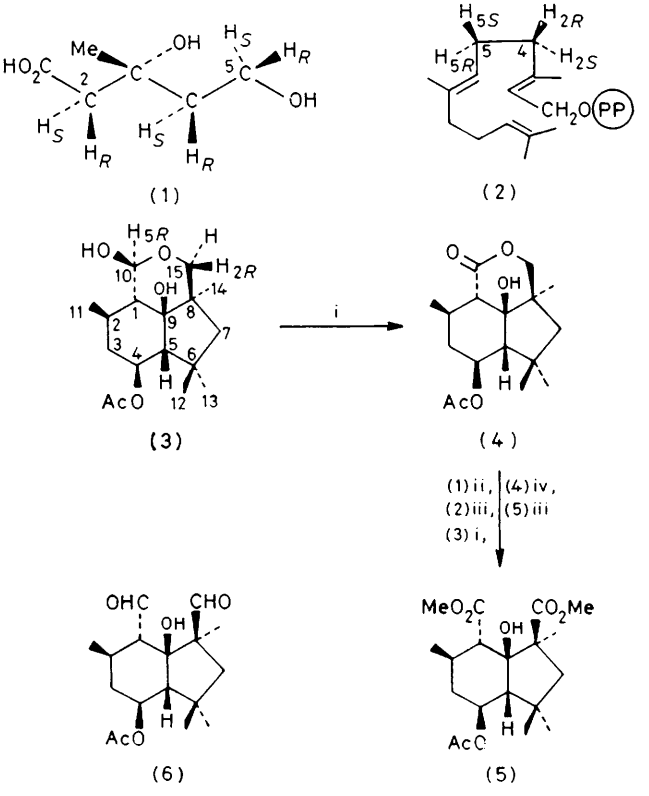
Formation of the Hemi-acetal Ring in the Sesquiterpenoid, Dihydrobotrydial

By A. PETER W. BRADSHAW and JAMES R. HANSON*
(*The School of Molecular Sciences, University of Sussex, Brighton, Sussex* BN1 9QJ)

Summary The formation of the hemi-acetal ring of dihydrobotrydial occurs with the retention of the *pro*-2(*R*) and *pro*-5(*R*) mevalonoid hydrogen atoms at C–15 and C–10, respectively, and proceeds with overall retention of configuration from farnesyl pyrophosphate at these centres *via* the corresponding dialdehyde.

THE fungus, *Botrytis cinerea*, is a serious pathogen of a number of commercial crops. A major phytotoxic metabolite is the sesquiterpenoid, dihydrobotrydial (**3**).[1] This contains a hemi-acetal ring which arises by scission of the 4,5-bond of a farnesyl pyrophosphate (**2**) precursor such that C-2 of mevalonate (**1**) becomes C-15 and C-5 of mevalonate becomes C-10.[2] We now report on the formation of the hemi-acetal ring.

The results of incubating 2- and 5-labelled mevalonates (**1**) with *Botrytis cinerea* are given in the Table. Oxidation of the dihydrobotrydial to the lactone (**4**) and to the diester (**5**) showed that the label at C–10 originated from the 5(*R*) position of mevalonate whilst only one 2-mevalonoid label which was from the *pro*-2(*R*)-position, remained at C–15. The stereochemistry of the labelling at C–15 was determined by deuterium labelling. The diastereotopic hydrogens at C–15 may be distinguished in the ^{1}H n.m.r. spectrum. The lower field resonance (δ 4·20), deshielded by the C–9 hydroxy group, undergoes a greater solvent shift [$\Delta\delta(CDCl_3$–$C_5D_5N)$ 0·3 p.p.m. *vs.* 0·05 p.p.m. for the 3·20 resonance] and was assigned to the *pro*-*S* (β-oriented) hydrogen atom. Sodium [2-$^2H_3$]acetate labels the 2-, 3′-, and 4-positions of mevalonate. When this acetate was incubated with *Botrytis cinerea*, the resultant dihydrobotrydial (**3**) bore a deuterium label at δ 4·20 in the ^{2}H n.m.r. spectrum but



Reagents: i, CrO_3, pyridine; ii, K_2CO_3, MeOH; iii, CH_2N_2; iv, aerial oxidation.

TABLE. Incorporation of mevalonates into dihydrobotrydial (**3**).

	[2-^{3}H, 2-^{14}C]MVA	[2(*R*)-2-^{3}H,2-^{14}C]MVA	[5-^{3}H,2-^{14}C]MVA	[5(*R*)-5-^{3}H,2-^{14}C]MVA
Initial MVA ^{3}H : ^{14}C	7·52 : 1	12·90 : 1	22·5 : 1	2·61 : 1
Amount ^{14}C fed μCi	17·3	20·2	24·1	1·28
Atom ratio	6 : 3	3 : 3	6 : 3	3 : 3
Metabolite ^{3}H : ^{14}C	6·14 : 1	12·30 : 1	14·68 : 1	2·89 : 1
Atom ratio	4·9 : 3	2·86 : 3	3·9 : 3	3·3 : 3
% Incorporation	0·14	1·28	0·52	0·7

not at δ 3·20.† The stereochemistry of labelling of farnesyl pyrophosphate (**2**) at C–4 and C–5 from *pro*-2(*R*)- and *pro*-5(*R*)-mevalonate is known.[3] Consequently the formation of the hemi-acetal proceeds with overall retention of configuration at both centres.

A number of mechanisms may be proposed for the bond cleavage involving, for example, an epoxide. However, the dialdehyde (**6**) was incorporated into dihydrobotrydial to the extent of 32% whereas the reverse reaction proceeded in 1·09% yield. Thus it seems likely that the cleavage occurs through the dialdehyde which in turn could be formed *via* a *trans*-15α, 10β-glycol. The oxidation of a *trans*-glycol would lead to a dialdehyde. The subsequent reduction of the aldehyde at C–15 proceeds with the re-stereospecificity typical of a microbial dehydrogenase.[4]

We thank Dr. F. W. Wehrli, Varian Associates, for the ^{2}H n.m.r. spectrum.

(*Received*, 12*th July* 1979; *Com.* 752.)

† Determined at 30·3 MHz.

[1] H. W. Fehlhaber, R. Geipal, H. J. Mercker, R. Tschesche, and K. Welmar, *Chem. Ber.*, 1974, **107**, 1720; H. J. Linder and B. Von Grosse, *ibid.*, p. 3332.
[2] J. R. Hanson and R. Nyfeler, *J.C.S. Chem. Comm.*, 1976, 72; A. P. W. Bradshaw, J. R. Hanson, and M. Siverns, *ibid.*, 1977, 819.
[3] J. W. Cornforth, R. H. Cornforth, C. Donninger, and G. Popjak, *Proc. Roy. Soc. Ser. B.*, 1965, **163**, 492; J. W. Cornforth, R. H. Cornforth, G. Popjak, and L. Yengoyan, *J. Biol. Chem.*, 1966, **241**, 3970.
[4] D. Arigoni, H. Weber, and J. Seibl, *Helv. Chim. Acta*, 1966, **49**, 741.