Tetrahedron Letters No. 15, pp. 1293-1296, 1970. Pergamon Press. Printed in Great Britain.

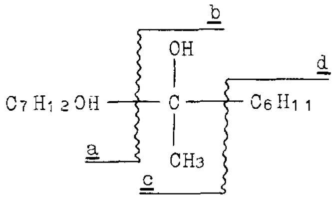
STRUCTURE OF CYCLONERODIOL

Shigeo Nozoe, Masami Goi, and Naoko Morisaki
Institute of Applied Microbiology, University of Tokyo
Bunkyo-ku, Tokyo

(Received in Japan 13 February 1970; received in UK for publication 3 March 1970)

During the course of the investigations on the biosynthesis of fungal isoprenoids, a new sesquiterpenediol, cyclonerodiol has been isolated from a certain strain of Trichothesium species fungi. We here report the structure of cyclonerodiol possessing a novel type of carbon skeleton in the field of sesquiterpenoids.

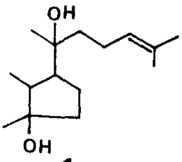
Cyclonerodiol **1**, $C_{15}H_{28}O_2$, mass peak at m/e 222 (M-18)1), $[\alpha]_D$ - 20° ($CHCl_3$), rrt., 0.76 2), shows nmr signals 3) for five methyl groups at 0.97 (d, J=7 Hz), 1.08 (s), 1.18 (s) 1.59 (bs) and 1.65 (bs) indicating that this compound might possess an unusual structural feature as a sesquiterpenic compound. The nmr spectrum of **1** shows an olefinic proton signal at 5.03 (bt, J=7 Hz). In the mass spectrum of **1**, fragmentation leading to the ions m/e (a) 113, 95 4) (b) 127, 109 4) (c) 157, 139, 121 and (d) 83 were observed. These fragmentation patterns indicate the electron impact cleavage of the C-C bond depicted in the following formula and the corresponding ions derived by loss of H_2O.

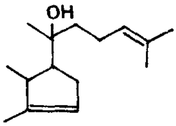


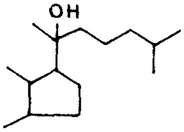
Heating **1** at 135° with phthalic anhydride gives a hydrocarbon, **2**, $C_{15}H_{24}$ (M^+, 204), which absorbs three moles of hydrogen to afford a saturated compound, **3**, $C_{15}H_{30}$ (M^+, 210). The second dehydration product **4**, $C_{15}H_{26}O$ (M^+, 222) shows new nmr signals at 1.67 (bs, 3H) and 5.14 (bt, 1H) due to a

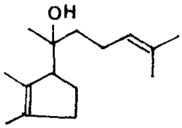
-C(CH_3)=CH- grouping. The prominent peaks in the mass spectrum of 4 are at m/e (a) 95, (b) 127, 109 (c) 139, 121 and (d) 83. Hydrogenation of 4 with two moles of hydrogen affords a saturated monoalcohol, 5, $C_{15}H_{30}O$ (M^+, 226), showing nmr signals of four secondary methyl groups at 0.86- 0.92 and a tertiary methyl at 1.07. The mass spectrum of 5 exhibits peaks at m/e (a) 97 (b) 129, 111 4) (c) 141, 123 4) and (d) 85, suggesting a ring must be in portion a. The main mass fragmentation of the third dehydration product 6 was very similar to that of 4, but four olefinic methyl signals occur at 1.60 and 1.67 in the nmr spectrum of 6.

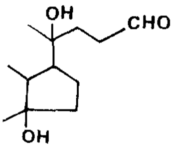
The spectroscopic properties described above indicate that the C_8-portion (b) must be a side chain possessing a tertiary methyl, a hydroxyl, and a double bond 5): the C_7-portion (a) must contain a hydroxyl, two methyl substituents, and hence, a five membered ring.

