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THE ISOLATION AND THE STRUCTURE OF SICCANOCHROMENES

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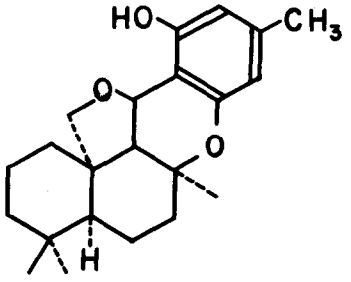
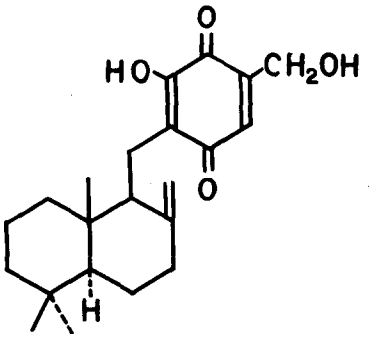
Previously we reported the structure of siccanin (I)[1], a physiologically active compound isolated from the cultured broth of Helminthosporium siccans Drechsler, which is a parasitic organism of rye-grass, Lolium multifolium Lam[2]. Siccanin has a unique structure in which the sesquiterpene portion——drimane skeleton——attached to the orcinol ring has a cis-syn-cis ring junction. Comparing this stereochemistry with that of tauranin (II)[3], which possesses an A/B trans ring juncture, we have been interested in the mechanism of cyclization of the acyclic precursors during the biosynthesis of siccanin.



I



II

In order to seek the biogenetical intermediates or related compounds of siccanin, the screening of the prenylphenols by autoradiography on thin layer chromatograms and by color reactions with diazonium salt solutions was attempted. Seven prenylphenols in the extract from Helminthosporium siccans were effectively screened by this method and were separated by preparative layer or column chromatography.

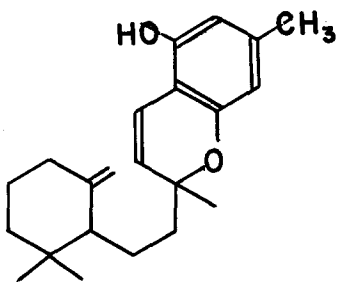
We here report the isolation of four new chromene derivatives which have been named siccanochromene-A, -B, -C, and -D. All these compounds resist crystallization; however, their homogeneity was confirmed by GLC, TLC, and nmr or mass spectroscopy.

Siccanochromene-A (r.t., 6.1)[4a], $C_{22}H_{30}O_2$[5] (M^+, 326), $[\alpha]_D^{9°}$ +68.8° (EtOH) showed characteristic ultraviolet absorption maxima[6] at 229.5 mμ (ε, 25,700), 278.5 mμ (ε, 9,320) and 286.5 mμ (ε, 8,700) in EtOH. The presence of the chromene chromophore was suggested from these data and from the infrared spectrum ($\nu_{max}^{CHCl_3}$ 1630, 1580 cm^{-1}). The nmr spectrum of siccanochromene-A (III) indicated the presence of a geminal dimethyl group (0.84 and 0.92, 6H)[7], a methyl α to an oxygen atom (1.26, 3H), an aromatic methyl group (2.17, 3H), an exocyclic methylene group (4.71, 4.48, 2H, d, J=2 cps), protons on a phenyl-conjugated disubstituted double bond (AB pattern at 6.55, 5.31, 2H, J=11 cps) and two aromatic protons (6.10, 6.96, 2H, J=1.5 cps). Hydrogenation of siccanochromene-A with Pd/C in EtOH afforded a dihydro derivative (VI), (r.t., 6.9), $C_{22}H_{32}O_2$ (M^+, 328). The signals due to the chromene double bond disappeared in the nmr spectrum of VI. The significant diamagnetic shift of the α proton of the chromene double bond (35 cps) upon acetylation of the phenolic hydroxyl group of III supports the substitution pattern of the aromatic ring[8]. On the basis of the above spectral properties as well as from biogenetical considerations, it was possible to postulate structure III for siccanochromene-A.

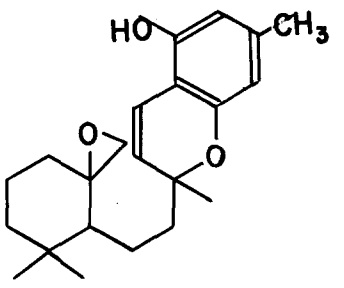
Siccanochromene-B (IV) (r.t., 15.0), $C_{22}H_{30}O_3$ (M^+, 342), $[\alpha]_D^{8.5}$ +121° (EtOH) showed an ultraviolet spectrum essentially the same as that of siccanochromene-A. The nmr spectrum of IV showed signals at 2.36 and 2.53 (2H, AB pattern, J=5 cps) due to the methylene protons of the oxirane ring instead of the exocyclic methylene protons of III. The nmr peaks are at 0.82, 1.04 (geminal dimethyl, 6H), 1.29 (methyl α to an oxygen atom, 3H), 2.16 (aromatic methyl, 3H), 6.55, 5.33 (protons on a disubstituted double bond, AB pattern, 2H, J=11 cps), 5.97, 6.08 (aromatic protons, 2H, J=1.5 cps).

