

IX with a large excess of sodium in boiling absolute ethanol and processing the reaction mixture as described above gave 45 mg. of product, m.p. 190–218°. Separation with digitonin and recrystallization of each component from the appropriate solvent gave 6 mg. of solanidine (m.p. and mixture m.p. was 215.5–218°) and 24 mg. of pseudosolanidine (m.p. was 235.7–236.5°, unchanged when mixed with previous material).

**Dihydropseudosolanidine (XVI).**—A solution of 22 mg. of XIV in glacial acetic acid was hydrogenated with 16 mg. of platinum oxide catalyst. The absorption was equivalent to 1 mole in excess of the catalyst requirement. After filtration and dilution, addition of potassium carbonate solution caused the separation of a gelatinous mass which was extracted with chloroform. The extract yielded a residue which after two crystallizations from methanol gave 6.5 mg. of XVI melting at 210–211°,  $[\alpha]_D^{25} +33.6^\circ$  ( $c$  0.52,  $chf$ ). The mother liquor yielded 2.5 mg. of less pure material, m.p. 209–211.5°. The reported constants for solanidin-3 $\alpha$ -ol are m.p. 211–213°,  $[\alpha]_D +31.9 \pm 4^\circ$ . An au-

thentic sample of solanidanol-3( $\alpha$ ) prepared by a modification of the method of Prelog and Szpilfogel<sup>11</sup> melted at 214.5–216.0°; acetate, 176.0–178.0° (reported 211–213° acetate, 174–176°). A mixture melting point with XV showed a marked depression; m.p. 182–201°. XVI therefore cannot be solanidan-3 $\alpha$ -ol.

**Infrared Spectra.**—Samples were prepared as Nujol mulls and the spectra determined from 2 to 14.5  $\mu$  without compensation on a Perkin-Elmer model 21 double beam spectrometer with sodium chloride optics, set at resolution 5, response 3, gain 8, suppression 1 and a scanning speed of 0.12  $\mu$  per minute on a chart scale of 2 inches for 1  $\mu$ .

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[CONTRIBUTION FROM THE NAGOYA INDUSTRIAL SCIENCE RESEARCH INSTITUTE,\* ROKUNO-CHO ATSUTA-KU, AND THE CHEMICAL INSTITUTE, NAGOYA UNIVERSITY\*\*]

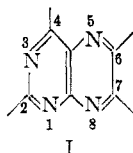
## Studies on Pteridines.<sup>1</sup> IV. Synthesis of 6- and 7-Hydroxypteridines

BY SADA O MATSUURA,\* SABUTO NAWA,\* HIROSHI KAKIZAWA\*\* AND YOSHIMASA HIRATA\*\*

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The synthesis, ultraviolet spectra and paper chromatography of several pteridines are described. The present work has been undertaken for the purpose of identifying the structures of pteridines isolated in our laboratory from the eggs of *Bombyx mori* (silk worm)<sup>2</sup> and the scale of carp.<sup>3</sup>

The 6- and 7-hydroxypteridines I have been synthesized by the condensation of 4,5-diamino-



pyrimidine derivatives with ethoxalyl (R-CO-CO<sub>2</sub>-C<sub>2</sub>H<sub>5</sub>) derivatives, the formation of the 6- or 7-hydroxy compounds depending mainly on the acidity of the medium and to some extent on the nature of the reagents. In general, weak acidity ( $pH$  5) favored the formation of 7-hydroxypteridines, whereas strong acid (2  $N$  HCl) favored that of the 6-hydroxypteridines; these results can be interpreted in terms of mono- and bivalent cation formation of the pyrimidine derivatives in weak and strong acid media.<sup>4</sup>

Paper chromatography (Table I) and ultraviolet spectra (Table II), together with several specific reactions such as Al-Hg reduction,<sup>5</sup> MnO<sub>2</sub> oxidation,<sup>2</sup> hydrolysis, decarboxylation, etc., were employed for the characterization of the products.

Comparison of  $R_f$  values of closely related pteridines in the two sets of solvents were consistent with the differences in their hydrophilic nature and were utilized in interpreting the nature of the products (*e.g.*, compounds XVIII to XXII).

(1) Previous paper, *Experientia*, **8**, 339 (1952).

(2) To be published.

(3) Y. Hirata and S. Nawa, *Compt. rend. soc. biol.*, **145**, 661 (1951). Recent results will be published in a forthcoming paper.

