dark red solution was stirred for 15 min. Then a solution of 8.0 g (0.04 mol) of diketone I in 30 ml of dimethyl sulfoxide was injected and the reaction mixture was stirred for 16 hr at room temperture and for 2 hr at 50–60°. The reaction mixture was poured on 200 g of crushed ice and the water–dimethyl sulfoxide mixture was extracted with pentane. The pentane solution was washed with aqueous dimethyl sulfoxide (1:1) and with a saturated salt solution and dried ($MgSO_4$). The dried pentane solution was chromatographed on neutral alumina to remove all of the triphenylphosphine oxide and the pentane was evaporated. The solid residue was recrystallized from petroleum ether (bp 40–60°). The yield of methoxymethylene ketone II, mp 109–110°, was 60–77%: ir ($CCl_4$) 1690, 1640, and 1100 $cm^{-1}$; uv max (95% ethanol) 242 mμ (ε 720), 308 (87); nmr ($CCl_4$), τ 8.87 and 8.84 s (ring methyl protons), 7.60 and 7.48 s (ring methylene protons), 6.47 s (ether methyl protons), 4.21 s (vinyl proton).

*Anal.* Calcd for $C_{12}H_{20}O_2S$ (228.35): C, 63.11; H, 8.82; S, 14.04. Found: C, 62.7, 63.0; H, 8.8, 8.8; S, 13.9, 14.0.

**5-Formyl-3,3,6,6,6-tetramethyl-1-thiacycloheptan-4-one (III).**—A solution of 4.0 g (0.017 mol) of methoxymethylene ketone II and 10 ml of perchloric acid in 50 ml of ether was refluxed for 30 min. The reaction mixture was poured into water and the ether layer was separated and washed with water and with sodium bicarbonate solution. The ethereal extract was dried ($Na_2SO_4$) and concentrated. The residue was recrystallized from petroleum ether (bp 40–60°). The yield of keto aldehyde III was 3.4 g (93%): mp 97–99°; ir ($CCl_4$) 1705 and 1735 $cm^{-1}$; uv (see discussion); nmr ($CCl_4$), τ 8.96, 8.84, and 8.78 s (methyl protons), 7.40 7.82, 7.58, 7.40, and 7.17 q (methylene protons), 6.58 and 6 .50d (proton at $C_4$), 0.30 and 0.22 d (aldehyde proton).

*Anal.* Calcd for $C_{11}H_{18}O_2S$ (214.32): C, 61.64; H, 8.47; S, 14.96. Found: C, 61.6, 61.5; H, 8.5, 8.3; S, 15.0, 15.0.

**4,4,8,8-Tetramethyl-4,5,7,8-tetrahydro-6-thiacyclohepta[*c*]pyrazole (IV).**—A solution of 1.0 g (0.0047 mol) of keto aldehyde III, 3 ml of hydrazine hydrate, and 1 drop of hydrochloric acid in 15 ml of acetic acid was refluxed for 1 hr. The reaction mixture was poured on ice and the precipitated compound was separated and washed with water. After recrystallization from aqueous methanol (1:1), 0.86 g (90%) of pyrazole IV was obtained: mp 186–188°; ir (KBr) 3200, 1570, and 1505 $cm^{-1}$; nmr ($CCl_4$), τ 8.63 s (methyl protons), 7.54 s (methylene protons), 2.80 s (C–H aromatic proton), 2.42 s (N–H proton).

*Anal.* Calcd for $C_{11}H_{18}N_2S$ (210.32): C, 62.81; H, 8.63; N, 13.32; S, 15.24. Found: C, 62.5, 62.6; H, 8.6, 8.7; N, 13.4, 13.4; S, 14.8, 14.8.

**4,4,8,8-Tetramethyl-4,5,7,8-tetrahydro-6-thiacyclohepta[*d*]isoxazole (V).**—A solution of 1.5 g (0.007 mol) of keto aldehyde III and 1.5 g (0.022 mol) of hydroxylamine hydrochloride in 25 ml of acetic acid was refluxed for 1 hr. The reaction mixture was poured on ice and the precipitated compound was separated and washed with water. Recrystallization from aqueous methanol (1:1) yielded 1.1 g (75%) of isoxazole V: mp 111–112°; ir (KBr) 1590 $cm^{-1}$; nmr ($CCl_4$), τ 8.65 and 8.55 s (methyl protons), 7.37 and 7.35 s (methylene protons), 2.12 s (aromatic proton).

