Tetrahedron Letters No. 40, pp 3701 - 3702, 1971. Pergamon Press. Printed in Great Britain.

# SYNTHESIS AND STEREOCHEMISTRY OF CYCLONERODIOL

Shigeo Nozoe, Masami Goi, and Naoko Morisaki

Institute of Applied Microbiology, University of Tokyo,

Bunkyo-ku, Tokyo, Japan

(Received in Japan 26 August 1971. received in UK for publication 1 September 1971)

We recently reported the plane structure of cyclonerodiol (1) which was isolated from the cultured broth of a strain of Trichothecium species fungi as a main sesquiterpenoid.[1] The carbon skeleton of cyclonerodiol possessing a substituted cyclopentane ring corresponds to the isoprene homologue of iridane skeleton[2].

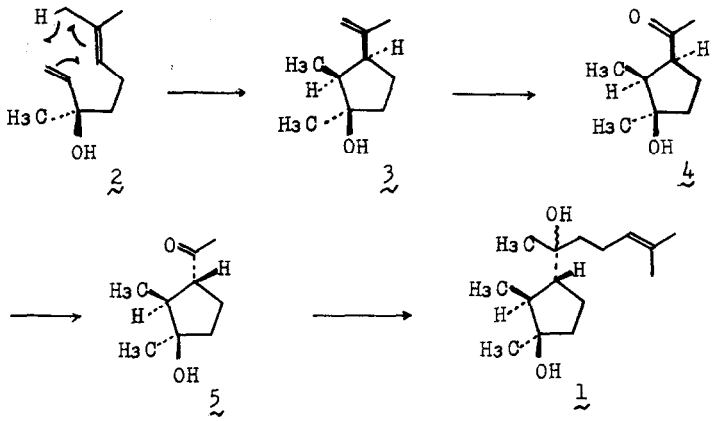
We here report the synthesis[3] of cyclonerodiol from linalool by a method which confirms the previous structural assignment and which additionally allows the relative stereochemistry of three adjacent alkyl substituents on the five membered ring.

Starting material used is a known isomer of the plinols which were first prepared by T. Ikeda et al.[4] from linalool by the intramolecular Alder "ene" reaction. The stereochemistry and the absolute configuration of the all possible diastereoisomers of the plinols were elucidated[5] and stereochemical course of the reaction were discussed in detail by H. Strickler et al[6].

Ozonization of plinol-C[7] (3) which is a major product of pyrolysis affords 1,2-dimethyl-3-acetylcyclopentan-1-ol having the stereochemistry shown in structure 4, nmr ($\delta$): 0.88 (d), 1.17 (s), 2.14 (s)[6]. Brief treatment of the ketone 4 with sodium methoxide in methanol gives a epimeric ketone 5, nmr: ($\delta$) 0.92 (d), 1.24 (s), 2.11 (s), in quantitative yield, possessing trans, trans arrangement of the alkyl substituents[6]. Treatment of the ketone 5 with Grignard reagent prepared from cyclopropylmethylketone by Julias' method[8] affords a sesquiterpenediol whose nmr spectrum ($\delta$, 0.97 (d, J=7 Hz), 1.08 (s), 1.18 (s), 1.59 (s), 1.65 (bs), and 5.03 (bt) in $CCl_4$), ir spectrum ($\nu$: 3600, 3500, 915, and 882 $cm^{-1}$ in $CHCl_3$), and mass spectrum (m/e 222, 207, 204, 189,

139, and 109) were indistinguishable from those of the natural cyclonerodiol[3].

In glc and tlc analysis, retention time and Rf value of the synthetic and the natural compound were identical at the various different conditions[3]. The products derived from trans,cis-, cis,cis-, and cis,trans- isomer of 1,2-dimethyl-3-acetylcyclopentan-1-ols and Grignard reagent were confirmed to be different from the natural compound. Above synthesis established the relative stereochemistry of the substituents as shown in structure 1.



REFERENCES

1. S. Nozoe, M. Goi, and N. Morisaki, Tetrahedron Letters, 1293 (1970).
2. "Cyclopentanoid Terpene Derivatives", Chaps. I and III: ed. by W. I. Taylor and A. R. Battersby, Marcel Dekker, Inc., New York (1969).
3. The synthetic sample of 1 assumed to be a mixture of diastereomer at an assymetric center on a side chain. The separation of the isomer was unsuccessful, however, the physicochemical properties examined so far were indistinguishable from the natural compound.
4. T. Ikeda and K. Wakatsuki, J. Chem. Soc. Japan, 57, 425 (1936).
5. H. Strickler, G. Ohloff, and E.sz.Kováts, Tetrahedron Letters, 649 (1964).
6. H. Strickler, G. Ohloff, and E.sz.Kováts, Helv. Chim. Acta., 50, 759 (1967)
7. T. Ikeda, and S. Takada, J. Chem. Soc. Japan, 58, 71 (1937).
8. M. Julia, S. Julia, and R.Guégan, Bull. soc. chim. France, 1072 (1960)

Acknowledgement: The authors are grateful to Professor S. Okuda for his interest to this work.