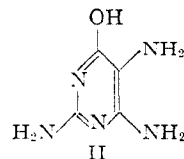
(4) G. B. Elion, G. H. Hitchings and P. B. Russell, *THIS JOURNAL*, **72**, 78 (1950); H. S. Forrest and J. Walker, *J. Chem. Soc.*, **79** (1949).

(5) Paper V, *THIS JOURNAL*, **75**, 4450 (1953).

Ultraviolet spectra (Table II) were measured in 0.1  $N$  NaOH solutions. All of the compounds belonging to the isoxanthopterin series possessed a maximum at 253–260  $m\mu$  ( $\log E$  3.9–4.2), a shoulder or maximum around 275  $m\mu$  ( $\log E$  3.44–3.72), and a maximum at 340–350  $m\mu$  ( $\log E$  4.0–4.2). Compounds belonging to the xanthopterin series possessed one or two maxima or shoulders around 250–280  $m\mu$  ( $\log E$  *ca.* 4.0) and maximum around 380–400  $m\mu$  ( $\log E$  *ca.* 3.7). Other pteridines also showed curves characteristic of their series and the ultraviolet spectra may serve for identification purposes. The pteridines which have been synthesized are listed in Table I.

In general the crude products were purified by several repetitions of the process of dissolution in dilute alkali, charcoal treatment and acidification with acetic acid.

When 2,4,5-triamino-6-hydroxypyrimidine (II)



and ethyl ethoxalylacetate were condensed in mineral media ( $pH$  2), a simultaneous hydrolysis and decarboxylation occurred giving a mixture of 6-methylisoxanthopterin (IV) and 7-methylxanthopterin (XXIII), whereas when condensed at  $pH$  5, an almost exclusive formation of ethyl isoxanthopteryl-6-acetate took place. The ester was subsequently hydrolyzed with alkali to give isoxanthopteryl-6-acetic acid (VIII). This compound is unstable to acids and is easily decarboxylated to

TABLE I  
 $R_f$  VALUES OF PTERIDINES<sup>a</sup>

Compounds III-XXXIV (in order)	$R_f$ values		Color of fluorescence of spot <sup>a</sup>
	Solv. A <sup>a</sup>	Solv. B <sup>a</sup>	
Isoxanthopterin <sup>b,c,d</sup>	0.35	0.40	p
6-Methylisoxanthopterin	.46	.37	p
6-Ethylisoxanthopterin	.69	.44	p
6-Propylisoxanthopterin	.86	.47	p
Isoxanthopteryl-6-carboxylic <sup>b,e</sup> acid	.12	.68	p
Isoxanthopteryl-6-acetic <sup>f,g</sup> acid	.32	.73	p
$\beta$ -(Isoxanthopteryl-6)-propionic acid	.33	.62	p
$\alpha$ -(Isoxanthopteryl-6)-propionic acid	.50	.78	p
$\alpha$ -(Isoxanthopteryl-6)-butyric acid	.73	.82	p
Isoxanthopteryl-6-succinic <sup>g</sup> acid	.79	.86	p
6-Acetonylisoxanthopterin	.51	.56	p
6-Propiomethylisoxanthopterin	.66	.58	p
6-Methoxymethylisoxanthopterin	.51	.52	p
6-( $\alpha$ -Hydroxyethyl)-isoxanthopterin	.43	.33	p
6-( $\beta$ -Hydroxypropyl)-isoxanthopterin	.59	.55	p
Isoxanthopteryl-6-hippuric acid ethyl ester	.98	.60	p
Isoxanthopteryl-6-hippuric	.83	.66	p
6-(Benzaminomethyl)-isoxanthopterin	.71	.13	p
6-Aminomethylisoxanthopterin	.15	.39	p
Isoxanthopteryl-6-glycine	.17	.70	p
7-Methylxanthopterin <sup>c,d</sup>	.50	.43	y
7-Ethylxanthopterin	.74	.50	y
Xanthopteryl-7-carboxylic <sup>e</sup> acid	.09	.76	y
7-Acetonylxanthopterin <sup>h</sup>	.68	.21	y
7-Propiomethylxanthopterin	.84	.22	y
2,4,7-Trihydroxy-6-methyl <sup>i</sup> -pteridine	.34	.53	p
2,4,7-Trihydroxypteridyl <sup>i</sup> -6-carboxylic acid	.12	.73	p
$\alpha$ -(2,4,7-Trihydroxypteridyl-6)-propionic acid	.41	.76	p
$\alpha$ -(2,4,7-Trihydroxypteridyl-6)-butyric acid	.78	.50	p
2,4,7-Trihydroxy-6-acetonylpteridine	.39	.63	p
2,4,6-Trihydroxy-(7-acetonyl)-pteridine	.51	.30	y
1-Methyl-4,7-dihydroxy-2-ketopteridyl-6-carboxylic acid	.25	.77	p