*Anal.* Calcd for $C_{11}H_{17}NOS$: C, 62.51; H, 8.11; N, 6.63; S, 15.18. Found: C, 62.7, 62.6; H, 8.3, 8.2; N, 6.7, 6.5; S, 14.7, 15.0.

**2-Amino-5,5,9,9-tetramethyl-5,6,8,9-tetrahydro-7-thiacyclohepta[*e*]pyrimidine (VI).**—A mixture of 2.0 g (0.009 mol) of keto aldehyde III, 2.0 g (0.017 mol) of guanidine carbonate, and 25 ml of absolute ethanol was heated in a sealed tube at 160–170° for 8 hr. The tube was opened and the contents were washed with water and ether. The water layer was separated and extracted with ether. The combined ether layers were extracted with dilute hydrochloric acid. The ethereal extract was dried ($CaCl_2$) and concentrated. The organic residue proved to be 3,3,6,6-tetramethyl-1-thiacycloheptan-4-one (VII). The yield of VII was 900 mg (52%). The hydrochloric acid extracts were neutralized with sodium hydroxide solution and extracted with ether. The ether solution was washed with water, dried ($CaCl_2$), and concentrated. The residue was recrystallized from petroleum ether (bp 60–80°). The yield of pyrimidine VI was 900 mg (42%): mp 109–110.5°; ir (KBr) 3400, 3230, 1645, 1580, and 1530 $cm^{-1}$; nmr ($CDCl_3$), τ 8.54 s (methyl protons), broad 7.25 s (methylene protons), broad 4.73 s ($NH_2$ protons), 1.72 s (aromatic proton).

*Anal.* Calcd for $C_{12}H_{19}N_3S$ (237.35): C, 60.72; H, 8.04; N, 17.70. Found: C, 61.0, 60.9; H, 8.2, 8.1; N, 17.8, 17.8.

**3,4-Di-*t*-butylpyrazole (VIII).**—A suspension of 20 g of Raney nickel W7 and 1.6 g (0.008 mol) of pyrazole IV in 150 ml of dioxane was stirred and refluxed for 5 hr. The reaction mixture was cooled to room temperature and filtered. The Raney nickel was refluxed twice with 200 ml of dioxane to remove the absorbed pyrazole. The dioxane was evaporated and 800 mg of residue was obtained. Recrystallization from aqueous methanol (1:1) yielded 500 mg (45%) of white crystalline 3,4-di-*t*-butylpyrazole: mp 129–130°; ir (KBr) 3200 and 1550 $cm^{-1}$; nmr ($CCl_4$), τ 8.63 and 8.58 s (*t*-butyl protons), 2.75 s (C–H aromatic proton), 2.03 s (N–H proton).

*Anal.* Calcd for $C_{11}H_{20}N_2$ (180.28): C, 73.28; H, 11.18; N, 15.54. Found: C, 73.4, 73.3; H, 11.1, 11.1; N, 15.6, 15.7.

**5-Cyano-3,3,6,6-tetramethyl-1-thiacycloheptan-4-one (IX).**—A suspension of 10 g of Raney nickel W7 and 1.1 g (0.005 mol) of isoxazole V in 200 ml of acetone was stirred and refluxed for 5 hr. After cooling to room temperature the mixture was filtered and the Raney nickel was refluxed twice with 200 ml of acetone to remove all of the absorbed materials. The combined acetone solutions were concentrated and the residue was dissoved in petroleum ether (bp 40–60°). The warm petroleum ether solution was filtered and upon cooling 300 mg of cyanide IX crystallized: mp 114–116°; ir (KBr) 2280 and 1720 $cm^{-1}$; nmr ($CDCl_3$), τ 8.83 and 8.75 s (methyl protons), 7.38 s and 7.61, 7.38, 7.28, and 7.00 q (methylene protons), 6.15 s (proton at $C_5$).

*Anal.* Calcd for $C_{11}H_{17}NOS$ (211.32): C, 62.51; H, 8.11; N, 6.63; S, 15.18. Found: C, 62.6, 62.7; H, 8.3, 8.2; N, 6.6, 6.6; S, 15.3, 15.3.

Concentration of the petroleum ether solution gave 200 mg of a solid. It was shown by tlc that at least three products were present. The infrared spectrum of this mixture showed a strong absorption at 1690 $cm^{-1}$.

**Registry No.**—II, 16867-90-6; III, 16867-91-7; IV, 16867-92-8; V, 16867-93-9; VI, 16867-94-0; VIII, 16867-95-1; IX, 16867-96-2.

