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THE CHEMICAL CONSTITUTION OF RUBROFUSARIN

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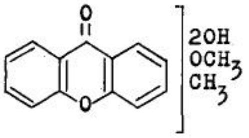
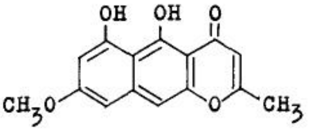
RUBROFUSARIN, $C_{15}H_{12}O_5$, was first isolated as a red pigment from the mycerium of Fusarium graminearum and F. culmolum by Ashley et al.[1], who proposed its structure as a methyltrihydroxyxanthone monomethyl ether (I) mainly from its general properties. Although further investigations have been performed by other workers[2,3], its orientation has not been determined and no degradation study has been reported.

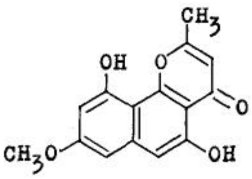
We now wish to report our finding that rubrofusarin is not the proposed methylxanthone, but is a derivative of 2-methylnaphtho-γ-pyrone and should be represented either by structure (II) or (III).



I



II



III

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[1] J.N.Ashley, B.C.Hobbs and H.Raistrick, Biochem. J. 31, 385 (1937).

[2] R.P.Mull and F.F.Nord, Arch. Biochem. and Biophys. 4, 419 (1944).

[3] N.A.Lund, Alexander Robertson and W.B.Whalley, J. Chem. Soc. 2434 (1953).

When rubrofusarin[4] was subjected to zinc dust distillation, naphthalene and a little anthracene were obtained, whereas no methylxanthene was detected. In connection with this fact, we have examined whether methylxanthones can give these polycyclic compounds or not, on that condition. The investigated samples were the four methylxanthone isomers and nor-lichexanthone[5]. From this zinc dust distillation study it was derived that anthracene is yielded from the xanthone[6] having a methyl group at the *o*-position to the carbonyl group, and that no naphthalene is afforded from any of the xanthones examined. Accordingly, we can assume the existence of a naphthalene nucleus in rubrofusarin.

The evidence for this assumption is further supplied by the alkaline degradation study of nor-rubrofusarin (i.e. demethylrubrofusarin). It was hydrolysed by refluxing for two hours with 20% aqueous sodium hydroxide in an atomosphere of nitrogen to give a naphthol[7] (IVa) in addition to acetone and acetic acid. IVa failed to crystallise owing to its in-

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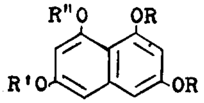
[4] The pigment was obtained from the dried mycerium of *F. graminearum* as reddish orange prisms, m.p. 213°, in 0.25% yield.

[5] (=1-Methyl-3,6,8-trihydroxyxanthone). Y.Asahina and H.Nogami, *Bull. Chem. Soc. Japan* **17**, 202 (1942).

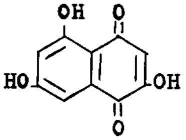
[6] 1-Methylxanthones may be regarded as a o-methylbenzophenone analogue. By analogy with a Elbs reaction the formation of anthracene as a main zinc dust distillate can be explained.

[7] The naphthol (IVa) shows λ_{max} 242.5, 306, 318, 327 and 332 mμ (log ε 4.68, 3.73, 3.76, 3.75 and 3.78 resp.), and gives an intense brown ferric reaction.

stability in air. It shows a considerable pH depression with boric acid and resists complete methylation with diazomethane. (The trimethyl ether (IVb), m.p. 141.5°, which gave a monoacetate, m.p. 107°.) A colourless alkaline solution of IVa on standing changed violet undergoing immediate aerial oxidation. In several hours, with an increase of a violet colour and a decrease of a bluish green fluorescence, the oxidation of the solution was advanced and it gave an amorphous red quinone on acidification. The quinone has an ultraviolet spectrum closely resembling that of flaviolin[8] (V) and appears to be identical with V. λ_{max} 268, 313, 384 and 462 mμ. IVa was characterized as the tetraacetate (IVc), m.p. 134° (Found: C, 59.90; H, 4.79; Ac, 49.2. $C_{18}H_{16}O_8$ requires: C, 60.00; H, 4.48; Ac, 48.0), λ_{max} 228, 286 mμ ($\log \epsilon$ 4.89, 3.77 resp.). Ozonolysis of IVc, followed by hydrolysis, gave 3,5-dihydroxyphthalic acid, which was identified as the dimethyl ether[9]. The above results and biogenetical considerations led us to presume that the naphthol (IVa) is 1,3,6,8-tetrahydroxynaphthalene. This has been established by the



IVa, R=R'=R"=H
b, $R=R'=CH_3$, R"=OH
c, R=R'=R"=Ac
d, R=R"=Ac, $R'=OCH_3$



V

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[8] B.D.Astill, J. Chem. Soc. 3302 (1953).

[9] The authentic sample was kindly supplied by Dr. Y. Hatsuda, Tottori University.

preparation of 1,3,6,8-tetraacetoxynaphthalene (IVc), m.p. 137°, from chromotropic acid by alkali fusion[10] and subsequent acetylation with acetic anhydride and pyridine. As expected, zinc dust distillation of IVa and IVc gave only naphthalene.

Thus it is evident that rubrofusarin has a naphthalene nucleus. According to the English workers[1,3], rubrofusarin has a C-methyl group in addition to an unreactive carbonyl group and an inert oxygen atom. By these data and the fission products of the above mentioned alkaline degradation, the presence of a 2-methyl-γ-pyrone ring in rubrofusarin (ν_{max}^{KBr} 1660 cm^{-1}) is indicated. It is further supported by the following reactions of rubrofusarin dimethyl ether; the ether gave a violet colour reaction with m-dinitrobenzene at the presence of alkali and condensed with piperonal to give a styryl compound, yellow needles, m.p. 254.5°.

From the above results, rubrofusarin is assigned the 2-methylnaphthopyrone structure (II or III) instead of the so far proposed xanthone structure (I). The position of the methoxy group is derived from the fact that acetylation of a alkaline degradate of rubrofusarin gave a methoxytriacetoxynaphthalene (IVd), m.p. 128°, showing a β-naphthol type ul-

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[10] Garden and Thompson reported that the fusion results in the formation of 2,4-dihydroxybenzoic acid. We have succeeded this attempt by carrying out the fusion using an alkali mixture ($Ba(OH)_2.8H_2O$, KOH and NaOH) in an atomosphere of nitrogen at 260° (oil bath) for 7 hrs. in 10% yield (as the tetraacetate).
J.F.Garden and R.H.Thompson, J. Chem. Soc. 2483 (1957).

traviolet spectrum. λ_{max} 235, 282, 317, 331 mμ (log ϵ 4.80, 3.69, 3.19, 3.24 resp.), λ_{min} 256, 312, 324 mμ (log ϵ 3.44, 3.15, 3.12 resp.). Both the structures II and III are in well accord with the acetate theory and with the statement of Lund et al.[3] that nor-rubrofusarin has a hydroxyl group in o-position to a carbonyl group. The ultraviolet spectrum of nor-rubrofusarin triacetate favours the structure II. Since a Wessely-Moser rearrangement between the structure II and III is expected, rubrofusarin should be examined for this isomeric change.

The details of this work and of further studies which are in progress will be found in the Bulletin of the Agricultural Chemical Society of Japan.

All melting points are uncorrected. Ultraviolet spectra were determined for 95% ethanol solutions on a Hitachi EPS-2 recording spectrophotometer.

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