<sup>a</sup> Ascending method. Since  $R_f$  values varied considerably with minor changes, parallel runs were always carried out for identification purposes. The values listed in the table show the relative positions of various compounds at 27° (Toyō filter paper No. 50); solvent A, BuOH:AcOH:H<sub>2</sub>O (4:1:1); solvent B, 4% sodium citrate solution. The fluorescences of the spots were identical for both solvents: y, yellow; p, purple. <sup>b</sup> G. B. Elion, A. E. Light and G. H. Hitchings, *THIS JOURNAL*, **71**, 741 (1949). <sup>c</sup> G. B. Elion, G. H. Hitchings and P. B. Russell, *ibid.*, **72**, 78 (1950). <sup>d</sup> G. B. Elion and G. H. Hitchings, *ibid.*, **69**, 2553 (1947). <sup>e</sup> R. Purmann, *Ann.*, **548**, 284 (1941). <sup>f</sup> R. Tschesche and F. Korte, *Ber.*, **84**, 801 (1951). <sup>g</sup> A. G. Renfrew and P. C. Piatt, *J. Am. Pharm. Assoc.*, **39**, 657 (1950). <sup>h</sup> R. Tschesche and F. Korte, *Ber.*, **84**, 77 (1951).

6-methylisoxanthopterin (IV). Similarly, 2,4,5-triamino-6-hydroxypyrimidine (II) gave  $\alpha$ -(isoxanthopteryl-6)-propionic acid (X) and 6-ethylisoxanthopterin (V) with ethyl  $\alpha$ -ethoxalylpropionate, EtO<sub>2</sub>CCOCH(CH<sub>3</sub>)CO<sub>2</sub>Et and  $\alpha$ -(isoxanthopteryl-6)-butyric acid (XI), and 6-propylisoxanthopterin (VI) with ethyl  $\alpha$ -ethoxalylbutyrate, EtO<sub>2</sub>CCOCH(Et)CO<sub>2</sub>Et. Treatment of

 TABLE II  
 SOME TYPICAL ULTRAVIOLET ABSORPTION SPECTRA<sup>a</sup>

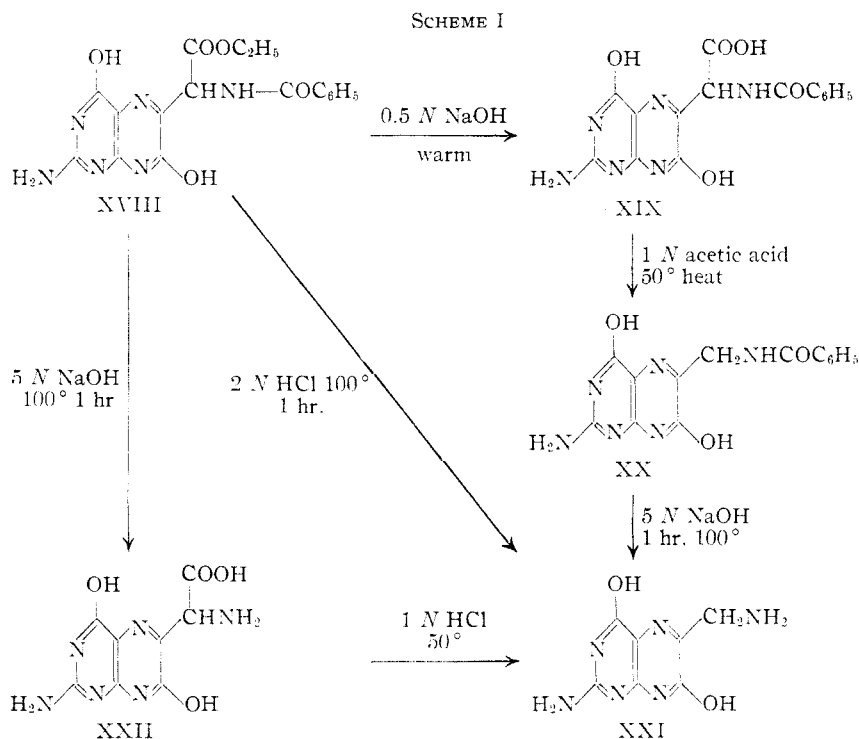
Compound	Max., m $\mu$	log $\epsilon$
Isoxanthopterin, III	253	3.93
	273 <sup>b</sup>	3.43
	340	4.02
Isoxanthopteryl-6-carboxylic acid, VII	259	3.92
	280 <sup>b</sup>	3.54
	350	4.01
6-Methylisoxanthopterin, IV	255	4.07
	276	3.67
	341	4.14
7-Ethylxanthopterin, XXIV	253	4.16
	272 <sup>b</sup>	3.98
	385	3.87
2,4,7-Trihydroxy-6-methylpteridine, XXVII	250	3.89
	260	3.89
	280	3.87
1-Methyl-4,7-dihydroxy-2-ketopteridyl-6-carboxylic acid, XXXIV	335	4.19
	257	4.07
	276 <sup>b</sup>	3.78
	347	4.24

