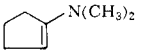
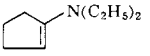
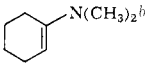
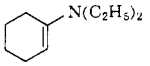
TABLE I

N,N-DIMETHYL- AND N,N-DIETHYLENAMINES

Enamine	Conv.,[a] %	Yield,[a] %	B.p., °C. (mm.)	$n^{25}D$	Anal. Calcd.	Anal. Found
	56	87	85–86 (104)	1.4801	C, 75.62 H, 11.76 N, 12.59	75.85 12.10 12.89
	65	63	99–101 (60)	1.4777	C, 77.63 H, 12.31 N, 10.06	77.81 12.19 9.66
 [b]	52	83	81 (35)	1.4851	C, 76.74 H, 12.08 N, 11.18	76.54 12.18 11.29
	35	51	64 (6)	1.4820	C, 78.36 H, 12.50 N, 9.14	78.28 12.42 8.86

[a] Based on ketone used. [b] R. A. Benkeser, R. F. Lambert, P. W. Ryan, and D. G. Stoffey, *J. Am. Chem. Soc.*, **80**, 6573 (1958) report this enamine but fail to give either a synthetic procedure or physical constants.

Pteridine Chemistry. IX. 2-Amino-4-hydroxy-6(and 7)-phenylpteridines

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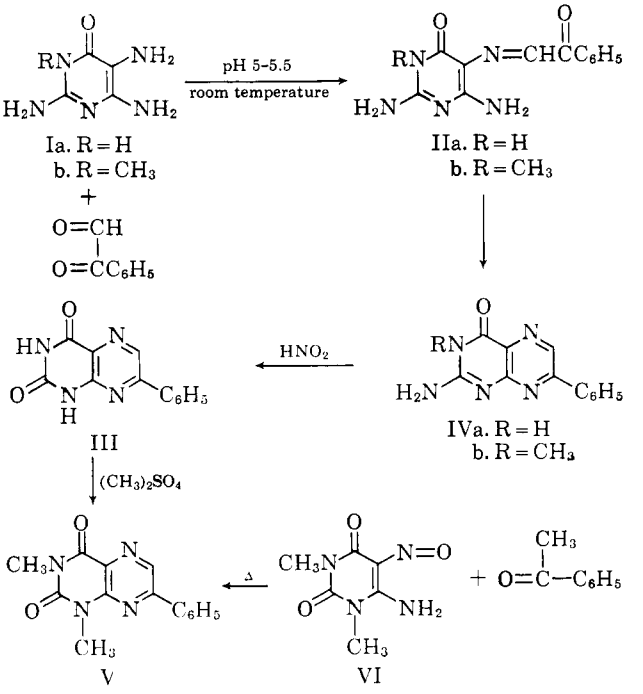
The isomeric 2-amino-4-hydroxy-6(and 7)-phenylpteridines (VIIa and IVa) and their 3-methyl derivatives were considered to be useful compounds for a continuation of the study of the methylation of 2-amino-4-hydroxypteridines.[1] However, the published reports by two groups of investigators on the synthesis of VIIa and/or IVa do not agree on the nature of the products obtained.

In 1952, King and Spensley[2] reported that the reaction between 2,4,5-triamino-6-hydroxypyrimidine (Ia) and phenylglyoxal or α-nitroacetophenone gave the 7-phenyl derivative IVa, while Ia and α,α-dichloroacetophenone gave the 6-phenyl derivative VIIa. In 1956, Dick, Wood, and Logan[3] re-examined the same three reactions and claimed that in each case the product was the 6-phenyl derivative VIIa. In connection with the use of phenylglyoxal in the above reaction, it should be noted that the reaction between 4,5-diaminopyrimidines and ketoaldehydes has been reported many times in the literature. Under weakly acidic conditions similar to those used by King and Spensley,[2] the primary product has almost invariably been a 7-substituted pteridine.[4,5] The 6-substituted derivatives have been prepared only in special systems containing either strong acid[5] or aldehyde binding agents such as hydrazine or sodium bisulfite.[4] Therefore, it was our opinion that King and Spensley were correct with respect to the phenylglyoxal reaction. This was verified as outlined.

