reagent tris(dipivalomethanato)europium has established that this α form has the *E* configuration (see text): nmr (100 MHz, $CDCl_3$) δ 2.37 (s, NCH_3, 3 H), ~2.40 (m, CH_2C=, 2 H), 2.71 (t, *J* = 7 Hz, NCH_2, 2 H), 3.78 (d, *J* = 13 Hz, 11 axial CH, 1 H), 4.42 (d, *J* = 13 Hz, 11 equatorial CH, 1 H), 6.22 (t, *J* = 7.5 Hz, vinylic CH, 1 H) 7.2–7.5 (m, aromatic CH, 7 H), 8.15 (d with fine structure, *J* = 8 Hz, C_9H, 1 H); nmr in presence of ~0.3 mol of $Eu(dpm)_3$ ($CDCl_3$) 4.13 (d, *J* = 13 Hz, 11 axial CH, 1 H), 4.42 (d, *J* = 13 Hz, 11 equatorial CH, 1 H), ~5.4 (broad, CH_2C=, 2 H), ~7.5 (broad, NCH_3, CH_2N, HC=, 6 H) 7.4–7.7 (m, aromatic H, 5 H), 7.85 (broadened d, *J* ≈ 8 Hz, C_1H, 1 H), 8.09 (broadened d, *J* ≈ 7–8 Hz, C_4H, 1 H), 8.31 (broadened d, *J* ≈ 8 Hz, C_9H, 1 H).

Supernatant B.—The supernatant benzene phase was concentrated to about 10 ml and allowed to stand. The solution was decanted from a small amount of oil that precipitated. This process was carefully repeated to give about 5 ml of a clear benzene solution. The benzene was evaporated to give 0.33 g of (*Z*)-*N*-methyl-3-(10,11-dihydro-10-oxo-5*H*-dibenzo[*a*,*d*]cycloheptene)-$\Delta^{5,\gamma}$-propylamine hydrochloride as a viscous oil that could not be crystallized. After being converted into the free base, expanded scale nmr examination showed a single *N*-methyl proton absorption peak at δ 2.30; nmr ($CDCl_3$) δ 1.21 (s, NH, 1 H), 2.2–2.9 (m, $-CH_2CH_2-$, with a singlet at 2.30 (NCH_3), 7 H), 3.78 and 4.40 (double d, J_{gem} = 13 Hz, $-CH_2CO-$, 2 H), 6.21 (t, *J* = 7 Hz, vinyl CH, 1 H), and 7.2–7.6 and 8.0–8.2 (m, aromatic CH, 8 H).

(*R*,*S*)-(*E*)-*N*-Methyl(10,11-dihydro-10-hydroxy-5*H*-dibenzo[*a*,*d*]cycloheptene)-$\Delta^{5,\gamma}$-propylamine (3).—To a solution of 1.56 g of the E ketone **8** dissolved in 25 ml of absolute methanol was added a solution of 1.56 g of sodium borohydride dissolved in 3 ml of water. The solution was stirred and refluxed for 1.5 hr. The methanol was evaporated, and the residue was dissolved in benzene. The benzene solution was washed with water, dried, and filtered, and the solvent was evaporated to give 1.56 g of the (*R*,*S*)-*E* amino alcohol **3**: ir (KBr) 3400 (s, broad, OH), 3300 (m, broad, NH), 1555 (w), 675 (w), 560 (w), and 540 (w) cm^{-1}. A comparison of the infrared spectra of (*R*,*S*)-(*E*)-**3** and (*R*,*S*)-(*Z*)-**2** showed that the bands at 675, 560, and 540 cm^{-1} were stronger in the *E* spectrum: R_f^1 0.57, R_f^2 0.31; nmr ($CDCl_3$, 10% w/v) δ 1.26 (S, NH, 1 H), 2.0–2.52 (m, with peaks at 2.03 and 2.19 (NCH_3)), 2.74–3.68 (broad, $-CH_2CHOH-$, 2 H), 4.66–5.1 (broad, OH, 1 H), 5.85 (t, vinyl CH, 1 H, *J* = 7 Hz), and 7.0–7.4 (m, aromatic CH). The hydrogen maleate salt was prepared and crystallized from isopropyl alcohol, mp 156–157.5°.

