The Structure and Biosynthesis of Foliamenthin

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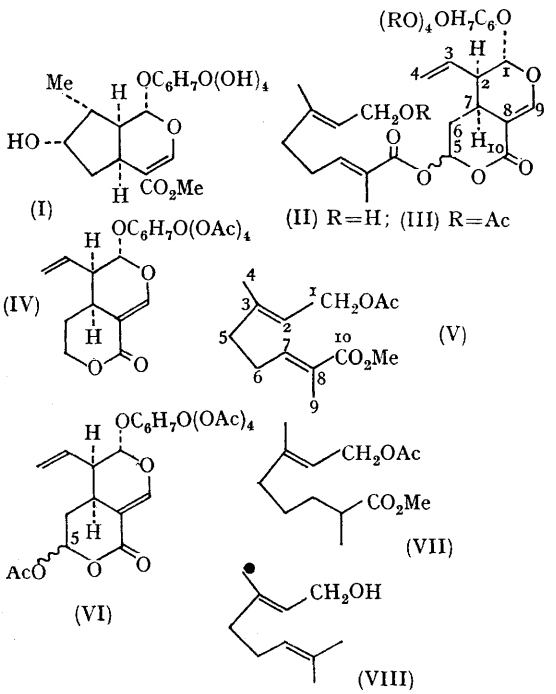
IN CONNECTION with current studies on the biosynthesis of loganin (I) in *Menyanthes trifoliata*,[1] we have isolated from the glycosidic fraction of the rhyzomes a new glucoside, foliamenthin, the structure of which has now been established as (II).

The free glucoside, $C_{26}H_{36}O_{12}$, $[\alpha]_D$ — 60° (MeOH), was first obtained by chromatography of the crude acetone extract on silica gel columns, but for large-scale work purification of the acetylated mixture by counter-current distribution proved more convenient. Interpretation of the mass spectrum of penta-*O*-acetylfoliamenthin (III), $C_{36}H_{46}O_{17}$, $[\alpha]_D$ — 55°, was complicated by the unexpected appearance of a temperature-dependent M + 2 peak (*m/e* 752);† however, the correct formula of the compound follows unambiguously from the chemical evidence below. The u.v. spectrum of (III), λ_{max} 228 mμ (ε 17,200), shoulder at 245 mμ, was consistent with the presence of two different chromophores, and further spectroscopic data indicated the presence of the group –O–CO–C=CH–O– (ν_{max} 1622 cm.$^{-1}$, τ 2·43) and of two methyl groups attached to double bonds (τ 8·12 and 8·21). Cleavage of (III) with sodium methoxide in methanol, followed by reduction with sodium borohydride and subsequent acetylation gave, in good yield, tetra-*O*-acetylsweroside (IV),[2-4] m.p. 165°, $[\alpha]_D$ — 173°, identified by direct comparison with an authentic specimen (provided by Dr. Linde). When the reduction step was omitted, two compounds could be isolated by chromatography on silica gel. The less polar one was an optically inactive *O*-acetyl methyl ester $C_{13}H_{20}O_4$, M^+ 240, λ_{max} 216 mμ (ε 12,000); its constitution and the *trans*-arrangement of the methoxycarbonyl group are shown to be as in (V) by the n.m.r. spectrum, in which all the signals can be assigned (*cf.* Table). The more polar component is a penta-acetate, $C_{26}H_{32}O_{15}$, $[\alpha]_D$ — 138°, λ_{max} 245 mμ (ε 8400). Since this compound contains one acetoxy-group more than its reduction product (IV), it must be assigned structure (VI), which is consistent with all the available spectroscopic data. The double n.m.r. signal for the C-5 proton (τ 3·61 and 3·50) provides evidence for the presence of two 5-epimers.

The penta-acetate (III) contains a tetra-acetylglucose residue, as shown by the characteristic and very intense peak at *m/e* 331; therefore reconstruction of the formula of foliamenthin from those of the two units related to the cleavage products (V) and (VI) is possible only in one way, which leads unequivocally to the structure represented in (II). No evidence is available for the configuration at C-5; in view of a plausible biogenetic relationship, the stereochemistry at C-1, C-2, and C-7 has been deliberately adjusted in (II) so as to



The 100 *MHz n.m.r. spectrum of substance* (V)

	Position of the protons							
	1	2	4	5 + 6	7	9	–OMe	–OAc
τ	5·41 d	4·55 t	8·21 m	7·72 m	3·25 m	8·12 d	6·25 s	7·95 s
J	7·5	7·5	0·5		7; 0·5	0·5		

† Similar results were obtained with other monoterpene glucosides and will be reported in detail elsewhere.

conform with the stereochemistry of loganin (I), which is now known in detail.[1,5,6] Different views, in particular with regard to C-1, have been expressed[2-4] for the relative configuration of the corresponding centres in sweroside and its tetra-acetate (IV); however, neither the present nor the previous arguments are compelling and further work is required to clarify this point.

With leaves rather than rhyzomes as starting material, mixtures of (III) and a new dihydro-derivative were usually obtained. The u.v. spectrum of such preparations showed a reduced intensity and this, together with the appearance of a new n.m.r. signal for a secondary methyl group (d, τ 8·88), made it clear that the dihydro-compound was lacking the conjugated double bond in the alicyclic C_{10}-component. Accordingly, methanolysis of these fractions followed by reacetylation gave, in addition to (VI), mixtures of (V) and a new compound (VII), $[\alpha]_D - 21°$, no u.v. absorption.

Foliamenthin (in crystalline form) and pure dihydro-foliamenthin have independently been isolated from the same source, together with a third related glucoside, by Prof. Battersby and his associates; the results of their studies are outlined in the accompanying Communication.[7]

The biosynthesis of foliamenthin has been investigated by feeding [4-^{14}C]geraniol (VIII) to whole rhyzomes of *M. trifoliata*. After rigorous purification, the labelled penta-acetate (III) (2·5% incorporation) was converted as above into the products (IV) and (V), which displayed a radioactivity ratio of 1 : 400. Kuhn–Roth oxidation of the dihydro-derivative from (IV) then gave propionic acid carrying 95% of the original activity, and this is consistent with the idea that the labelled precursor is incorporated intact in the seco-iridoid segment of foliamenthin.

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