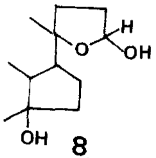

1

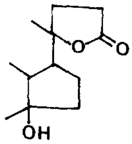

4

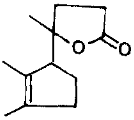

5

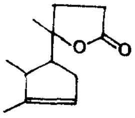

6


7


8

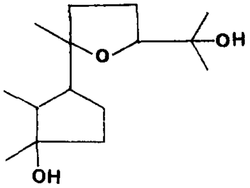

9


10

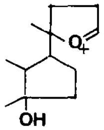

11

Ozonolysis of 1 yields a mixture of the trisnor compounds 7, 8, and 9. The mixture of the products shows an aldehydic proton signal at 9.15, a hemiacetal proton signal at 5.38 in the nmr spectrum and an absorption band at 1766 cm^{-1} in the ir spectrum. Treatment of the mixture with Jones' reagent in acetone gives a single product, **9**, m.p. 66-8°, $[\alpha]_D$ -52.5° ($CHCl_3$), $C_{12}H_{20}O_3$ (M^+, 212, intense peaks at m/e 99 and 95); nmr; 1.04 (d, J=7, 3H), 1.26 (s, 3H), and 1.39 (s, 3H), and 2.26 (m, 2H) exhibiting ir absorption at 1766 cm^{-1} (γ-lactone). Dehydration of the lactone **9** with thionyl chloride in pyridine affords compound **10**, $C_{12}H_{18}O_2$ (M^+, 194); nmr, 1.62, 1.63 (two olefinic methyls), and 1.28 (methyl on a lactone ring); ir, 1766 cm^{-1}. This finding indicates that two methyl groups on the five membered ring are adjacent. Heating of the lactone **9** at 130° with phthalic anhydride gives the lactone **11**, $C_{12}H_{18}O_2$ (M^+, 194); nmr, 1.62 (bs, 3H), 1.23 (d, J=7 Hz, 3H), and 5.13 (m, 1H); ir, 1766 cm^{-1} along with the afore-mentioned lactone **10** in a ratio of 7:3. The multiplicity of the signal of the trisubstituted olefinic proton at 5.13 of lactone **11** reveals the presence of an allylic methylene group in **11**. All of the experimental results mentioned support that cyclonerodiol possesses the planary structure **1**.

As a minor constituent of the metabolite, compound **12**, rrt, 1.20[2]; $C_{15}H_{28}O_3$[1], $[\alpha]_D$ -36.7° ($CHCl_3$), was also isolated from the same source. The nmr spectrum of **12** shows five methyl signals at 1.03 (d, J=7 Hz), 1.13 (s), 1.17 (s), 1.21 (s), 1.26 (s) and a methine proton at 3.74. The mass fragmentation leading to the ion m/e 197, 179, 143 (base peak), 113, 95 and 59 can be explained as shown below[6]. Oxidation of **12** with Jones' reagent[7] gives γ-lactone which was proved to be identical with **9**.



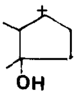
12



m/e 197

-H_2O

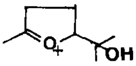
m/e 179



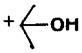
m/e 113

-H_2O

m/e 95



m/e 143



m/e 59

Acknowledgement: The authors are grateful to Professor S. Okuda for providing us the strain of *Trichothesium* sp. fungi which was used for the present investigation and to Dr. Y. Nakayama, Nippon Kayaku Co., Ltd., for kindly supplying fermentation materials.

References

1. The mass spectrum did not show the molecular ion peak, but gave (M-18) ion peak [4]. Satisfactory analytical data were obtained for this compound.
2. Herein rrt indicates relative retention time (on the 1.5% OV-17 on Shimalite W, 4mm x 1m column, N_2 flow rate, 40 ml/min., column temp. 120°) to *trans*,*trans*-farnesol (1.00, rt, 9.8 min.)
3. All nmr spectrum were measured in CCl_4 solution and signals given in δ-value.
4. The metastable peaks were observed at expected positions.
5. A. Chawla, S. Dev, *Tetrahedron Letters*, 4837 (1967).
6. G. Ohloff, K.-H. Schulte-Elte, B. Willhalm, *Helv. Chim. Acta.*, *47* 602 (1964)
7. C. M. M. Halls, E. W. Warnhoff, *Chem.* and *Ind.*, 1986 (1963)