Anal. Calcd for $C_{19}H_{21}NO \cdot C_4H_4O_4$: C, 69.85; H, 6.37; N, 3.54. Found: C, 69.70; H, 6.62; N, 3.60.

Attempts to analyze this salt by differential thermal analysis (dta), differential scanning calorimetry (dsc), and phase solubility analysis were unsuccessful.

A crystalline neutral naphthalene-1,5-disulfonate salt was prepared and recrystallized from methanol, mp 242°.

Anal. Calcd for $(C_{19}H_{21}NO)_2 \cdot C_{10}H_8O_6S_2$: C, 68.06; H, 5.95; N, 3.31; S, 7.57. Found: C, 67.67; H, 5.97; N, 3.22; S, 7.50.

On attempted analysis by dta, this salt showed a sharp endotherm at 242° (in air) (234° *in vacuo*), followed by a very sharp exotherm of crystallization to give presumably norcyclobenzaprine naphthalene-1,5-disulfonate which then melted at 309°.

Phase solubility analysis of the (*R*,*S*)-(*E*)-naphthalene-1,5-disulfonate salt showed it to be 99.8% pure.

(*R*,*S*)-(*Z*)-*N*-Methyl(10,11-dihydro-10-hydroxy-5*H*-dibenzo[*a*,*d*]cycloheptene)-$\Delta^{5,\gamma}$-propylamine (2).—In a manner similar to that described for reduction of the *E* isomer **8**, the *Z* isomer **9** (0.33 g) was reduced to **2** using 0.10 g of sodium borohydride: ir (KBr) 3400 (s, broad, OH), 3300 (m, broad, NH), 675 (m), 560 (w), and 540 (w) cm^{-1}. A comparison of the infrared spectra of (*R*,*S*)-(*E*)-**3** and (*R*,*S*)-(*Z*)-**2** showed that the OH stretching band at 3400 was stronger in the *Z* spectrum. The band at 1555 cm^{-1}, seen in the spectrum of **3**, is not present in the spectrum of **2**: R_f^1 0.52, R_f^2 0.24; nmr ($CDCl_3$, 10% w/v) δ 1.26 (s, NH, 1 H), 2.0–2.6 (m, with peaks at 2.21 (NCH_3) and 2.39), 2.82–3.7 (broad, $-CH_2CHOH-$, 2 H), 4.66–5.1 (broad, OH, 1 H), 5.85 (t, vinyl CH, 1 H, *J* = 7 Hz), and 7.0–7.4 (m, aromatic). The (*R*,*S*)-*Z* isomer **2** did not form a crystalline hydrogen maleate salt on long standing. The hydrogen oxalate salt was prepared and recrystallized from absolute ethanol, mp 135–137° (foaming).

Anal. Calcd for $C_{19}H_{21}NO \cdot C_2H_2O_4$: C, 68.28; H, 6.28; N, 3.79. Found: C, 67.93; H, 6.50; N, 3.52.

Attempts to analyze this salt by dta and dsc were unsuccessful.

Registry No.—**2**, 37439-87-5; **2** hydrogen maleate, 37439-88-6; **3**, 37439-89-7; **3** hydrogen maleate, 37439-90-0; **3** naphthalene-1,5-disulfonate salt, 37439-91-1; **4**, 37439-92-2; **5**, 37439-93-3; **6**, 37439-94-4; **7**, 37440-21-4; **8**, 37508-15-9; **8** HCl, 37440-24-7; **9**, 37440-22-5; (*R*,*S*)-*N*,*N*-dimethyl-3-(10,11-dihydro-10-hydroxy-5*H*-dibenzo[*a*,*d*]cycloheptene)-$\Delta^{5,\gamma}$-propylamine, 37440-23-6.

