to give a clear light-yellow solution. Norit was added and the filtrate treated cautiously with 50 ml. of 50% sulfuric acid. The solution was cooled to 0°, the white crystalline sulfate collected by filtration, washed with a generous amount of cold water and dried; yield 9.98 g. (68.5%).

4-Amino-2-mercapto-6,7-dimethylpteridine.—A solution of 1.0 g. (0.0039 mole) of 4,5,6-triamino-2-mercaptopyrimidine sulfate[25] in 125 ml. of boiling water was adjusted to *p*H 7 with dilute sodium hydroxide and treated with a solution of 0.5 g. (0.0058 mole) of biacetyl in 5 ml. of 50% aqueous ethanol. A heavy lemon-yellow crystalline precipitate separated almost at once from the boiling solution. The mixture was cooled to 0°, the solid collected by filtration and washed with water followed by acetone to give 0.755 g. (93%). The product was purified by dissolving in hot 0.1 *N* sodium hydroxide, treating with Norit and pouring into an excess of boiling 0.1 *N* acetic acid. Recrystallization from 60% aqueous dimethylformamide gave yellow rhombohedral platelets decomposing slowly upon heating above 280°.

Anal. Calcd. for $C_8H_9N_5S$: C, 46.4; H, 4.4; N, 33.8. Found: C, 46.6; H, 4.4; N, 33.9.

4-Amino-2-methylmercapto-6,7-dimethylpteridine.—This compound was prepared in a similar manner from 4,5,6-triamino-2-methylmercaptopyrimidine sulfate and biacetyl

(23) All melting points are corrected unless otherwise stated.

(24) H. L. Wheeler and G. S. Jamieson, *Am. Chem. J.*, **32**, 342 (1904).

(25) A. Bendich, J. F. Tinker and G. B. Brown, THIS JOURNAL, **70**, 3109 (1948).

(26) J. Baddiley, B. Lythgoe, D. McNeil and A. R. Todd, *J. Chem. Soc.*, 383 (1943).

in 59% yield. The yellow plate-like crystals decomposed sharply at 274–275°.

Anal. Calcd. for $C_9H_{11}N_5S$: C, 48.9; H, 5.0; N, 31.7. Found: C, 49.0; H, 5.0; N, 31.4.

4-Amino-2-mercapto-6,7-diphenylpteridine.—To a suspension of 1.0 g. (0.00392 mole) of 4,5,6-triamino-2-mercaptopyrimidine sulfate in 25 ml. of boiling water adjusted to *p*H 9 with dilute sodium hydroxide was added a solution of 0.95 g. (0.00452 mole) of benzil in a mixture of 10 ml. of ethanol and 10 ml. of ethyl methyl ketone and the mixture heated under reflux for three hours. After the first five minutes, a clear orange solution resulted which shortly deposited a yellow crystalline solid. The organic solvents were removed by distillation under reduced pressure and the residual aqueous suspension was acidified with acetic acid. The yellow crystals were collected by filtration and extracted with boiling petroleum ether (30–60°) to remove any residual benzil; yield 1.09 g. (84%). Recrystallization from 50% aqueous dimethylformamide gave lemon-yellow prisms melting with decomposition at 283°.

Anal. Calcd. for $C_{18}H_{13}N_5S$: C, 65.3; H, 3.9; N, 21.2. Found: C, 65.2; H, 3.9; N, 21.0.

4-Amino-2-methylmercapto-6,7-diphenylpteridine. A. From 4,5,6-Triamino-2-methylmercaptopyrimidine and Benzil.—This preparation was carried out in a manner similar to that described above. Recrystallization from ethanol gave a 47% yield of the desired product in the form of slender needles melting at 252.5–253°.

Anal. Calcd. for $C_{19}H_{15}N_5S$: C, 66.1; H, 4.4; N, 20.3. Found: C, 66.2; H, 4.3; N, 20.2.

B. From 4-Amino-2-mercapto-6,7-diphenylpteridine and Methyl Iodide.—To a suspension of 0.15 g. (0.00045 mole) of 4-amino-2-mercapto-6,7-diphenylpteridine in 50 ml. of absolute ethanol was added 0.10 g. (0.0007 mole) of methyl iodide and the mixture heated under reflux for one-half hour. The clear yellow solution was evaporated nearly to dryness under diminished pressure, the residue suspended in 40 ml. of 0.1 *N* ammonium hydroxide and the mixture evaporated to dryness. The residue was dissolved in 50 ml. of boiling ethanol, treated with Norit and the filtrate diluted with 50 ml. of hot water. On cooling, 0.110 g. (71%) of yellow platelets separated; m.p. 252.5–253°. A mixed melting point with a sample prepared by method A showed no depression.

Reaction of 4-Amino-2-mercapto-(or methylmercapto)-pteridines with Ammonia and Amines.—The following reactions were carried out by heating a sealed glass bomb containing approximately 0.20 g. of pteridine, approximately 1.0 g. of ammonia or amine and 50 ml. of absolute ethanol at 180–190° for ten hours. The alcoholic solution of the product was treated with Norit, filtered and evaporated to dryness. The solid product was recrystallized from the appropriate solvent.