2,4,5-Triamino-6-hydroxypyrimidine (Ia) was condensed with phenylglyoxal hydrate in a weakly acidic water–ethanol solution at room temperature.[2] An ultraviolet absorption spectrum of the initial product indicated that it was primarily the anil IIa. When this product was dissolved in 2.5 *N* sodium hydroxide, ring closure occurred to give a pteridine which was 2-amino-4-hydroxy-7-phenylpteridine (IVa) contaminated with a small amount of 6-phenyl isomer as shown by paper chromatography and ultraviolet absorption spectra (see p. 1399). The impurity was successfully removed by crystallization. The structure of IVa was proved by its conversion to 2,4-dihydroxy-7-phenylpteridine (III)[3] followed by methylation to produce 1,3-dimethyl-7-phenyl-2,4(1*H*,3*H*)-pteridinedione (V). The latter compound V was then synthesized unequivocally as described by Dick, Wood, and Logan[3] from 6-amino-1,3-dimethyl-5-nitroso-2,4-(1*H*,3*H*)-pyrimidinedione (VI) and acetophenone. The two products were identical as shown by infrared and ultraviolet absorption spectra and mixture melting point.

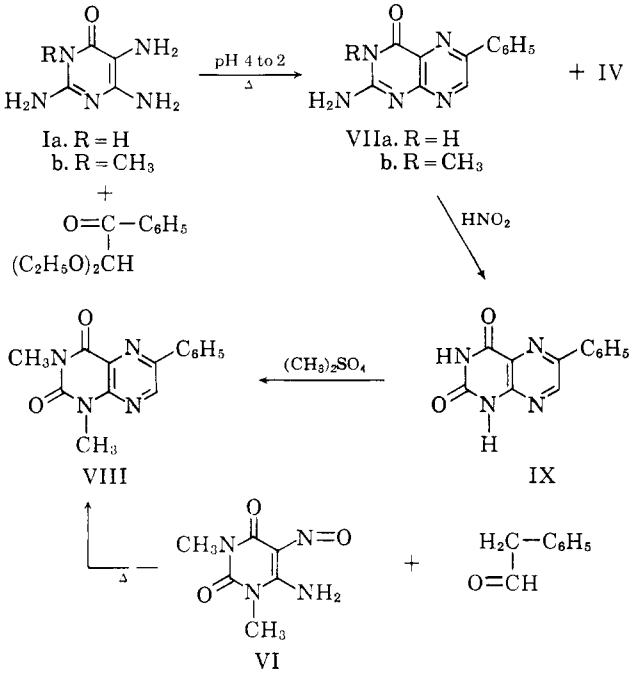


A synthesis of the isomeric 6-phenyl derivative VIIa was discovered during an attempt to utilize directly commercially available phenylglyoxal diethyl acetal. 2,4,5-Triamino-6 hydroxypyrimidine (Ia) was con-

(1) R. B. Angier and W. V. Curran, *J. Org. Chem.*, **27**, 892 (1962).
(2) F. E. King and P. C. Spensley, *J. Chem. Soc.*, 2144 (1952).
(3) G. P. G. Dick, H. C. S. Wood, and W. R. Logan, *ibid.*, 2131 (1956).
(4) A. Albert, *Quart. Rev.*, **6**, 227, 228 (1952).
(5) W. R. Boon, *J. Chem. Soc.*, 2146 (1957).

densed with phenylglyoxal diethyl acetal in a weakly acidic water–ethanol solution under reflux for ten hours. The product was primarily 2-amino-4-hydroxy-6-phenylpteridine (VIIa) which was readily purified, although with considerable loss of material.

Since our results differed from those of Dick, *et al.*,[3] the structure of VIIa was also proved by conversion to 2,4-dihydroxy-6-phenylpteridine (IX) followed by methylation to give 1,3-dimethyl-6-phenyl-2,4(1*H*,3*H*)-pteridinedione (VIII). Compound VIII was then synthesized unequivocally from the nitrosopyrimidine VI and phenylacetaldehyde.[3] The two products were identical as shown by infrared and ultraviolet absorption spectra and mixture melting point.



Attempts were made to utilize both sodium bisulfite[4] and 6 *N* sulfuric acid[5] in the reaction between Ia and phenylglyoxal in order to produce the 6-phenyl isomer VIIa. In each case the added reagent did increase the per cent of 6-isomer produced. However, the product was always a mixture of isomers which could not be separated by the methods used in the reactions described previously.