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N-Hydroxypteridines Structurally Analogous to Oncogenic *N*-Hydroxypurines. Covalent Hydration of 1-Hydroxy-2-oxo-1,2-dihydropteridine[1]

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1-Hydroxy-2,4-dioxo-1,2,3,4-tetrahydropteridine has been synthesized and its properties compared with the analogous 3-hydroxypurine derivative. A technique was devised for the catalytic reduction of 5-nitrocytosine 3-oxide to the requisite 5-aminocytosine 3-oxide necessary for the synthesis of the 1-hydroxy-2-oxo-1,2-dihydropteridine. The latter undergoes facile covalent hydration, including addition of methanol and ethanol.

The biological importance of pteridines and the existence of oncogenic[2] purine *N*-oxides suggested that consideration should be given to the possible chemical and biological properties of structurally analogous pteridine *N*-oxide derivatives. Few pteridine *N*-oxides are known[3,4] and the only one structurally analogous to the oncogenic 3-hydroxyxanthine (**1**, R = H) is 1-hydroxy-2,4-dioxo-1,2,3,4-tetrahydro-6,7-dimethylpteridine[3] (6,7-dimethyl **2**, R = H).

The desired 1-hydroxy-2,4-dioxo-1,2,3,4-tetrahydro-

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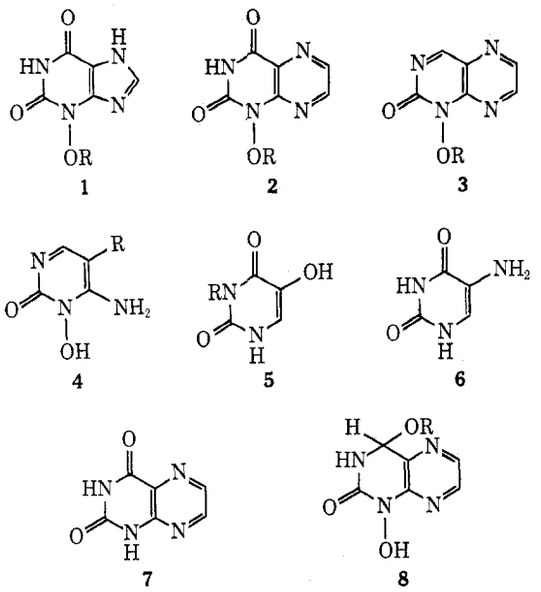

pteridine (2, R = H) and its *O*-benzyl derivative (2, R = $C_6H_5CH_2$) were prepared from condensation of 1-hydroxy- or 1-benzyloxy-5,6-diaminouracil[3,5] with glyoxal.

The synthesis of 1-hydroxy-2-oxo-1,2-dihydropteridine (3, R = H) required the synthesis of a series of new intermediates. That synthesis involved the nitration of the cytosine 3-oxide,[6] in concentrated sulfuric acid at room temperature with potassium nitrate, to give 4 (R = NO_2) in good yield and high purity. Reduction of the nitro group without reducing the *N*-oxide function was accomplished by catalytic hydrogenation with palladium on charcoal in water. The 5-aminocytosine 3-oxide (4, R = NH_2) tends to be oxidized when in contact with air and, immediately after the completion of hydrogenation, 1 equiv of 1 *N* HCl was added to the mixture to stabilize the amino derivative. Hydrogenation in 1 *N* HCl, to avoid the air oxidation after hydrogenation, was found to give a considerably lower yield because of the unexpected formation of 5-hydroxyuracil 3-oxide (5, R = OH) and at least six other minor by-products. The identity of 5 was confirmed by elemental analysis, nmr, and by its reduction to the known 5-hydroxyuracil.[7] Sodium dithionite was found to be an excellent selective reducing agent for reducing nitrosouracil *N*-oxides,[3,5] but was not as satisfactory for reducing nitrocytosine *N*-oxide, since it yielded both 4 (R = NH_2) and 5-aminouracil (6). The latter may arise by a mechanism similar to that proposed for the deamination of cytosine with sodium bisulfite.[8,9]

1-Hydroxy-2,4-dioxo-1,2,3,4-tetrahydropteridine (2, R = H) can exist in many tautomeric forms, but the neutral species is predominantly the dioxo form, as indicated by the similarity of the ultraviolet spectrum of 2 (R = H) in neutral solution to those of 2,4-dihydroxypteridine (7), known to exist predominately in dioxo form,[10] and of 1-benzyloxy-2,4-dioxo-1,2,3,4-tetrahydropteridine (2, R = $C_6H_5CH_2$). Comparison of the ultraviolet spectra of the neutral species of 3-hydroxyxanthine derivatives with those of the parent xanthines showed[11] that introduction of the *N*-hydroxy group at the 3 nitrogen caused a bathochromic shift of 6 ± 1 nm in the main absorption band. The neutral species of 2,4-dihydroxypteridine and of its 1-hydroxy derivative shows a similar difference.

