Tetrahedron Letters No.29, pp. 2457-2460, 1969. Pergamon Press. Printed in Great Britain.

THE STRUCTURE OF THE TRIPRENYL PHENOL DERIVATIVES BIOSYNTHETICALLY RELATED TO SICCANIN

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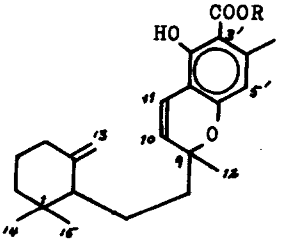
(Received in Japan 2 May 1969; received in UK for publication 14 May 1969)

Previously, we reported the structure of siccanin (1) and siccanochromenes (2) which were isolated from the cultured broth of the plant pathogenic fungi, Helminthosporium siccans Drechsler.

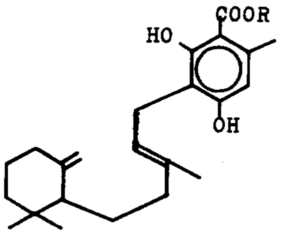
We here report the isolation of the additional triprenyl phenol derivatives I, II (R=H) and III which were thought to be biosynthetic intermediates of siccanin and siccanochromenes.

When the above mentioned fungi was grown in a medium containing 2-^{14}C-mevalonic acid lactone, it was observed that considerable radioactivity was transfered into carboxylic acid fraction (4% of the total activity). The total crude acidic fraction was esterified with diazomethane and chromatographed on silica gel to afford two ester derivatives, methyl siccanochromenate (I, R=Me) and methyl presiccanochromenate (II, R=Me).

Methyl siccanochromenate (I, R=Me), $C_{24}H_{32}O_4$ (M^+, 384, base peak at 233) showed uv absorption maxima (3) at 256, 262, 293 and 330 nm (ε, 22000, 23000, 3150 and 2040); ir bands at 1654 and 1166 cm^{-1} which indicate the presence of a methoxycarbonyl group on the aromatic ring (4). The nmr spectrum of I (R=Me) was similar to that of siccanochromene-A (2) except for the presence of only one aromatic proton and the low field shifts of the aromatic methyl and aromatic proton signals. The position of the methoxycarbonyl group at $C_{3'}$ was deduced from the chemical shift of the phenolic proton at very low field by hydrogen bonding (11.53). Decarboxylation of I with methanolic KOH yielded afore-mentioned siccanochromene-A (2).



I



II

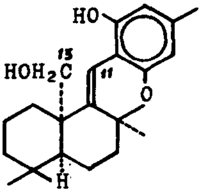
Methyl presiccanochromenate (II, R=Me), $C_{24}H_{34}O_4$ (M^+, 386) showed uv absorption maxima at 223, 272 and 306 nm (ε, 19650, 11050 and 3330); ir bands at 3600, 3430, 1650, 1625 and 1582 cm^{-1}. The nmr spectrum of II (R=Me) exhibits the presence of the geminal dimethyls (0.84 and 0.91, 6H, s), an olefinic methyl (1.78, 3H, bs), which coupled with the olefinic proton at 5.23 (1H, t, t, J=7, 1 Hz), an aromatic methyl (2.38, 3H, s), benzylic protons (3.32, 2H, d, J=7 Hz), an ester methyl (3.85, 3H, s), an exocyclic methylene (4.44 and 4.68, 2H, d, J=2 Hz), an aromatic proton (6.10, 1H, s), a hydrogen bonded hydroxyl group (11.93, 1H, s), and a hydroxyl group (5.98, 1H, s).

Heating of II in methanolic alkali solution afforded the decarboxylated product, $C_{22}H_{32}O_2$, (M^+, 328); nmr; geminal dimethyls (0.81 and 0.89, 6H, s), an olefinic methyl (1.75, 3H, bs), an aromatic methyl (2.12, 3H, s), benzylic protons (3.27, 2H, d, J=7 Hz), an exocyclic methylene (4.44, 4.67, 2H, d, J=2 Hz), an olefinic proton (5.13, 1H, t, J=7 Hz) and aromatic protons (6.05, 2H, s). This compound was also found to occur in the metabolites of the fungi. Treatment of the compound II (R=Me) with DDQ in benzene solution (5) yielded quantitatively methyl siccanochromenate I (R=Me) as a diastereomeric mixture, whose nmr spectrum exhibits two pairs of signals at 5.30 and 5.34 due to the C_{10} proton in a ratio of 1:1.

On the basis of the above data, the structure of II was assigned as presiccanochromenic acid. The geometry of the trisubstituted olefinic linkage of II was suggested to be trans by the measurement of NOE of C_{10} proton signal (only ca. 8% increase by the irradiation of C_{12} methyl signal, comparing ca. 27% increase of $C_{5'}$ proton signal by the irradiation of aromatic methyl signal under the same conditions), and confirmed by an independent synthesis (6).

Among the other minor metabolites, a new siccanochromene derivative named siccanochromene-E, which possesses longer uv absorption maxima of 2.5-5 nm than those of other siccanochromene derivatives, has been isolated. The structure of siccanochromene-E was assigned as III on the following physicochemical properties and chemical interrelation.

Siccanochromene-E(III), $C_{22}H_{30}O_3$, m.p., 191-2°, $[\alpha]_D^{19°}$ -86° (EtOH), M^+, 342 (intense peak at 327 (M-15), 311 (M-31)), λ_{max}^{EtOH} 233.6, 287 and 293 nm (ε, 26000, 13900 and 14100), gave diacetate, $C_{26}H_{34}O_5$ (M^+, 426) on acetylation. The nmr spectrum of III exhibits four methyl signals at 0.94, 1.01 (6H, s, gem.-dimethyls), 1.39 (3H, s, C_9-Me) and 2.18 (aromatic Me) and C_{13}-methylene signals at 3.25 and 3.80 (2H, ABq, J=11 Hz) which shift to low field upon acetylation. The signal at 6.59 (1H, s) can be assigned to the olefinic proton of C_{11} position, and this signal shifts to high field by 0.38 ppm on acetylation.



III

The structure and stereochemistry of III was confirmed by the chemical correlation with siccanin. Treatment of siccanin with boron trifluoride in acetic anhydride yielded two products. one of which was found to be identical with natural siccanochromene-E diacetate.(6)

The biosynthetic relationship and intermediary role of these compounds on siccanin biosynthesis are now under investigation.

Acknowledgement: The authors are grateful to Professor S. Okuda for his lively interest, to Dr. G. Sunagawa, Director of Sankyo Central Research Laboratories for fermentation materials of H. siccans, and to Mr. H. Kuwano for measurement of NOE. Thanks also due to Mr. Masami Goi for his technical assistance.

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3) Uv was measured in EtOH, nmr(δ) in CCl_4, ir in $CHCl_3$ solution unless otherwise mentioned.

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