

ISOLATION AND STRUCTURE OF TRICHODIOL, A NEW SESQUITERPENOID

FROM Trichothesium roseum.

Shigeo Nozoe and Yoshimasa Machida

Institute of Applied Microbiology, University of Tokyo

Bunkyo-ku, Tokyo, Japan

(Received in Japan 4 February 1970; received in UK for publication 24 February 1970)

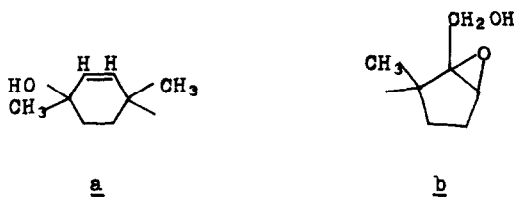
During the course of the investigations on the biosynthesis of fungal isoprenoids, trichodiol (1), a new sesquiterpenediol, was isolated from a certain strain of the Trichothesium species fungi. The evidence outlined below establishes the structure 1 for this compound.

Trichodiol, 1, m.p. 81-3°, $[\alpha]_D^{+52}$ (CHCl₃). C₁₅H₂₆O₃ (M-18 at m/e 234), ν_{\max} 3460 cm⁻¹, exhibits the nmr signals at δ 0.86 (3H, s), 0.96 (3H, s), 1.15 (3H, s) due to three tertiary methyl groups, 3.48, 4.06 (2H, ABq, J=12 Hz: -CH₂OH), 3.17 (1H, bs, methine on an oxirane ring) and at 5.46 and 6.73 (2H, ABq, J=10 Hz: -CH=CH-)¹. Acetylation of 1 gives a monoacetate, 2, C₁₇H₂₆O₄, (M⁺, 294), nmr(δ), 4.33 and 4.54 (2H, ABq, J=12 Hz: -CH₂OAc), which has ir absorption at 3600 cm⁻¹, indicating the presence of a tertiary hydroxyl group in both 1 and 2. The main feature of the mass spectrum of 1 is the fragmentation leading to two ions: fragment a, C₈H₁₃O (calcd. m/e 125.097, obsd. m/e 125.099), and fragment b, C₇H₁₁O₂ (calcd. m/e 127.076, obsd. m/e 127.074). Other prominent peaks appeared at m/e 107.088 (C₈H₁₁, a-H₂O), and m/e 108.094 (C₈H₁₂, a-OH, base peak), m/e 109.065 (C₇H₉O, b-H₂O) and at m/e 96.058 (C₈H₈O, b-CH₂OH). The mass spectrum of the acetate 2 shows peaks at m/e 125 (a) and at m/e 169 (b+CH₂CO), which indicates that the CH₂OH group exists in the b portion.

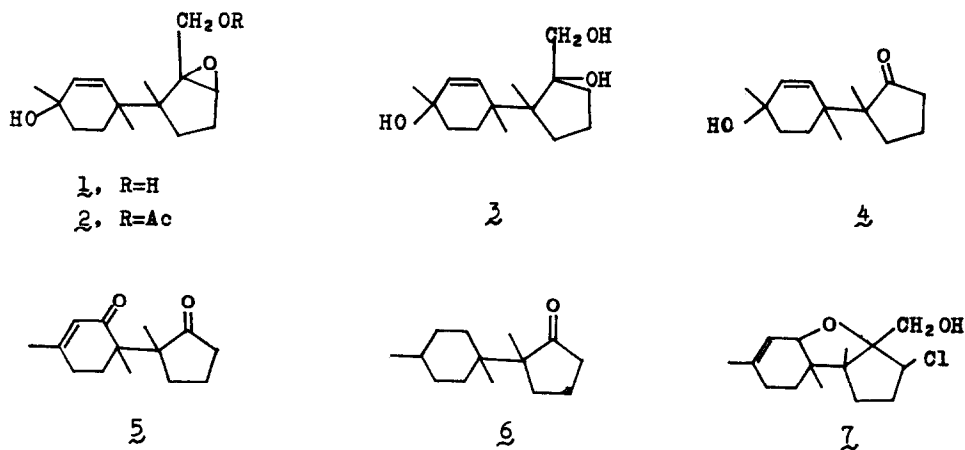
Treatment of 1 with lithium aluminum hydride reductively cleaves the oxirane ring, giving a triol, 3, C₁₅H₂₆O₃, mass spec., m/e 236 (M-H₂O), 125 (a), 107 (a-H₂O), nmr (δ), 0.88 (6H, s), 1.17 (3H, s), 3.35, 3.79 (2H, ABq, J=12 Hz) 5.48, 6.07 (2H, ABq, J=10 Hz). Oxidative cleavage of the triol 3 with

