BIOSYNTHESIS OF THE 3-ETHYLCHROMONE PHYTOALEXIN LATHODORATIN IN LATHYRUS ODORATUS

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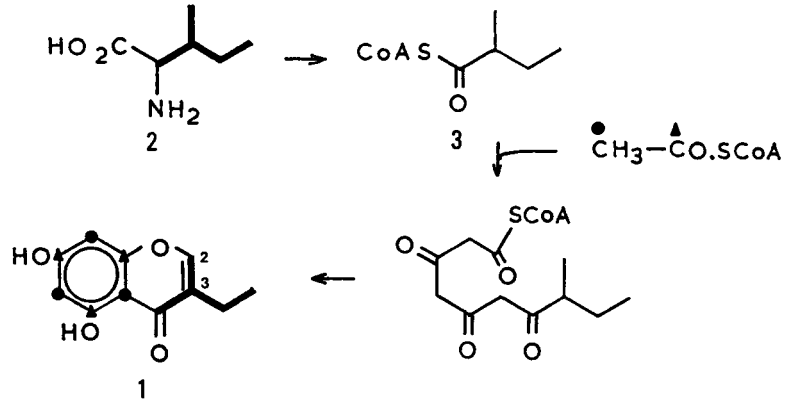
Lathodoratin (1) is an antifungal 3-ethylchromone derivative, produced as a phytoalexin by the sweet pea Lathyrus odoratus as a result of fungal infection or other forms of stress (Robeson, Ingham and Harborne, 1980). Its structure is unusual and does not relate readily to other classes of natural chromones. Most simple chromones encountered in nature have a substituent at C-2 rather than C-3, and are good examples of polyketide structures derived from acetate-malonate. As part of a broad programme relating to natural antifungal agents, we have investigated its biosynthetic origin by feeding likely precursors to C. odoratus pods, previously treated with 2% aqueous $CuSO_4$ as inducing agent.



Postulated biosynthetic sequences to lathodoratin (Robeson, Ingham and Harborne, 1980) were immediately excluded since in a series of feeding experiments, ^{14}C-labelled phenylalanine and methionine were not incorporated. However, acetate (incorporation 0.10%) labelled the phloroglucinol ring of (1) as demonstrated by partial degradation by alkali fusion, giving phloroglucinol containing 97% of the incorporated activity. This was confirmed by using [$^{13}C_2$]acetate as precursor and analysing satellites flanking the aromatic signals in the ^{13}C NMR spectrum. In addition, [$^{13}C_2$]acetate was incorporated intact, at a rather lower level, into the ethyl substituent at C-3. These results are consistent with the phloroglucinol ring having a polyketide origin, and the remaining five carbon "isoprene unit" being derived from the amino acid isoleucine (2). [U-^{14}C] Isoleucine was subsequently confirmed to be incorporated (0.9%) specifically into this five carbon fragment. Alkali fusion gave phloroglucinol essentially unlabelled (1%), and alkaline hydrolysis indicated C-2 contained 22% (i.e. about one-fifth) of the activity. Leucine and valine were rather poorly incorporated into lathodoratin, probably via prior metabolism to acetate.

The results suggest that isoleucine provides a starter unit, probably 2-methylbutanoate (3), for acetate-malonate chain extension. Although many organisms are known to use starter molecules other than acetate for chain extension, we know of no other example for the participation of isoleucine as source of the starter unit.

Robeson, D.J., Ingham, J.L. and Harborne, J.B. (1980) Phytochemistry, 19, 2171.