Using modifications of methods outlined previously, the 3-methyl derivatives IVb and VIIb were synthesized. 2,5,6-Triamino-3-methyl-4(3*H*)-pyrimidinone (Ib) and phenylglyoxal hydrate at room temperature gave the anil IIb which was recrystallized to give a pure product. Cyclization of this anil IIb to a pteridine could not be carried out in an alkaline solution since the product, a 3-methyl-4-pteridinone IVb, would be expected[6] to rearrange to a 2-methylamino derivative. However, cyclization of IIb was accomplished in refluxing 2-methoxyethanol using a take-off to remove water formed during the reaction. A good yield of 2-amino-3-methyl-7-phenyl-4(3*H*)-pteridinone (IVb) was obtained uncontaminated with any of the 6-phenyl isomer.

The reaction between 2,5,6-triamino-3-methyl-4(3*H*)-pyrimidinone (Ib) and phenylglyoxal diethyl acetal under weakly acidic conditions gave a product which was shown by paper chromatography to be a mixture of approximately equal parts of the 6-phenyl VIIb and 7-phenyl IVb isomers. However, a fortunate and unexpected difference in solubilities permitted a rather easy separation of pure 2-amino-3-methyl-6-phenyl-4(3*H*)-pteridinone (VIIb). The structures of these 3-methyl derivatives (VIIb and IVb) were confirmed through the use of ultraviolet absorption spectra, discussed below.

In order to resolve the other differences between King and Spensley,[2] and Dick, Wood, and Logan[3] the reaction between pyrimidine Ia and α-nitroacetophenone was repeated[2] and found to give the 6-phenyl derivative VIIa in a poor yield. This is in agreement with Dick, Wood, and Logan. Furthermore, this is the expected product since the intermediate anil should logically involve the 5-amino group of Ia rather than the 4-amino group as suggested by King and Spensley.[2] The two groups agreed that Ia and α,α-dichloroacetophenone gave the 6-phenyl isomer VIIa. We concur in this, but in our limited study of this reaction the product always contained enough of the 7-phenyl isomer IVa to make purification difficult. Finally, the synthesis of 2,4-dihydroxy-7-phenylpteridine as reported by Dick, *et al.*,[3] was repeated and the product was found to be identical with our compound III.

Ultraviolet Absorption Spectra and Structure.—Although the infrared absorption spectra of pure 6-phenyl and 7-phenyl isomers (VIIa and IVa) are distinctively different, the best method for differentiating these compounds and for determining isomer ratios in reaction mixtures involves the use of their ultraviolet absorption spectra. Petering and Schmitt[7] have shown that isomer contents of crude mixtures of 2-amino-4-hydroxy-6(and 7)-alkylpteridines can be determined by measuring the ratio of the absorptions at two specific wave lengths. In the same manner we have found that in 0.1 *N* hydrochloric acid the ratio *E* 276 mμ/*E* 351 mμ is 2.1 for 2-amino-4-hydroxy-6-phenylpteridine (VIIa) *vs.* 0.30 for the isomeric 7-phenyl derivative IVa. A curve prepared from known mixtures of VIIa and IVa was then used to calculate the isomer contents described in the experimental section. We have also shown[8] that in 0.1 *N* hydrochloric acid 3-methyl derivatives of 2-amino-4-hydroxypteridines have essentially the same ultraviolet absorption spectra as the parent 2-amino-4-hydroxypteridines. Thus the structures of the isomeric 3-methyl-6(and 7)-phenylpteridines (VIIb and IVb) were confirmed by comparison of their absorption spectra with those of the parent 2-amino-4-hydroxy-6-(and 7)-phenylpteridines (VIIa and IVa).

Experimental[9]

All evaporations were carried out under reduced pressure.

Descending paper chromatography on Whatman no. 1 paper was used routinely to follow reactions and purifications. Isopropyl alcohol–1 *N* ammonium hydroxide (7:3) was the most useful solvent for separating and identifying the 6- and 7-phenyl isomers of 2-amino-4-hydroxypteridine and their 3-methyl derivatives. The spots were detected using an ultraviolet lamp provided with a filter to give primarily light of wave length 254 mμ.

(6) W. V. Curran and R. B. Angier, *J. Am. Chem. Soc.*, **80**, 6095 (1958).

(7) H. G. Petering and J. A. Schmitt, *ibid.*, **71**, 3977 (1949).

(8) R. B. Angier and W. V. Curran, *J. Org. Chem.*, **26**, 2129 (1961).

(9) All melting points are corrected for the exposed stem of the thermometer.

