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STRUCTURE OF TRICHODIENE

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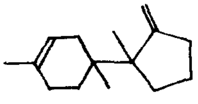
The naturally occuring esters of the group of sesquiterpenoids having the "trichothecene" nucleus[1], such as trichothecin[2], verrucarins and roridins[3], antibiotics isolated from *Trichothecium* and *Myrothecium* species fungi and the toxic substances[4] produced by *Fusarium* species fungi constitute an important class of the physiologically active terpenoids.

During the course of our investigations on the biosynthesis of the fungal isoprenoids, we have found that a strain of *Trichothecium roseum* produces a hydrocarbon possessing the structure **1** which has been assumed to be a biogenetic precursor of the afore-mentioned substances. We here describe the structural elucidation of the hydrocarbon, trichodiene, by a chemical correlation with a known compound.

Trichodiene, **1**, $C_{15}H_{24}$ (M^+ 204) $[\alpha]_D$ +21° ($CHCl_3$, c, 1.35) shows nmr signals[5] at δ0.85, (3H, s), 1.04 (3H, s), 1.63 (3H, bs), 5.23 (1H, m) and 4.71 and 4.92 (1H, each, bs), and ir absorption bands at 3065, 1645, and 890 cm^{-1} ($CHCl_3$), suggesting the presence of two tertiary methyl groups, an olefinic methyl group ($CH_3\text{-}\underset{|}{C}\text{=}CH\text{-}$) and an exocyclic methylene group. In the mass spectrum of **1**, the intense peaks occur at m/e 189, 161, 133, 121, 119, 109 (base peak, C_8H_{13}, **a**), 95 (C_7H_{11}, **b**), 93 and 67. Treatment of **1** with *m*-chloroperbenzoic acid afforded a monoepoxide, **2**, $C_{15}H_{24}O$, mass spec. m/e 220 (M^+), 125 ($C_8H_{13}O$, **a** + 16), 107, 96, and 95 (**b**); nmr (δ) 0.85, (3H, s), 1.02 (3H, s), 1.26 (3H, s), 2.76 (1H, d, J=5 Hz, a methine proton on an oxirane ring), 4.69 and 4.93 (2H, exocyclic methylene protons).



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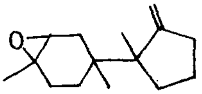

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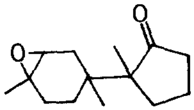

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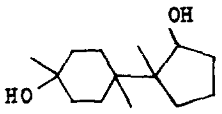

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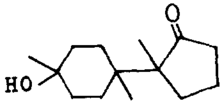

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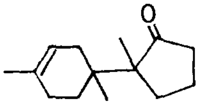

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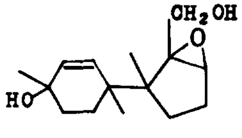
Ozonolysis of the epoxy-olefin 2 yielded a norketone, 3, $C_{14}H_{22}O_2$, mass spec. m/e 125, 107, and 98; nmr (δ), 0.89 (3H, s), 0.96 (3H, s), 1.23 (3H, s) and 2.74 (1H, t, J=2.5 Hz), which exhibits ir absorption due to a five membered ring ketone at 1732 cm^{-1}. Reduction of the norketone 3 with lithium aluminum hydride in ether afforded an epimeric mixture of diols, 4, $C_{14}H_{26}O_2$, which on Jones oxidation gave a ketoalcohol, 5, $C_{14}H_{24}O_2$, mass spec., m/e 224 (M^+), 206, 126, 125, 109 and 98; nmr (δ) 0.92 (3H, s), 0.97 (3H, s), 1.12 (3H, s): ir, νmax 3600, 1734 cm^{-1}. Treatment of 3 with sodium iodide, sodium acetate, and zinc in acetic acid yielded the compound 6, $C_{14}H_{22}O$, mass spec. m/e 108 (base peak), 98, 93, and 67; nmr (δ) 0.88 (3H, s), 0.98 (3H, s), 1.62 (3H, bs), and 5.20 (1H, m); ir νmax, 1735 cm^{-1}.

Since the data described above are compatible with the structure 1 for trichodiene, chemical interrelation of the compound 5 and trichodiol, 7^6), whose structure has already been established, was attempted.



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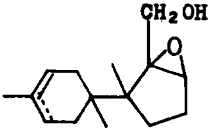

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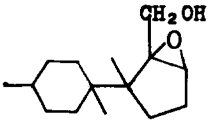

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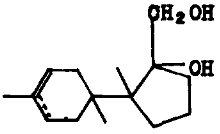

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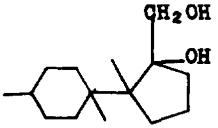

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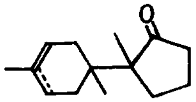

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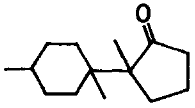

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Trichodiol 7 was hydrogenated over Pd/C with one mole of hydrogen, affording a mixture of compound 8 and the saturated derivative 9. Lithium aluminum hydride reduction of this mixture gave glycols 10, $C_{15}H_{26}O_2$, and 11, $C_{15}H_{28}O_2$, which on periodate oxidation yielded a mixture of norketones 12, $C_{14}H_{22}O$, mass spec., m/e 108, 98, and 93, and 13, $C_{14}H_{24}O$. The unsaturated and saturated norketones could be separated by means of silver nitrate impregnated silica gel column chromatography. It was found that the norketone 12 was a mixture of two double bond isomers, which might be formed by isomerization during hydrogenation. The mass and ir spectra of compound 12 were same with compound 6, but the nmr spectrum was slightly different in intensity, suggesting 6 is identical with one of the isomers of 12. Treatment of 12 with m-chloroperbenzoic acid afforded a mixture of two isomeric epoxides, whose nmr spectrum suggests that one of the isomers is identical with 3. Lithium aluminum hydride reduction of this compound followed by Jones oxidation gave a ketoalcohol, which was found to be identical in all respects (mass, nmr, ir spectra, and tlc, vpc behaviors) with the compound 5. From these results, the structure of trichodiene is establised as 1.

Preparation of the isotopically labelled trichodiene, 1, to follow metabolic fate of this hydrocarbon in a growing cell system of some *Trichothecium* and *Fusarium* species fungi are in progress.

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References

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