Tetranortriterpenoids. Part XVI.[1] Partial Syntheses of Andirobin, Methyl Angolensate, Mexicanolide, and 1-Deoxymexicanolide

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Methyl angolensate (16; R = O) has been synthesised from 7-oxo-7-deacetoxykhivorin (2), thus confirming the proposed 1α-configuration of the ether oxygen atom. The diene lactone (11a) has also been prepared from the same starting material and it readily cyclises by Michael addition to give mexicanolide (18). 1-Deoxymexicanolide (25) has similarly been synthesised from 7-oxo-7-deacetoxygedunin (20). Partial syntheses of andirobin (17) and isoandirobin (19) are also reported.

It is an attractive suggestion [2] that the characteristic bicyclo[3.3.1]nonane ring system of the swietenine group of tetranortriterpenoids is formed from the normal tetracyclic triterpene nucleus by oxidative cleavage of ring B in a compound similar to (2), followed by intramolecular Michael addition of a C-2 carbanion to the diene lactone system in (4) to give (8) [*cf.* arrows in structure (4)]. We have now successfully tested this suggestion *in vitro*.

The hydrolytic cleavage of ring B has previously been reported in deoxylimonin (1) [3] and in 7-deacetoxy-7-oxodeoxygedunin (5).[4] This leads to a monounsaturated lactone, and the introduction of a second conjugated double bond is difficult.[3] We have investigated the application of the Baeyer–Villiger oxidation, which is a more likely analogue of the biosynthetic process [5] and gives a product of the correct oxidation level. This has the additional advantage that the oxidation can be applied in the epoxy- or the deoxy-series, whereas hydrolytic cleavage is limited to deoxy-derivatives.

Since our preliminary communications [6] a second synthesis of mexicanolide has been published,[7] in which ring B is cleaved by Beckmann rearrangement of the oxime of a 7-ketone.

Our present work started with 7-deacetoxy-7-oxokhivorin (2), readily available as a natural product

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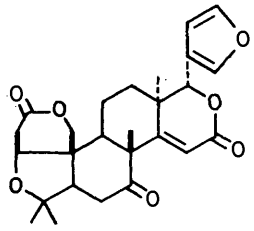
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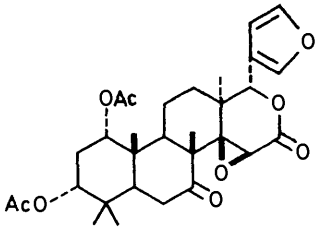
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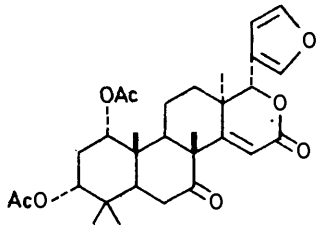
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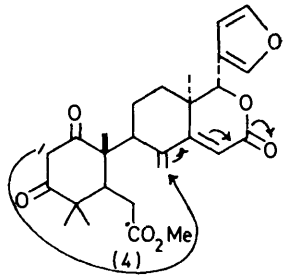
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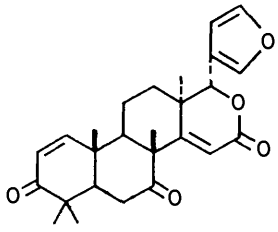
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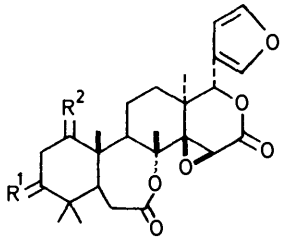
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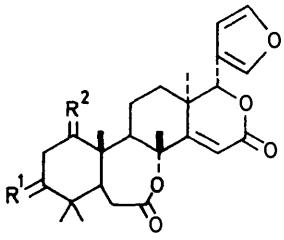
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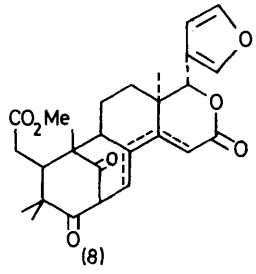
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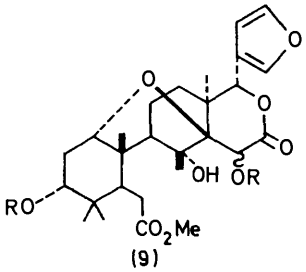
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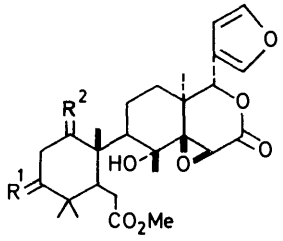
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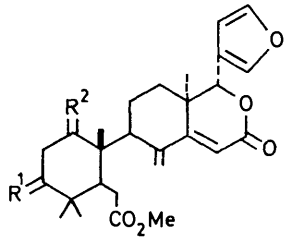
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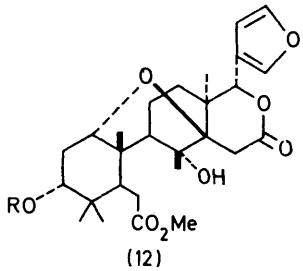
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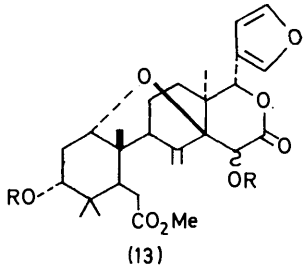
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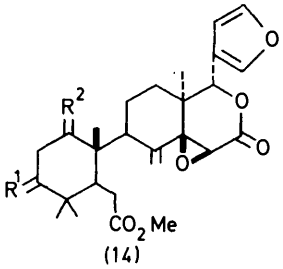
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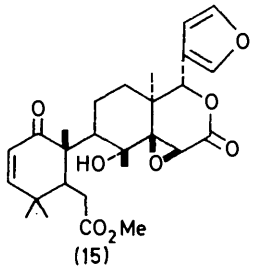
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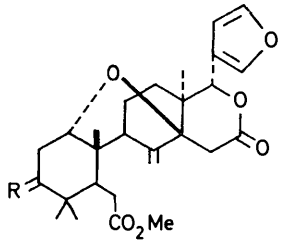
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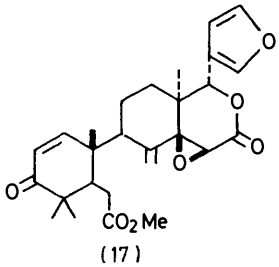
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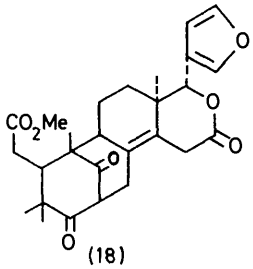
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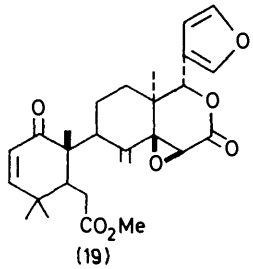
(19)

