The Incorporation of a Labdadienol into the Tetracyclic Diterpenes

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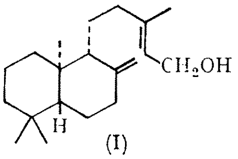
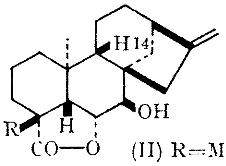
WE have shown[1] that the enantiomer of the bicyclic alcohol (I), *i.e.* with the normal A/B fusion, acts (as its pyrophosphate) as a precursor of the tricyclic diterpene rosenonolactone. Biogenetic theory suggests[2] that it should also act as a precursor of the tetracyclic diterpenes. We now present experimental evidence to support this. These cyclizations have formed the subject of a number of model *in vitro* studies.[3]

Extraction of the copal of *Trachylobium verrucosum* from Malaysia[4] afforded a bicyclic ester and its dihydro-derivative. Reduction gave the bicyclic alcohol (I)[5] with the antipodal A/B fusion. Oxidation with manganese dioxide afforded the corresponding aldehyde, which was reduced with sodium borotritiide to give the labelled alcohol. This was converted into its pyrophosphate by Cramer's method[1,6] and fed to *Gibberella fujikuroi*. The metabolites were isolated. 7-Hydroxykaurenolide (II) showed an incorporation of 0·54%, 7,18-dihydroxykaurenolide (III) 0·45%, and gibberellic acid (IV) purified as its methyl ester, 5·13%.

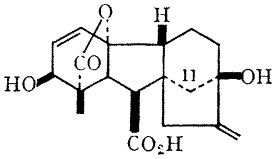
Specificity was demonstrated as follows. Methyl gibberellate was converted into methyl allogibberate, which was in turn rearranged to methyl gibberate (V). These retained the radioactivity. Oxidation of methyl gibberate to methyl gibberdionate (VI)[7] removed the radioactivity which was thus specifically located at C-11 (C-14 kauranoid numbering) in the original gibberellic acid. The level of incorporation of the pyrophosphate into gibberellic acid is comparable to that of (−)-kaurene.[8] It contrasts with that of (−)-pimaradiene (VII)[9] suggesting that either solubility and transport phenomena may affect the tricyclic hydrocarbon or that it may have a different status in the biosynthesis as perhaps an enzyme-bound intermediate (at C-8). It should be pointed out that although the incorporation is specific and clearly exists, no tricyclic pimaradiene metabolites have so far been found in *Gibberetta fujikuroi* whereas both bicyclic and tetracyclic compounds have been found.[10]



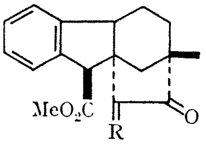
(I)



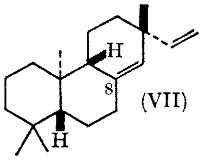
(II) R=Me
(III) R=CH$_2$OH



(IV)



(V) R=H$_2$
(VI) R=O



(VII)

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