2-Amino-4-hydroxy-7-phenylpteridine[2] **(IVa). A.**—A solution containing 14.0 g. (67.5 mmoles) of phenylglyoxal diethyl acetal, 80 ml. of dioxane, 20 ml. of water, and 2.0 ml. of concentrated hydrochloric acid was heated for 3 hr. on a steam bath. This was evaporated to a small volume, diluted with 50 ml. of 50% dioxane–water and 1.2 ml. of concentrated hydrochloric acid, and heated 3.5 hr. on a steam bath. The solution was evaporated to a sirup, redissolved in *ca.* 30 ml. of ethanol, and added to a solution of 9.76 g. (45.6 mmoles) of 2,4,5-triamino-6-hydroxypyrimidine dihydrochloride and 22.0 g. (244 mmoles) of sodium acetate in 120 ml. of water. The mixture stood at room temperature for 3 hr. and in an ice bath for 2 hr., after which the solid was collected. This was primarily the anil IIa.[10] It was cyclized to the pteridine by dissolving in 800 ml. of hot 2.0 *N* sodium hydroxide which was treated with charcoal, filtered, acidified to pH 4, and cooled; yield 11.0 g.; the pteridine content consisted of 92% 7-phenyl and 8% 6-phenyl derivatives.[11]

This was dissolved in 400 ml. of hot 0.2 *N* sodium hydroxide which was clarified with charcoal and treated with 160 ml. of 10.0 *N* sodium hydroxide to give a crystalline sodium salt. The mixture stood several hours at room temperature and 2 hr. in the chill room. The product was collected and redissolved in 800 ml. of hot water. The solution was treated with charcoal, filtered and acidified to pH 2.5 with hydrochloric acid; yield 4.5 g. (41%); 95% 7-phenyl derivative IVa.

To remove the last traces of the 6-phenyl isomer the reaction product[12] was dissolved in 225 ml. of hot dimethylformamide by adding 3.6 ml. of concentrated hydrochloric acid. After clarifying the solution with charcoal it was reheated, 110 ml. of water was added slowly, and after a few minutes the crystalline product was collected while still hot; yield 3.5 g. (32%); R_f 0.5 [isopropyl alcohol–1.0 *N* ammonium hydroxide (7:3)], 0.38 (0.1 *N* HCl) (light blue); $\lambda_{max}^{0.1\ N\ NaOH}$ 237 mμ (ε 19,800), 264 mμ (ε 19,900), 373 mμ (ε 12,900); $\lambda_{max}^{pH\ 7.0}$ 236 mμ (ε 20,800), 275 mμ (ε 16,700), 362 mμ (ε 13,800), $\lambda_{max}^{0.1\ N\ HCl}$ 225 mμ (ε 23,900), 260–280 mμ (sh) (ε 6,200), 347 mμ (ε 21,500); *E* 276 mμ/*E* 351 mμ in 0.1 *N* HCl = 0.30; λ_{max}^{KBr} 8.1, 12.3 μ. (These two peaks are absent in the 6-phenyl isomer.)

Anal. Calcd. for $C_{12}H_9N_5O$ (239): C, 60.2; H, 3.8; N, 29.3. Found: C, 60.5; H, 3.9; N, 29.8.

B.—This reaction was also carried out using crystalline phenylglyoxal hydrate. The results were the same as described under A.

2,4-Dihydroxy-7-phenylpteridine[3] **(III).**—2-Amino-4-hydroxy-7-phenylpteridine (500 mg., 2.1 mmoles) was suspended in 220 ml. of boiling water to which was added 15 ml. of concd. hydrochloric acid. Sodium nitrite (8.0 g.) was added in portions to the hot solution. The mixture was again brought to boiling for a few minutes, then cooled to 40°, and filtered; yield of product 400 mg. (80%); m.p. 374–378° dec.; R_f 0.13 (0.1 *N* HCl) (deep blue); $\lambda_{max}^{0.1\ N\ NaOH}$ 234 mμ (ε 17,800), 268 mμ (ε 18,000), 371 mμ (ε 10,600); $\lambda_{max}^{pH\ 9.2}$ 230 mμ (ε 19,200), 273 mμ (ε 15,600), 363 mμ (ε 12,900); $\lambda_{max}^{0.1\ N\ HCl}$ 221 mμ (ε 20,400), 350 mμ (ε 20,200).

