742. *The Chemistry of Fungi. Part XXXVIII.*[1] *Further Evidence for the Structure of Rubropunctatin.**

By E. J. HAWS and J. S. E. HOLKER.

Oxidation of both *O*-methylaporubropunctataminol methiodide and hexahydro-*O*-methylaporubropunctatin with alkaline potassium permanganate has given anisole-2,3,5,6-tetracarboxylic acid. Consideration of this result, together with findings previously published,[1] confirms structures (I) and (XIII) for aporubropunctatamine and hexahydroaporubropunctatin respectively.

IN a recent account[1] of the chemistry of rubropunctatin, $C_{21}H_{22}O_5$, this compound was shown to react with aqueous ammonia under very mild conditions to give a nitrogen analogue, rubropunctatamine, $C_{21}H_{23}O_4N$, which, on reduction with zinc and acetic acid, was degraded to aporubropunctatamine, $C_{20}H_{25}O_2N$, and one mol. of carbon dioxide. A detailed study of the chemistry of aporubropunctatamine led to structure (I) for this compound although the alternative structure (III) could not be excluded. Since the proposed structures (V) and (VI) for the parent pigment and its nitrogen analogue respectively were based primarily on structure (I) for aporubropunctatamine, it was essential to confirm this structure.

Differentiation between structures (I) and (III) for aporubropunctatamine would be possible by oxidation of the methyl ether (II or IV) to an anisolepolycarboxylic acid. In the isoquinoline series oxidative fission of the heterocyclic ring is best achieved by treatment of quaternary salts with alkaline potassium permanganate, the reaction proceeding with formation of an *N*-alkylisocarbostyril.[2] Accordingly, *O*-methylaporubropunctatamine was converted into its methiodide which had $\lambda_{max.}$ 262 and 375 mμ (log ε 4·65 and 3·85) in ethanol. On addition of 0·01N-sodium hydroxide a large bathochromic shift to $\lambda_{max.}$ 300, 345, and 500 mμ (log ε 4·14, 4·07, and 4·15) occurred, the spectrum reverting to that of the quaternary salt on acidification. This unexpected behaviour could not be interpreted in terms of either quaternary ammonium hydroxide or *N*-methylisocarbostyril formation in alkaline solution, but rather suggested the formation of an anhydro-base of type (VII) or (VIII). A similar phenomenon has been observed[3] with the pyridinium salt (IX) which

---

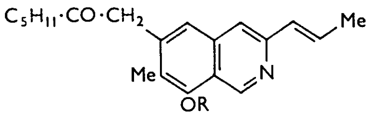
* A brief report of this work is included in a preliminary communication on the chemistry of monascorubrin (*Tetrahedron Letters*, 1960, No. 5, 24).

[1] Part XXXVII, Haws, Holker, Kelly, Powell, and Robertson, *J.*, 1959, 3598.

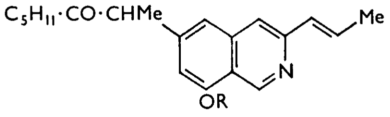
[2] Gensler, in Elderfield's "Heterocyclic Compounds," Chapman and Hall Ltd., London, 1952, Vol. IV, p. 407.

[3] Katritzky, *J.*, 1955, 2586.

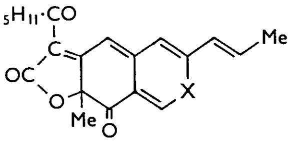
is converted into the anhydro-base (X) in alkaline solution. It appeared, therefore, that *O*-methylaporubropunctatamine methiodide would not be suitable for the envisaged oxidation and, indeed, the only product isolated on oxidation of this compound with alkaline potassium permanganate was oxalic acid.



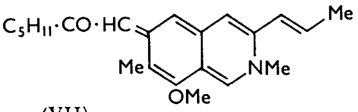
(I) R = H. (II) R = Me.



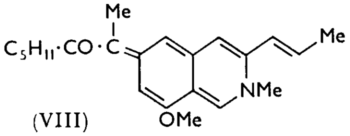
(III) R = H. (IV) R = Me.



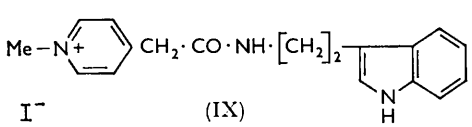
(V) X = O. (VI) X = NH.



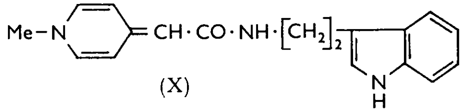
(VII)



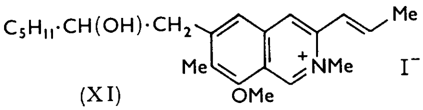
(VIII)



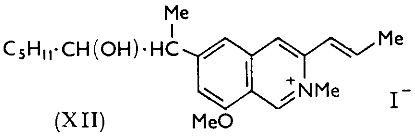
(IX)



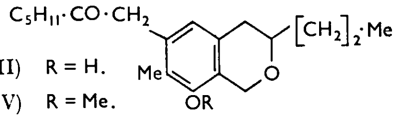
(X)



(XI)



(XII)



(XIII) R = H.
(XIV) R = Me.