The nmr spectrum of 1-hydroxy-2-oxo-1,2-dihydropteridine (3, R = H) disclosed an unusually facile covalent hydration.[12] The crystals obtained from water correspond to a monohydrate. An nmr spectrum in DMSO suggested an equilibrium mixture of 3 (R = H) and 8 (R = H).[11b] The only signals expected for 3 (R = H) were a pair of doublets with coupling constants of ~2–3 Hz, a singlet for the aromatic proton, and a deuterium-exchangeable and relatively broad signal for the NOH proton. There are also broad aliphatic resonance at τ 4.41 and deuterium-exchangeable protons with signals at τ −0.18, 1.52, and 3.42, features not to be expected for the species 3 (R = H). The broad signal at τ 4.41, which became a sharp singlet upon the addition of D_2O, indicated that the protons influencing the broadening of the peak were exchanged. It was, therefore, concluded that the formation of 8 (R = H) was the cause of the additional signals. As in other cases of covalent hydration the addition reaction was acid catalyzed. The complete covalent hydration of 3 (R = H) to 8 (R = H) occurred when DCl was added to it in DMSO, as shown by the disappearance of all signals attributed to the anhydrous species.[11b]

Boiling of 3 (R = H) in methanol or ethanol yielded corresponding addition products 8 (R = Me or Et), which were isolated in crystalline form. The nmr spectrum of 8 (R = Me)[11b] indicated the presence of a single pure species. Doublets at τ 4.65 (J = 6 Hz) and 1.11 (J = 6 Hz) are assigned to the 4-H and 3-H. The nmr spectrum of the ethoxy isomer[11b] was similar to that for 3 (R = Me) except that the two doublets of H-6 and H-7 in the region τ 1.50–1.73 were converted to a multiplet when D_2O was added. This suggested that the ethanol adduct equilibrated with D_2O rapidly to form a new additional species of D_2O adduct. Under such conditions, the methanol adduct was stable, since the addition of D_2O, DCl, or NaOD caused only exchange of the labile protons, and did not dissociate the adduct.

The ultraviolet spectra of 1-hydroxy-2-oxo-1,2-dihydropteridine (8, R = H) in both neutral and basic aqueous solution are almost identical with those of the methanol adduct in neutral or in basic methanol, respectively. Since the methanol adduct is stable in methanol, the close similarity of its ultraviolet spectra in methanol to that of 1-hydroxy-2-oxo-1,2-dihydro-

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pteridine in water indicates that the latter exists in the covalently hydrated form in aqueous solution.

2-Hydroxypteridine is known[13] to form a covalent hydration adduct stable only in acid and neutral media. The present data show that the covalent hydration adduct of the *N*-hydroxy derivative could also be observed in a nonaqueous medium, and furnishes another example of the influence of the *N*-hydroxy group in increasing[14] the susceptibility of the molecule to attack by nucleophiles.

The 1-hydroxy-2,4-dioxo-1,2,3,4-tetrahydropteridine (**2**, R = H) formed stable *N*-acetoxy, mesyloxy, or tosyloxy derivatives (**2**, R = Ac, Ms, or Ts). From **3** similar derivatives were obtained, but nmr evidence indicated that they were in the covalently hydrated forms corresponding to **8**. Rapid hydrolysis of those intermediates prevented their isolation in a pure state.

