UDC 547.854'861.1'456:582.284

105. Toru Masuda, Toyokazu Kishi, and Mitsuko Asai : Application of Chromatography. XXXIII.* V-Compound Isolated from the Mycelium of *Eremothecium ashbyii*.

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Formerly Kuwada and Masuda,$^{1)}$ and Shimizu, Ohara, and Minoura$^{2)}$ successively discovered a purple fluorescent substance in the mycelium of *Eremothecium ashbyii* by paper partition chromatography. Katagiri and Imai$^{3)}$ also detected a substance in the acetone-butanol fermentation broth which gave a blue fluorescent spot on the chromatogram and assumed that the substance might be a pteridine derivative and related to the biosynthesis of flavins.

Thereafter, Shimizu$^{4)}$ made a more extensive study on the substance and pointed out that the substance might not be a pteridine derivative as Katagiri *et al.* presumed. On the other hand, Masuda,$^{5,6)}$ in his study on the biosynthesis of FAD in *Er. ashbyii*, reconfirmed the formation of the purple fluorescent substance and isolated it in crystalline form, and he announced its detailed properties including its melting point, analytical values, and ultraviolet spectrum in a preliminary report. This was tentatively designated as V-compound.

The foregoing is the outline of the investigations hitherto made on the V-compound. None of them, however, give even a clue to the elucidation of the structure of the compound. Although the present report also furnishes no positive evidences for its structure, the authors are confident that some progress has been made towards its elucidation.

Experimental Results

I. Extraction of V-Compound from the Mycelium of *Er. ashbyii*—Twenty kilograms of the wet mycelium was extracted with $MeOH-H_2O$ (1 : 1) at 70° and the extract, after being concentrated *in vacuo*, was shaken with benzyl alcohol to remove riboflavin therein. The solution was further concentrated and $Na_2S_2O_4$ was added, whereupon FAD precipitated in reduced form.

The FAD was filtered off, the filtrate was diluted with water to 2 L., acidified by addition of 100 cc. of AcOH, and poured onto a column of 90 g. of activated carbon. The column was washed with 3 L. of water and the substances adsorbed were developed with water containing 2% of pyridine. The first ca. 3 L. of the eluate which was non-fluorescent was discarded and the next 3.5 L. which exhibited purple fluorescence under ultraviolet rays was collected. This fraction was concentrated *in vacuo* to ca. 300 cc., the same volume of EtOH was added, and the deposited precipitate was filtered off. The filtrate was concentrated to 15 cc. and developed on a column of 100 g. of powdered cellulose with the upper layer of a mixture of $AcOH-BuOH-H_2O$ (1 : 4 : 5). The first 180 cc. of the eluate was discarded and the next 240 cc. which was fluorescent was collected. This fraction, after being freed from BuOH, was again subjected to chromatography on activated carbon.

This time, 40 g. of activated carbon was used and the sample was applied after it was acidified with AcOH. The column was washed with 2 L. of water and the substances adsorbed were

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* This constitutes a part of a series entitled "Application of Chromatography" by S. Kuwada. Part XXXII : This Bulletin, **5**, 136(1957).

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1) S. Kuwada, T. Masuda : Vitamins (Japan), **5**, 29(1952).

2) S. Shimizu, T. Ohara, K. Minoura : J. Fermentation Technol. (Japan), **30**, 13(1952).

3) H. Katagiri, K. Imai : Vitamins (Japan), **5**, 160(1952).

4) S. Shimizu : *Ibid.*, **6**, 766(1953).

5) T. Masuda : This Bulletin, **3**, 434(1955).

6) *Idem* : *Ibid.*, **4**, 72(1956).

developed with water containing 2% pyridine. The first 1.5 L. of the eluate was discarded and the next 2.5 L. which had purple fluorescence was collected. The fraction was concentrated *in vacuo* to 3 cc. and allowed to stand overnight, when brownish crystals separated out. After 3 recrystallizations from water the product was obtained as needle crystals (ca. 300 mg.)