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## Pteridines. XIII.[1] Aromatization during the Attempted Synthesis of a 6,6-Disubstituted 5,6-Dihydropteridine

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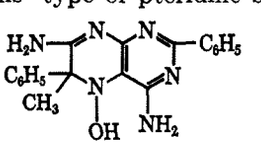
In the course of our work on the diuretic pteridines we wished to prepare 4,7-diamino-5-hydroxy-6-methyl-2,6-diphenyl-5,6-dihydropteridine (I) as an example of a pteridine in which a 5,6-dihydro form has been fixed by the presence of two stable substituents at position 6. In an approach to this, 2-phenylpropionitrile was condensed with 4,6-diamino-5-nitroso-2-phenylpyrimidine (III) in ethanol in the presence of alkali in a Timmis[2] type of pteridine synthesis. The



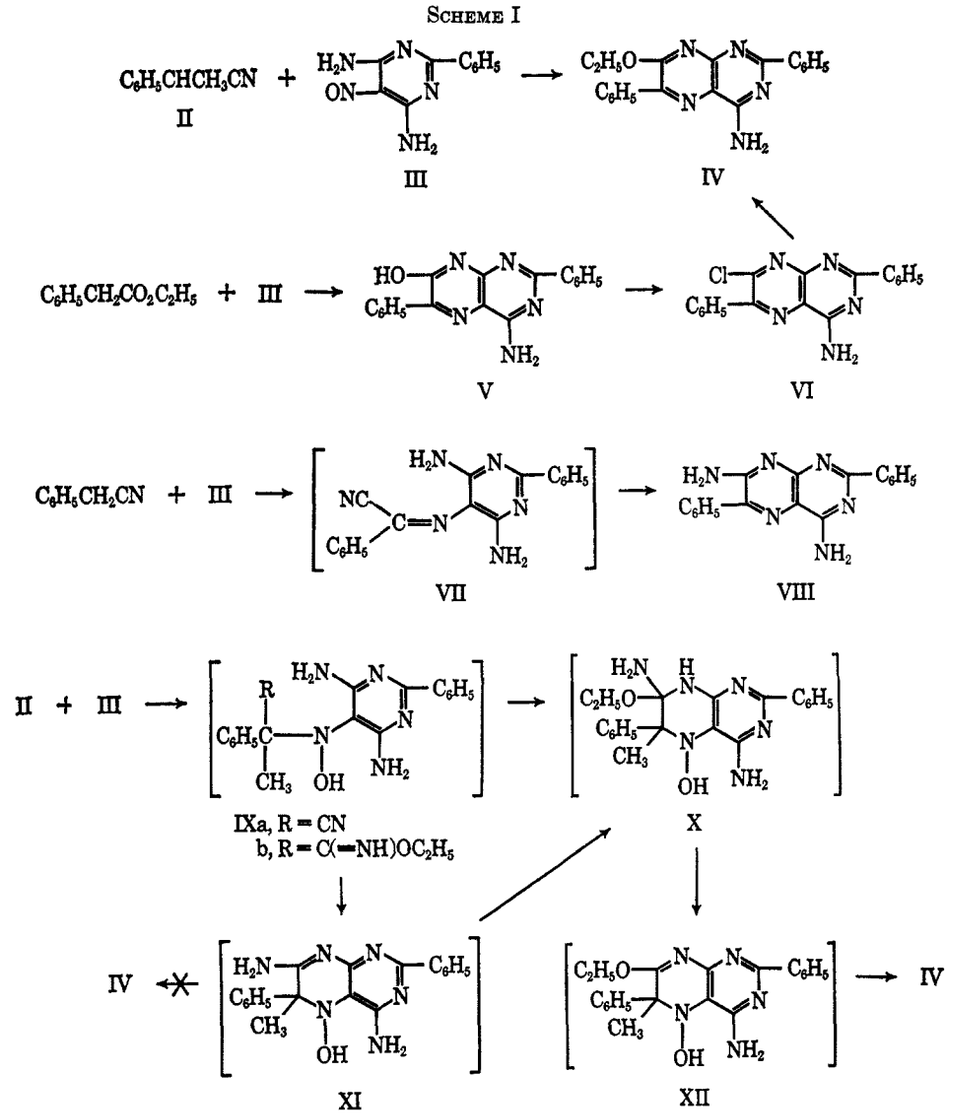
I

only product isolated (in 16% yield) was 4-amino-7-ethoxy-2,6-diphenylpteridine (IV). The structure of

(1) Previous paper in this series: J. Weinstock, J. W. Wilson, V. D. Wiebelhaus, A. R. Maass, F. T. Brennan, and G. Sosnowski, *J. Med. Chem.*, **11**, 573 (1968).