lead tetraacetate in benzene yields a norketone, 4, $C_{14}H_{22}O_2$, mass spec., m/e 222 (M^+), 125 (a), 107 (a- H_2O), nmr (δ), 0.92, 1.02, 1.17 (three methyl groups), 5.53 and 5.68 (2H, ABq: $-CH=CH-$), exhibiting an ir absorption band at 1732 cm^{-1} due to a five membered ring ketone. These facts indicate that fragment b contains a five membered ring, an oxirane ring and a primary hydroxyl group.

Jones' oxidation of the norketone 4 affords a diketone, 5, $C_{14}H_{20}O_2$, mass spec., m/e 220 (M^+), 124, 123 and 82 (base peak), uv, λ_{max} 237 nm (ϵ , 12, 600), ir, ν_{max} 1735 cm^{-1} (five membered ring ketone), 1665 cm^{-1} ($\alpha\beta$ -unsaturated ketone), showing the nmr signals at 0.97 (3H, s), 1.09 (3H, s), 1.89 (3H, bs: $CH_3 > C=CH-CO-$), and at 5.58 (1H, bs: $CH_3 > C=CH-CO-$). Formation of a β -methyl- $\alpha\beta$ -unsaturated carbonyl system upon oxidation of 4 suggests the presence of an allylic carbinol system such as $CH_3 > C(OH)-CH=CH-C-$ in compound 4. The position of the absorption band of the $\alpha\beta$ -unsaturated carbonyl group in 5 reveals that the ring existing in fragment a must be six membered, and hence two tertiary methyl substituents are in fragment a and one is in fragment b. Since both carbons linked directly to the double bond of 4 are quaternary (from nmr), it can be deduced that fragment a possesses partial structure shown below.



Compound 5, $C_{14}H_{24}O$, mass spec., m/e 208 (M^+), 111 (a+2H), 98, ir, ν_{max} 1732 cm^{-1} , nmr (δ), 0.90 (3H, s), 0.935 (3H, s), 0.905 (3H, d, $J=6\text{ Hz}$) obtained by hydrogenation of 4 (Pd/C) followed by lithium aluminum hydride reduction and successive periodate oxidation, shows in its nmr spectrum only two proton absorption in the field lower than 1.90 ppm, indicating that one of the carbons next to the carbonyl group is quaternary. This and the above data lead to the partial structure b for this moiety. Therefore, the structure of trichodiol is established as 1.



Treatment of $\underline{1}$ with hydrochloric acid affords compound $\underline{7}$, $C_{15}H_{23}O_2Cl$ (M^+ , 270), nmr (δ), 0.81 (3H, s), 1.03 (3H, s), 1.71 (3H, bs: $CH_3-C=CH-$), 3.64 3.79 (2H, ABq, $J=12$ Hz: CH_2OH), 3.64 (1H, bd, $J=5$ Hz: $-C=C-\underline{CH}-O-$), 4.20 (1H, t, $J=4$ Hz: $-CHCl$ in cyclopentane ring), and 5.44 (1H, bd, $J=5$ Hz: $-C=CH-$). This reaction indicates that the allyl carbinol system present in $\underline{1}$ is easily attacked by an intramolecular nucleophile and provides further support for the structure.

The studies on the biosynthesis of this compound in-connection with trichothecin and the related compounds are in progress.

The authors are grateful to Professor S. Okuda for providing them the strain of Trichothesium -6157 which was used for the present investigation, to Dr. Y. Nakayama, Nippon Kayaku Co., Ltd., for kindly supplying the fermentation materials, and to Mr. T. Kinoshita, Central Research Laboratories, Sankyo Co., Ltd., for measurement of high resolution mass spectrum. We also thank the Hohansha for its financial support of this work.

- All nmr spectra were measured in CCl_4 solutions and signals given in δ values.