II. Properties of V-Compound—As shown in Fig. 1, this compound occurs as uniform crystals and is colorless in pure state, m.p. 263°(decomp.); $[\alpha]_D^{20}$ +4.5°(c=3.3%, H_2O, l=1 dm.), +11.45°(c=2.6%, 0.1*N* NaOH, l=1 dm.).7)

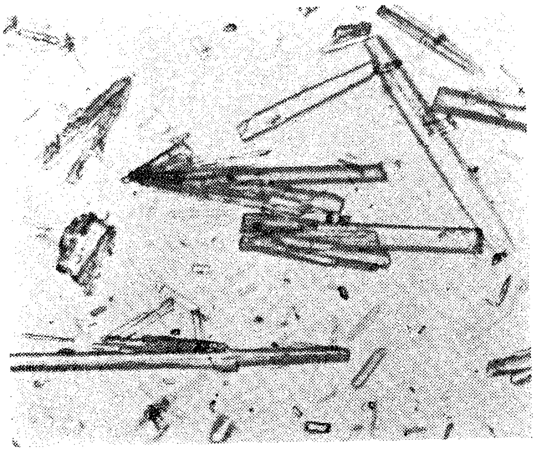

Fig. 1.

Crystals of V-Compound

The aqueous solution of this compound shows strong purple fluorescence and the solution, when applied on filter paper and sprayed with 5% aqueous solution of $AgNO_3$, forms a yellow spot. This compound contains C, H, O, and N but neither S nor P. *Anal.* Calcd. for $C_{12}H_{16}O_7N_4$: C, 43.90, H, 4.91, N, 17.07; mol. wt., 328. Found : C, 43.98; H, 4.92; N, 17.03; mol. wt. (Barger method), 300 ±30 (H_2O). The ultraviolet spectrum curves of this compound at various pH's are as shown in Fig. 2, and the infrared spectra of this compound, its deuterium-substituted compound and calcium salt are shown in Figs. 3 and 4.

This compound dissolves in $NaHCO_3$ solution under foaming and its 3% aqueous solution shows pH 2.42. Titration of the solution with 0.1*N* NaOH gives the curve shown in Fig. 5, indicating

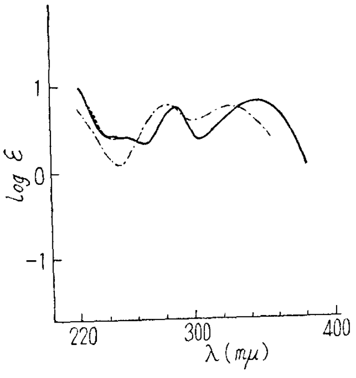

Fig. 2.

Ultraviolet Spectra of V-Compound

—— in pH 7.0 buffer
– – – in pH 2.1 〃
········ in pH 10.5 〃

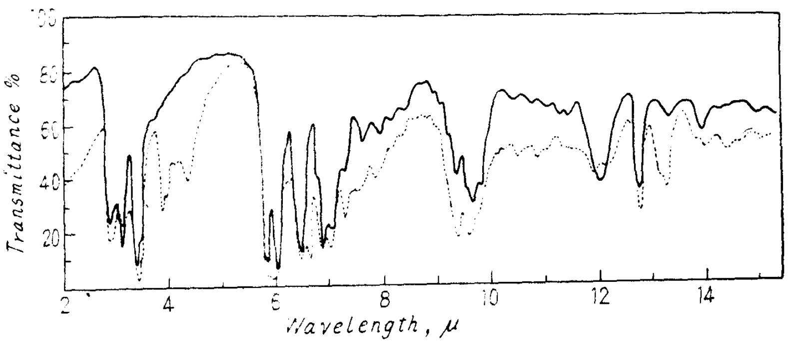

Fig. 3.

Infrared Spectra of V-Compound (——) and Deuterium-Substd. V-Compound (------)

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7) The m.p. and $[\alpha]_D$ were previously reported (Masuda : This Bulletin, 4, 72(1956)) as m.p. 239~243°(decomp.), $[\alpha]_D^{20}$: ±0, respectively, which are hereby corrected.

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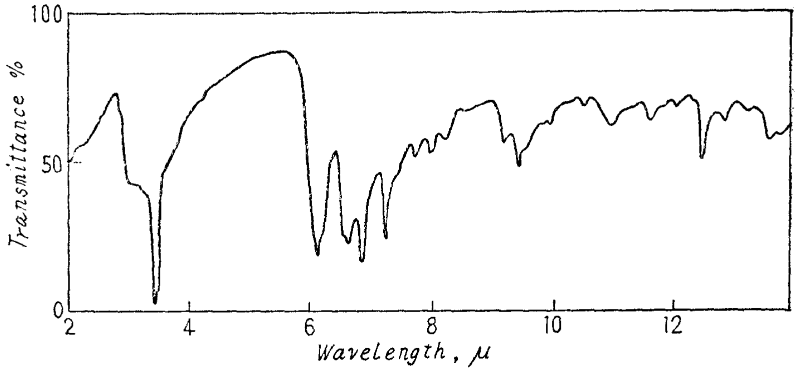

Fig. 4.

