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THE STRUCTURE OF SICCANIN

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In a program of investigation on the metabolite of the plant pathogenic fungus in these laboratories, one of us (K.I) isolated a phenolic antibiotic named siccanin[1] from the cultured broth of Helminthosporium Siccans Drechsler, which is parasitic organism of rye-grass, Lolium multifilium Lam., and is moderately harmful to the foliage. Siccanin exhibits inhibitory activities against a variety of fungi, especially strong activity against Trichophyton interdigitale and T. asteroids at 0.1 mcg/ml.

Siccanin, $C_{22}H_{30}O_3$[2], M^+ at 342, m.p. 138°, $[\alpha]_D^{16}$-150° ($CHCl_3$, C=7.75) λ_{max}^{EtOH} 278 mu (sh.) and 285 mu (ε=1,800), $\nu_{max}^{CHCl_3}$ 3500, 1633, and 1575 cm^{-1}, contains phenolic structure. The n.m.r. spectrum[3] shows the signals at 0.80, 0.84 (6H, gem-dimethyls), 1.25 ($-O-C-CH_3$), 2.20 (aromatic methyl), 6.15 and 6.30 (aromatic protons), 3.46, 4.24 (2H, AB quartet, $-CH_2-O-$), 5.16 (1H, doublet, benzylic methine), 1.94 (methine) and at 6.57 (-OH).

We now report the complete molecular structure, stereochemistry and absolute configuration from a three dimentional X-ray diffraction study of the siccanin p-bromobenzenesulfonate ester, m.p. 156°, $C_{28}H_{33}O_5S$ Br. Crystals are orthorhombic. The space group is P $2_12_12_1$. There are four molecules in a cell of dimensions a=11.06Å, b=22.87Å, c=10.34Å.

Three dimentional intensity data were collected from the a- and c-axis by means of equi-inclination Weissenberg photographs. A total of 1537 reflections were estimated visually. The structure was solved by the heavy atom method with several Fourier and difference Fourier syntheses. The parameters were then refined by three cycles of full matrix least squares calculations to an R-value of 0.155[4]. The above results establish that the p-bromobenzenesulfonate has the structure shown in Fig.1, and it follows, therefore, that siccanin has structure I. The absolute configuration shown was determined by the anomalous dispersion effect of the bromine atom for Cu Kα radiation.

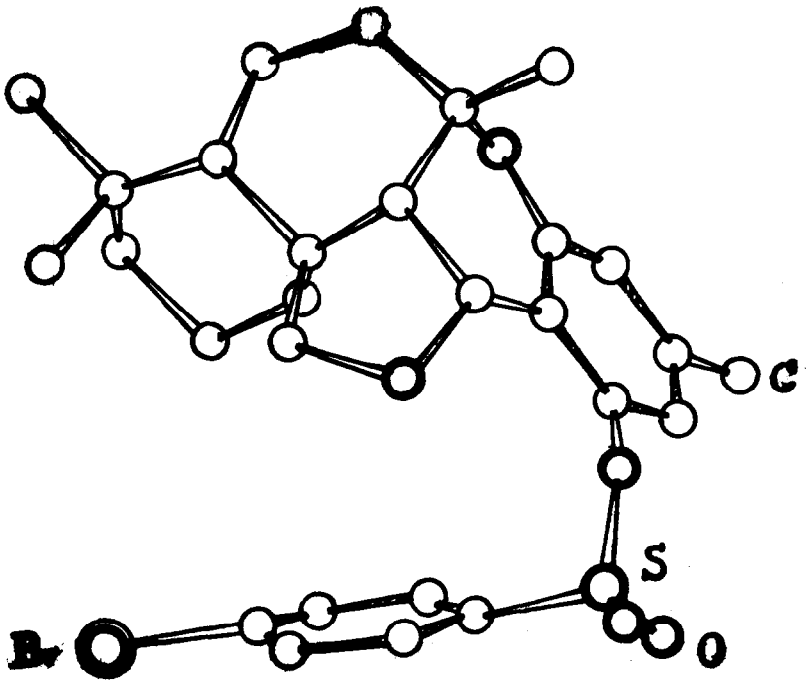
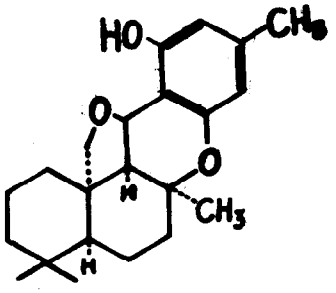
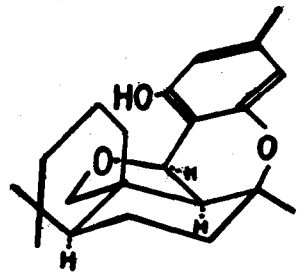


Fig. 1

The structure of siccanin can be derived biogenetically from farnesylpyrophosphate and orcinol (hence, orsellinic acid); however, this structure is unique in that it has <u>cis</u> fusion of decalin system which may be the first example of the naturally occuring drimane skeleton.





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Siccanin shows biogenetical and / or structural similarities with other natural products, tauranin[5] and griforin[6]. The synthesis of siccanin and the simpler analogues are now under investigation.

REFERENCES

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

2) The molecular formula was previously reported as $C_{30}H_{40}O_4$.

3) n.m.r. were measured at 100 Mc in $CDCl_3$. Shifts are expressed as δ-value.

4) Refinement is being continued and the full account of the analysis will be published elsewhere.

5) K. Kawashima, K. Nakanishi, H. Nishikawa, Chem. Pharm. Bull., Japan, 12 796 (1964)

6) T. Goto, H. Kakisawa, Y. Hirata, Tetrahedron 19 2079 (1963)