Crystallographic Structure Determination of Utilin, $C_{41}H_{52}O_{17}$, a Complex Meliacin with a 1,29-Cycloswietenan Skeleton

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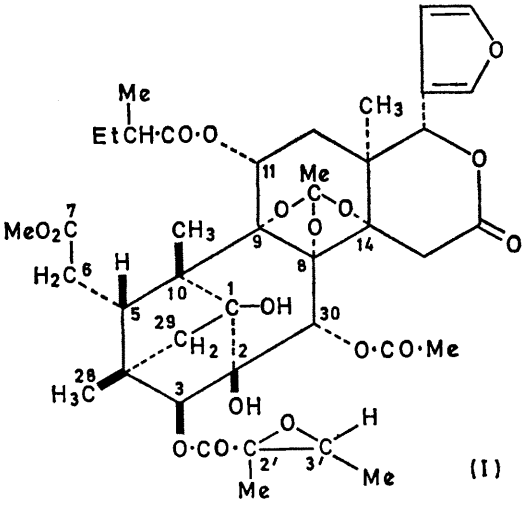
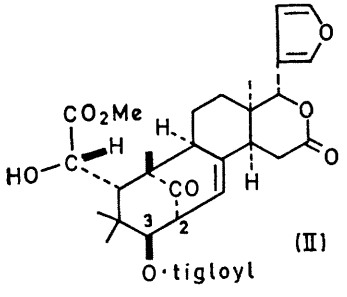
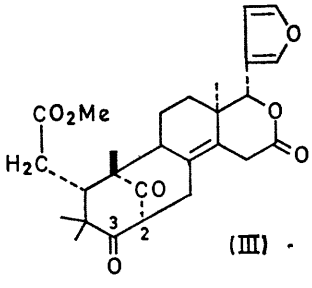
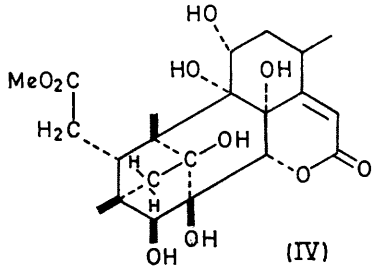
Summary The structure of utilin, $C_{41}H_{52}O_{17}$, a complex meliacin has been shown by *X*-ray analysis to be the 1,29-cycloswietenan derivative (I); the functional groups are methoxycarbonyl, acetate, orthoacetate, *R*-2-methylbutyrate, 2*S*,3*R*-2,3-epoxy-2-methylbutyrate, two hydroxyls, and a δ-lactone; and a β-substituted furan ring is also present.

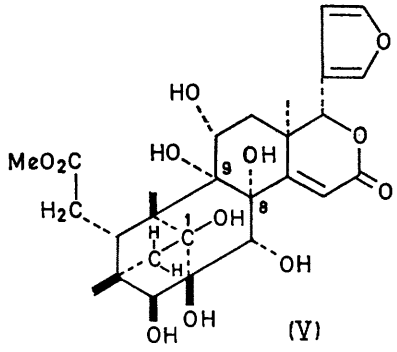
UTILIN, $C_{41}H_{52}O_{17}$, is a complex meliacin isolated from the timber of *Entandrophragma utile*.[1,2] It has been shown[2] to contain one 2,3-epoxy-2-methylbutyrate group, one 2-methylbutyrate group, one normal acetate group, and one concealed acetate group. On alkaline hydrolysis it affords[1] β-furfuraldehyde and on methanolysis it gives[2,3] two αβ-unsaturated δ-lactones, (A), $C_{22}H_{30}O_{10}$, and a second which, after acetylation with acetic anhydride in acetic acid containing toluene-*p*-sulphonic acid,[4] affords a penta-acetate (B) $C_{37}H_{42}O_{16}$ containing four normal acetate groups and one concealed acetate group. These results and the botanical source of utilin suggested[3] that it was a complex meliacin. Attempts to prepare a heavy-atom derivative for *X*-ray analysis were unsuccessful, so an *X*-ray analysis was attempted on the parent compound. This proved successful.











Utilin forms monoclinic crystals in the non-centrosymmetric space group $P2_1$, with $a = 10{\cdot}38$, b (unique) = 17·79, $c = 10{\cdot}99$ Å, $\beta = 95{\cdot}52°$, $Z = 2$. All data out to $\theta = 80°$ were collected on a computer-controlled, four-circle diffractometer with nickel-filtered, Cu-K_α radiation. 4051 independent reflections were measured with intensities greater than four standard deviations.

The structure was solved with a computer programme based on the tangent formula of Karle and Hauptman.[5] The phases of two suitable *h*0*l* reflections and one suitable *h*1*l* reflection were specified to define the origin.[6] Next three other reflections which, with the first three, appeared to lead to good phase determination were also chosen and were given trial numerical values. Of the 32 final sets from the tangent formula refinement, two were clearly indicated

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to be better than the rest, having considerably lower Karle R-factors[7] and the largest number of Σ_2 interactions in use. The $|E|$-map calculated on the first set (319 phases) proved uninterpretable, but the map calculated with the second set (314 phases) gave a 48-atom, chemically reasonable fragment. An $|F|_{obs}$ map with all 4051 reflections phased on these sites revealed thirteen new positions and indicated five of the old ones to be incorrect. A further $|F|_{obs}$ map showed the remaining two positions and allowed differentiation between carbon and oxygen atoms. The molecular structure of utilin is revealed as (I), with formula $C_{41}H_{52}O_{17}$, in agreement with the original chemical analysis. The absolute configuration of (I) follows from the isolation of D(−) [*i.e.* *R*]-α-methylbutyric acid on hydrolysis of utilin.[8] Refinement is still in the early stages, with the present $R = 8\%$.

Structure (I) is formally a 1,29-cycloswietenan derivative and is related to the meliacins containing the bicyclononane system such as swietenine (II)[9] and mexicanolide (III).[10] The stereochemistry of the bicyclononane system is given relative to the cyclo-octane ring. The 2,3-epoxy-2-methylbutyrate group is a tiglate epoxide and has the *S*-configuration at C-2′ and *R* at C-3′. The possible biosynthesis of the additional ring will be discussed in detail later. It may simply involve bonding between C-1 and C-29 of a swietenan derivative but there are more complex possibilities involving fission between C-2 and C-3. Cyclisation and recyclisation can then occur either between C-1 and C-29 and between C-2 and C-3 of the original skeleton or between C-1 and C-3 and between C-2 and C-28. If the latter pathway is correct then C-3, C-28, and C-29 of utilin are originally C-28, C-29, and C-3 of the swietenan precursor.

The elucidation of the structure of utilin enables the methanolysis product (A) to be formulated as (IV) and the acetylated product (B) as a tetra-acetyl orthoacetyl derivative of (V). There are four possible positions for the orthoacetyl group in (B). The sterically most favourable appears to be the one involving the 1,8,9-hydroxy-groups.

Utilin has been inter-related[2] with entandrophragmin, $C_{43}H_{56}O_{17}$, which differs from utilin in containing an isobutyrate group instead of an acetate group. Entandrophragmin also affords under identical conditions as were used with utilin the two products (A) and (B). The n.m.r. spectra of utilin and entandrophragmin are identical except in the methyl region, so entandrophragmin must have the same basic structure as utilin. The most likely distribution of acyl groups in it is as in utilin with an isobutyrate group replacing the acetate group at C-30.

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