2,4-Diamino-6,7-diphenylpteridine. A. From 4-Amino-2-mercapto-6,7-diphenylpteridine and Ammonia.—The crude reaction product obtained as described above was purified by dissolving in boiling 0.1 *N* hydrochloric acid and pouring into an excess of boiling 0.1 *N* ammonium hydroxide to give a light yellow solid in 84% yield. One recrystallization from 80% aqueous formic acid gave crystals melting at 280–283° (uncor.) in good agreement with the previously reported value.[5a] The ultraviolet absorption spectrum was identical with that of an authentic sample.

B. From 4-Amino-2-methylmercapto-6,7-diphenylpteridine and Ammonia.—The product was obtained in 79% yield after one recrystallization from aqueous formic acid. Its identity was established by melting point and ultraviolet absorption spectrum determinations.

4-Amino-2-methylamino-6,7-diphenylpteridine. A. From 4-Amino-2-mercapto-6,7-diphenylpteridine and Methylamine.—The product was obtained in 97% yield. Recrystallization from 25% aqueous ethanol gave yellow prisms melting at 264–265°.

Anal. Calcd. for $C_{19}H_{16}N_6$: C, 69.5; H, 4.9; N, 25.6. Found: C, 70.0; H, 5.0; N, 25.5.

B. From 4-Amino-2-methylmercapto-6,7-diphenylpteridine and Methylamine.—The compound was obtained in 68% yield and was shown to be identical with the product from A by melting point and ultraviolet absorption spectrum determinations.

4-Amino-2-dimethylamino-6,7-diphenylpteridine. A. From 4-Amino-2-mercapto-6,7-diphenylpteridine and Dimethylamine.—The product was obtained in 97% yield. Recrystallization from methanol gave yellow needles melting at 192–195°.

Anal. Calcd. for $C_{20}H_{18}N_6$: C, 70.0; H, 5.3; N, 24.6. Found: C, 70.2; H, 5.3; N, 24.8.

B. From 4-Amino-2-methylmercapto-6,7-diphenylpteridine and Dimethylamine.—The product was obtained in 94% yield and was shown to be identical with the product from A by melting point and ultraviolet absorption spectrum determinations.

4-Amino-2-dimethylamino-6,7-dimethylpteridine. A. From 4-Amino-2-mercapto-6,7-dimethylpteridine and Dimethylamine.—The product was obtained as a yellow powder in 93% yield. Recrystallization from methanol gave yellow prisms which decompose slowly upon heating above 260°.

Anal. Calcd. for $C_{10}H_{14}N_6$: C, 55.0; H, 6.5; N, 38.5. Found: C, 54.9; H, 6.3; N, 38.6.

B. From 4-Amino-2-methylmercapto-6,7-dimethylpteridine and Dimethylamine.—The product was obtained in 53% yield and was shown to be identical with the product from A by an ultraviolet absorption spectrum determination.

4-Amino-2-piperidino-6,7-diphenylpteridine.—A mixture of 1.0 g. of 4-amino-2-mercapto-6,7-diphenylpteridine, 15 ml. of freshly distilled piperidine and 10 ml. of dimethylformamide was heated under reflux to give a clear red solution. Evolution of hydrogen sulfide ceased after 12 hours of heating. Excess piperidine was removed by distillation under reduced pressure and the residual sirup was poured into 100 ml. of water. The oil which separated was dissolved in a few milliliters of acetone and added to 50 ml. of ice-water. A yellow solid separated which was collected by filtration, washed thoroughly with water and dried; yield 0.75 g. (65%). Recrystallization from methylene chloride–petroleum ether gave stubby rectangular prisms melting at 209°.

Anal. Calcd. for $C_{23}H_{22}N_6$: C, 72.2; H, 5.8; N, 22.0. Found: C, 72.3; H, 6.1; N, 21.9.

4-Amino-2-morpholino-6,7-diphenylpteridine.—A solution of 0.70 g. of 4-amino-2-mercapto-6,7-diphenylpteridine in 10 ml. of freshly distilled morpholine was heated under reflux for ten hours. Water was added to the cooled reaction solution and the mixture allowed to stand at 2° overnight. The precipitate which separated was collected by filtration, washed thoroughly with water and dried. It was then dissolved in acetone, thoroughly decolorized with Norit and the filtrate evaporated to dryness. Extraction of the residue with ether and evaporation of the ether extracts gave a light yellow solid which was obtained as long yellow prisms upon recrystallization from aqueous acetone; yield 0.37 g. (45%); m.p. 231–232°.

Anal. Calcd. for $C_{22}H_{20}N_6O$: C, 68.7; H, 5.2; N, 21.9. Found: C, 69.0; H, 5.3; N, 22.1.

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