Infrared Spectrum of Ca Salt of V-Compound

the pK of the compound to be 3.95. If this compound is regarded as a monobasic acid, its molecular weight is calculated to be 347 from the quantity of NaOH required for its neutralization. This value is in close agreement with that obtained by the Barger method, as well as by calculation from the molecular formula described before.

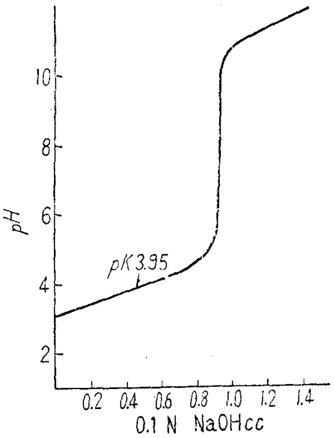

Fig. 5.

Titration Curve of V-Compound

Polarography—This compound shows 2 reduction waves at a suitable pH. Their first step implies reduction of an undissociated molecule by 2 electrons and 2 protons, and the second step, reduction of the dissociated molecule by 2 electrons. Both steps can be observed in the vicinity of pH 9.0, The apparent pKa is about 8.5, differing from the true pKa (such a phenomenon is observed with 4-oxopteridines and their carboxyl derivatives but not with quinoxaline or riboflavin). From the wave height the molecular weight is presumed to be ca. 300.

III. Degradation of V-Compound by Alkali—A solution of 10 mg. of V-compound in 2 cc. of *N* NaOH was heated on a water bath for 3 hrs. and then passed through a column of Amberlite 1R-120 (H-form). The weakly acid eluate, after being concentrated, was subjected to paper chromatography. The results are shown in Table I.

TABLE I. Rf of the Alkali Degradation Products of V-Compound

Solvent System	Sample	Fluorescence under ultraviolet rays				Band detected by Ehrlich reagent
$AcOH \cdot BuOH \cdot H_2O$ (1 : 4 : 5)	Alkali degradation products of V-compound	0.01 V +	0.14 V ⧻	0.17 V ?	0.26 V +	0.37
	Urea					0.37
$EtOH \cdot BuOH \cdot H_2O$ (15 : 50 : 35)	The above degradation products	0.06 V +	0.20 V ⧻	0.25 V ±	0.28 V +	0.40
	Urea					0.40

V : violet. ⧻, +, ± Intensity of fluorescence.

Riboflavin can be determined by treating it with *N* NaOH at 100° for 20 mins. and submitting the produced urea to Iwasaki's azotometry.[8] This method was applied to the V-compound, but as shown in Table II, the formation of urea was not quantitative even after prolonged heating. The same treatment of a 0.0110 g./20 cc. solution of 6,7-dimethyllumazine[9] gave no urea.

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8) M. Yamagishi, M. Yokoo, S. Inoue : J. Pharm. Soc. Japan, **75**, 1386(1955).

9) T. Masuda : This Bulletin, **4**, 375(1956).

Table II. Formation of Urea by Alkali Degradation of V-Compound (0.0114 g/20 cc.)

Period of degradation (min.)	Urea detected (mg.)	Urea detected (%)
10	20.4	19.4
20	27.6	26.5
30	31.4	30.2
40	38.6	36.2

IV. Acetylation of V-Compound—To a mixture of 1 cc. of pyridine and 1 cc. of Ac_2O, 100 mg. of V-compound was added and the whole was left standing at room temperature. After 3 days the reaction mixture was concentrated *in vacuo* and the residue was allowed to stand with 1 cc. of EtOH, whereupon colorless crystals separated out. Recrystallization of the product from EtOH gave 30 mg. of crystals, m.p. 184°. This product showed Rf 0.51 when developed with AcOH•BuOH•H_2O and its analytical data were in accord with the tetraacetate of V-compound. *Anal.* Calcd. for $C_{20}H_{24}O_{11}N_4$: C, 48.39; H, 4.87; N, 11.29; $COCH_3$ 34.4 (tetraacetate), 28.2 (triacetate). Found: C, 48.44; H, 4.92; N, 11.29; $COCH_3$, 31.83.

