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MONASCORUBRIN

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WE recently reported[1] that rubropunctatin, a pigment from Monascus rubropunctatus Sâto has structure (I). Parallel with this investigation we have examined 'monascorubrin'[2] first isolated by Nishikawa[3] from Monascus purpureus Wentii. Although our work on this substance is incomplete, a recent publication[4] in which structure (IV) is suggested for monascorubrin makes it desirable to record some of our observations, particularly as these

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[1] E.J. Haws, J.S.E. Holker, A. Kelly, A.D.G. Powell and A. Robertson, J. Chem. Soc. 3598 (1959).

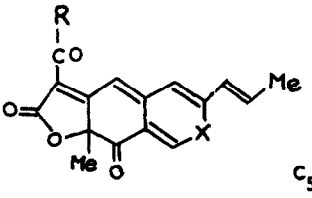
[2] As will become apparent in the sequel 'monascorubrin' is a mixture of rubropunctatin and a second component, present in major amount and for which we now reserve the name monascorubrin. In this communication trivial names enclosed in quotation marks refer to mixtures.

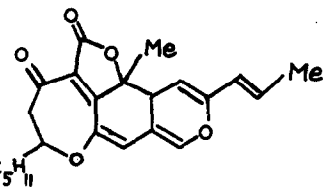
[3] H. Nishikawa, J. Agric. Chem. Soc. Japan 8, 1007 (1932).

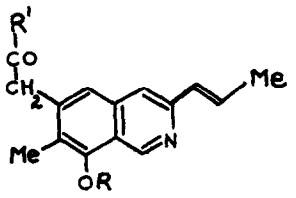
[4] K. Nakanishi, M. Ohashi, S. Kumasaki and S. Yamamura, J. Amer. Chem. Soc. 81, 6339 (1959).

allow us to exclude structure (IV) and to propose a more suitable alternative.

For a long time we were unable to differentiate between rubropunctatin and 'monascorubrin' since both compounds underwent parallel reactions and corresponding products derived from the two natural products exhibited closely similar properties. Thus, 'monascorubrin', m.p. 134-136° (decomp.) $[\alpha]_D$ - 3390° (c 1.03 in $CHCl_3$) λ_{max} (cyclohexane) 236 (sh.), 246, 278 and 410 mμ (log ε 4.17, 4.20, 4.07 and 4.40) ν_{max} 1757(s), 1727(s), 1658(s), 1631(s) and 1570(s) $cm.^{-1}$ (Found: C, 71.7; H, 6.9; (C)-Me, 11.3%) on treatment with dilute ammonium hydroxide gave 'monascorubramine', m.p. 198° (decomp.) λ_{max} (in 95% ethanol) 255, 306, 375(sh.), 430 and 560 mμ (log ε 4.11, 4.35, 4.00, 3.94 and 3.91) ν_{max} 3188(m), 1734(s), 1712(s), 1645(w), 1620(m), 1605(s), 1568(s) and 1530(s) cm^{-1} (Found: C, 71.8; H, 6.9; N, 3.7%). Reduction of 'monascorubramine' with zinc and acetic acid gave one molecular equivalent of carbon dioxide and 'apomonascorubramine' m.p. 190° λ_{max} 257, 305 and 358 mμ (log ε 4.72, 3.84 and 3.67) ν_{max} 3125 (m sh.), 1712(s), 1656(w), 1634(s), 1592(w) and 1570(s) cm^{-1} (Found: C, 77.9; H, 8.4; N, 4.3%) which was characterised as the 'methyl ether', m.p. 65° (Found C, 77.3; H, 8.4; N. 4.5; OMe, 9.0%) and as an 'O-acetate', m.p. 82° (Found: C, 75.0; H, 7.9; N, 4.0; Ac, 10.4%). These compounds have closely similar properties to rubropunctatin (I), rubropunctatamine (II), aporubropunctatamine (V), O-methyl-aporubropunctatamine (VI) and O-acetylaporubropunctatamine (VII) respectively. Analogues of all derivatives of rubropunctatin so far reported[1] have been prepared from 'monascorubrin'. In each case a close parallel exists. The only consistent difference between the two series is that 'monascorubrin' derivatives have a slightly higher carbon and hydrogen content that the corresponding rubropunctatin derivatives.







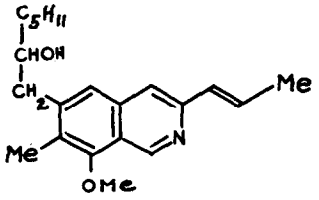
I	$R=C_5H_{11}$	X=O	IV	V	R=H	$R'=C_5H_{11}$
II	$R=C_6H_{11}$	X=NH		VI	R=Me	$R'=C_5H_{11}$
III	$R=C_7H_{15}$	X=O		VII	R=Ac	$R'=C_5H_{11}$
				VIII	R=Me	$R'=C_7H_{15}$

The situation has now been resolved by comparative mass spectrometric examination of 'O-methylapomonascorubramine' and the corresponding rubropunctatin derivative (VI) when it was found that whereas the latter compound was essentially one component of M.W. 325 in agreement with formula (VI), the former substance was a mixture of two major components of M.W.'s 325 and 353 present in an approximate ratio of 1:4. Gas liquid chromatography showed that the component M.W. 325 had the same retention time as (VI). Thus the component M.W. 353 probably differs from compound (VI) only by two additional methylene groups. The position of these methylene groups has been established by oxidation of 'dihydroapomonascorubramine' (in which the double bond of the propenyl group has been saturated) with potassium permanganate and isolation of the aliphatic carboxylic acids by steam distillation. Separation of these acids as their ammonium salts on paper gave two spots having $\underline{R_f}$ values of hexanoic and octanoic acids respectively. Thus '<u>O</u>-methylapomonascorubramine' appears to be a mixture of compounds (VI) and (VIII) and hence 'monascorubrin' as isolated by us is a mixture of rubropunctatin (I) and (III) now called monascorubrin. Although

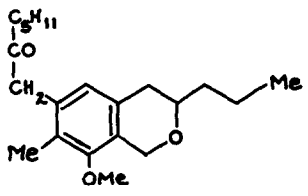
the Japanese workers[4] do not state that their monascorubrin is a mixture this seems likely since the melting point of their substance is identical with that of ours.

The formula (III) for monascorubrin, unlike formula (IV) is in complete agreement with the biogenesis of rubropunctatin recently suggested.[1]

It should be noted that structure (I) for rubropunctatin is derived from the structure (V) for aporubropunctatamine. The evidence previously presented[1] for this structure did not completely exclude other possibilities, but we have now shown that there is an unsubstituted position para to the phenolic hydroxyl group and hence, that aporubropunctatamine is correctly represented by structure (V). Thus, the alcohol (IX) derived from O-methyl-aporubropunctatamine was treated with methyl iodide to give the methiodide, m.p. 118-120° (decomp.) (Found: C, 55.8; H, 7.1; N, 2.9. $C_{22}H_{32}O_2NI$ requires C, 56.3; H, 6.9; N, 3.0%). Oxidation of this with alkaline potassium permanganate gave anisole-2:3:5:6-tetracarboxylic acid, characterised as the tetramethyl ester. The same acid has also been isolated by similar oxidation of O-methylhexahydroaporubropunctatin (X).



IX



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