(2) G. M. Timmis, *Nature*, **164**, 139 (1949).

SCHEME I



IV was first indicated by elemental analysis and the presence of the typical ethoxy proton pattern in the nmr spectrum. The structure was established by an unequivocal synthesis as shown in Scheme I. Condensation of ethyl phenylacetate with III in a Timmis reaction gave 4-amino-7-hydroxy-2,6-diphenylpteridine (V), which on reaction with phosphorus pentachloride in phosphorus oxychloride gave VI. Reaction of this with sodium ethoxide in ethanol gave IV, whose infrared spectrum and melting point were in agreement with those of the sample isolated from the 2-phenylpropionitrile condensation.

A possible mechanism for the formation of IV from II and III is indicated in Scheme I. A postulated initial adduct IXa could not have lost the elements of methanol to form VII because this would have given VIII, the 7-amino analog of IV. The condensation of phenylacetonitrile with III under similar conditions gave an excellent yield of VIII. A ring-closed intermediate X could form from the imino ether IXb or by addition of ethanol to XI (or its 8-H tautomer). The 8-H tautomer of XI could be formed by the usual addition of the pyrimidine 4-$NH_2$ in IXa to the nitrile. The elements of methanol could not be lost from XI because this would also lead to VIII. However, XII, formed by loss of the elements of ammonia from X, could have given rise to the observed product IV by loss of the elements of methanol. We have no evidence to indicate the exact nature of these transformations, but this reaction illustrates the ease with which a 5,6-dihydropteridine will become aromatic, even if a carbon–carbon bond must be broken in the process. Similar driving forces play a role when hydropteridines are involved as cofactors in biological systems.[3]

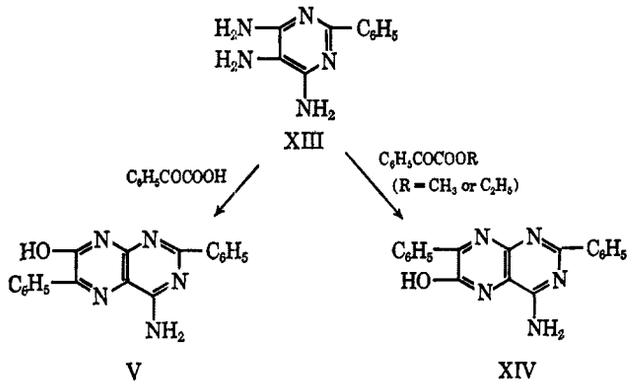
In our first attempt to prepare IV, methyl phenylglyoxylate was treated with 4,5,6-triamino-2-phenylpyrimidine (XIII) in ethanol. We had anticipated the formation of V because the reaction of tetraaminopyrimidine with ethyl phenylglyoxylate in 1 *N* acetic acid[4] and with phenylglyoxylic acid at pH 5[5] gave 2,4-diamino-7-hydroxy-6-phenylpteridine. However, the product obtained after purification was different from authentic V prepared *via* the Timmis reaction, and thus must be 4-amino-6-hydroxy-2,7-diphenylpteridine (XIV). This was converted into the corresponding 6-chloro- and 6-ethoxypteridines, each of which was different from the authentic 7 isomers described above.

(3) A. Ehrenberg, P. Hemmerick, F. Müller, T. Okada, and M. Viscontini, *Helv. Chim. Acta*, **50**, 411 (1967).

(4) A. G. Renfrew, P. C. Piatt, and L. H. Cretcher, *J. Org. Chem.*, **17**, 467 (1952).

(5) R. G. W. Spickett and G. M. Timmis, *J. Chem. Soc.*, 2887 (1954).

SCHEME II




The course of the condensation to form the 6-hydroxypteridine can be rationalized by assuming that in methyl phenylglyoxylate the ester carbonyl is more reactive than the ketone carbonyl, and that the former condenses with the 5-amino group of XIII which is the most reactive amino group.[6,7] The previously reported condensations can be rationalized by assuming that in aqueous media ester hydrolysis precedes amine condensation, and that in an $\alpha$-keto acid the ketone carbonyl is more reactive than the acid carbonyl. This rationalization is supported by the synthesis of V in excellent yield by the reaction of phenylglyoxylic acid with XIII in ethanol. Since many 7-hydroxypteridines have been prepared by the reaction of methyl pyruvate with 4,5-diaminopyrimidines in alcohols, the order of reactivity in $\alpha$-keto acids and esters appears to be $-COOH < -COC_6H_5 < -CO_2CH_3 < -COCH_3$.

