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Fungus Pigments. XXIV*. Peniolactol Obtained from Wood Attacked by the Fungus *Peniophora sanguinea* Bres.

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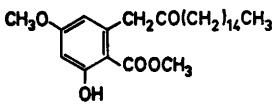
On the basis of spectral analysis, the structure 3,4-dihydro-3,6,8-trihydroxy-3-pentadecyl-1*H*-2-benzopyran-1-one (*1b*) is assigned to peniolactol.

In a paper describing the isolation of the pigment peniosanguin methyl ether from the extract of wood attacked by the fungus *Peniophora sanguinea* Bres.[1], it was noted that the pigment was accompanied by a colourless compound.

The structure *1*, which can exist in the two tautomeric forms *a* and *b*, is now proposed for this colourless compound which has been termed peniolactol. This structure proposal is based on the spectral properties of the compound and its derivatives, as outlined below.



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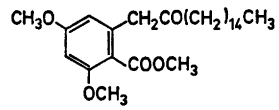

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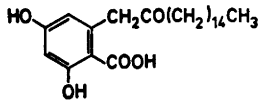
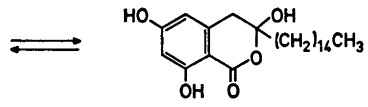
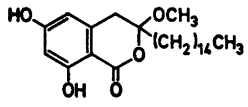


1a



1b



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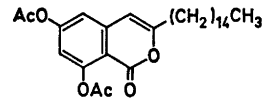

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Peniolactol has the composition $C_{24}H_{38}O_5$. In the mass spectrum only a very weak peak is found at *m/e* 406, corresponding to this molecular formula. There are instead two strong peaks at *m/e* 388 and 362, formed by loss of water and carbon dioxide, respectively. The base peak of the spectrum is at *m/e* 239, corresponding to $C_{15}H_{31}CO$.

Methylation of peniolactol with diazomethane gives a dimethyl derivative (*2*), and methylation with dimethyl sulphate and potassium carbonate of either peniolactol or its dimethyl derivative gives a trimethyl derivative (*3*).

IR-absorptions at 1654 and 1712 cm^{-1} in *2*

* Part XXIII, *Tetrahedron Lett.* (1974) 619.

and at 1712 and 1720 cm^{-1} in *3* show the presence of two carbonyl groups, one of which is an unconjugated aliphatic keto group and the other an aromatic methyl ester which is strongly chelated in *2*. Peniolactol shows only one carbonyl absorption at 1640 cm^{-1}, the aliphatic keto group being masked by lactol formation as indicated in *1b*. This requires that the aliphatic keto group is situated in a side chain *ortho* to the carboxyl group and the latter therefore lies between the aliphatic side chain and one phenolic hydroxyl. The position of the second phenolic hydroxyl in the *para*-position to the carboxyl group may be deduced from the NMR spectra of *2* and *3*, which show the presence of two *meta*-coupled aromatic protons. These NMR spectra also contain the expected two proton singlet for a methylene group between an aromatic ring and a carbonyl group.[2-4]

The structures of *2* and *3* are also supported by their UV spectra. Thus the spectrum of *2* is almost identical with that of ethyl 2-acetonyl-4-benzyloxy-6-hydroxybenzoate [2] and the mono- and diethyl esters of α-carboxy-6-hydroxy-4-methoxy-*o*-toluic acid.[5] Similarly that of *3* is almost identical with the spectrum of α-carboxy-4,6-dimethoxy-*o*-toluic acid.[6]

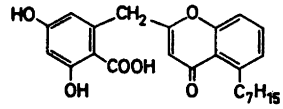
Esterification of peniolactol with methanol and sulphuric acid gives a monomethyl derivative, which must be the pseudo-ester *4*, because there is no absorption due to the aliphatic carbonyl group in its IR spectrum.

Acetylation of peniolactol gives an anhydrodiacetate (*5*). This structure is supported by the absence of the NMR signal due to the methylene group and the appearance of a one proton singlet at δ 6.09.

The NMR spectra of all the derivatives of peniolactol contain, in addition to the signals from the groups directly attached to the aromatic ring (discussed above), a very strong and somewhat broadend singlet at $\delta \sim 1.27$ which is accompanied by a three proton distorted triplet on the high field side and a two proton ill defined triplet on the low field side. This part of the spectrum is very similar to that of straight chain aliphatic acids and ketones, indicating that the group $-(CH_2)_{14}CH_3$ in the structures above is indeed the normal one.