Anal. Calcd. for $C_{12}H_8N_4O_2$ (240): C, 60.0; H, 3.4; N, 23.3. Found: C, 59.7; H, 3.4; N, 23.2.

This was identical with a sample prepared from phenylglyoxal hydrate and Ia in the presence of sodium bisulfite and sodium sulfite as described by Dick, *et al.*[3]

1,3-Dimethyl-7-phenyl-2,4(1*H*,3*H*)-pteridinedione[3] **(V).**—2,4-Dihydroxy-7-phenylpteridine (360 mg., 1.5 mmoles) (III), 9 ml. of dimethylformamide (DMF), 12 ml. of water, 1.5 ml. of 1 *N* sodium hydroxide and 0.15 ml. of dimethyl sulfate were mixed and stirred with a magnetic stirrer. At 15-min. intervals four 0.15-ml. portions of dimethyl sulfate were added followed each time by the addition of 1.5 ml. of 1 *N* sodium hydroxide over a 2–3 min. interval. After an additional 30 min. of stirring the pH was adjusted to 5, the mixture was cooled and the product was collected; yield 325 mg. (81%). Two recrystallizations from dimethylformamide using decolorizing charcoal gave 170 mg. of product; m.p. 308–309°. Using infrared and ultraviolet absorption spectra and mixture melting point this material was found to be identical with a sample prepared unequivocally from 6-amino-1,3-dimethyl-5-nitroso-2,4-(1*H*,3*H*)-pyrimidinedione (VI) and acetophenone as described by Dick, Wood, and Logan[3] and recrystallized from DMF: $\lambda_{max}^{CH_3OH}$ 230 mμ (ε 23,600), 274–282 mμ (plateau) (ε 8,900), 352 mμ (ε 19,500); λ_{max}^{KBr} 7.0 μ. (This peak is not present in the isomeric 6-phenyl derivative VIII.)

Anal. Calcd. for $C_{14}H_{12}N_4O_2$ (268); C, 62.7; H, 4.5; N, 20.9. Found: C, 62.8; H, 4.6; N, 21.1.

2-Amino-4-hydroxy-6-phenylpteridine (VIIa).—A mixture of 10.3 g. (40 mmoles) of 2,4,5-triamino-6-hydroxypyrimidine·H_2SO_4·H_2O, 9.8 g. (40 mmoles) of barium chloride, and 110 ml. of water was heated on a steam bath for 15 min. and then filtered through a Celite pad. The filtrate was mixed with 3.6 g. (44 mmoles) of sodium acetate and a solution of 8.6 g. (41 mmoles) of phenylglyoxal diethyl acetal in 20 ml. of ethanol and heated on a steam bath for 3.5 hr. The mixture was cooled overnight and the product collected, washed with water, then ether and air-dried under suction in the funnel, thus evaporating the ether in the filtrate; yield 2.7 g.; 46% 6-phenyl isomer VIIa and 54% 7-phenyl isomer IVa.[11]

The filtrate was mixed with 20 ml. of ethanol, heated on a steam bath for 6.5 hr., cooled, and filtered; yield 6.0 g.; 91% 6-phenyl isomer VIIa.[11]

This second crop was recrystallized from 2500 ml. of 1.0 *N* hydrochloric acid using 6.0 g. of Norit. The product was collected, the damp filter cake was slurried in hot water containing a little pyridine to remove hydrochloric acid. The mixture was cooled and the product was collected; yield 2.2 g. (23%); R_f 0.3 [isopropyl alcohol–1.0 *N* ammonium hydroxide (7:3)] (blue), R_f 0.4 (0.1 *N* HCl); $\lambda_{max}^{0.1\ N\ NaOH}$ 271 mμ (ε 23,200), 377 mμ (ε 10,000); $\lambda_{max}^{pH\ 7.0}$ 293 mμ (ε 18,900), 370 mμ (ε 8,100); $\lambda_{max}^{0.1\ N\ HCl}$ 276 mμ (ε 20,000), 351 mμ (ε 9,600); *E* 276 mμ/*E* 351 mμ in 0.1 *N* HCl = 2.1; λ_{max}^{KBr} 6.75, 7.8 and 11.85 μ. (These three peaks are absent in the 7-phenyl isomer II.)

Anal. Calcd. for $C_{12}H_9N_5O$ (239): C, 60.2; H, 3.8; N, 29.3. Found: C, 59.8; H, 4.1; N, 29.1.