### Experimental Section[8]

Infrared spectra were obtained on a Perkin-Elmer Infracord, ultraviolet spectra on a Cary Model 14 spectrometer, and nmr spectra on a Varian A-60 spectrometer. Paper chromatography was done by the circular system using a cotton wick to bring the solvent to the paper. The following systems were used: (1) EtOH–$H_2O$ (2:1) on mineral oil pretreated paper; (2) 5.6 *N* $NH_4OH$–BuOH (4:5); (3) EtOH–$H_2O$ (2:1) on mineral oil–castor oil (1:1) pretreated paper.

**4-Amino-2,6-diphenyl-7-ethoxypteridine (IV). A.**—To a solution of 4.6 g (0.20 mol) of sodium in 200 ml of absolute ethanol was added 6.66 g (0.02 mol) of 4-amino-7-chloro-2,6-diphenylpteridine and the mixture refluxed for 3 hr. Chilling gave a yellow-orange solid whose infrared spectrum was identical with that of the sample obtained in B. Recrystallization from ethanol gave 1.75 g (25%) of yellow crystals, mp 239–241°.

**B.**—A solution of 2.15 g (0.010 mol) of 4,6-diamino-5-nitroso-2-phenylpyrimidine, 2.00 g (0.015 mol) of 2-phenylpropionitrile,[9] and 1.35 g (0.012 mol) of potassium *t*-butoxide in 300 ml of absolute ethanol was refluxed for 20 hr. Addition of 250 ml of water and chilling gave 0.54 g (16%) of a light tan solid. Recrystallization of this from 125 ml of ethanol gave 0.40 g of pink crystals: mp 241.5–242° (a second recrystallization from the same solvent did not change the melting point); $R_f$ 0.65 (system 1); $\lambda_{max}^{4.5\%\ HCOOH}$ 273, 359 m$\mu$ (log $\epsilon$ 4.45, 4.40).

*Anal.* Calcd for $C_{20}H_{17}N_5O$: C, 69.95; H, 4.99; N, 20.40. Found: C, 70.00; H, 5.00; N, 20.22.

**4-Amino-7-hydroxy-2,6-diphenylpteridine (V). A.**—A solution of 21.5 g (0.10 mol) of 4,6-diamino-2-phenyl-5-nitrosopyrimidine in 500 ml of absolute ethanol was treated with 20 g (0.122 mol) of ethyl phenylacetate and 6.6 g (0.122 mol) of sodium methoxide. After refluxing for 80 min, acetic acid was added to bring the pH to 6. The solid formed was collected by filtration, washed with hot ethanol, and dried to give 22.8 g (72%) of yellow crystals. Recrystallization from dimethylformamide–water gave 16.6 g (53%) of yellow crystals: mp >300°; $R_f$ 0.53 (system 2), blue fluorescence under ultraviolet light; $\lambda_{max}^{0.1\ N\ HCl\text{-}C_2H_5OH}$ 227.5, 256, 378.5 m$\mu$ (log $\epsilon$ 4.38, 4.29, 4.41); $\lambda_{max}^{C_2H_5OH,\ pH\ 11.5}$ 250, 377.5 m$\mu$ (log $\epsilon$ 4.75, 4.69).

**B.**—A solution of 1.0 g (0.005 mol) of 4,5,6-triamino-2-phenylpyrimidine and 1.0 g (0.0067 mol) of phenylglyoxylic acid in 35 ml of absolute ethanol was refluxed for 1.5 hr. Filtration of the chilled reaction mixture gave 1.45 g (92%) of a yellow solid whose infrared spectrum and paper chromatographic behavior were identical with those of the sample obtained above.

**4-Amino-6-hydroxy-2,7-diphenylpteridine (XIV).**—A mixture of 10.0 g (0.05 mol) of 4,5,6-triamino-2-phenylpyrimidine and 9.85 g (0.06 mol) of methyl phenylglyoxylate in 350 ml of absolute ethanol was refluxed for 16 hr. Cooling and filtration gave a yellow solid. Recrystallization from dimethylformamide–water gave 11.2 g (71%) of yellow crystals: mp > 300°; $R_f$ (system 2), 0.85, major, yellow fluorescence under uv light; 0.95, minor, blue fluorescence under uv light. This was dissolved in dilute ammonium hydroxide and an insoluble portion removed by filtration. Adjustment of the pH to 8 with acetic acid gave a product which was recrystallized once from dimethylformamide–water to give yellow crystals: mp >310°; $R_f$ 0.66 (system 3), $R_f$ 0.85 (system 2), yellow-green fluorescence under ultraviolet light; $\lambda_{max}^{4.5\%\ HCOOH}$ 284, 382 m$\mu$ (log $\epsilon$ 4.37, 4.29); $\lambda_{max}^{1N\ NaOH}$ 281, 401 m$\mu$ (log $\epsilon$ 4.36, 4.15).

