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THE SYNTHESES OF SICCANOCHROMENE-A AND THE RELATED COMPOUNDS

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Recently, we reported the structural elucidation of siccanochromene-A, -B (1) and presiccanochromenic acid (2), which were isolated from the cultured broth of the plant pathogenic fungi, Helminthosporium siccans Drechsler. We describe here the syntheses of the racemic siccanochromene-A (I), presiccanochromene-A (II) and episiccanochromene-B (X).

The keto ester III, prepared by the reported procedure (3) was converted into the ethylene ketal IV. The ketal IV was treated with methylsulfinyl carbanion in dimethyl sulfoxide to afford β-keto sulfoxide which was successively treated with aluminum amalgam in aqueous tetrahydrofuran (4). Condensation of the resulting keto ester V with ethyl diethylphosphonoacetate and sodium hydride in dimethyl sulfoxide gave αβ-unsaturated ester VI as a separable mixture of cis-trans geometrical isomers in a ratio of 1 : 3. The mixture of the ester VI was converted into the corresponding aldehyde VII by lithium aluminum hydride reduction followed by active manganese dioxide oxidation. The aldehyde VII, $C_{16}H_{26}O_3$, showed uv absorption maximum at 238 nm, ir bands at 2730, 1680 and 1630 cm^{-1}, and nmr signals at 0.87, 0.94 (6H, s, gem-dimethyls), 2.15 (3H, s, methyl on a double bond), 3.86 (4H, methylenes α to an oxygen), 5.77 and 10.0 (1H, 1H, d, J=7 Hz, αβ-unsaturated aldehyde). The olefinic methyl and aldehydric proton signals of the cis isomer appear at δ1.94 and 9.90 respectively.

Condensation of the unsaturated aldehyde VII with lithium salt of orcinol bistetrahydropyranyl ether (5) at room temperature afforded benzylalcohol derivative

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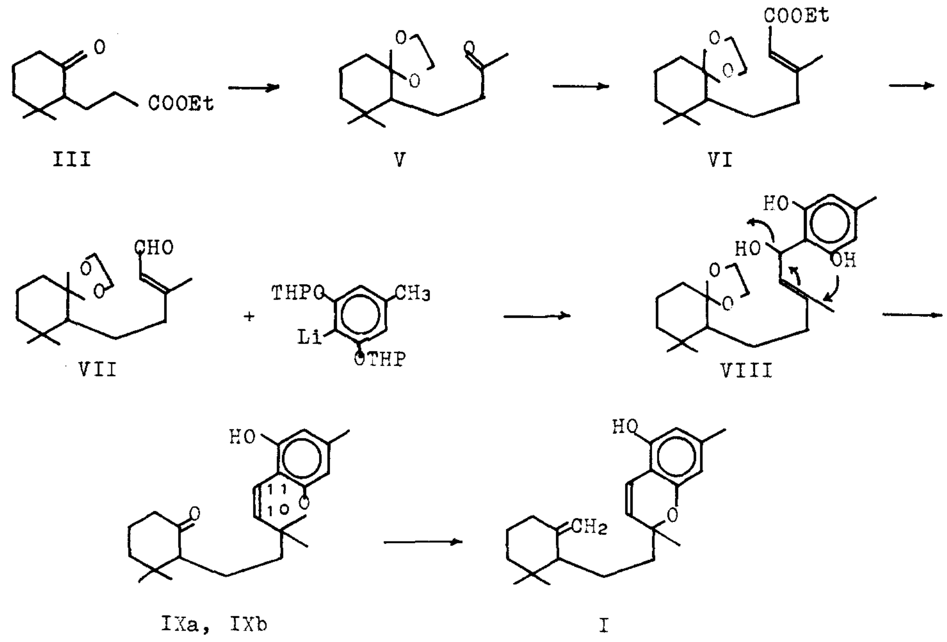
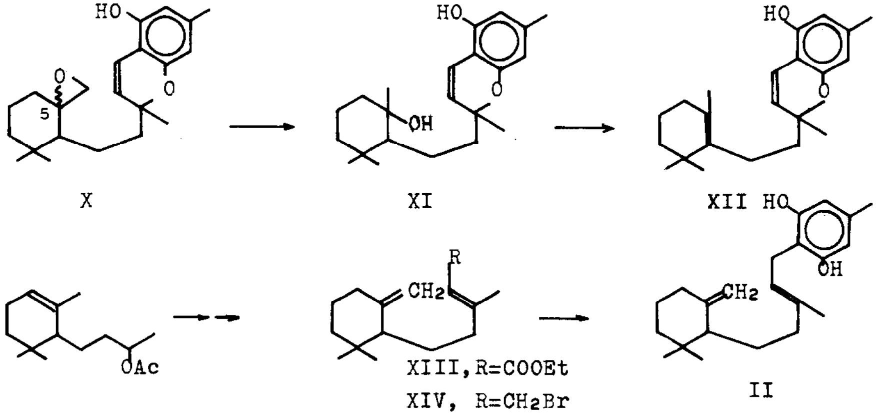
VIII. The mild acid treatment of VIII with oxalic acid in aqueous tetrahydrofuran gave chromene IX as a 1 : 1 diastereomeric mixture. The keto chromene IX, $C_{21}H_{28}O_3$ (M^+, 328) exhibits uv absorption maxima at 229, 278 and 284.5 nm (ε, 22000, 8100 and shoulder) and ir bands at 1710, 1630 and 1580 cm^{-1}. Extensive chromatographic separations of the diastereomeric mixture of IX were carried out through silica gel column to yield isomers IXa and IXb, both of which showed almost identical nmr spectrum except for the signals due to the olefinic protons at C_{10} and C_{11}.