<sup>a</sup> Taken in 0.1 N NaOH. <sup>b</sup> Those marked with an asterisk represent shoulders.

II with ethyl methoxyethoxalylacetate, EtO<sub>2</sub>C-COCH(OCH<sub>3</sub>)CO<sub>2</sub>Et, gave the corresponding pterin which was also extremely vulnerable toward acids and gave 6-methoxymethylisoxanthopterin (XV).

Treatment of II with ethyl ethoxalylsuccinate gave isoxanthopteryl-6-succinic acid (XII). The decarboxylation of isoxanthopteryl-6-succinic acid (XII) yielded a compound which was identical with that obtained from II and ethyl  $\alpha$ -ketoglutarate, *i.e.*,  $\beta$ -(isoxanthopteryl-6)-propionic acid (IX). Hence the decarboxylation of isoxanthopterin side-chains in acid media is specific for those carboxyl groups attached to an  $\alpha$ -carbon and does not occur with other carboxyl groups under normal mild conditions. This can be compared with the easy decarboxylation of  $\beta$ -keto acids, nitroacetic acid,  $\alpha$ -dicarboxylic acids, etc.; and the fact that isoxanthopterin-6-carboxylic acid (VII) is stable toward 2 N HCl and is decarboxylated only when heated to 270° suggest that the isoxanthopteryl nucleus is a strong electron attracting group.

Condensation of II with ethoxalylacetone under usual conditions gave a mixture of 6-acetonylisoxanthopterin (XIII) and 7-acetonylxanthopterin (XXVI), whereas almost pure XIII resulted when ethoxalylacetone was added to the 1 N NaOH solutions of II prior to acidification and heating; condensation in mineral acid media gave pure 7-acetonylxanthopterin (XXVI). 6-Acetonylisoxanthopterin (XIII) can be recrystallized from 20% acetic acid but is unstable to alkali and is converted into 6-methylisoxanthopterin (IV) when heated with 3% NaOH; mineral acids and light converted it into an unidentified brown substance. Reduction of 6-acetonylisoxanthopterin with NaBH<sub>4</sub> yielded a crystalline product which was inert to MnO<sub>2</sub> oxidation, aluminum amalgam treatment and was recovered unchanged after 3% alkali treatment.



Since it was found that  $\text{NaBH}_4$  does not reduce the pteridyl nucleus from model experiments, presumably the compound formed is 6-( $\beta$ -hydroxypropyl)-isoxanthopterin (XVII).

The reaction of II and ethyl ethoxalylhippurate gave isoxanthopteryl-6-hippuric acid ethyl ester (XVIII); the transformations related to XVIII are summarized in scheme I; results were confirmed from their chromatographic behavior.