Even under mild conditions, such as in aqueous solution at pH's near 7 and at room temperature, 3-acetoxyxanthine (**1**, R = Ac) and related compounds undergo a "3-acyloxypurine 8-substitution" reaction[15-18] which involves replacement of the 3-acetoxy group by hydrogen and substitution at C-8 by nucleophiles such as water, chloride ion, or methionine. Unlike the purine *N*-oxide derivatives, the analogous acetoxy-, mesyloxy-, or tosyloxypteridines (**2** or **3**, R = Ac, Ms, or Ts) are quite stable even under more vigorous conditions. The failure of esters of **2** and **3** (R = Ac, Ms, or Ts) to undergo rearrangement can be attributed to the relatively π-deficient character of the pyrazine moiety, as compared to the π-excessive state of the imidazole. The ring system of **2** or **3** must be inefficient in transmitting a π electron from the pyrazine ring *via* delocalization to the N–O position to facilitate the cleavage of that bond in a manner similar to that which can occur with 3-acetoxyxanthine (**1**, R = Ac).[17,18]

The possible relationship of the 3-acyloxypurine 8-substitution reaction to the oncogenicity[2] of **1**, R = H, has been considered.[18,19] From the absence of a counterpart to that reaction in the analogous pteridines, it would not now be suggested that they would be oncogenic.

Experimental Section

Uv absorption spectra were determined with a Unicam SP800 recording spectrophotometer. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn. The nmr spectra were determined with a Varian A-60 spectrometer in DMSO-d_6 with the use of tetramethylsilane as an internal reference. The melting points are uncorrected. Paper chromatography, ascending, on Whatman No. 1 paper was used to check the purity of each of the compounds prepared. The pK_a's were determined in 0.01 *M* buffers[20] by methods described.[21] For Dowex-50 chromatography BioRad AG-50, 8X, 200–400 mesh [H$^+$] resin was used, in a column 4.5 × 26 cm, unless otherwise specified.

1-Benzyloxy-1,2,3,4-tetrahydro-2,4-dioxopteridine.—1-Benzyloxy-5,6-diaminouracil, prepared[8,22] by reduction of 1-benzyloxy-5-nitrosouracil (5.60 g) with sodium dithionite, was added to a boiling solution of glyoxal (1.20 g) in water (100 ml) in small portions. After 1 hr the hot suspension was filtered and the insoluble material was washed twice with 100 ml of boiling water. The combined filtrates yielded the benzyloxypteridine (720 mg) on cooling. Concentration of the mother liquors yielded an additional 250 mg. The yield based on nitrosouracil was 970 mg (18%), mp 212° (from 50% EtOH).

Anal. Calcd for $C_{13}H_{10}N_4O_3$: C, 57.78; H, 3.73; N, 20.73. Found: C, 57.67; H, 3.75; N, 20.56. Uv max at (pH 5.0) (neutral species) nm ($\epsilon \times 10^{-3}$), 232 (12.9), 245 (10.0) inflection, 282 (3.39), 329 (6.61). Chromatography of the filtrate from benzyloxypteridine solution over a column of Dowex-50 eluting with water yielded 2,4-dihydroxypteridine[23] (800 mg, 25%), uv max at pH 5.9 (neutral species), nm ($\epsilon \times 10^{-3}$), 230 (10.0), 324 (6.92); at pH 10.1 monoanion, 235 (10.5), 270 (8.91), 347 (4.90).

1-Hydroxy-2,4-dioxo-1,2,3,4-tetrahydropteridine.—5,6-Diamino-1-hydroxyuracil[8] from the reduction of 6-amino-1-hydroxy-5-nitrosouracil (1.92 g) with sodium dithionite was added to a glyoxal solution (650 mg in 25 ml of water) which was preheated for 5 min to permit the glyoxal to dissolve. After gentle refluxing for 1.5 hr the insoluble solid (500 mg) was separated and washed twice with 10 ml of boiling water. The filtrates were passed over a Dowex-50 [H$^+$] column which was eluted with water that was concentrated to yield 1-hydroxypteridine (1.0 g, overall yield 50%). Recrystallization from water (30 ml) gave needles, mp 321° dec.