As mentioned above, the IR spectrum indicates that, at least in the crystalline state, peniolactol exists in the lactol form *1b*. The position of this equilibrium in *o*-(2-oxoalkyl)-benzoic acids appears to depend to some extent on the substitution of the aromatic ring, although there seems also to be some confusion in the literature in this respect. Thus Buckley, Ritchie and Taylor [7] have made an extensive study of the unsubstituted 2-acetonylbenzoic acid and they conclude, on the basis of the IR spectrum in different media, that the equilibrium lies far towards the open chain form. In derivatives with a hydroxy or methoxy group in the 6-position,[2,8-10] there is no IR absorption that can be ascribed to the unconjugated carbonyl group as in peniolactol. They should therefore be regarded as existing in the lactol form, although some workers [2,10] still depict them as the open chain tautomers.

Peniolactol is evidently acetate derived and a number of compounds of analogous structure, but with a shorter aliphatic sidechain, have been isolated from fungi.[3,10,11-18] They are sometimes in a different state of oxidation or are ring closed to an isocoumarin or to a macrocyclic lactone. A number of depsides and depsidones [19] also belong to the same type of structure and a particularly interesting compound in this connection is siphulin (*6*),



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which has been isolated from the lichen *Siphula ceratites* [6] and has the same number of carbon atoms as peniolactol.

Since the extract from which peniolactol was isolated was obtained from decaying wood coloured red by the mycel of *Peniophora sanguinea* the question arises whether or not peniolactol is produced by *Peniophora sanguinea* or by some other fungus present in the decaying wood. The possibility that peniolactol is not a fungus product at all but a constituent of the wood, appears to be very improbable. In view of the very large amount of work which has been carried out on wood extracts it seems very unlikely that peniolactol, which is a nicely crystalline compound, should have been overlooked.

The presence of peniolactol in an extract can

easily be detected on TLC plates by spraying the plate with bis-diazotised benzidine. Examination of extracts obtained from different parts of the same piece of decaying wood revealed that peniolactol was never detected in those extracts obtained from non-coloured parts of the wood, whereas its presence could always be demonstrated in extracts which also contained the pigments. Furthermore, in a few fortunate cases it was possible to isolate the mycel of *Peniophora sanguinea*, seemingly free from contaminants, and in these cases the extract always contained peniolactol. It may therefore be concluded that peniolactol is indeed produced by *Peniophora sanguinea*.

EXPERIMENTAL

Melting points were determined by means of a Kofler melting point microscope and are uncorrected. Spectra were obtained using the following instruments: UV spectra on a Beckman DK-2, IR spectra on a PE 125, NMR spectra on a Varian A 60 and mass spectra on a PE 270B. Elemental analyses were carried out by Ilse Beetz, Mikroanalytisches Laboratorium, Kronach, German Federal Republic.

Isolation of peniolactol. The crude peniosanguin methyl ether [1] was dissolved in pyridine to which solution water was added until precipitation occurred. The peniosanguin methyl ether thus obtained was separated and more water was added to the mother liquor causing the precipitation of peniolactol. Further reprecipitation from pyridine gave peniolactol as slightly grey crystals. It melts at about 150 °C with decomposition. (Found: C 71.45; H 8.75, $C_{24}H_{38}O_5$ requires C 70.90; H 9.42) Mass spectrum: *m/e* 388, 362, 239, 205, 192, 150, 123. IR maxima: 3480, 2920, 2850, 1640, 1615 cm^{-1}. UV spectrum (EtOH): λ_{max} 214(4.44), 246(3.92), 264(4.02), 299(3.76); λ_{min} 240(3.82), 250(3.89), 286(3.68) nm (log ε).