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### Experimental

**Isoxanthopteryl-6-acetic Acid (VIII),  $\alpha$ -(Isoxanthopteryl-6)-propionic Acid (X) and butyric Acid (XI).**—A solution of 4 g. of 2,4,5-triamino-6-hydroxypyrimidine sulfate in 100 ml. of 1 N NaOH was acidified with 200 ml. of 1 N acetic acid and 8 g. of ethyl ethoxalyl acetate was added. The mixture was heated on the bath for 30 min., cooled and the precipitate was collected, 3 g. This was dissolved in 100 ml. of 0.2 N NaOH and after treating with charcoal, 150 ml. of 1 N acetic acid ( $50^\circ$ ) was added. The precipitate was filtered and the purification was repeated thrice. Finally the product was dissolved in 50 ml. of 0.2 N NaOH, 350 ml. of water was added and made  $50^\circ$ , and finally 500 ml. of 0.5 N acetic acid was added, when colorless needles of VIII were obtained.

*Anal.* Calcd. for  $\text{C}_8\text{H}_7\text{O}_4\text{N}_5$ : N, 29.53. Found: N, 28.86.

Paper chromatography showed the absence of the 6-methyl compound (IV). The corresponding 6-propionic (X) and 6-butyric acid (XI) derivatives were obtained by similar treatment of II with ethyl  $\alpha$ -ethoxalylpropionate and ethyl  $\alpha$ -ethoxalylbutyrate, respectively.

*Anal.* Calcd. for  $\text{C}_9\text{H}_9\text{O}_4\text{N}_5$ : N, 27.88. Found: N, 27.59. Calcd. for  $\text{C}_{10}\text{H}_{11}\text{O}_4\text{N}_5$  (XI): N, 26.41. Found: 26.14.

**6-Methyl (IV), 6-Ethyl (V), 6-Propyl (VI)-isoxanthopterin and 7-Ethylisoxanthopterin (XXIV).**—A solution of 800 mg. of

isoxanthopterin-6-acetic acid (VII) in 20 ml. of 0.5 N NaOH was added dropwise to a boiling solution of 150 ml. of 2 N HCl, and after boiling for five more minutes, the mixture was cooled and the crystals collected, 480 mg.

*Anal.* Calcd. for  $\text{C}_7\text{H}_7\text{O}_2\text{N}_5$  (IV): N, 36.26. Found: N, 36.30.

6-Ethylisoxanthopterin (V) and 6-propylisoxanthopterin (VI) were obtained from the corresponding acids. V was also obtained together with 7-ethylisoxanthopterin (XXIV) in the following manner. To a solution of 2.8 g. of II in 20 ml. of 1 N NaOH, there was added 3 g. of  $\alpha$ -ketobutyric acid<sup>6</sup> in 100 ml. of 1 N acetic acid and the mixture heated for 45 min. The crude precipitate (2.3 g.) was dissolved in a small amount of 1 N NaOH, treated with charcoal and poured into boiling 2 N HCl when white precipitates of 6-ethylisoxanthopterin (V) were obtained. Adjustment of the pH of the red filtrate to 5 gave yellow precipitates of 7-ethylisoxanthopterin (XXIV). Repetition of dissolution and precipitation of the respective precipitates gave 1.3 g. (48%) of V and 0.9 g. (32%) of XXIV.

*Anal.* Calcd. for  $\text{C}_8\text{H}_9\text{O}_2\text{N}_5$  (V): N, 33.80. Found: N, 33.64. Calcd. for  $\text{C}_9\text{H}_{11}\text{O}_2\text{N}_5$  (XXIV): N, 33.80. Found: N, 33.61. Calcd. for  $\text{C}_9\text{H}_{11}\text{O}_2\text{N}_5$  (VI): N, 31.52. Found: N, 31.58.

**6-(Methoxymethyl)-isoxanthopterin (XV).**—Ethyl ethoxalylmethoxyacetate (8 g.) was added to a warm solution of 25 g. of (II)-sulfate in 200 ml. of 0.5 N NaOH, the mixture was acidified with acetic acid and heated on the bath for an hour. A small amount of precipitate was removed and the solution was cooled, when 1.8 g. of yellow precipitates was obtained. This was dissolved in 50 ml. of 1 N NaOH, and after treating with charcoal, 500 ml. of 10% acetic acid at  $70^\circ$  was added when yellow needles were obtained.

*Anal.* Calcd. for  $\text{C}_8\text{H}_9\text{O}_3\text{N}_5$ : N, 31.38. Found: N, 30.82.

