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ANDIROBIN

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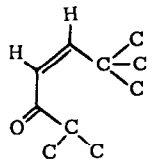
The oxidative modification of triterpenoids related to euphol has provided an interesting group of natural products characterised by the presence of a β-substituted furan ring in association with a modified euphol skeleton. Many variants upon this theme are now known including structures associated with the oxidative cleavage of ring A (e.g. dammarenolic acid,[1] nyctanthic acid,[1,2] limonin,[3] and canaric acid[4]), cleavage of ring C (e.g. nimbin[5]), and cleavage of ring D (e.g. limonin,[3] gedunin,[6] khivorin,[7] and obacunone[8]). We now wish to report on the constitution of andirobin which reveals a new variant in that its structure contains a cleaved ring B.

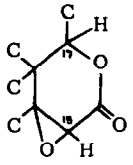
Andirobin, m.p. 195-197°, isolated from the seeds of Carapa guayanensis Aubl. (Meliaceae) was shown to have the molecular formula $C_{27}H_{32}O_7$ [M 468 (mass spectrum kindly determined by Dr. C.P. Falshaw)]. The n.m.r. spectrum of andirobin was particularly informative in that it showed the presence of two α-furan protons (τ 2.54), one β-furan proton (τ 3.62), an AB system characteristic of an $\alpha\beta$-unsaturated carbonyl group (τ 2.80 and 3.88; J = 11 c.p.s.), four protons associated with singlets (τ 4.47, 4.55, 4.67, and 5.92), one methoxyl group (τ 6.25), and four tertiary C-methyl groups (τ 8.88, 8.88, 9.01, and 9.05). Alkaline hydrolysis of andirobin gave the corresponding carboxylic acid, $C_{26}H_{30}O_7$, which reformed andirobin by reaction with diazomethane. This required the presence of a CO_2Me group (τ 6.25) in andirobin in accord with ester carbonyl absorption at 1745 cm^{-1}. Andirobin contained no hydroxyl group, but reduction of andirobin with sodium borohydride yielded a tetrahydro-derivative, andirobindiol, characterised as a diacetate which showed a U.V. maximum (λ_{max} 209 mμ, ε_{max} 9,100) characteristic of a β-substituted furan. There were thus two carbonyl groups present in the andirobin structure which were reduced with borohydride. One of these was associated with an $\alpha\beta$-unsaturated ketone (ν_{max} 1680 cm^{-1}.) and the other with a δ-lactone (ν_{max} 1760 cm^{-1}.). Subtraction of the U.V. spectrum of andirobindiol diacetate from that of andirobin gave a subtraction curve (λ_{max} 235 mμ, ε_{max} 9,500) corresponding with the $\alpha\beta$-unsaturated-3-keto-chromophore of triterpenoids and steroids. This chromophore was clearly associated with the structural feature also responsible for the AB system (τ 2.80 and 3.88; J = 11 c.p.s.) in

andirobin and the absence of further splitting suggested the presence of the structural feature (I) with a cis-disubstituted double bond and a tertiary γ-carbon atom.

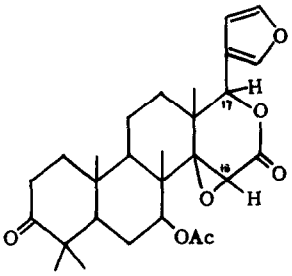
The presence of a C_{26} skeleton in andirobin in association with a β-substituted furan ring made us suspect that andirobin belonged to the oxidatively modified euphol group of natural products, and this suspicion was encouraged on phytochemical grounds. Many naturally occurring substances of this group contain an $\alpha\beta$-epoxy-δ-lactone structure (II), and comparison of the n.m.r. spectrum of andirobin with that of dihydrogedunin (III),[9] which showed two singlets at τ 4.40 and 6.48, suggested that the singlets (τ 4.47 and 5.92) in the andirobin spectrum could be assigned to similarly located protons at C_{15} and C_{17}. The presence of an $\alpha\beta$-epoxy-δ-lactone structure in andirobin was fully confirmed by its smooth reduction with chromous chloride[3] to deoxyandirobin, $C_{27}H_{30}O_6$. These reactions thus defined the functions of the seven oxygen atoms in the andirobin molecule.



(I)

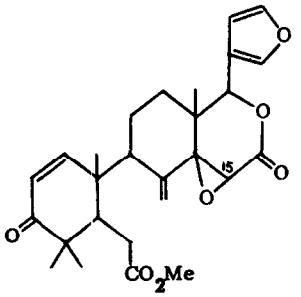


(II)

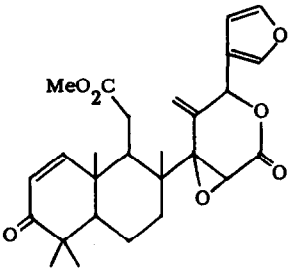


(III)

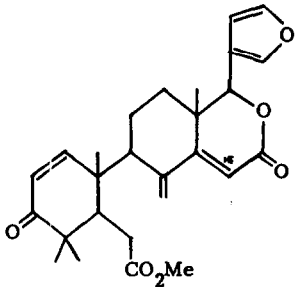
Thus the probable presence in the structure of andirobin of the partial structures (I) and (II) in association with a β-substituted furan ring, a methoxycarbonyl group, and four tertiary C-methyl groups suggested two structures (IV or V) for andirobin which were biogenetically attractive. Furthermore, these two structures (IV or V) immediately provided an acceptable interpretation for the presence of two singlets (τ 4.55 and 4.67) in the n.m.r. spectrum of andirobin; these two singlets could be associated with the two protons of the exocyclic methylene group.