Reduction of IV with lithium aluminum hydride led to a tertiary alcohol (V), (r.t., 13.3), $C_{22}H_{32}O_3$ (M^+, 344), $[\alpha]_D^{19}$ +115° (EtOH). The nmr spectrum of V showed a new signal at 1.32 (3H, singlet). Treatment of V with thionyl chloride in pyridine gave siccanochromene-A in 80% yield. This result indicates the

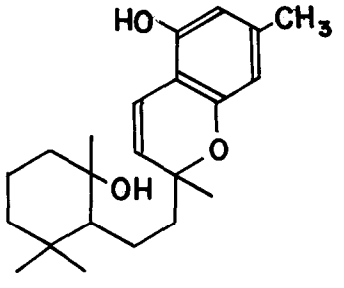
stereochemistry of oxirane in which the C-O bond occupies an equatorial position.



III

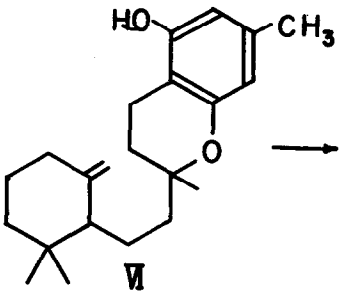


IV

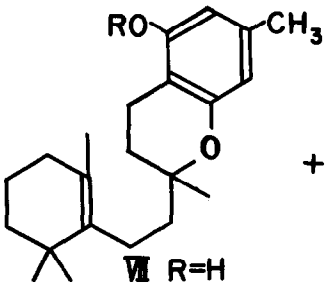


V

Treatment of dihydrosiccanochromene-A (VI) with stannic chloride in benzene yielded the isomerized chromane derivatives VII and VIII in the ratio of 9:1, which proved separable by silver nitrate-silica gel column chromatography of their acetates (IX and X). Compound VII was synthesized from dihydro-α-ionone via compound XI[9], and the identity of the naturally derived compound and the synthesized one was confirmed.

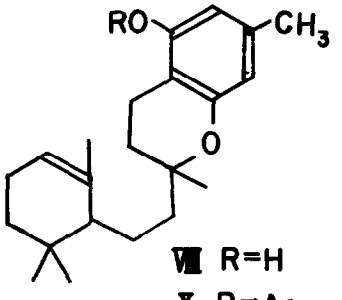


VI

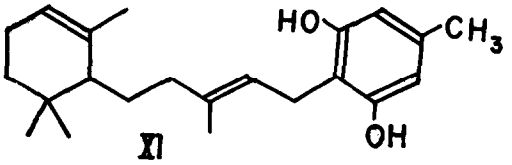


VII R=H
IX R=Ac

+



VIII R=H
X R=Ac



XI

The structure of siccanochromene-C, (r.t., 12.2)[4b], $C_{22}H_{30}O_3$ (M^+, 342) and siccanochromene-D, (r.t., 13.2)[4b], $C_{22}H_{32}O_3$ (M^+, 344) and the stereochemistry of these compounds are under investigation. We are also studying the biosynthetic pathway of siccanin and siccanochromenes.

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References

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2) K. Ishibashi, J. Antibiotics, Ser A 15, 161 (1962).

3) K. Kakisawa, K. Nakanishi, and H. Nishikawa, Chem. Pharm. Bull., Japan, 12, 796 (1964).

4a) R.t. indicates retention time on the 1.5% OV-17 on chromsorb W 100/120 (150cm x 4mm. i.d., N_2 flow rate 73 ml./min., column temp. 229°C) unless otherwise mentioned.

4b) R.t. indicates retention time on the 1.0% XE-60 on chromsorb W 100/120 (150cm x 4mm. i.d., N_2 flow rate 58 ml./min., column temp. 225°C).

5) Satisfactory elemental analyses were obtained for all compounds.

6) Y. Gaoni and R. Mechoulam, Chem. Commun., 20 (1966).

7) All nmr spectra were measured in CCl_4 with a JEOL 100 Mc spectrometer. The signals are reported in δvalue from TMS as internal standard.

8) A. Arnone, G. Cardillo, L. Merlini and R. Mondelli, Tetrahedron Letters, 4201 (1967).

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