*Anal.* Calcd for $C_{18}H_{13}N_5O$: C, 68.56; H, 4.16; N, 22.21. Found: C, 68.56; H, 4.41; N, 22.34.

The reaction of XIII with ethyl phenylglyoxylate was carried out as described above. Cooling the reaction mixture to room temperature and filtering gave an 85% yield of yellow crystals of XIV in which ir and chromatography (system 2) showed the presence of a small quantity of V. Interruption of the reaction after 7 hr of reflux gave only a 51% yield of product. Thus this reaction is much slower than that of the corresponding acid.

**4-Amino-7-chloro-2,6-diphenylpteridine (VI).**—A mixture of 16.65 g (0.053 mol) of 4-amino-7-hydroxy-2,6-diphenylpteridine, 83.4 g (0.40 mol) of phosphorus pentachloride, and 600 ml of phosphorus oxychloride was heated for 2 hr on a steam bath. The excess phosphorus oxychloride was evaporated under vacuum and the residue poured onto ice. A yellow solid formed which was collected and washed with ether. Recrystallization from dimethylformamide–water gave 13.25 g (75%) of a yellow solid: mp 274–276°; $R_f$ 0.35 (system 3).

*Anal.* Calcd for $C_{18}H_{12}N_5Cl$: C, 64.77; H, 3.62; N, 20.98. Found: C, 65.74; H, 3.99; N, 21.22.

**4-Amino-6-chloro-2,7-diphenylpteridine.**—A mixture of 10.0 g (0.0317 mol) of 4-amino-6-hydroxy-2,7-diphenylpteridine, 50 g (0.24 mol) of phosphorus pentachloride, and 500 ml of phosphorus oxychloride was refluxed for 2 hr. The phosphorus oxychloride was removed under vacuum and the residue treated with an ice–water mixture. The aqueous suspension was warmed briefly on a steam bath and then chilled and filtered. Neutralization of the filtrate gave an additional quantity of product. Recrystallization from a dimethylformamide–water mixture gave 7.0 g (66%) of a yellow solid: mp 257–258°; $R_f$ 0.49 (system 3); $\lambda_{max}^{4.5\%\ HCOOH}$ 281, 367 m$\mu$ (log $\epsilon$ 4.30, 4.32).

*Anal.* Calcd for $C_{18}H_{12}ClN_5$: C, 64.77; H, 3.62; N, 20.98. Found: C, 64.95; H, 3.52; N, 21.06.

**4-Amino-2,7-diphenyl-6-ethoxypteridine.**—A suspension of 1.0 g (0.003 mol) of 4-amino-6-chloro-2,7-diphenylpteridine in a solution of 0.69 g (0.03 mol) of sodium in 30 ml of absolute ethanol was refluxed for 3 hr. Addition of water gave a yellow-orange solid, mp 241–244°. Three recrystallizations from methanol gave a bright yellow solid, mp 248–249.5°.

*Anal.* Calcd for $C_{20}H_{17}N_5O$: C, 69.95; H, 4.99; N, 20.40. Found: C, 69.92; H, 4.81; N, 20.64.

(6) With methylglyoxal, XIII forms 2-phenyl-4-amino-7-methylpteridine: J. Weinstock, R. Y. Dunoff, J. E. Carevic, J. G. Williams, and A. J. Villani, *J. Med. Chem.*, **11**, 618 (1968).

(7) A referee suggested that the formation of XIV might be favored by the use of the methyl ester which would be expected to react at the ester carbonyl more rapidly than the corresponding ethyl ester. To check this point, ethyl phenylglyoxylate was treated with XIII in absolute ethanol. This also gave XIV as the predominant product. However, the ir spectrum and chromatography of the crude reaction product did show the presence of a small amount of V. It is noteworthy that XIII undergoes reaction more slowly with these esters than with phenylglyoxylic acid.

(8) We wish to thank Mr. Richard J. Warren for spectral data, Miss Margaret Carroll and her staff for microanalytical data, and Mr. Alex Post for chromatographic data.

(9) M. S. Newman and R. D. Closson, *J. Amer. Chem. Soc.*, **66**, 1553 (1944).

