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10,11-OXIDOSQUALENE FROM SCLEROTINIA FRUCTICOLA

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In the course of our study on a sporulation-inducing substance of fungi, we have found that the mycelia of Sclerotinia fructicola[1] cultured under shaking in the dark produced a new metabolite. Although the metabolite had no biological activity, we determined its structure as 10,11-oxidosqualene (1) as described in this report.

The hexane soluble neutral extracts of the mycelia, upon chromatography on silica gel (elution with ethyl acetate in n-hexane) gave a fraction containing 1 as well as several known compounds such as squalene, ergosterol and 24-methylenedihydrolanosterol.[2] 1 was produced so poorly by this fungus that its substantial isolation in pure form could not be carried out. However when the eluate from the chromatography was subjected to GC-mass spectrometry,[3] 1 was detected as a single peak at Rt 19.8 min, and its mass spectrum (Fig. 1a) revealed that it has an interesting structure as follows. A high resolution mass spectrum established its molecular formula as $C_{30}H_{50}O$ (observed 426.3823; calcd. 426.3860). A series of fragment ions in two sets, one of which is those of m/e 357 [M - 69 ()], 289 [M - 137 ()] and 221 [M - 205 ()], and the other, m/e 69, 137 and 205, suggested it to be an acyclic isoprenoid having an oxygen atom, most probably oxidosqualene. When its mass spectrum was compared with that of 2,3-oxidosqualene (Fig. 1c), the both spectra were found to be quite similar to each other but different at the ion peak of m/e 153 which appeared only in the latter spectrum. With strong speculation that 1 is a regioisomer of 2,3-oxidosqualene, the remaining 6,7- and 10,11-isomers were synthesized from all trans-squalene upon epoxidation (m-chloroperbenzoic acid in CH_2Cl_2). The synthetic mixture was separated by preparative TLC (silica gel, 10% ethyl acetate in n-hexane) into 3 and a mixture of 1 and 2. The latter was further fractionated into each component by preparative TLC on $AgNO_3$-impregnated silica gel (30% ethyl acetate in benzene). As the structural differentiation between the purified products, 1 and 2, could not be achieved from their spectral analysis, they were converted by acid hydrolysis ($HClO_4$ in THF-H_2O) into respective diol derivative (4 and 5), whose structures were established by the characteristic ion peaks at m/e 195 and 177 in the mass spectrum of 4, and m/e 127 and 109 in that of 5. Thus, the metabolite (1) was shown in the mass spectra (Figure 1) to be identical with 10,11-oxidosqualene, but was significantly different from the 6,7-isomer. The synthetic specimens of oxidosqualenes, 1, 2 and 3, had Rf's 0.50, 0.65 and 0.42, respectively, on a $AgNO_3$-impregnated silica gel plate (30% ethyl acetate in benzene), and showed in their nmr spectra the methine proton signal of the oxirane ring at slightly different chemical shifts, δ 2.51, 2.49 and 2.48, respectively. The present finding that 10,11-oxidosqualene occurs naturally as a fungal metabolite may be interestin in relation to the important role of 2,3-oxidosqualene[4] already established in the terpenoid

biosynthesis.

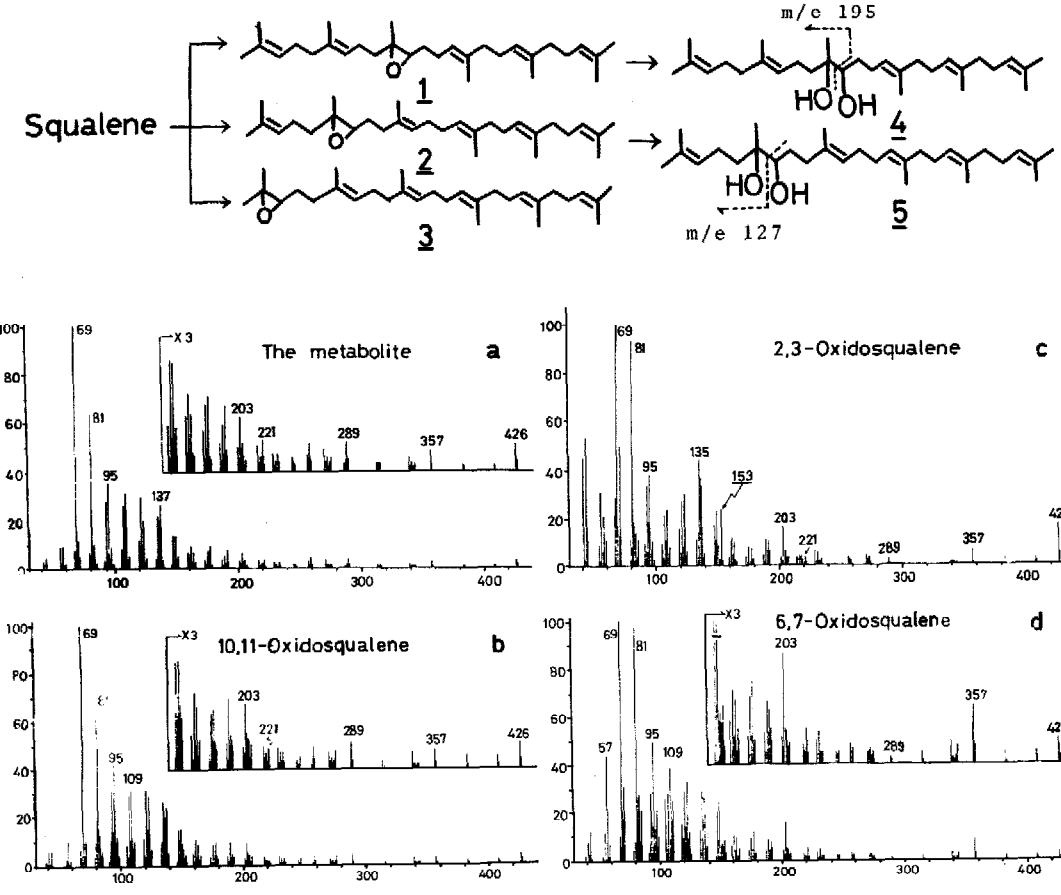

Figure 1. Mass Spectra of the Metabolite of S. fructicola and the Oxidosqualene Isomers.

References and Notes

1. The strain of S. fructicola was sent kindlily from Commonwealth Mycological Institute, England.
2. T. Kato, S. Tanaka, M. Ueda and Y. Kawase, Agric. Biol. Chem., 39, 169 (1975).
3. GC-mass analysis was performed using JEOL JMS-D 100 mass spectrometer interfaced with a column (2 mm 1 m) of 5% silicone OV-210 on 80/100 Gas Chrom Q, temperature 187°.
4. E. J. Corey, W. E. Russey, P. R. O. de Montellano, J. Am. Chem. Soc., 89, 4750 (.966); E. E. van Tamelen, J. D. Willet, R. B. Clayton and K. E. Lord, J. Am. Chem. Soc., 89, 4752 (1966).