V. Oxidation of V-Compound by Pb(AcO)$_4$—Fifty milligrams of V-compound was placed in the boiling flask of a simple distilling apparatus fitted with a trap containing a saturated solution of dimedone in acetate buffer of pH 4.6. A slow stream of N_2 was passed through the apparatus. 20 cc. of 0.1N Pb(AcO)$_4$ solution in AcOH was added to V-compound and the flask was heated on a water bath for 1.5 hrs., when crystals began to separate out in the dimedone solution already after about 1 hr. At the end of the time, 20 cc. of water was added to the content in the flask to decompose the residual Pb(AcO)$_4$, the solution was filtered, and the residual formaldehyde in the filtrate was distilled into the dimedone trap. The dimedone solution was left standing for 1 day, the separated crystals were collected, and recrystallized from 50% EtOH. The product had a melting point of 190°, which coincides with that of formaldehyde dimedone reported in the literature, and showed no depression of m.p. on admixture with formaldehyde dimedone prepared by the oxidation of riboflavin with Pb(AcO)$_4$ according to the method of Plaut, *et al.*[10]

The reaction mixture in the flask was diluted with water and passed through a column of Amberlite IRC-50 (H-form) to remove Pb. The eluate was concencentrated and developed on a filter paper or submitted to paper ionophoresis at 300 v/3 hrs. using Theorell buffer of pH 7.0 as the medium. The results are shown in Table III.

Table III.

Solvent system	Rf and migration distance in ionophoresis (cm.)								
AcOH•BuOH•H_2O (1 : 4 : 5)	0.07 V+	0.10 V+	0.17 V+	0.20 V+	0.24 V+	0.35 V+	0.40 V+++	0.46 V+	0.56 V+
pH 7.0, 300 V, 3 hrs. in Theorell buffer	−1.5 V+	+2.0 V++	+4 V±	+8 V+					

On the other hand, the concentrated solution was applied on a large sheet of filter paper and developed, and the part corresponding to Rf 0.4 was cut out and extracted with water at various pH's. Ultraviolet spectra of the extracts are shown in Fig. 6.

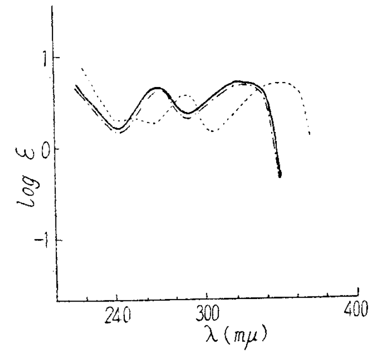

Fig. 6. Ultraviolet Spectra of the Substance showing Rf 0.40, obtained by Oxidation of V-Compound with Lead Tetraacetate

——— in aq. soln.
------- in 0.05N HCl
.... in 0.05N NaOH

VI. Photodecomposition of V-Compound—When a neutral aqueous solution of V-compound was exposed to direct sunlight for 5 days, it lost the fluorescence and the characteristic absorption in the ultraviolet region, showing its decomposition. To effect the photodecomposition more mildly,

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10) G. W. E. Plaut, P. L. Broberg: J. Biol. Chem., **219**, 131(1956).

100 mg. of V-compound was dissolved in 100 cc. of 0.6*N* NaOH and the solution, after addition of 10 cc. of 30% H_2O_2, was irradiated in a glass dish with an electric lamp of 100 w from a distance of 15 cm., when white crystals separated after ca. 10 hrs. The crystals, basic and soluble in water, were dissolved in water, the pH was adjusted to 3~4 with AcOH, and the separated crystals were recrystallized from water to fine needles (30 mg.), m.p. >360°. This product dissolves in $NaHCO_3$ solution with foaming and its aqueous solution exhibits purple fluorescence like V-compound, though the fluorescence is a little weaker than that of the original compound. When the aqueous solution is applied on filter paper and sprayed with $AgNO_3$ solution, it gives the same color reaction as V-compound. *Anal.* Calcd. for $C_7H_6O_4N_4$: C, 40.00; H, 2.88; N, 26.66. Found (1. After dryng *in vacuo* at 120° for 3 hrs.) : C, 40.32; H, 3.14; N, 26.49. (2. After dryng *in vacuo* at 180° for additional 2 hrs.) : C, 40.35; H, 2.91.