Attention was next turned to *O*-methylaporubropunctataminol methiodide (XI) or (XII), which no longer contains a ketonic carbonyl group in the side-chain and hence would be less likely to give an anhydro-base.[3] Treatment of this compound with sodium hydroxide gave a pale yellow sticky solid, typical of a pseudo-base, and oxidation of this material with potassium permanganate gave anisole-2,3,5,6-tetracarboxylic acid, characterised as its tetramethyl ester. This result excludes structure (III) for aporubropunctatamine and equivalent structures for its derived products, and when considered in conjunction with the evidence previously presented[1] confirms beyond reasonable doubt that aporubropunctatamine has structure (I).

In our account of the chemistry of rubropunctatin,[1] the compound, $C_{20}H_{30}O_3$, obtained in low yield by exhaustive catalytic hydrogenation of rubropunctatin was considered to be hexahydroaporubropunctatin (XIII). Support for this view has now been obtained by oxidation of the *O*-methyl ether (XIV) with potassium permanganate to give anisole-2,3,5,6-tetracarboxylic acid.

EXPERIMENTAL

O-Methylaporubropunctatamine and O-Methylaporubropunctataminol Methiodides.—When prepared by dissolving *O*-methylaporubropunctatamine[1] (250 mg.) and *O*-methylaporubropunctataminol[1] (200 mg.) in methyl iodide (1·5 ml. and 5 ml. respectively) and setting the mixtures aside for 24 hr. at room temperature, the methiodides crystallised from the reaction mixtures. Thus isolated, O-*methylaporubropunctatamine methiodide* formed chunky yellow prisms (310 mg.), m. p. 163—165° (decomp.), $\nu_{max.}$ 1704s, 1621s, 1558m, and 1506w cm.$^{-1}$ (in mineral oil) (Found: C, 55·6; H, 6·6; N, 3·4; I, 26·9. $C_{22}H_{30}INO_2$ requires C, 56·3; H, 6·9; N, 3·0; I, 27·0%), and O-*methylaporubropunctataminol methiodide* formed yellow needles (220 mg.), m. p. 118—120° (decomp.), $\lambda_{max.}$ 262 and 375 mμ (log ε 4·23 and 3·80) (in EtOH), $\nu_{max.}$ 3311m, 1629s, 1563m, and 1513w cm.$^{-1}$ (in mineral oil) (Found: C, 54·8; H, 7·1; N, 2·9. $C_{22}H_{32}INO_2,H_2O$ requires C, 54·2; H, 7·0; N, 2·9%). Both compounds were thermally unstable and decomposed on attempted recrystallisation.

Oxidation of Rubropunctatin Derivatives.—(a) O-*Methylaporubropunctataminol methiodide.* To a suspension of this compound (380 mg.) in N-sodium hydroxide (50 ml.), initially at room temperature and later at 90°, was added powdered potassium permanganate in portions (8 × 0·5 g.) during 12 hr., each portion being completely reduced before addition of the next. Manganese dioxide formed in the reaction was then collected and washed well with hot water, and the combined filtrate and washings were acidified with concentrated hydrochloric acid. The resultant mixture was then warmed to 70° and treated with potassium permanganate (1·0 g.) and after 15 min. the excess of reagent was destroyed with sulphur dioxide. The product was isolated in ether by continuous extraction for 6 hr. and methylated with diazomethane, and the crude ester (92 mg.) was adsorbed on a column of aluminium oxide (10 × 1·5 cm.) from solution in ether (5 ml.) and light petroleum (b. p. 40—60°) (15 ml.). Elution with the same solvent mixture (100 ml.) gave tetramethyl anisole-2,3,5,6-tetracarboxylate which separated from ether–light petroleum (b. p. 40—60°) in rods (43 mg.), m. p. and mixed m. p. with an authentic sample 106° (Found: C, 52·8; H, 5·0. Calc. for $C_{15}H_{16}O_9$: C, 52·9; H, 4·7%).

(b) *Hexahydro*-O-*methylaporubropunctatin.* Oxidation of this compound (500 mg.), as in the foregoing procedure, gave tetramethyl anisole-2,3,5,6-tetracarboxylate, rods (115 mg.) [from light petroleum (b. p. 40—60°)–ether], m. p. and mixed m. p. 106° (Found: C, 52·9; H, 4·7%).

(c) O-*Methylaporubropunctatamine methiodide.* Oxidation of this compound (1 g.) in N-sodium hydroxide (100 ml.) with potassium permanganate (8 × 1 g.) at 90°, followed by removal of manganese dioxide with sulphur dioxide and acidification with 2N-sulphuric acid, gave oxalic acid (isolated in ether by continuous extraction), needles (50 mg.) (from acetic acid–benzene), m. p. and mixed m. p. with anhydrous oxalic acid 189° (decomp.).

The authors thank the Department of Scientific and Industrial Research for a Maintenance Grant (to E. J. H.), and Mr. D. H. Marrow of this Department for a synthetic sample of anisole-2,3,5,6-tetracarboxylic acid.

UNIVERSITY OF LIVERPOOL.

[*Received, April 7th*, 1961.]