**Isoxanthopteryl-6-succinic Acid (XII).**—To a solution of 4 g. of (II)-sulfate in 100 ml. of 0.5 N NaOH, there was added 150 ml. of 2 N acetic acid and after heating on the bath, 10 g. of ethyl ethoxalylsuccinate was added and the mixture heated for one hour. The orange pterin (4 g.) was collected, dissolved in 100 ml. of 0.25 N NaOH, treated with charcoal and precipitated by the addition of 2 N acetic acid. This was repeated four times. The product was contaminated with a small amount of the decarboxylated compound (IX).

*Anal.* Calcd. for  $\text{C}_{10}\text{H}_9\text{O}_6\text{N}_5$ : N, 23.73. Found: N, 24.33.

**$\beta$ -(Isoxanthopteryl-6)-propionic Acid (IX). Method A. From Isoxanthopterylsuccinic Acid (XII).**—A solution of 900 mg. of (XII) in 500 ml. of 0.5 N NaOH was poured into 150 ml. of boiling 2 N HCl and cooled after 15 min. when 500 mg. of product was obtained.

**Method B. From Ethyl  $\alpha$ -Ketoglutarate.**—To a solution of 1 g. of (II)-sulfate in 25 ml. of 0.5 N NaOH, there was added 40 ml. of 2 N acetic acid and 3 g. of ethyl  $\alpha$ -ketoglutarate, and the mixture was heated for 30 min. on the bath. After cooling, the precipitate was collected and purified, 400 mg.

*Anal.* Calcd. for  $\text{C}_8\text{H}_9\text{O}_4\text{N}_5$ : N, 27.88. Found: N, 28.29.

**6-Acetonylisoxanthopterin (XIII).**—Ethoxalylacetone (20 g.) and 200 ml. of water were added to (II)-sulfate (15 g.) in 200 ml. of 1 N NaOH and after neutralizing with acetic

(6) This was obtained by heating ethyl ethoxalyl propionate in 10%  $\text{H}_2\text{SO}_4$  for 5 hr., extracting with ether and distilling in vacuum.

acid to pH 7, the mixture was heated on the bath when a brown gelatinous product was obtained. Upon addition of 10 ml. of acetic acid and boiling for 1 min., this was converted into a yellow precipitate, 10.5 g., which was recrystallized from one liter of 2 *N* acetic acid to give light yellow needles.

*Anal.* Calcd. for  $C_9H_9O_3N_5$ : N, 29.78. Found: N, 29.52.

**6-Propiomethylisoxanthopterin (XIV).**—Also obtained by similar treatment of (II)-sulfate with ethoxalylmethyl ethyl ketone.

*Anal.* Calcd. for  $C_{10}H_{11}O_3N_5$ : N, 28.10. Found: N, 28.05.

**6-( $\alpha$ -Hydroxyethyl)-isoxanthopterin (XVI).**—Ethyl  $\alpha$ -ethoxalylacetate (15 g.) was added to a solution of 5 g. of (II)-sulfate in 1 *N* NaOH and the mixture was acidified with acetic acid under heating, when red-brown precipitates were formed. This was purified through the conventional method upon which an amorphous orange-yellow product was obtained; however, owing to the partial formation of a red-purple product, further purification was abandoned. The  $MnO_2$  oxidation of the compound yielded isoxanthopterylcaboxylic acid,<sup>2</sup> a result which was plausible for the structure (XVI).

**6-( $\beta$ -Hydroxypropyl)-isoxanthopterin (XVII).**—A mixture of 100 mg. of 6-acetonilysoxanthopterin (XIII) in 20 ml. of 3% NaOH and 18 mg. of  $NaBH_4$  in 10 ml. of water was left overnight at room temperature. The solution was acidified with acetic acid and the 0.5 *N* NaOH solution of the precipitate was added to 10 ml. of boiling 1 *N* acetic acid; repetition of this purification gave light yellow needles.

*Anal.* Calcd. for  $C_9H_{11}O_3N_5$ : N, 29.53. Found: N, 29.48.

**6-Benzaminomethylisoxanthopterin (XX).**—To a solution of 10 g. of (II)-sulfate in 200 ml. of 1 *N* NaOH, 550 ml. of water was added, and while heating on the bath, 10 g. of ethyl ethoxalylhippurate was added and the solution was acidified with acetic acid. After heating for 1 hour, 7.3 g. of isoxanthopteryl-6-hippuric acid ethyl ester (XVIII) was collected; upon dissolution in 0.5 *N* NaOH and gentle warming, XVIII was converted into a substance with an  $R_f$  value shown in Table I, which suggested the hydrolysis of the ester group. Charcoal treatment and gentle heating of the solution after acidification with acetic acid gave white needles, for which the 6-benzaminomethylisoxanthopterin structure has been assigned because of its paper chromatographic behavior.