The above product, when subjected to paper ionophoresis at 300 v for 3 hrs. using Theorell buffer (pH 7.0, $\mu=0.1$) as the medium, migrated toward the anode by 4 cm. Since lumazine-6-carboxylic acid prepared from folic acid according to the method of Angier, *et al.*[11] also migrates toward the anode by 7.5 cm. by the same treatment, the above result seems to furnish a reference for discussion of the structure of V-compound. Ultraviolet spectra of this product at various pH's and infrared spectra of the product and its sodium salt are shown in Figs. 7 and 8, respectively.

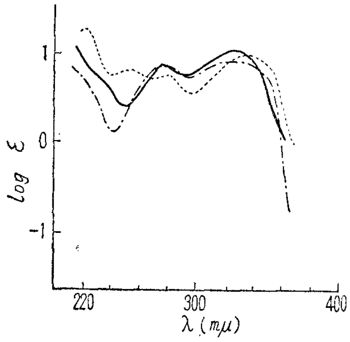

Fig. 7. Ultraviolet Spectra of the photodecomposition product of V-compound

——— in aq. soln. (pH 5.9)
------- in 0.05*N* HCl (pH 1.4)
··········· in 0.05*N* NaOH (pH 11)

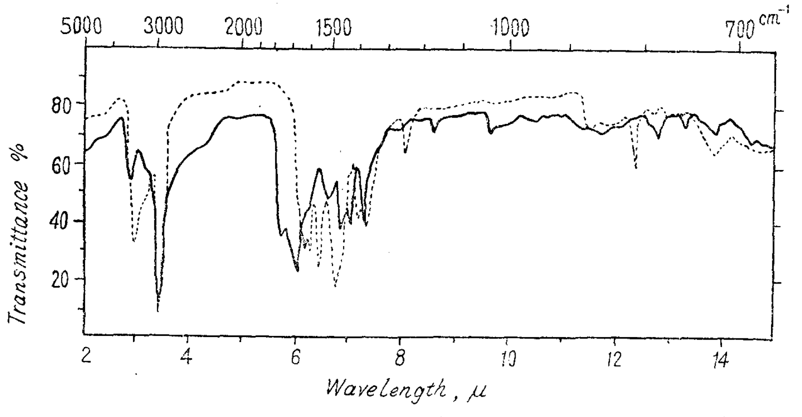

Fig. 8. Infrared Spectra of the photodecomposition product of V-compound and its sodium salt

——— Photodecomposition product of V-compound
-------- 〃 〃 〃 Sodium salt

Discussion

As mentioned at the beginning, it is already known that a purple fluorescent substance is contained in the mycelium of *Er. ashbyii* as well as of the microörganism used for acetone-butanol fermentation. Katagiri, *et al.*[3] assumed the substance to be a compound akin to 2-amino-4-hydroxypteridine-6-carboxylic acid, but Shimizu[4] negated the opinion. The present state as to the investigation of the substance is that

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[11] R. B. Angier, J. H. Boothe, J. H. Mowat, C. W. Waller, J. Semb : J. Am. Chem. Soc., **74**, 408 (1952).

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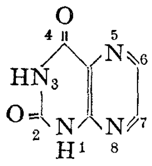
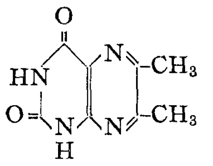
there are found no opinions cogent enough to elucidate the structure in the literature at home or abroad.

The purple fluorescent substance obtained by the present authors is a crystalline substance, m.p. 263°(decomp.), and dissolves in sodium hydrogen carbonate solution with foaming, showing that it is an acid. If this substance is regarded as a monobasic carboxylic acid, its molecular weight is found to be 347 from the quantity of alkali required for its neutralization, and this value coincides with the molecular weight obtained by Barger method and polarography. From its analytical value it is reasonable to assign the molecular formula, $C_{12}H_{16}O_7N_4$, to this compound.

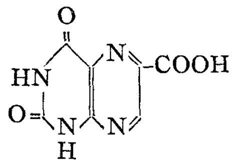
The aqueous solution of this substance forms a yellow precipitate with 5% aqueous solution of silver nitrate, and the solution, when applied on filter paper and sprayed with silver nitrate solution, produces a yellow spot. Lumazine (2,4-dioxopteridine) (I), 6,7-dimethyllumazine (II), lumazine-6-carboxylic acid (III), 2-amino-4-oxopteridine-7-carboxylic acid (IV), and 2-amino-4-oxo-6-methylpteridine (V) are all positive to these tests, but such pyrimidine derivatives as uracil (2,4-dioxopyrimidine), 4,5-diaminouracil, 4-aminouracil, 4-amino-5-nitrosouracil, and barbituric acid are negative.



