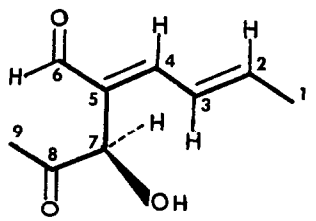
Tetrahedron Letters No. 38, pp 3527 - 3528. 0040-4039/78/0915-3527$02.00/0

METABOLITES OF PYRENOMYCETES IX[1]. STRUCTURE AND ABSOLUTE CONFIGURATION OF (+)-R-AVELLANEOL, AN ANTIBIOTIC METABOLITE OF HYPOCREA AVELLANEA.

L.Ananthasubramanian, Susan T. Carey and M.S.R. Nair*
The New York Botanical Garden, Bronx N.Y. 10458

Hypocrea avellanea Rogerson and Carey[2] produces an antibacterial culture liquid from which (+) avellaneol was isolated as a colorless viscous oil. This compound is assigned structure I on the basis of the data presented here.



I

Avellaneol $\alpha_D^{20} = +39^\circ$ (c, 2.58%, $CHCl_3$), $C_9H_{12}O_3$, MW 168.0783(ms), had λ_{max}^{EtOH} 278(ε 19500), ν_{max} 3400, 1720, 1680, 1638, 1360 and 970 cm^{-1}. Its ^1H NMR spectrum showed signals at δ 1.95 (3H, d, J=6Hz) for C_1 protons, 2.08(3H, s) for the $COCH_3$, 4.10(1H, broad, exchanges with D_2O) for the -OH, 5.15(1H, s, shifts to 6.18 on acetylation) for the CHOH, 6.25-6.80(2H, m) for C_2 and C_3 protons, 7.05 (1H, d, J=9.5Hz) for C_4 proton and 9.43(1H, s) for the aldehyde proton. Proton-noise and CW-off resonance decoupled ^{13}C NMR spectra showed the presence of two methyls at δ 19.3(C_1) and 24.9(C_9), one CHOH at 72.0, three sp^2 tertiary carbons at 126.7(C_2), *145.9 and *153.3(C_3 and C_4) a quaternary carbon at 135.1(C_5), one CHO at 193.1 and a C=O at 206.6. Thus avellaneol is an open chain compound with a dienealdehyde moiety, a CHOH group which has no vicinal protons, a $COCH_3$ group and an allylic methyl on a quarternary carbon. Structure I is the only one which satisfies all these requirements.

Avellaneol formed a monoacetate which showed λ_{max}^{EtOH} 278(ε 19000), ν_{max} 1748 1686, 1640 and 1231 cm^{-1}. The ^1H NMR spectrum showed a peak at δ 2.10(3H, s) for the acetate and another at 6.18(1H, s) for the CHOAc; rest of the spectrum closely resembled that of avellaneol.

In the ^1H NMR spectrum of (I) the C_3 and C_4 proton signals shifted downfield on adding $Eu(FOD)_3$, away from the multiplet for C_2 proton. On decoupling the CH_3, this multiplet appeared as a doublet (J=14Hz). Therefore C_2 and C_3 protons are trans to each other. Coupling constant of 9.5Hz between C_3 and C_4 protons show that they too are trans to each other. The chemical shift δ 19.3 for C_1 carbon and the UV and IR data are in agreement with this assignment.

In comparable dienone systems[3] and in retinals[4], when the carbonyl is cis to the γ carbon, the proton attached to it absorbs at $\delta>7.1$ and shows strong NOE with the aldehyde proton. When they are trans to each other, the proton appears at a higher field and no NOE is observed. C_3 proton in (I) has a chemi cal shift of $\sim \delta$ 6.6 and it shows no NOE on irradiating the aldehyde frequency Therefore avellaneol has the trans - trans dienal system.

The absolute configuration of avellaneol was determined by Horeau's method[5] and was found to be (R).

In serial dilution tests avellaneol was active against Staphylococcus aureus at a concentration of 30ppm and against Escherichia coli, Klebsiella pneumoniae, Bacillus subtilis and Mycobacterium smegmatis at a concentration of 60ppm.

Avellaneol is probably formed from 3 acetate units and one propionate unit We are studying the biogenesis by incorporating ^{13}C acetates and propionates. The results will be published in a fuller paper.

Acknowledgements:This work was supported by grants AI-13074, AI-00226 and AI-13247 from the Institute of Allergy and Infectious Diseases of National Institutes of Health and a grant RR05621 from the Division of Research Resources of NIH. We thank Mr. F.Manginelli, Miss S.Yost and Mrs. R.Beecher for technical assistance.

Foot notes and references:

1. For part VIII see, S.T.Carey and M.S.R.Nair, Lloydia,40,602(1977).
2. S.T.Carey and C.T.Rogerson, Brittonia,28,381(1976).
3. A.F.Kluge and C.P.Lillya, J.Org.Chem.,36,1977(1971).
4. R.Rowan III and B.D.Sykes, J.Am.Chem.Soc.,97,1023(1975).
5. A.Horeau, Tetrahedron Letters,15,506(1961).

(Received in USA 5 May 1978; received in UK for publication 18 July 1978)