Loganin as Precursor of the Indole Alkaloids

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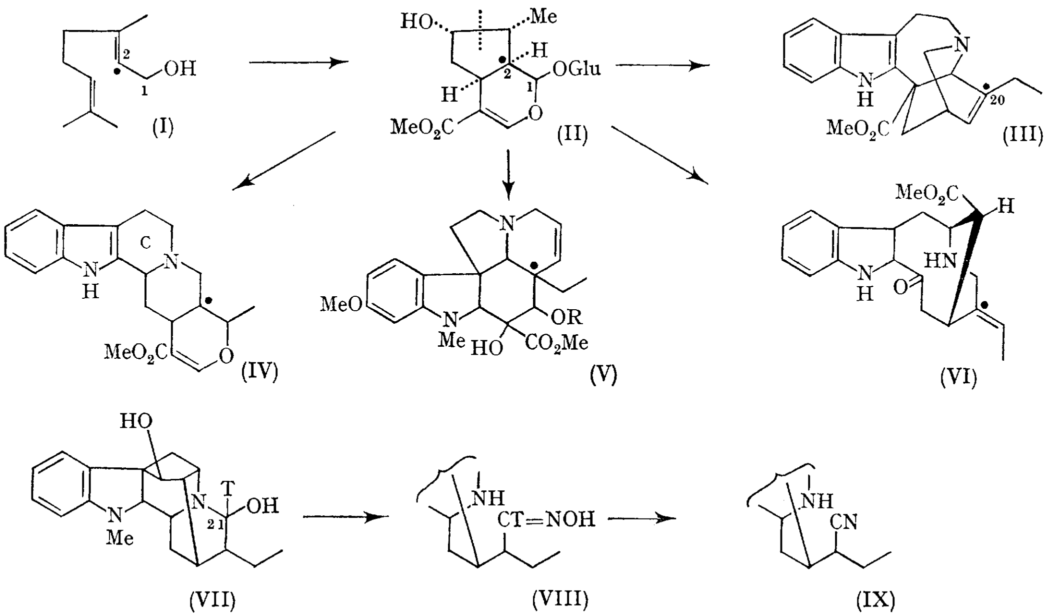
EXPERIMENTS[1] with *O*-methyl labelled loganin strongly supported the view that loganin (II) is a key intermediate for the biosynthesis of indole alkaloids and evidence was presented against the possibility of *O*-methyl transfer. The work now described rigorously establishes the validity of this interpretation of our earlier studies.[1]

A mixture (*ca.* 3 : 1) of [2-^{14}C]geraniol (I) and [2-^{14}C]nerol was prepared in 70% radiochemical yield from [2-^{14}C]bromoacetic acid through the Wittig reaction involving 2-methylheptan-2-one; the esters so formed were reduced with lithium aluminium hydride. This product (1·33 mc.) was administered to *Menyanthes trifoliata* plants and the glycosides were extracted from batches harvested over the period 1—6 days following the initial feeding. Fractionation of the combined extracts gave pure loganin which was checked for radiochemical purity by conversion of part into the penta-acetate; repeated recrystallisation caused no change in molar activity.

When the biosynthetic loganin, labelled specifically with carbon-14, was fed to *Vinca rosea* plants, the following radioactive alkaloids were isolated (incorporations as %): catharanthine (III; 0·50%), serpentine (IV; ring C aromatised; 0·60%), ajmalicine (IV; 0·46%), vindoline (V; R=Ac; 0·23%) and perivine (VI; 0·04%). Kuhn–Roth oxidation of catharanthine (III) afforded propionic acid (100% of total activity) and radio-inactive acetic acid, both acids being isolated as *p*-bromophenacyl esters. The alkaloid was thus proved to be labelled solely at C-20. Similar degradation of deacetylvindoline (V; R=H) and of dihydroperivine (VI; with ethylidine group reduced) proved that 102% and 96% of their total activities, respectively, was located at the indicated positions. Loganin is thereby firmly proved to be a precursor of representative examples from the three major groups of indole alkaloids comprising the *Corynanthe*, *Iboga*, and *Aspidosperma* families.[3] This knowledge allows rational study of the steps by which (a) the cyclopentane ring is cleaved[4] and (b) rearrangement of the skeleton occurs to generate the *Iboga* and *Aspidosperma* systems. Appropriate experiments are in progress.

Further evidence was obtained by feeding [1-^{3}H]loganin (II), prepared biosynthetically,[2] to *Rauwolfia serpentina* plants. The isolated radioactive ajmaline (VII; 0·04% incorp.) was converted into ajmaline oxime[5] (VIII) without significant change of molar activity but dehydration to yield the nitrile[5] (IX) caused complete loss of ^{3}H-activity. It follows that ajmaline (VII) was labelled with tritium at C-21 and that loganin acts as a specific precursor of a *Corynanthe* type alkaloid in a second plant species.



Related independent experiments are reported by Loew and Arigoni in an accompanying Communication.

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[1] A. R. Battersby, R. T. Brown, R. S. Kapil, J. A. Martin, and A. O. Plunkett, *Chem. Comm.*, **1966, 890;** A. R. Battersby, *Pure and Appl. Chem.*, 1967, **14**, 117.

[2] A. R. Battersby, R. S. Kapil, and R. Southgate, *Chem. Comm.*, 1968, preceding Communication.

[3] Outlined in part at the Gordon Conference on "Steroids and Other Natural Products," New Hampton, U.S.A., August, 1967.

[4] R. Thomas, *Tetrahedron Letters*, **1961, 544;** E. Wenkert, *J. Amer. Chem. Soc.*, 1962, **84**, 98.

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