Anal. Calcd for $C_6H_4N_4O_3$: C, 40.00; H, 2.24; N, 31.10. Found: C, 40.01; H, 2.25; N, 31.00. Uv max at pH 3.0 (neutral species), nm ($\epsilon \times 10^{-3}$), 232 (11.5), 252 (7.50) inflection, 332 (6.72); at pH 7.9 monoanion, 234 (9.79), 261 (10.2), 302 (6.96); at pH 12.0 dianion, 238 (8.53), 271 (19.8), 307 (3.46) inflection; $pK_{a_1} = 6.50 \pm 0.05$, $pK_{a_2} = 9.35 \pm 0.05$.

1-Acetoxy-2,4-dioxo-1,2,3,4-tetrahydropteridine.—The 1-hydroxypteridine (200 mg) was boiled with a mixture of acetic anhydride (2 ml) and acetic acid (1.5 ml) for 2 hr and cooled. This yielded the acetoxypteridine (220 mg, 89%) as fine crystals, mp 255°.

Anal. Calcd for $C_8H_6N_4O_4$: C, 43.25; H, 2.72; N, 25.22. Found: C, 43.22; H, 2.72; N, 24.98. Uv max at pH 5.0 (neutral species), nm ($\epsilon \times 10^{-3}$), 229 (11.2), 323 (7.94).

1-Mesyloxy-2,4-dioxo-1,2,3,4-tetrahydropteridine.—1-Hydroxy-2,4-dioxo-1,2-dihydropteridine (85 mg) with mesyl chloride (0.1 ml) in pyridine (1.0 ml) was stirred at room temperature for 2 hr. This was absorbed on a Dowex-50 [H$^+$] column, and eluted with water to give 1-hydroxy-2,4-dioxopteridine (13 mg) followed by the 1-mesyloxypteridine (85 mg, 70%), mp 130°. The mesyloxypteridine is stable in water at room temperature but does hydrolyze to the hydroxypteridine upon heating.

Anal. Calcd for $C_7H_6N_4O_5S$: C, 32.57; H, 2.34; N, 21.70. Found: C, 32.68; H, 2.36; N, 21.85. Uv max at pH 5.0 (neutral species), nm ($\epsilon \times 10^{-3}$), 229 (11.2), 315 (6.76).

2,4-Dioxo-1-tosyloxy-1,2,3,4-tetrahydropteridine.—The 1-hydroxypteridine (180 mg) and 1 *N* NaOH (1.5 ml) were added to a suspension of tosyl chloride (290 mg) in a mixture of water (2 ml) and ethanol (3 ml), and stirred at 90° for 15 min and at room temperature overnight. A white precipitate (320 mg, 96%) was washed with water, ethanol, and ether, mp 224° dec.

Anal. Calcd for $C_{13}H_{10}N_4O_5S$: C, 46.72; H, 3.02; N, 16.76. Found: C, 46.78; H, 3.09; N, 16.60. Uv max at pH 5.0 (neutral species), nm ($\epsilon \times 10^{-3}$), 234 (21.9), 315 (6.17).

5-Nitrocytosine 3-Oxide.—Finely ground potassium nitrate (2.22 g, 0.022 mol) was slowly added with stirring to a solution of cytosine 3-oxide[6] (2.90 g, 0.02 mol) in 10 ml of concentrated H_2SO_4. The solution was warmed to 30° for 30 min, then added to 200 g of crushed ice, and carefully neutralized with 50% NaOH to pH 6 at a temperature below 10°. A yellow precipitate was collected, washed repeatedly with water, and dried (2.95 g, 86%), mp 220°. The bright yellow nitrocytosine 3-oxide gave a dark orange-brown color with ferric chloride.

Anal. Calcd for $C_4H_4N_4O_4$: C, 27.92; H, 2.34; N, 32.55. Found: C, 27.78; H, 2.28; N, 32.35. Uv max at pH 2.0 (neutral species), nm ($\epsilon \times 10^{-3}$), 245 (5.77) inflection, 270 (6.63),

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330 (9.73); at pH 10 monoanion, 240 (7.86) inflection, 276 (8.98), 347 (12.7).