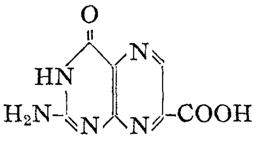
(I)



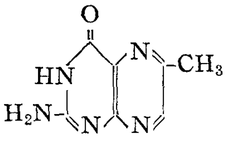
(II)



(III)



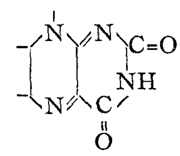
(IV)



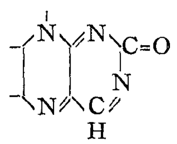
(V)

Therefore, the presence of pteridine ring as the parent structure in the V-compound is readily presumed even only from these tests. The ultraviolet spectrum of the substance also suggests the existence of a pteridine ring, and that the infrared absorption at 5.9 μ observed in the substance is absent in its calcium salt seems to indicate the presence of a carboxyl group.

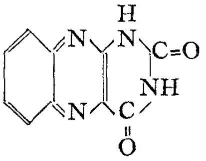
Paper chromatography of the alkali degradation products of the substance formed four bands detectable under ultraviolet rays. Although they could not be identified, one band detected by the Ehrlich reagent agreed with the spot of urea. If the substance contains a pteridine ring such as (VI) or (VII), it is natural that the substance produces urea by its alkali degradation.



(VI)



(VII)



(VIII)

As mentioned in the experimental part, this phenomenon is not observed with 6,7-dimethyllumazine. Further, from the fact that Kuhn, *et al.*[12] confirmed the formation of urea by the alkali degradation of riboflavin or lumiflavin but observed the reaction to be difficult with alloxazine (VIII), it is assumed that one of the nitrogens in the pyrazine ring of the substance has a substituent group. If so, the group would be

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[12] R. Kuhn, H. Rudy, T. Wagner-Jauregg: Ber., **66**, 1950(1933).

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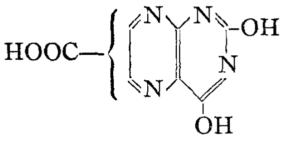
eliminated by photodecomposition of the substance, in view of the experience with riboflavin.

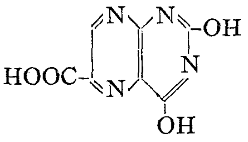
Following the experiment in which Fukamachi and Sakurai[13] obtained lumichrome, lumiflavin, and 6,7-dimethylflavin-9-acetic acid by the photodecomposition of riboflavin, an alkaline solution of V-compound was irradiated with a 100-watt. electric lamp in the presence of hydrogen peroxide and white crystals were obtained, which did not melt below 360° and its analytical value coincides with $C_7H_6O_4N_4$. Like V-compound, it is an acid substance and gives yellow color with silver nitrate solution showing the presence of a pteridine ring. The ultraviolet spectrum of the product also supports the pteridine structure. On the other hand, it is an evidence of the presence of a carboxyl group that the product has infrared absorptions at 5.9, 9.7 μ, and 3.8~4.5 μ, but its sodium salt lacks these absorptions and has new absorptions at 6.1 and 6.8 μ.

Since the analytical data of the product agreed with $C_7H_6O_4N_4$, it was provisionally assumed that two of the four oxygens are in COOH and the remaining two are in hydroxyl groups. It is possible that, if V-compound has the parent structure represented by (VII), not to speak of the case where it has the structure of (VI), oxygen may enter 4-position during photodecomposition to form a 2,4-dihydroxy compond. If so, the photodecomposition product probably has the structure of (IX).

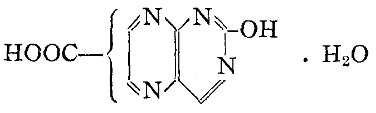
However, as shown in Table IV, the ultraviolet absorption maxima of lumazine-6-carboxylic acid (X), m.p. 345° (decomp.), prepared by Angier *et al.*[11] from folic acid and those of the present product are different (especially in alkaline solution) in position. Although the two subtances migrate toward the anode in ionophoresis, they are different in the velocity of the migration showing that the latter has lower negative charge than the former.