The isomer IXa showed these proton signals at δ5.40 and 6.63 and IXb at 5.30 and 6.57 (2H, ABq, J=10 Hz). The methylenation of IXa with methylenetriphenyl phosphorane afforded siccanochromene-A (I) (6), identical with natural substance in vpc, tlc, nmr, ir, uv and mass spectrum. The same treatment of IXb yielded diastereoisomer of I, which exhibits nmr signals at δ5.35 and 6.57 (2H, ABq, J=10 Hz) instead of the corresponding signals at δ5.31 and 6.57 in the natural compound.

Treatment of the acetate of keto chromene IXa with dimethylsulfonium methylide (7) in dimethyl sulfoxide gave the oxyrane derivative X, $C_{22}H_{30}O_3$, (M^+, 342), λmax; 231 and 281 nm (ε, 25500, 6700); νmax; 1628, 1580, 3620 and 3400 cm^{-1}, nmr; δ2.42 and 2.52 (2H, ABq, J=5.0 Hz, oxyrane methylene). The compound X was found to be epimeric at C_5 with siccanochromene-B. The tertiary alcohol XI derived from X by lithium aluminum hydride reduction was dehydrated to give rise to a compound XII as a major product by treatment with thionyl chloride in pyridine, while, as previously reported, the tertiary alcohol derived from the natural siccanochromene-B gave I by the same treatment.



X XI XII

XIII, $R=COOEt$
XIV, $R=CH_2Br$

II

The unsaturated ester XIII (8) synthesized from dihydro-γ-ionone, which was prepared from dihydro-α-ionyl acetate by the photosentized isomerization (9) was converted into the bromide XIV by lithium aluminum hydride reduction followed by treatment with phosphorous tribromide. Condensation of the bromide XIV with the lithium salt of orcinol bistetrahydropyranyl ether in hexane followed by mild hydrolysis with oxalic acid gave the phenolic compound, which was found to be identical in all respects with the natural presiccanochromene-A (II) (2).

The biosynthetic studies of the antibiotic, siccanin (10) using isotope-labelled substrates, I and II are under investigations.

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