Methyl 2-hydroxy-4-methoxy-6-(2-oxoheptadecyl)benzoate (2). Peniolactol (50 mg) dissolved in ether was treated with an excess of diazomethane. After standing over night the ether was evaporated and the residue purified by preparative TLC. Yield 35 mg, m.p. 96 – 97 °C (Found: C 71.54, H 9.42; $C_{26}H_{42}O_5$ requires C 71.85, H 9.74), Mass spectrum: *m/e* 434(M^+), 402, 239, 219, 206, 196, 164. IR maxima: 2920, 2850, 1712, 1654, 1620 cm^{-1}. UV spectrum (EtOH): λ_{max} 214(4.40), 263(4.13), 302(3.79); λ_{min} 239(3.60), 282 (3.55) nm (log ε). NMR spectrum ($CDCl_3$): δ 0.89 (3 H, br tr), 1,28(26 H, s), 2.41(2 H, br tr), 3.81(3 H, s), 3.82(3 H, s), 3.90(2 H, s), 6.23 (1 H, d; $J = 2.5$ Hz), 6.43 (1 H, d; $J = 2.5$ Hz), 11.62(1H, s).

Methyl 2,4-dimethoxy-6-(2-oxoheptadecyl)benzoate (3). Peniolactol (30 mg) dissolved in acetone was stirred for 8 h at room temperature with potassium carbonate (0.5 g) and dimethyl sulphate (0.2 ml). After filtration, addition of water and removal of the acetone under vacuum, a white precipitate was obtained which was purified by preparative TLC and recrystallisation from methanol. M.p. 71 – 72 °C. The same compound was also obtained when (*2*) was treated in the same way. (Found: C 72.30, H 9.22. $C_{27}H_{44}O_5$ requires C 72.28;, H 9.89). Mass spectrum: *m/e* 448(M^+), 416, 233, 220, 210, 196, 179, 178. IR maxima: 2920, 2850, 1720, 1712 1604 cm^{-1}. UV spectrum(EtOH): λ_{max} 250(3.81), 286(3.56); λ_{min} 239(3.77), 271 (3.41) nm (log ε). NMR spectrum ($CDCl_3$): δ 0.90(3 H, br tr), 1.27(26 H, s), 2.45(2 H, br tr), 3.67(2 H, s), 3.80(6 H, s), 3.82 (3H, s), 6.32(1 H, d; $J = 2$ Hz), 6.42(1 H, d; $J = 2$ Hz).

3,4-Dihydro-6,8-dihydroxy-3-methoxy-3-pentadecyl-1H-2-benzopyran-1-one (4). Peniolactol (40 mg) was refluxed for 8 h in methanol containing two drops of conc. sulphuric acid. Water was then added and the methanol removed under vacuum. Extraction with ether and recrystallisation from light petroleum gave (*4*). M.p. 92 – 93 °C (Found: C 71.35, H 9.74. $C_{25}H_{40}O_5$ requires C 71.39, H 9.59). IR maxima: 3250, 2910, 2850, 1660, 1615 cm^{-1}. UV spectrum (EtOH): λ_{max} 214(4.35), 230(infl.; 4.16), 246 (3.86), 270(4.15), 302(3.87); λ_{min} 242(3.80), 249(3.83), 291(3.84) nm (log ε). NMR spectrum ($CDCl_3$): δ 0.90(3 H, br tr), 1.28(26 H, s), 2.00(2 H, br tr), 3.08(2 H, br s), 3.38(3 H, s), 6.22(1 H, d; $J = 2.5$ Hz), 6.34(1 H, d; $J = 2,5$ Hz), 11.12(1 H, br s; exch. with D_2O).

6,8-Diacetoxy-3-pentadecyl-1H-2-benzopyran-1-one (5). Peniolactol dissolved in acetic anhydride containing a drop of pyridine was kept over night at room temperature. The anhydroacetate was precipitated with water and purified by preparative TLC. M.p. 86 – 87 °C. (Found: 70.96, H 8.38. $C_{28}H_{40}O_6$ requires C 71.16, H 8.53). Mass spectrum: *m/e* 472(M^+), 430, 388, 205, 192, 177, 163. IR maxima: 2950, 2880, 1770, 1730, 1660 cm^{-1}. UV spectrum(dioxan): λ_{max} 237(4.56), 243(infl.; 4.47), 262(3.95), 270 (4.00), 280(3.91), 323(3.67); λ_{min} 257(3.91), 264(3.94), 276(3.86), 292(3.13) nm (log ε). NMR spectrum(CCl_4): δ 0.89(3 H, br tr), 1.24(26 H, s), 2.27(3 H, s), 2.33(3 H, s), 2.20 – 2.30(2 H, m), 6.09(1 H, s), 6.77(1 H, d; $J = 3$ Hz), 6.95(1 H, d; $J = 3$ Hz).

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