**Registry No.**—IV, 16878-41-4; V, 16878-42-5; VI, 16878-43-6; XIV, 16878-44-7; 4-amino-6-chloro-2,7-diphenylpteridine, 16878-45-8; 4-amino-2,7-diphenyl-6-ethoxypteridine, 16878-46-9.

## Synthesis of a 10,10a-Dihydro-1H-imidazo-[3,4-*b*][1,2]benzothiazine 5,5-Dioxide

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Chlorosulfonation of an aromatic, followed by treatment of the resulting sulfonyl chloride with ammonia, is a generally useful method for the preparation of aryl sulfonamides.[1] We applied this sequence to 5-(4-chlorophenyl)-5-methylhydantoin (**1**) and its 3-chloro isomer (**4**), with different results in each instance. As anticipated from steric considerations, **1** gave 5-(4-chloro-3-sulfamylbenzyl)-5-methylhydantoin (**2**)[2] in 83% yield, and this was hydrolyzed with barium hydroxide to give 4-chloro-$\alpha$-methyl-3-sulfamylphenylalanine. However, when **4** was treated with chlorosulfonic acid followed by ammonia, it gave a product in 72% yield; the composition differed from that of **4** by two less hydrogens and an additional $SO_2$. Barium hydroxide hydrolysis gave a product which displayed a peak at 5.92 $\mu$ in its infrared spectrum, characteristic of a carboxylic acid, and which lacked peaks at 6.3 and 6.55 $\mu$, characteristic of amino acids.

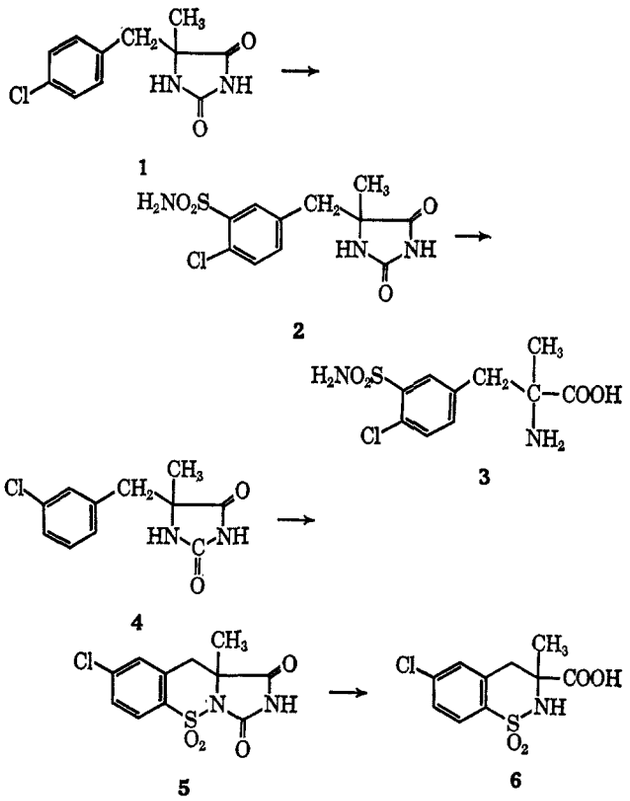
These data are best explained by assuming that the chlorosulfonation of **4** proceeded *para* to the chlorine, and that the sulfonyl chloride cyclized to structure **5** when treated with base. Basic hydrolysis of **5** then opened the hydantoin portion of **5** and the elements of $NCO^-$ were lost, to give 6-chlorobenzo-1,2-thiazine 1,1-dioxide (**6**). The orientation of the chlorosulfonation is confirmed by the nmr spectrum of **5**, which shows a doublet at $\delta$ 7.93 ($J$ = 8 Hz). This is expected for an aromatic proton *ortho* to a sulfonyl group which is one of an AB pair.

This orientation is in accord with the generalization that the *para* directive influence of a halogen in sulfonation is greater than that of a methyl group.[3a] However, the results with the 4-chloro isomer are not in agreement with the generalization[3] that a methyl is more strongly *ortho* directing than halogen.[3b]

### Experimental Section[4]

The chromatographic $R_f$ values were determined in the following systems: (1) tlc, silica gel G, chloroform–acetone (1:1); (2) 3 MM Whatman paper, 5.6 $N$ ammonium hydroxide–butanol (125:80); (3) tlc, silica gel G, ethyl acetate–acetic acid (99:1); and (4) tlc, Avicel, 5.6 $N$ ammonium hydroxide–butanol (125:80).

