The Meliacins (Limonoids): Boron Trifluoride-catalysed Rearrangements of 14,15-Epoxides in the Meliacins[1]

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Summary 14,15-Epoxides of meliacins in which ring D is a δ-lactone have been rearranged by treatment with boron trifluoride etherate in benzene; only compounds with 7-OH groups rearrange.

A COMMON structural feature of the meliacins is a 14,15-epoxide in ring D of the molecule. Recently Chan, Gibbs, and Taylor[2] and Taylor and Okorie[3] studied the action of dilute acid on the cyclopentanoid epoxides [*e.g.* in havanensin and related compounds (I)]. Such epoxides are very reactive, and either a 15-ketone or a 14-methyl-15-hydroxy-compound containing a 13,17-double bond is formed depending on the nature of the oxygen function at C-7.

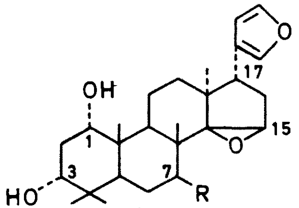
In contrast the αβ-oxido-δ-lactones such as gedunin, khivorin, and limonin (7-oxo or 7α-OAc) are stable to acid.[4] We find that αβ-oxido-δ-lactones having 7α- or 7β-hydroxy-groups undergo acid-catalysed rearrangements not previously detected.

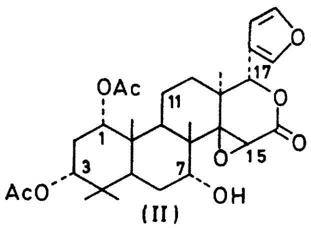
Thus 7-deacetylkhivorin (II) on reaction with boron trifluoride etherate in benzene gave two compounds A and B. A is formulated as (III).† Its n.m.r. spectrum retained most of the features of the spectrum of 7-deacetylkhivorin. In particular, the 7-hydroxy-group was still there, as indicated by a hydroxy-proton signal at τ 3·79 (exchangeable with D_2O) as well as the 7-H triplet now displaced downfield to τ 5·47 from τ 6·5. However 15-H had disappeared. The u.v. spectrum λ_{max} 215 (ε 5000) and 262 nm, (ε 5400) in methanol; 216 and 300 nm. in alkaline methanol] supports an enolisable α-keto-δ-lactone.

Compound B is formulated as (V), consistent with its n.m.r. spectrum: τ 4.90, 1H, m (11-H); 3.60, 1H, m (7-H); 5.50, s, 1H, *H*COH (15-H); and 6.50 bs, 1H exchangeable with D_2O (OH). The signal at τ 5·5 moves downfield to τ 4·2 on acetylation, and disappears on Jones oxidation. We suggest that following the formation of a C-14 carbonium ion there is a methyl shift from C-8 to form the allyl alcohol (IV), which under the acidic conditions of the reaction readily eliminates water to form (V). The low-field absorption of 7-H is due to interaction with the 15-OH. When the latter is acetylated, the 7-H signal moves upfield to τ 4·45. The structure is further supported by the u.v. spectrum of the product: λ_{max} 247nm (ε 12,000).

The same compound is also obtained by vigorously heating khivorin with a strong solution of toluene-*p*-sulphonic acid in benzene. The intermediate here would be the *O*-acetate of the allyl alcohol (IV) which eliminates acetic acid.

The reaction of 7-deacetylgedunin (IV) with boron trifluoride also afforded two compounds with corresponding structures to (III) and (V). When 1,2-epoxy-7-deacetylgedunin was similarly treated only the 14,15-epoxy-group reacted, giving the corresponding 15-ketone. This underlines the assistance given by the 7-OH group to the opening of the 14,15-epoxide.


