Isolation and Enzymic Formation of *trans*-γ-Monocyclofarnesol

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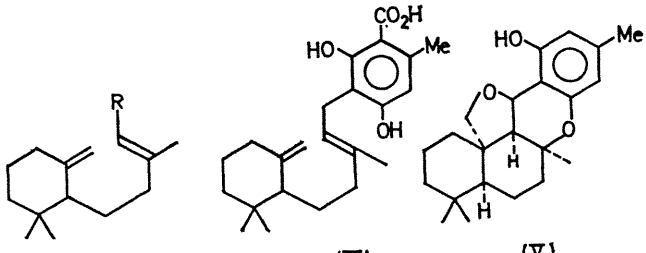
Summary *trans*-γ-Monocyclofarnesol (I) was formed by incubation of mevalonic acid lactone with the soluble enzyme preparation from the mycelia of *Helminthosporium siccans*, which was known to produce an antibiotic, siccanin.

RECENTLY we reported the isolation and structural elucidation of presiccanochromenic acid (IV)[1] which was thought to be a biogenetic precursor of an antibiotic, siccanin (V).[2] We have found that the soluble enzyme system prepared from the disrupted cells of the fungi converts mevalonic acid lactone into *trans*-γ-monocyclofarnesol (I), with a high conversion ratio, which is corresponding to the terpenic portion of the above compounds.

Mevalonic acid [2-^{14}C]lactone was incubated with the cell free system from *H. siccans*, in 0·1M phosphate buffer (pH, 7·22), in the presence of adenosine triphosphate and $MgCl_2$ (0·1mM). Products were isolated by saponification. The nonsaponifiable fraction which was extracted with ether contained on average, 30—60% of the added radioactivity; of this radioactivity, >80% was found to be located at a position with R_F 0·11 on a silica gel t.l.c. plate developed with benzene.

A sesquiterpene alcohol which behaved exactly like the enzymically formed product on t.l.c. has been isolated from the mycelia of the fungi as a minor constituent. Its identity with the enzymically formed compound was confirmed by autoradiography on t.l.c. developed with different solvent systems on silica gel, silica gel impregnated with silver nitrate, and on paraffin-coated silica gel plates as well as by tracer gas chromatography. Acetylation and oxidation of the radioactive specimen gave products which were identified on t.l.c. under various conditions as the acetate (II) and the aldehyde (III) respectively. The locations of the radioactivity on t.l.c. plates were determined by autoradiography with or without carriers.

The structure of compound (I), $C_{15}H_{26}O$, was determined as *trans*-γ-monocyclofarnesol from the following data: M^+ 222; $[\alpha]_D$ +17·6° (EtOH); ν_{max} 3350 (OH), 3060, 887 (=CH_2), 1387, and 1366 cm^{-1} (*gem*-dimethyls); n.m.r. (CCl_4) δ 0·87, 0·94 (3H each, s, *gem*-dimethyls), 1·66 (3H, s, an olefinic methyl), 4·04 (2H, d, *J* 7 Hz, a methylene α to an oxygen), 4·55, 4·75 (2H, an exocyclic methylene), and at 5·34 p.p.m. (1H, bt, *J* 7 Hz, an olefinic proton). In



(I) R = CH_2OH
(II) R = CH_2OCOMe
(III) R = CHO

(IV) (V)

the mass spectrum of (I), the intense peaks appeared at *m/e* 207, 204, 189, 108, and 81. Oxidation of (I) with manganese oxide affords an aldehyde, (III), $C_{15}H_{24}O$ (M^+, 220); λ_{max} (EtOH) 240 nm (ε, 9800); υ_{max} 2720 and 1682 cm^{-1}, n.m.r. (CCl_4) at δ 2·15 (3H, s), 5·79 (1H, d, *J* 7·5 Hz), and 9·92 p.p.m. (1H, d, *J* 7·5 Hz) due to a β-methyl-αβ-unsaturated aldehyde grouping, and indicating the *trans* geometry of the trisubstituted double bond.[3]

The double bond isomer of (I) and farnesol (and their pyrophosphate esters) were not observed in the incubation mixture.

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[1] S. Nozoe and K. T. Suzuki, *Tetrahedron Letters*, 1969, 2457.
[2] K. Hirai, S. Nozoe, K. Tsuda, Y. Iitaka, K. Ishibashi, and M. Shirasaka, *Tetrahedron Letters*, 1967, 2177.
[3] L. M. Jackman and R. H. Wiley, *J. Chem. Soc.*, 1960, 2886.