2,4-Dihydroxy-6-phenylpteridine (IX).—2-Amino-4-hydroxy-6-phenylpteridine (300 mg., 1.26 mmoles) was suspended in 150 ml. of boiling water and dissolved by the addition of 2.0 ml. of 1.0 *N* sodium hydroxide. The clear, hot solution was acidified with 15.0 ml. of concentrated hydrochloric acid, reheated almost to boiling, and treated with 5.0 g. of sodium nitrite which was added in portions with swirling. The mixture was reheated to boiling, allowed to stand at room temperature for one hour, and filtered; yield of solid 200 mg. (67%). This was recrystallized from 20 ml. of 2-methoxyethanol; yield 120 mg. (40%); m.p. 380–382°; R_f 0.17 (0.1 *N* HCl); $\lambda_{max}^{0.1\ N\ NaOH}$ 280 mμ (ε 22,300), 382 mμ (ε 9,100); $\lambda_{max}^{pH\ 9.2}$ 292 mμ (ε 21,600), 370 mμ (ε 8,000); $\lambda_{max}^{0.1\ N\ HCl}$ 272 mμ (ε 21,600), 353 mμ (ε 9,600).

Anal. Calcd. for $C_{12}H_8N_4O_2$(240): C, 60.0; H, 3.4; N, 23.3. Found: C, 59.7; H, 3.6; N, 23.2.

1,3-Dimethyl-6-phenyl-2,4-(1*H*,3*H*)-pteridinedione[3] **(VIII).**—2,4-Dihydroxy-6-phenylpteridine (360 mg., 1.5 mmoles) (IX) was methylated exactly as described above for the isomeric 7-phenyl derivative; yield 350 mg. Two recrystallizations from dimethylformamide gave 185 mg. of product, m.p. 258–259°. Using infrared and ultraviolet absorption spectra and mixture melting point this was found to be identical with a sample prepared unequivocally from 6-amino-1,3-dimethyl-5-nitroso-2,4-(1*H*,3*H*)-pyrimidinedione (VI) and phenylacetaldehyde as described by Dick, Wood, and Logan[3] and recrystallized from DMF; $\lambda_{max}^{CH_3OH}$ 280 mμ (ε 21,200), 357 mμ (ε 8,500); λ_{max}^{KBr} 6.7, 7.4, 8.9 and 13.65 μ. (These 4 peaks are not present in the isomeric 7-phenyl derivative V.)

Anal. Calcd. for $C_{14}H_{12}N_4O_2$(268); C, 62.7; H, 4.5; N, 20.9. Found: C, 63.0; H, 4.6; N, 20.5.

2,6-Diamino-3-methyl-5[N-(2-phenyl-2-oxoethylidene)amino]-4-(3*H*)-pyrimidinone (IIb).—3-Methyl-2,5,6-triamino-4-hydroxypyrimidine hydrochloride[6] (0.4 g., 2.1 mmoles) and 0.67 g. (8.4 mmoles) of sodium acetate were dissolved in 8.0 ml. of water and immediately mixed with a solution of 0.35 g. (2.3 mmoles) of phenylglyoxal hydrate in 6.0 ml. of 50% ethanol. An orange precipitate appeared immediately. After 3 hr. at room temperature the mixture was diluted with 10 ml. of water and the product was collected; yield 0.6 g. (98%).

A solution of 200 mg. of this material in 20 ml. of hot ethanol was clarified with charcoal and then diluted with 15 ml. of water and cooled to give reddish hair-like crystals; yield 120 mg.; dried at room temperature; $\lambda_{max}^{CH_3OH}$ 262 mμ (ε 15,000), 415 mμ (ε 18,800).

Anal. Calcd. for $C_{13}H_{13}N_5O_2 \cdot H_2O$ (289): C, 54.0; H, 5.2; N, 24.2. Found: C, 53.9; H, 5.3; N, 24.2.

(10) The ultraviolet absorption spectra of this anil IIa showed maxima in methanol at 263 mμ and 415 mμ. This is similar to the anil IIb and entirely different from the 7-phenylpteridine IVa.

(11) This isomer ratio was determined as described under "Ultraviolet Absorption Spectra and Structure."

(12) As prepared by previous investigators the 7-phenyl isomer IVa undoubtedly contained a small amount of the 6-phenyl isomer VIIa.

A sample of this material recrystallized from ethanol gave orange prisms which also contained a mole of solvent.