(I)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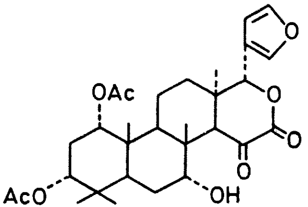
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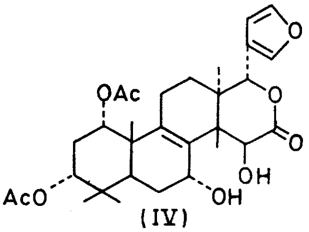
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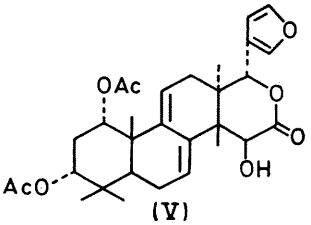
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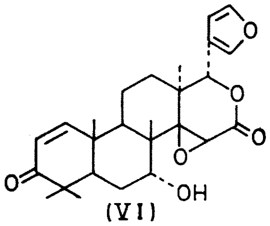
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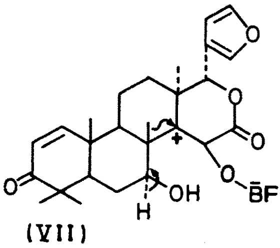
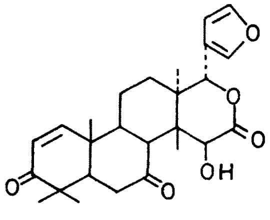
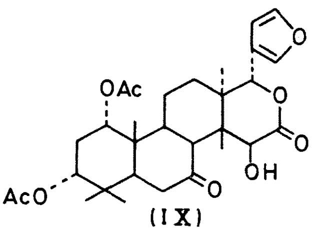

(VII)


(VIII)


(IX)

The rearrangement of the 7β-hydroxy-compounds took a different course. 7β-Hydroxy-7-deacetoxygedunin was obtained in good yield by partial reduction of 7-oxo-7-deacetoxygedunin at ice-bath temperature with sodium borohydride. On reaction with boron trifluoride it gave (VIII), the n.m.r. spectrum of which indicated the disappearance of 7-H. It further showed a 2H singlet signal at τ 5·82. One of these hydrogens is exchangeable with D_2O, the exchange rendering the remaining signal sharper. Also, on acetylation, one of them disappears and the remaining signal moves downfield to τ 4·48. The peak at τ 5·82 thus

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† Satisfactory elemental analyses and mass spectral molecular weights were obtained for all new compounds.

represents a singlet HCOH. The u.v. spectrum of the product is similar to that of gedunin. The first stage of the reaction is also most probably the opening of the oxide ring to form a C-14 carbonium ion which in this case is followed by a methyl shift from C-8 as shown in (VII) leading to structure (VIII). That the C-7 ketone is formed *via* the enolate is supported by the incorporation of deuterium into the product when the reaction mixture is worked-up in deuterium oxide and the product crystallised from methanol. A doublet at τ 6·98 (J 12 Hz) is assigned to 8-H. It disappears in the spectrum of the deuteriated product.

7β-Hydroxy 7-deacetoxykhivorin gave small amounts of (V) but the major product was (IX). Like the product from the corresponding gedunin derivative, its n.m.r. spectrum indicated the absence of 7-H and the presence of a singlet HCOH (τ 4·15, moving downfield to τ 3·20 on acetylation and disappearing on Jones oxidation). The oxidation product is a non-enolisable α-keto-lactone: λ_{max} 243 nm (ϵ 2000).

The stability of the $\alpha\beta$-oxido-δ-lactones is further enhanced if the furan at C-17 is oxidised to a carboxyl. Such compounds are stable in dilute acid even when they possess a 7-OH group.

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[1] Presented in part at the 3rd Natural Products Symposium, Kingston, Jamaica, January 1970.

[2] W. R. Chan, J. A. Gibbs, and D. R. Taylor, *Chem. Comm.*, 1967, 720.

[3] D. A. Okorie and D. A. H. Taylor, *Chem. Comm.*, 1968, 737.

[4] For a review see D. L. Dreyer, *Fortschr. Chem. org. Naturstoffe*, 1968, **26**, 191.