Reduction of 5-Nitrocytosine 3-Oxide to 5-Aminocytosine 3-Oxide. A. By Sodium Dithionite.—Sodium dithionite (12.2 g, 70 mmol) was added, in small portions at 25°, to a solution of 5-nitrocytosine 3-oxide (3.44 g, 20 mmol), stirred at the same temperature for 0.5 hr, and the mixture was absorbed on a Dowex-50 [H^+] column and eluted with water (800 ml). Further inorganic material and a small amount of starting material was removed with 1 *N* hydrochloric acid (300 ml). With 2 *N* hydrochloric acid (400 ml) 5-aminocytosine 3-oxide hydrochloride (1.01 g, 28%) was obtained; further elution with 2 *N* hydrochloric acid (1200 ml) gave a small amount of unknown byproducts.

B. By Catalytic Hydrogenation in 1 *N* Hydrochloric Acid.—A suspension of 5-nitrocytosine 3-oxide (1.72 g, 10 mmol) with 10% palladium on charcoal in 1 *N* hydrochloric acid (250 ml) was hydrogenated at 1 atm for 2 days, at which time 3 equiv of hydrogen had been absorbed. The filtrate was evaporated to dryness *in vacuo*, and the residue was dissolved in 5 ml of water and chromatographed over a Dowex-50 [H^+] column. By elution with water, and stepwise with 1 *N* to 4 *N* hydrochloric acid, two major products were isolated and six minor products were detected. The major product eluted by water was the 5-hydroxyuracil 3-oxide derivative: uv max (pH 4) 275 (pH 11) 299, 232 nm; (500 mg) nmr τ 3.05, 3.45 (NH), broad absorption between 0.67 and 0.0 (NH + 3 H).

Anal. Calcd for $C_4H_4N_2O_4$: C, 33.34; H, 2.80; N, 19.44. Found: C, 33.37; H, 2.78; N, 19.45.

Its identity was confirmed by reduction to the known 5-hydroxyuracil. The desired 5-aminocytosine 3-oxide (340 mg, 18.0%) was eluted with 2 *N* hydrochloric acid.

C. By Catalytic Hydrogenation in Water.—5-Nitrocytosine 3-oxide (3.44 g, 20 mmol) in water (500 ml) with 10% palladium on charcoal (800 mg) was hydrogenated for 2 days. To minimize air oxidation 20 ml of 1 *N* hydrochloric acid was added immediately after the hydrogenation. The catalyst was separated, the filtrate was absorbed on Dowex-50 [H^+], and elution with 1 *N* hydrochloric acid yielded 5-aminocytosine 3-oxide (3.4 g, 95%). This darkened on standing and was stored cold and used as soon as possible without further purification.

Reduction of 5-Hydroxyuracil 3-Oxide.—To 5-hydroxyuracil 3-oxide (30 mg) in 1 *N* hydrochloric acid (10 ml), powdered zinc (100 mg) was added with stirring. After 3 days at 25° 5-hydroxyuracil (10 mg) was obtained as a white precipitate. Its identity was confirmed by comparison of the uv spectrum with that of an authentic sample.[7]

1-Hydroxy-2-oxo-1,2-dihydropteridine.—Glyoxal (400 mg) was depolymerized by heating under reflux in water (50 ml) until the solid was dissolved. The clear solution was allowed to cool to 50°, 5-aminocytosine 3-oxide hydrochloride (1.02 g) was added, and the solution was stirred at 50–60° for 2.5 hr. A white precipitate formed, and at room temperature the *N*-hydroxypteridine **3** (719 mg, 70%) was collected as light gray needles from water, mp 267° dec.

Anal. Calcd for $C_6H_4N_4O_2 \cdot H_2O$: C, 39.56; H, 3.32; N, 30.76. Found: C, 39.59; H, 3.29; N, 30.79. Uv max at pH 5.0 (neutral species), nm ($\epsilon \times 10^{-3}$), 227 (6.76) inflection, 241 (7.59), 289 (4.27) inflection, 311 (7.41); pH 12 (anion) 258 (15.1), 275 (17.4), 415 (3.31). Nmr (DMSO) τ 4.41 (broad, 4-H of **8**, R = H), 3.42 (broad, 4-OH of **8**, R = H), 1.78, 1.62 (doublet pair, J = 3 Hz, 6-H + 7-H of **8**, R = H), 1.52 (broad, 3-H of **8**, R = H), 1.29, 1.07 (doublet pair, J = 3 Hz, 6-H + 7-H of **3**, R = H), 0.57 (singlet, 4-H of **3**, R = H), −0.18 (broad, 1-H of **8**, R = H), −0.41 (broad, 1-H, **3**, R = H). Nmr (DCl added) 4.41 (singlet, 4-H of **8**, R = H), 1.78, 1.62 (doublet pair, J = 3 Hz, 6-H + 7-H of 8, R = H).