(IX)



(X)



(XI)

Table IV.

Substance	Ultraviolet absorption max. (mμ)								
	Neutral			Alkaline			Acidic		
Lumazine-6-carboxylic acid	230	258	325		267.5	370	237	264	330
Photodecomposition product	–	277	326	249	277	333	–	277	324

Consequently, it seems most natural to think that the photodecomposition product is a monohydroxy-monocarboxylic acid having one mole of hardly removable water of crystallization as represented by (XI).

The $C_5H_{12}O_4$ obtained by subtracting the molecular formula $C_7H_4O_3N_4$ of the photodecomposition product from that of V-compound ($C_{12}H_{16}O_7N_4$) must be the group split from one of the nitrogens in the pyrazine ring by photodecomposition. On the other hand, the optical rotation of V-compound and the fact that the acetylation product of this compound agreed with its tetraacetate, that the relation between the infrared spectra of V-compound and its deuterium-substituted compound was the same as that observed with G-compound,[9,14] and that formation of formaldehyde by oxidation of V-compound with lead tetraacetate was confirmed as was made by Plaut, *et al.*[10] all suggest the presence of a polyhydric alcohol which has $-CH_2OH$ as the terminal

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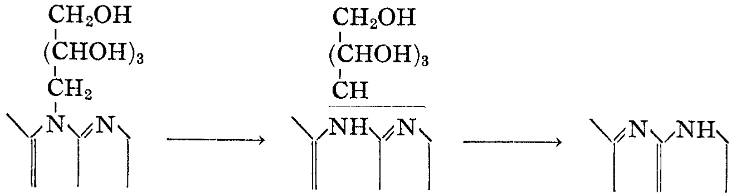
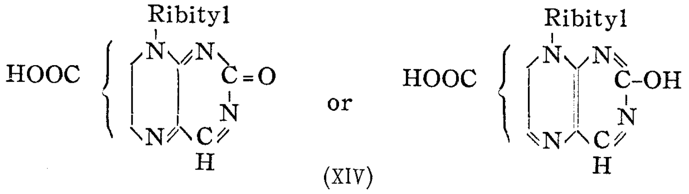
[13] C. Fukamachi, Y. Sakurai: J. Vitaminology, **1**, 217(1955).

[14] T. Kanzawa, T. Masuda: This Bulletin, **4**, 316(1956).

group. If the polyhydric alcohol is regarded as ribityl, the experimental results mentioned above are well explained and riboflavin can be well related to V-compound. However, considering that the $C_5H_{12}O_4$ was split off in the same manner as the formation of lumichrome (XIII) by the photodecomposition of riboflavin, the decomposition product obtained in the present experiment has two less hydrogens. This may be due to the simultaneous dehydrogenation of the parent structure at the time of the cleavage of the ribityl group, as Forrest, *et al.*[15] observed with the photodecompositon of 2-amino-4-hydroxy-7,8-dihydro-8-lactylpteridine-6-carboxylic acid, and this is understood from the fact that the substituent in V-compound is ribityl group, as well as from the opinion of Albert[16] that partial saturation of the pyrazine ring in the pteridine ring decreases its stability to chemicals.


(XII) (XIII)

From the reasons mentioned above the authors propose the structure of (XIV) for the V-compound. Studies are now under way to confirm the conclusion more positively.


(XIV)

The authors gratefully acknowledge the technical assistance of Mr. Yutaka Shiraishi for the cultivation of *Er. ashbyii*, of Dr. Tokunosuke Kanzawa, Mr. Hideo Kamio, and Mr. Masao Nishikawa for their measurement and analysis of the infrared spectrum, and to Mr. Yutaka Asahi for his measurement of the polarography. Thanks are also due to the members in charge of elementary analysis.

