The Biosynthesis of Portentol: Assembly of a Linear Pentapropionate from Acetate and Methionine

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Summary Portentol (**1**) is synthesised *in vivo* from acetate or malonate and methionine.

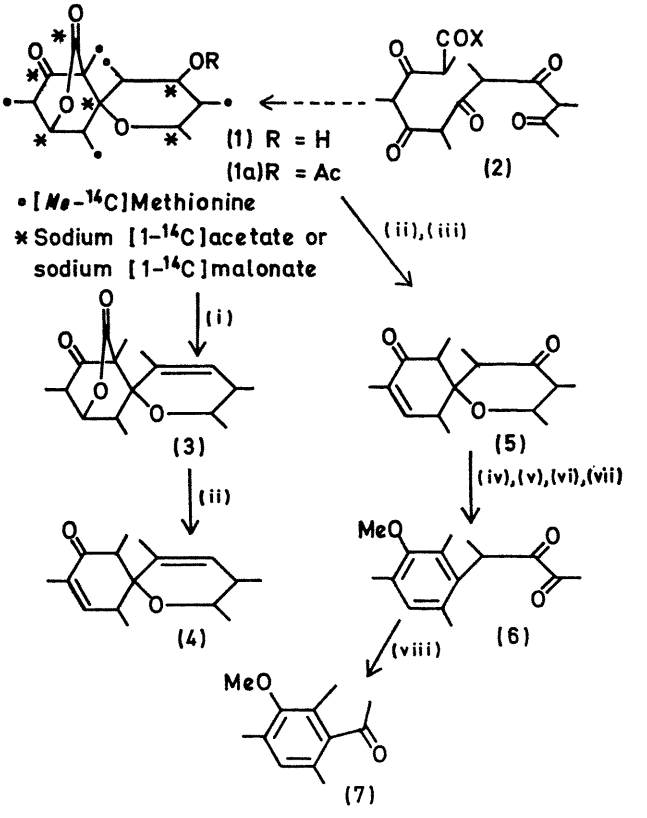
THE structure of the lichen metabolite portentol (**1**)[1,2] suggests that it may be formed *via* a linear polyketide (**2**) consisting of one acetate and five propionate units.

Apparently analogous polypropionate chains feature in the mycocerosic acid of *M. tuberculosis*,[3] the branch-chain fatty acids of goose preen glands[4] and, most important, in the lactone rings of the macrolide antibiotics.[5] In these cases it has been demonstrated[3,4,5b] that propionate is incorporated intact into each C_3 unit, while the methyl of methionine does not enter the carbon chain. More detailed studies[6–8] with the heptapropionate erythronolide A, the aglycone of erythromycin, have shown that propionate acts as the chain starter, and methyl malonate as the chain propagator.

We have investigated the biosynthesis of portentol acetate (**1a**) and find that its mode of formation differs from that of the linear polypropionates previously studied.

Roccella fuciformis DC (10 g) was, within seven days of removal from its natural habitat, suspended in sterilised water (50 ml) containing 50 μc of precursor and 0·1% of Tween 80, and aerated at 20° for 4 days under illumination (200 w).

Our results (see Table) can be interpreted in terms of a polyketide intermediate [as (**2**) (see Scheme)]. We find, however, that (i) Propionate and methyl malonate are not incorporated into the carbon chain of portentol acetate; (ii) Acetate† and malonate are incorporated uniformly (within experimental limits) into the carbon chain of portentol acetate. This implies ready equilibration between acetate and malonate in either direction, which is unusual. Accordingly, in mixed feeding experiments with acetate and



SCHEME. (i) H_2SO_4–AcOH; (ii) KOH–MeOH; (iii) Jones Reagent; (iv) H_2SO_4–EtOH–H_2O; (v) MeI–K_2CO_3; (vi) OsO_4–C_6H_6; (vii) $NaIO_4$; (viii) H_2O_2–OH^-.

† Four-fifths of the total activity incorporated from acetate appears in the ester function which to a minor extent also incorporates activity from propionate.

TABLE

Compound	Sodium [1-^{14}C]-acetate	Sodium [2-^{14}C]-acetate	[*Me*-^{14}C]-Methionine	Sodium [1-^{14}C]-malonate	Sodium [1-^{14}C]-acetate + malonate	Sodium [1-^{14}C]-malonate + acetate	Sodium [1-^{14}C]-propionate	Sodium [2-^{14}C]-propionate
	Incorporation (%)							
(**1a**)	0·2	0·062	0·11	0·28[a]	0·13	0·36	0·02[b]	0·03[b]
(**3**)	0·04	0·013	0·11	0·20	0·075	0·29	0	0
	R.M.A. × 10^{-3}							
(**1a**)	83·8	30·8	43·5	160	130	192	4·65	10·4
(**3**)	16·7	6·4	43·0	114	74	156	0	0
(**4**)	13·5 obs.	6·28		98·0	61·6	128		
	13·9 calc.	6·40		95·2	61·6	130		
(**5**)	13·7 obs.	6·38	44·0	96·6	61·4	130		
	13·9 calc.	6·40	43·5	95·2	61·6	130		
(**6**)[d]	10·6 obs.	5·26	43·5	77·4	47·8	102		
	11·1 calc.	5·33	43·5	76·0	49·4	104		
(**7**)	8·15 obs.	4·17	33·9					
	8·35 calc.	4·27	34·4					

[a] Allowing for loss of r.a. by decarboxylation.
[b] R.m.a. not constant (–OCOMe + –OCOEt).
[c] Calculated on the basis of labelling as in (**1**) [malonate ⇋ acetate assumed complete].
[d] As the quinoxaline derivative.

malonate there is no significant preferential incorporation of acetate into the starter, or of malonate into the propagator units; (iii) while the terminal secondary methyl group originates from C-2 of acetate, the remaining five methyls derive from methionine; (iv) mevalonate is not incorporated into portentol acetate.

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