Biosynthesis of Isoprene Derivatives: Origin of the Furan Ring in the Quinoline Alkaloid Dictamnine

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Summary The hydroxyisopropyldihydrofuranoquinoline alkaloid, platydesmine, has been shown to be an efficient precursor of the furanoquinoline alkaloid, dictamnine, in *Skimmia japonica* Thunb.

THE specific incorporation of the ^{14}C-labelled dimethylallylquinolone (Ia) into dictamnine (IIIa) indicated the isoprenoid origin of the furan ring of the alkaloid,[1] and it was shown later[2] that the furan ring of the related alkaloid, skimmianine (IIIb), was derived from mevalonate. The quinolone (Ia) is also a precursor of the hydroxyisopropyldihydrofuranoquinoline quaternary salt (IV)[1], and epoxide intermediates have been suggested for this process.[3] Birch and Smith[4] suggested that hydroxyisopropyl deri-

vatives might be involved in the biosynthesis of furan rings in aromatic natural products and we have now tested this hypothesis using the shrub *Skimmia japonica* Thunb., which contains dictamnine (IIIa), (+)-platydesminium metho-salt (IV), and traces of skimmianine (IIIb).[5]

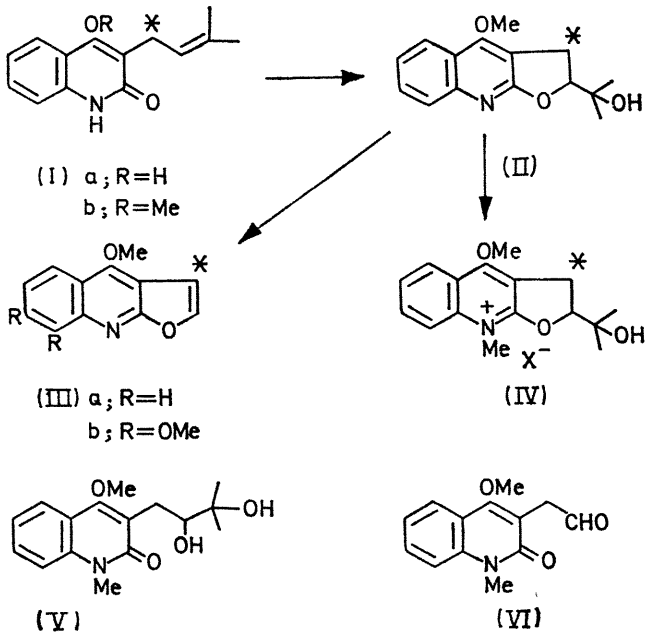
The tertiary alkaloid (+)-platydesmine (II), specifically labelled with ^{14}C, was fed to shoots of *Skimmia japonica*. After 3 days, incorporations into the alkaloids were: platydesminium metho-salt (IV) (4·3%), dictamnine (IIIa) (18·9%), and skimmianine (IIIb) (0·1%). Platydesmine is clearly an efficient precursor of the quaternary alkaloid and of dictamnine; the figures given are minimum values, since probably the plant utilises only one enantiomer of the racemic precursor. The isolation of radioactive skimmianine (IIIb) suggests that hydroxylation of the homocyclic ring occurs later in the biosynthetic pathway.

Degradation of dictamnine by a method similar to that reported by Spencer and his co-workers[6] showed that no randomisation of the label occurred. Treatment of the quaternary alkaloid (IV) with aqueous base gave the diol (V)[5] which was converted with periodic acid into the aldehyde (VI);[7] as expected, almost all the radioactivity of the diol (96%) was retained in the aldehyde.

Platydesmine (II) has been isolated from rutaceous plants[8] but has not hitherto been detected in *Skimmia japonica*. Accordingly, we carried out a trapping experiment by feeding ^{14}C-quinolone (Ib) to *S. japonica* in the presence of unlabelled (±)-platydesmine. After 24 h, extraction afforded platydesmine containing 0·86% of the original radioactivity of quinolone (Ib) confirming that platydesmine is a key biosynthetic intermediate.

The possibility that the quaternary alkaloid (IV) was involved in the biosynthesis of dictamnine was tested by feeding ^{14}C-platydesminium methiodide but the low incorporation (0·03%) into dictamnine indicates that this is not a major pathway.

The results establish the main features of the biosynthetic pathway to furanoquinoline alkaloids and we are now studying the biosynthetic mechanism of the loss of the hydroxyisopropyl fragment. The recent work with furanocoumarins employing compounds generally labelled with tritium[9] suggests that the scheme also applies to other aromatic systems containing furan rings.



Asterisks in formulae (I)—(IV) indicate the position of ^{14}C-labelling.

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