Biosynthesis of the 3-Benzylchroman-4-one Eucomin

By PAUL M. DEWICK
(*Department of Pharmacy, University of Nottingham, University Park, Nottingham* NG7 2RD)

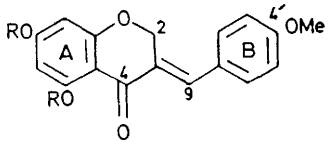
Summary Labelling patterns produced in the 3-benzylchroman-4-one eucomin are consistent with a biosynthetic mechanism involving addition of an extra carbon atom derived from methionine on to a C_{15} skeleton such as a chalcone.

THE genus *Eucomis* (Liliaceae) has recently provided[1,2] a new group of phenolic compounds based upon a 3-benzylchroman-4-one skeleton.

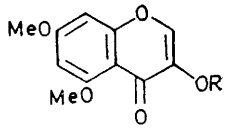
The biosynthesis of eucomin (**1**) has now been investigated by feeding aqueous solutions of labelled phenylalanine, methionine, and sodium acetate *via* the roots to plants of *Eucomis bicolor*. The incorporation of activity into eucomin was poor (0·0002—0·0022%, see Table) but of sufficient magnitude to permit degradative studies and provide a reasonably accurate assessment of the labelling pattern produced by these expected precursors. Degradation of the labelled eucomin was as follows: the fully methylated derivative (**2**) was cleaved (OsO_4–$KClO_3$) to anisaldehyde and the chromone (**3**). Anisaldehyde was oxidised to anisic acid (**5**); the chromone was either treated with alkaline H_2O_2 to yield 4,6-dimethoxysalicylic acid (**6**) or, after methylation to (**4**), hydrolysed to give the acetophenone (**7**). The two aromatic acids were degraded further by standard methods as required. The relative specific activities of these degradation products are presented in the Table.

The results indicate that within the limits of experimental error, activity from [1-^{14}C]phenylalanine was entirely localised at C-4 of eucomin. Approximately one-ninth of the activity from [*U*-^{14}C]phenylalanine was recovered in (**6**) and seven-ninths in (**5**). Thus, a C_6–C_3 unit from phenylalanine is incorporated intact into the eucomin molecule, becoming C-4, C-3, C-9, and the aromatic ring B. The *O*-methyl on ring B is supplied by methionine, and since (**7**) was virtually inactive, by difference it is concluded that methionine also acts as the source of C-2. The aromatic ring A is acetate-derived.

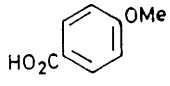
The labelling patterns set up in the eucomin skeleton by these simple precursors are similar to those demonstrated in flavonoid biosynthesis,[3] but differ in that an extra carbon atom derived from methionine is added to produce the heterocyclic ring. The fundamental C_{15} skeleton of flavonoids is provided by the chalcones,[3] and it now seems highly probable that a 2-methoxychalcone [*e.g.* (**8**)] may be



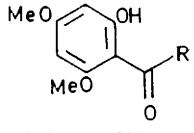
(1) R = H
(2) R = Me



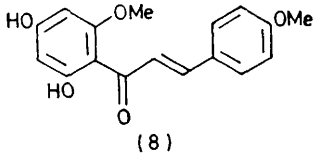
(3) R = H
(4) R = Me



(5)



(6) R = OH
(7) R = CH_2OMe



(8)

an intermediate in the biosynthesis of eucomin, the 2-*O*-methyl providing the 'extra' carbon atom.[2,4] The utilisation of an *O*-methyl group to form a carbon–carbon linkage has been demonstrated in the biosynthesis of rotenoids,[5] and it is also believed to occur during the formation of peltogynol and related compounds by analogy with *in vitro* processes.[6]

TABLE. *Incorporation of precursors into eucomin in* Eucomis bicolor, *and relative specific activities of degradation products*

Compound fed	% Incorporation	Relative specific activities (2)	(5)	$MeEt_3N^+I^-$ (4′-OMe)	(6)	$BaCO_3$ (C-4)	(7)
DL-[1-^{14}C]Phenylalanine[a]	0·0022	1·00	0·02		1·00	0·92	
L-[*U*-^{14}C]Phenylalanine[a]	0·0010	1·00	0·73		0·14		
Sodium [2-^{14}C]acetate[a]	0·0002	1·00	0·08		0·91		
L-[*Me*-^{14}C]Methionine[a]	0·0005	1·00	0·46		0·06		
L-[*Me*-^{14}C]Methionine[b]	0·0014	1·00	0·40	0·38			0·07

[a] Feeding period 72 h; [b] Feeding period 48 h.

That the name 'homoisoflavonoid' has been coined for 3-benzylchroman-4-one derivatives (see refs. 1 and 2) is perhaps unfortunate. The formation of isoflavonoid compounds in Nature involves a characteristic 1,2-aryl migration step,[3] but no such rearrangement occurs during the biosynthesis of eucomin. The 'homoisoflavonoids' seem to represent a further modification of the unrearranged flavonoid skeleton.

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