Anal. Calcd. for $C_{13}H_{13}N_5O_2 \cdot C_2H_5OH$ (317): C, 56.8; H, 6.0; N, 22.1. Found: C, 56.6; H, 6.2; N, 22.6.

2-Amino-3-methyl-7-phenyl-4(3*H*)-pteridinone (IVb).—A mixture of 8.0 g. (42 mmoles) of 2,5,6-triamino-3-methyl-4(3*H*)-pyrimidinone hydrochloride[6] and 13.6 g. (165 mmoles) of sodium acetate was slurried in 160 ml. of water and quickly mixed with a warm (35°) solution of 7.0 g. (45 mmoles) of phenylglyoxal hydrate in 120 ml. of ethanol. After several hours at room temperature the product was collected; yield 11.6 g. (97%).

A solution of this anil in 450 ml. of 2-methoxyethanol was heated to reflux for 5.5 hr. using a take-off intermittently to remove water (about 150 ml. of fresh 2-methoxyethanol was added during this period while a total of 300 ml. of distillate was collected). The reaction solution was evaporated to a small volume and slurried with warm water to give a volume of about 450 ml. This was cooled well and the product was collected; yield 10 g. (98%). This material was chromatographically pure and contained none of the 6-phenyl isomer. It was recrystallized from 450 ml. of acetic acid. The product was collected, air-dried and then dried in an oven at 100° for 4 hr.; yield 6.7 g. (63%); m.p. 352–355°; R_f 0.6 [isopropyl alcohol–1.0 *N* NH_4OH (7:3)] (blue); $\lambda_{max}^{pH\ 7.0}$ 236 mμ (ε 21,800), 277 mμ (ε 18,400), 369 mμ (ε 11,900); $\lambda_{max}^{0.1\ N\ HCl}$ 225 mμ (ε 24,800), 260–280 (sh) (ε 6,600), 347 mμ (ε 21,000); the spectrum in 0.1 *N* sodium hydroxide was essentially the same as at pH 7.0. The spectrum in 0.1 *N* hydrochloric acid is almost superimposable on the spectrum of 2-amino-4-hydroxy-7-phenylpteridine (IVa).

Anal. Calcd. for $C_{13}H_{11}N_5O$ (253): C, 61.6; H, 4.4; N, 27.7. Found: C, 61.4; H, 4.4; N, 27.9.

2-Methylamino-4-hydroxy-7-phenylpteridine.—2-Amino-3-methyl-7-phenyl-4(3*H*)-pteridinone (200 mg., 0.8 mmole) (IVb) was suspended in a solution of 10 ml. of 2-methoxyethanol and 15 ml. of 1.0 *N* sodium hydroxide and heated on a steam bath for 1.5 hr. The hot solution was acidified with 1.5 ml. of acetic acid and cooled; yield 125 mg. This was recrystallized from 15 ml. of dimethylformamide; yield 85 mg.; R_f 0.5 [isopropyl alcohol–1.0 *N* ammonium hydroxide (7:3)] (blue); $\lambda_{max}^{0.1\ N\ NaOH}$ 238 mμ (ε 20,500), 270 mμ (ε 25,300), 388 mμ (ε 12,900); $\lambda_{max}^{pH\ 7.0}$ 239 mμ (ε 21,500), 281 mμ (ε 20,800), 369 mμ (ε 13,100); $\lambda_{max}^{0.1\ N\ HCl}$ 230 mμ (ε 28,200), 349 mμ (ε 22,000).

Anal. Calcd. for $C_{13}H_{11}N_5O$ (253): C, 61.6; H, 4.4; N, 27.7. Found: C, 61.9; H, 4.0; N, 27.5.

2-Amino-3-methyl-6-phenyl-4(3*H*)-pteridinone (VIIb) and Its Isomer IVb.—A solution of 10.2 g. (53.0 mmoles) of 2,5,6-triamino-3-methyl-4(3*H*)-pyrimidinone·hydrochloride[6] in 270 ml. of water was mixed with a solution of 12.0 g. (58.0 mmoles) of phenylglyoxal diethyl acetal in 75 ml. of water and heated to reflux for 8 hr. This was cooled overnight, the product was collected, and washed with water and ether and dried; yield 12.4 g. (92%). (Paper chromatography showed this to be a mixture of the isomeric 6-phenyl VIIb and 7-phenyl IVb derivatives).