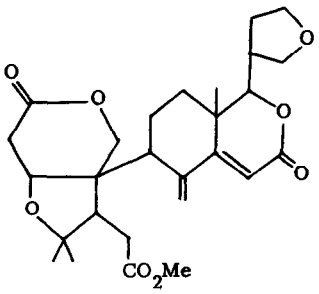
(IV)



(V)



(VI)

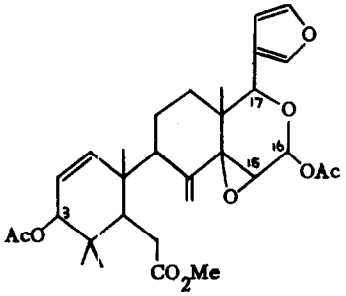


(VII)

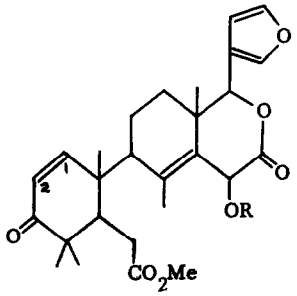
The $\gamma\delta$-location of the vinyl double bond with respect to the $\alpha\beta$-epoxy-lactone carbonyl group in andirobin was clearly indicated by subtraction of the U.V. spectrum of andirobin from that of deoxyandirobin. This gave a maximum at 257 mμ (ε_{max} 8,300) which is at a higher wavelength than would be expected for an isolated $\alpha\beta$-unsaturated lactone grouping. However, these chromophoric characteristics precisely matched those (λ_{max} 255 mμ, ε_{max} 7,800) of a trans-formation product (VII) of limonin.[3] This close spectral similarity also demonstrated that deoxyandirobin had the chromophoric situation required by structure (VI) rather than the alternative corresponding to the structure (V).

Thus a decision in favour of the structure (IV) for andirobin rather than the alternative (V) was possible on the following grounds: (i) the spectroscopic characteristics of deoxyandirobin (see above); (ii) the stability of deoxyandirobin to acid under conditions when deoxyandirobin would have been isomerised to an α-pyrone if its structure had corresponded to formula (V); (iii) comparison of the chemical shift of the C_{17}-proton in andirobin and its derivatives with suitable models (e.g. III and XII) showed that the C_{17}-proton was not allylically placed with respect to the vinyl group.

The n.m.r. spectrum of deoxyandirobin (VI) was similar in many respects to that of andirobin except that the C_{15}-proton in andirobin (IV) (τ 5.92) was shifted downfield in deoxyandirobin (VI) giving a singlet (τ 3.58). The n.m.r. spectrum of andirobindiol diacetate was in full accord with the structure (VIII); in particular the protons at C_3 (τ 4.73; J = 2 c.p.s.), C_{15} (τ 6.23; J = 3 c.p.s.), and C_{16} (τ 3.58; J = 3 c.p.s.) gave doublet signals. Clearly the C_{15}- and C_{16}-protons in andirobindiol diacetate are in the cis-relationship.



(VIII)

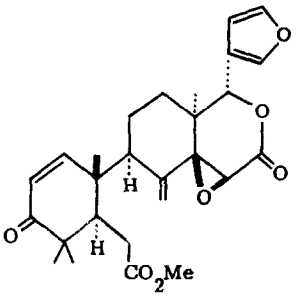


(IXa, R = H; IXb, R = Ac)

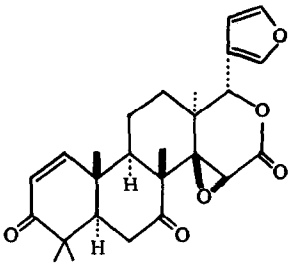
(Xa, R = H; Xb, R = Ac
C_1 - C_2 double bond reduced)

The structure of andirobin (IV) was confirmed by catalytic hydrogenation which yielded either dihydroandirobin (IXa) or tetrahydroandirobin (Xa). These compounds and their mono-acetates (IXb and Xb) had n.m.r. spectra in accord with these structures and their spectra showed as expected the absence of the exocyclic methylene group and its replacement by a low field vinylic methyl group.

Biogenetic analogy suggests that andirobin has the absolute stereochemistry shown in formula (XI). Another substance, $C_{26}H_{30}O_6$, m.p. 260-263°, also isolated with andirobin from Carapa guayanensis, showed properties which suggested that it was identical with the known 7-deacetoxy-7-ketogedunin (XII);[10] its n.m.r. spectrum was in complete accord with this proposal.



(XI)



(XII)

The co-occurrence of andirobin (XI) and the compound (XII) is of biogenetic interest in that it is clearly compatible with the earlier suggestion[1] that the ring cleavage reactions of the type (XII) → (XI) are biosynthetically probable. Ring B cleavage among the diterpenes has been recently recognised with the elucidation of the structure of enmein.[11]

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