a; $R^1 = R^2 = O$
d; R^1 = H,αOAc, R^2 = O

b; $R^1 = R^2$ = H,αOAc
e; R^1 = H,αOH, R^2 = O

c; $R^1 = R^2$ = H,αOH
f; R^1 = O, R^2 = H, αOH

from certain specimens of *Khaya senegalensis*.[8] This was reduced with chromium(II) chloride to the deoxy-derivative (3), which on oxidation with peracetic acid gave the ε-lactone (7b) (characteristic shift of C-8 methyl group downfield to δ 1·68). The lactone ring was opened by the action of toluene-*p*-sulphonic acid in benzene, giving the unsaturated acid, which was characterised as the methyl ester (11b). The n.m.r. spectrum of the ester (11b) indicated loss of one tertiary methyl group and the introduction of an exocyclic methylene group. (δ 5·22 and 5·28, each one 1H, s). No trace was found of the corresponding $\Delta^{8,9}$-isomer. Mild alkaline hydrolysis of the ester (11b), followed by acidification, did not give the expected diol (11c) but instead the cyclisation product (16; R = H,αOH), identical with an aluminium isopropoxide reduction product of methyl angolensate.[9,10] Oxidation of the synthetic alcohol then gave methyl angolensate (16; R = O), identical in all respects with a natural sample. This synthesis from a khivorin derivative, for which the 1α-configuration has been established [11] confirms the previously proposed configuration of methyl angolensate.[12]

Mild alkaline hydrolysis of the lactone (7b), followed by methylation gave a dihydroxy-ester, in which there was no n.m.r. signal corresponding to that expected for the vinyl H-15 proton. This shows that the Michael cyclisation has occurred again, and the product has the structure (12; R = H). The monoacetate (12; R = Ac) (H-1, δ 3·95; H-3, δ 4·63), was dehydrated with thionyl chloride in pyridine at 0 °C, giving the exo-methylene derivative (16; R = H,αOAc), also obtained by acetylation of (16; R = H,αOH).

In connection with this partial synthesis of methyl angolensate, the aluminium isopropoxide reduction [10,12] was re-investigated. It was discovered that reduction for a short period of time gives the 3α-isomer (16; R = H,αOH) while if the time of the reaction is increased, the 3β-isomer is produced by equilibration. This result parallels that reported for many similar reductions.