Summary

The purple fluorescent substance (V-compound) obtained by the authors from the mycelium of *Er. ashbyii* occurs as colorless needles, m.p. 263°(decomp.), $[\alpha]_D^{20}$: +4.5° (in H_2O), +11.45°(in 0.1*N* NaOH). The molecular weight of this substance was found to be about 300 by Barger method, titration (as monobasic acid), and from the wave height in polarography. A molecular formula of $C_{12}H_{16}O_7N_4$ was assigned to the substance from its analytical value. From its ultraviolet and infrared spectra the presence of a pteridine ring, COOH, and OH was presumed. Since the substance gave urea by treatment with alkali solution, it was assumed to be a pteridine compound having a carbonyl group at 2-position, substituted by a group at one of the nitrogens in the pyrazine ring. From the fact that the acetylation product of the substance was in accord with its tetraacetate, and that it gave formaldehyde by oxidation with lead tetraacetate, the group was presumed to be ribityl. Photodecomposition of this substance furnished more important data. Although exposure of an aqueous solution of the substance to direct sunlight destroyed even the pteridine ring, irradiation of its alkaline solution with light from an electric lamp in the presence of hydrogen

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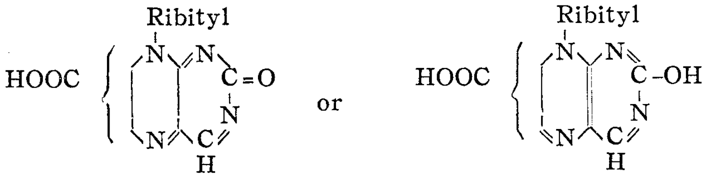
[15] H. S. Forrest, H. K. Mitchell : J. Am. Chem. Soc., **76**, 5658(1954).
[16] A. Albert : Quart. Rev.(London), **6**, 197(1952).

peroxide yielded crystals of m.p. >360°. The product exhibited the ultraviolet spectrum characteristic to pteridine compounds. Comparison of the product with lumazine-6-carboxylic acid by ionophoresis indicated that the former has lower negative charge than the latter. Therefore, the molecular formula, $C_7H_6O_4N_4$, calculated from the analytical value was concluded to be $C_7H_4O_3N_4 \cdot H_2O$. This may be due to the dehydrogenation of the parent ring during cleavage of the group at the nitrogen of the pyrazine ring by photodecomposition of the V-compound. From these results, the authors gave the following structure to the V-compound.



(Received August 26, 1957)

UDC 547.833.3.07

107. Eiji Ochiai und Yutaka Kawazoe: Polarisation der heterocyklischen Ringe mit aromatischem Charakter. CXX.[1] Eine neue Synthese von 1-Halogeno-5,6,7,8-tetrahydroisochinolin.

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Ochiai und Ikehara[2] nahmen an, dass Isochinolin bei der katalytischen Reduktion zuerst auf seiner Benzolhälfte hydriert werden würde, wenn man dasselbe zuvor auf seiner Pyridinhälfte mit einem Substituenten von grossem +E Effekt blockiert. In Bestätigung dieser Vermutung erhielten sie das 4-Amino-5,6,7,8-tetrahydroisochinolin in 78%iger Ausbeute, indem sie 4-Aminoisochinolin mit Platinoxyd in Eisessig-Lösung unter Zusatz einiger Tropfen konz. Schwefelsäure katalytisch hydrierten. 4-Amino-5,6,7,8-tetrahydroisochinolin wurde dabei über die Diazostufe in das 5,6,7,8-Tetrahydroisochinolin mit ca. 65%iger Ausbeute überführt. Seither wurde diese Synthese in unserem Laboratorium, anlässlich der Versuche zur Synthese von Morphinan-Derivaten[3] oftmals nachgeprüft und festgestellt, dass die Ausbeute der Reaktion an der Desaminierungsstufe beträchtlich schwankt, obwohl die katalytische Reduktion glatt mit fast konstanter Ausbeute verläuft. 4-Amino-5,6,7,8-tetrahydroisochinolin zeigte bei der Desaminierung eine grosse Neigung in das entsprechende 4-Oxyderivat überzugehen. Eine verbesserte Synthese mit konstanter Ausbeute ist also wünschenswert.

In Berücksichtigung der Lage unserer Versuche, die das 1-Halogeno-5,6,7,8-tetrahydroisochinolin benötigen, haben wir nun versucht, Isocarbostyril, 1-Alkoxyisochinoline bzw. 1-Aminoisochinolin ganz analog zu hydrieren, weil jedes 5,6,7,8-Tetrahydroderivat dieser Verbindungen ziemlich glatt in das 1-Halogeno-5,6,7,8-tetrahydroisochinolin überführbar sein könnte.

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* Hongo, Tokyo (落合英二, 川添 豊).

[1] CXIX. Mitt.: Dieses Bulletin, **5**, 313(1957).

[2] Diese Bulletin, **2**, 72(1954).

[3] *Ibid.*, **2**, 109(1954); **3**, 291(1955).