*Anal.* Calcd. for  $C_{14}H_{12}O_3N_5$ : N, 26.91. Found: N, 26.75.

**6-Aminomethylisoxanthopterin (XXI).**—Heating 800 mg. of (XX) in 20 ml. of 5 *N* NaOH on the bath for 1 hour, addition of 100 ml. of water, charcoal adsorption and acidification (acetic acid) gave an amorphous yellow-brown powder, which could not be further decolorized. The same compound also resulted from XVIII and XXII through proce-

dures shown in scheme I, and these reactions suggested the given structure for the product.

*Anal.* Calcd. for  $C_7H_8O_3N_5$ : N, 40.37. Found: N, 39.23.

**7-Acetonilyxanthopterin (XXVI).**—(II)-Sulfate (5 g.) was dissolved in 60 ml. of 2 *N* NaOH and, after addition of 300 ml. of 2.5 *N* HCl, 8 g. of ethoxalylacetone was added under heating. The mixture was heated for an additional 30 min., when yellow needles were obtained, 4.5 g.

*Anal.* Calcd. for  $C_9H_9O_3N_5$ : N, 29.78. Found: N, 29.78.

**$\alpha$ -(2,4,7-Trihydroxypteridyl-6)-propionic Acid (XXX).**—To 2.5 g. of 2,4-dihydroxy-5,6-diaminopyrimidine sulfate in 10 ml. of 2 *N* NaOH, there was added 120 ml. of 1 *N* acetic acid containing 6 ml. of ethyl  $\alpha$ -ethoxalylpropionate and the mixture was heated for 45 min. at 100°. When the solution was frozen overnight yellow crystals were obtained; a second crop precipitated from the mother liquid. The combined crystals were dissolved in a small amount of 2%  $Na_2CO_3$ , treated with charcoal and poured into a cold 2 *N* HCl solution to give light yellow crystals. After repeating this procedure once more, the product was dissolved in the minimum amount of 2%  $Na_2CO_3$ , acidified with 2 *N* acetic acid and left overnight to give a crystalline product. This was washed with dil. acetic acid, alcohol and ether; 1.4 g. (56%).

*Anal.* Calcd. for  $C_9H_8O_5N_4$ : N, 22.22. Found: N, 22.16.

**$\alpha$ -(2,4,7-Trihydroxypteridyl-6)-butyric Acid (XXXI).**—This was obtained in a 62% yield from 2,4-dihydroxy-5,6-diaminopyrimidine sulfate and ethyl  $\alpha$ -ethoxalylbutyrate in an analogous manner.

**2,4,7-Trihydroxy-6-acetonilypteridine (XXXII) and 2,4,6-Trihydroxy-7-acetonilypteridine (XXXIII).**—The former compound (XXXII) was produced by the reaction of 2,4-dihydroxy-5,6-diaminopyrimidine sulfate with ethoxalylacetone under conditions mentioned for the preparation of 6-acetonilysoxanthopterin (XIII), and the latter compound (XXXIII) from the same two reagents under the conditions of 7-acetonilyxanthopterin (XXVI) production.

**4,7-Dihydroxy-2-keto-1-methylpteridyl-6-carboxylic Acid (XXXIV).**—To a suspension of 1-methyl-2-keto-4-hydroxy-5,6-diaminopyrimidine<sup>7</sup> in 10 ml. of water (containing 1 drop of HCl), there was added 0.5 ml. of ethyl oxamalonate and the mixture was heated on the bath for 1 hr.

The precipitate was collected, dissolved in 10 ml. of 0.2 *N* NaOH, treated with charcoal and added to 10 ml. of boiling 2 *N* HCl, when yellow crystals were obtained. Three repetitions of the purification gave 160 mg. (50%) of white fine crystals.

*Anal.* Calcd. for  $C_8H_6O_5N_4$ : N, 23.53. Found: N, 23.45.

NAGOYA, JAPAN

(7) W. Traube, *Ber.*, **33**, 3048 (1900).