The Reaction of Methanol (or Ethanol) with 1-Hydroxy-2-oxo-1,2-dihydropteridine.—1-Hydroxy-2-oxo-1,2-dihydropteridine (100 mg) was boiled with methanol (10 ml) until the solid dissolved (1 hr), and the solution was evaporated. The nmr of the residue indicated the addition of methanol at the 3,4 bond. The 1-hydroxy-4-methoxy-2-oxo-1,2,3,4-tetrahydropteridine crystallized from methanol as needles, mp 176° dec.

Anal. Calcd for $C_7H_8N_4O_3$: C, 42.86; H, 4.11; N, 28.56. Found: C, 42.70; H, 4.20; N, 28.63. Uv max in methanol, nm ($\epsilon \times 10^{-3}$), 228 (6.76) inflection, 242 (7.99), 290 (5.53) inflection, 312 (6.64); in 0.01 *N* methanolic NaOH, 260 (11.3), 278 (12.5), 415 (2.09). Nmr (DMSO) τ 6.70 (singlet, CH_3), 4.65 (doublet, J = 6 Hz, 4-H), 1.75, 1.58 (doublet pair, J = 3 Hz, 6-H + 7-H), 1.11 (broad doublet, J = 6 Hz, 3-H), −0.22 (singlet, 1-H). Nmr (D_2O, NaOD, or DCl added) 6.70 (singlet, CH_3) 4.65 (singlet, 4-H), 1.75, 1.58 (doublet pair, J = 6 Hz, 6-H + 7-H).

Similar treatment of the 1-hydroxy-2-oxo-1,2-dihydropteridine with ethanol gave 1-hydroxy-4-ethoxy-2-oxo-1,2,3,4-tetrahydropteridine, mp 176° dec (from hexane).

Anal. Calcd for $C_8H_{10}N_4O_3$: C, 45.71; H, 4.80; N, 26.66. Found: C, 45.80; H, 4.91; N, 26.58. Nmr (DMSO) τ 8.86 (triplet, J = 7 Hz, CH_3), 6.42 (quartet, J = 7 Hz, CH_2), 4.44 (doublet, J = 4 Hz, 4-H), 1.71, 1.53 (doublet pair, J = 3 Hz, 6-H + 7-H), 1.10 (doublet, J = 4 Hz, 3-H), −0.33 (broad, 1-H). Nmr (D_2O added) 8.86 (triplet, J = 7 Hz, CH_3), 6.42 (quartet, J = 7 Hz, CH_2), 4.41 (singlet, 4-H), 4.31 (singlet, 4-H of **8**, R = D), 1.50–1.73 (multiplet, 6-H + 7-H of **8**, R = Et and R = D).

Registry No.—**2** (R = benzyl), 37440-26-9; **2** (R = H), 37440-27-0; **2** (R = Ac), 37440-28-1; **2** (R = mesyl), 37440-29-2; **2** (R = tosyl), 37440-30-5; **3**, 37440-31-6; **4** (R = NO_2), 37440-39-4; **4** (R = NH_2), 37440-40-7; **4** (R = NH_2, HCl), 37440-41-8; **5** (R = OH), 37440-32-7; **8** (R = Me), 37440-33-8; **8** (R = Et), 37440-34-9; 1-benzyloxy-5,6-diaminouracil, 37440-35-0; glyoxal, 107-22-2; 2,4-dihydroxypteridine, 525-77-9; 5,6-diamino-1-hydroxyuracil, 37440-37-2; cytosine 3-oxide, 37440-38-3.

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