SCHEME I




**5-(4-Chlorobenzyl)-5-methylhydantoin (1).**—A mixture of 1-(4-chlorophenyl)-2-propanone[5] (8.4 g, 0.05 mol), ammonium carbonate (45 g), potassium cyanide (5.0 g), water (75 ml), and ethanol (75 ml) was heated at 55–60° for 8 hr. After cooling, 50 ml of water was added and the mixture was chilled and filtered to give 10.1 g (84%) of white crystals, mp 215–217°. Recrystallization from ethanol–water gave white crystals: mp 214–215°; $R_f$ 0.43 (system 1).

*Anal.* Calcd for $C_{11}H_{11}ClN_2O_2$: C, 55.35; H, 4.64; N, 11.74. Found: C, 55.57; H, 4.77; N, 11.97.

**5-(3-Chlorobenzyl)-5-methylhydantoin (4).**—Using 1-(3-chlorophenyl)-2-propanone,[6] the above procedure gave 82.4% of product: mp 240–242°; $R_f$ 0.43 (system 1); nmr ($D_2O$/KOH), $\delta$ 1.42 (S, 3, $CH_3$), 2.89 (S, 2, $CH_2$), and 7.23 (m, 4).

*Anal.* Calcd for $C_{11}H_{11}ClN_2O_2$: C, 55.35; H, 4.64; N, 11.74. Found: C, 55.29; H, 4.69; N, 11.87.

**5-(4-Chloro-3-sulfamybenzyl)-5-methylhydantoin (2).**—A 32.9-g sample of **1** (0.14 mol) was added in portions to 200 ml of $ClSO_3H$ at 0°. The reaction mixture was then stirred at 100–110° for 3 hr, cooled, and added dropwise to 1500 g of ice. This gave a tan solid, mp 208–210°, which was immediately added to 250 ml of 14 $N$ $NH_4OH$. After being stirred for 1 hr on a steam bath, the cooled reaction mixture was brought to pH 1 with concentrated HCl, and a tan solid, mp 143–148°, was collected. When this solid was purified by dissolving in dilute NaOH and reprecipitating with HCl, it gave 32.5 g (73%) of white crystals: mp 144–147°; $R_f$ 0.30 (system 1); nmr ($D_2O$/KOD), $\delta$ 1.42 (s, 3, $CH_3$), 2.98 (d, 2, $J$ = 0.5 Hz, $CH_2$), 7.34 (q, 1, $J_{5,6}$ = 8 Hz, $J_{2,6}$ = 3 Hz, 6 H of phenyl), 7.57 (d, 1, $J$ = 8 Hz, 5 H of phenyl), and 7.89 (d, 1, $J$ = 3 Hz, 2 H of phenyl).

*Anal.* Calcd for $C_{11}H_{12}ClN_3O_4S \cdot {}^1/_4H_2O$: C, 41.00; H, 3.91; N, 13.04. Found: C, 40.95; H, 4.06; N, 12.84.

**4-Chloro-3-sulfamylphenyl-$\alpha$-methylalanine (3).**—A stirred mixture of 3.2 g (0.01 mol) of **2**, 15.8 g (0.05 mol) of $Ba(OH)_2 \cdot 8H_2O$, and 60 ml of $H_2O$ was refluxed for 48 hr. The cooled

(1) C. M. Suter, "The Organic Chemistry of Sulfur," John Wiley and Sons, Inc., New York, N. Y., 1944, p 573.

(2) This structural assignment is supported by the difference of $\delta$ 0.09 observed for the $-CH_2-$ in the nmr spectra of **2** and **4**. In comparison, the difference of $\delta$ between the $CH_3$ of toluene and the 2-$CH_3$ and the 5-$CH_3$ of 2,5-dimethylbenzenesulfonamide is $\delta$ 0.37 and 0.085.

(3) (a) See ref 1, p 217. (b) At least 86% of the sulfonation product of 4-chlorotoluene is 3-chloro-6-methylbenzenesulfonic acid: W. P. Wynne and J. Bruce, *J. Chem. Soc.*, 731 (1898).

(4) We wish to thank Mr. R. Warren for nmr spectral data, Miss M. Carroll and staff for microanalytical data, and Mr. A. Post for thin layer and paper chromatographic data.

(5) C. G. Overberger and H. Biletch, *J. Amer. Chem. Soc.*, **73**, 4880 (1957).

(6) J. H. Biel, A. E. Drukker, T. F. Mitchell, E. P. Sprengeler, P. A. Nuhfer, A. C. Conway, and A. Horita, *ibid.*, **81**, 2805 (1959).