This material was suspended in a solution of 250 ml. of dimethylformamide (DMF) and 6.2 ml. of concentrated hydrochloric acid, which was heated to boiling for several minutes and filtered hot; yield 5.5 g. (fraction A). (Paper chromatography showed this product to be the 6-phenyl derivative VIIb contaminated with a small amount of 2-amino-4-hydroxy-6-phenylpteridine but verv little of the 7-phenyl isomer.) Fraction A was probably sufficiently pure for most purposes. However, it was purified further as follows. It was suspended in 900 ml. of dimethylformamide and 24 ml. of concentrated hydrochloric acid, heated to boiling, and filtered; yield 2.5 g. (fraction B). The filtrate was cooled, diluted with 600 ml. of water, and cooled some more; yield 2.4 g. (fraction C). Fraction B was dissolved in a solution of 600 ml. of dimethylformamide and 18 ml. of concentrated hydrochloric acid which was then cooled and diluted with 300 ml. of water; yield 2.2 g. (fraction D).

Fractions C and D were combined, added to a hot solution of sodium acetate, mixed well, and cooled; yield 4.1 g. (30%) of the 6-phenyl isomer.

For analyses a small sample was recrystallized from a dimethylformamide–hydrochloric acid solution and then freed of hydrochloric acid by slurrying in a sodium acetate solution just as described above; m.p. 355–358°; R_f 0.5 [isopropyl alcohol–1.0 *N* NH_4OH (7:3)] (blue); $\lambda_{max}^{pH\ 7.0}$ 296 mμ (ε 23,800), 375 mμ (ε 8,500); $\lambda_{max}^{0.1\ N\ HCl}$ 278 mμ (ε 19,700), 352 mμ (ε 9,400). The spectrum of this compound in 0.1 *N* hydrochloric acid is almost superimposable on the spectrum of 2-amino-4-hydroxy-6-phenylpteridine (VIIa).

Anal. Calcd. for $C_{13}H_{11}N_5O$ (253): C, 61.6; H, 4.4; N, 27.7. Found: C, 61.6; H, 4.4; N, 28.1.

The filtrate from fraction A was warmed, diluted with 375 ml. of water, adjusted to pH 5.5 with sodium acetate, and cooled; yield 4.7 g. This was recrystallized from 180 ml. of acetic acid and a second time from 80 ml. of acetic acid using charcoal to clarify the solution each time. The product was dried in an oven at 100°; yield 2.2 g.; m.p. 346–349°. Chromatography indicated that this was fairly pure 7-phenyl isomer IVb.

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Synthesis of 5-Amino-5-deoxy Derivatives of L-Idose[1]

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Synthesis of suitably substituted C-5 hydroxyls of aldopentoses and aldohexoses offers a direct route for the introduction of selected hetero atoms into pyranose rings. Preparation of a thiapyranose and thiapyranosides, obtained through the placement of a mercapto group on carbon 5 of several pentoses and hexoses, has been reported recently.[2–5]

This work describes the synthesis of 5-amino-5-deoxy derivatives of L-idose from new derivatives of D-glucose.

3-*O*-Benzyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (I) is hydrolyzed selectively to remove the 5,6-*O*-isopropylidene group. Subsequent tritylation of compound I gives crystalline 3-*O*-benzyl-1,2-*O*-isopropylidene-6-*O*-triphenylmethyl-α-D-glucofuranose (II) in 94% yield. Tosylation of compound II then affords crystalline 3-*O*-benzyl-1,2-*O*-isopropylidene-5-*O*-*p*-tolylsulfonyl-6-*O*-triphenylmethyl-α-D-glucofuranose (III) in 95% yield. A heterogeneous solution, observed in a conventional hydrazinolysis[6] of compound III, markedly diminishes the yield of 3-*O*-benzyl-5-deoxy-5-hydrazino-1,2-*O*-isopropylidene-6-*O*-triphenyl-β-L-idofuranose (IV). However, when compound III is dissolved in absolute 1-butanol with anhydrous hydrazine, a homogeneous solution is maintained and the reaction gives a smooth SN2 displacement of the 5-*O*-tosyloxy group with the formation of crystalline compound IV in 75% yield. Thus, hydrazinolysis of compound III is more seriously inhibited by solution heterogeneity, than by molecular steric effects. An L-idose configuration is assigned to compound IV, since experimental evidence presented by previous in-

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