The discovery of how easily the 1–14 oxide bridge was formed made it necessary to postpone removal of the 14,15-epoxide until later in the reaction sequence. We therefore carried out the Baeyer–Villiger oxidation of 7-deacetoxy-7-oxokhivorin itself, obtaining the ε-lactone (6b). Attempts to open the ε-lactone ring with toluene-*p*-sulphonic acid in benzene failed, possibly because the C-8 oxygen atom is now not allylic. Basic hydrolysis of the lactone gave a number of products, depending on the reaction conditions. Mild conditions gave mainly the corresponding diacetoxy-acid, with the dihydroxy-lactone (6c). In acidic solution the di-acetoxy-acid slowly re-lactonised. Under more vigorous conditions, the triol acid (10c) was obtained, together with equal amounts of a second compound of equal polarity to which we assign the structure (9; R = H) (see below). This was not useful for the further stages of the synthesis.

The diol (6c) (H-1, H-3, δ 3·66 and 3·74; multiplets sharpening on addition of D_2O) was oxidised with Jones reagent to the β-diketone (6a) [2 × H-2, δ 3·45br (s)]. Unfortunately, attempts to remove the epoxide ring in this compound with chromium(II) chloride failed. This reaction normally occurs readily and the reason for its failure is obscure.

We then turned to the diacetoxy-acid, which was obtained in high yield together with a little of the corresponding ester (10b), by hydrolysis of the lactone (6b) with potassium carbonate in aqueous methanol. Methylation of the mixture with ethereal diazomethane converted it completely into the ester (10b) ($\nu_{max.}$ (CCl_4) 3590 cm^{-1}), which was dehydrated with thionyl chloride in pyridine to give the required exomethylene compound (14b) (=CH_2, δ 5·06 and 5·4; only 4 tertiary methyl groups). Again, no trace of the endocyclic isomer could be found. Mild alkaline hydrolysis of (14b) removed the two acetate groups, giving the non-crystalline diol (14c) (H-1, H-3, δ 3·57 and 3·74, m) and a minor amount of a second compound (13; R = H) (see below).

Oxidation of the diol gave the β-diketone (14a), with the expected spectroscopic properties [$\lambda_{max.}$ 261 nm (ε 9300); in alkali $\lambda_{max.}$ 289 nm (ε 22,600); 2 × H-2, δ 3·89br, (s)]. The hydroxy-ketone (14f) was also obtained in small amounts; this is discussed later.

Reduction of the diketone (14a) with chromium(II) chloride then removed the epoxide, giving the required diene lactone (11a). This proved to be labile, undergoing spontaneous cyclisation to mexicanolide, and was difficult to purify by t.l.c. or by crystallisation. Our best sample had m.p. 204—210 °C [$\lambda_{max.}$ 259 nm (ε 22,800)]. Owing to the extreme lability of mexicanolide to base,[13,14] strong alkaline reagents could not be used for the cyclisation, but stirring a chloroform solution with aqueous sodium hydrogen carbonate completed cyclisation to give mexicanolide (18), identical with the natural product. No trace of the double bond isomers [*cf.* (8)] was detected.

Treatment of the hydroxy-ketone (14f) with thionyl chloride in pyridine dehydrated it, yielding andirobin [15] (17), identical with the natural product. This synthesis proves the structure of the hydroxy-ketone. The isomeric 1-oxo-3-hydroxy-compound which would have

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the structure ascribed to mahoganin,[16,17] was not detected; its dehydration product, isoandirobin (19) was, however, obtained in the following way. The triol acid was methylated and the resulting methyl ester (10c) oxidised with Jones reagent. Two products were obtained, the β-diketone (10a) and the dihydroxy-ketone (10e). Acetylation of the latter gave a mixture of two compounds separated with difficulty by preparative t.l.c. The more polar was the expected acetate (10d) (H-3, >C*H*OAc, δ 4·93, m), the less polar the dehydration product (15) ($\nu_{max.}$ 3600, 1675, and 1740 cm^{-1}; H-2, H-3, δ 5·86 and 6·59, *J* 10Hz). The chemical shifts of the vinyl protons are characteristic of a $\Delta^{2,3}$-1-oxo-compound.[18] The formation of this enone confirms the structure of the hydroxy-ketone (10e). Dehydration of the enone with thionyl chloride then gave isoandirobin (19), as a gum, ($[\alpha]_D$ +22°, $\nu_{max.}$ 1675 cm^{-1}, δ 5·86, 5·29, and 5·62, each 1H, s, exomethylene protons and H-17). Dehydration of the acetate (10d) under the same conditions gave, in poor yield, the exomethylene derivative (14d), not obtained crystalline [δ 4·90 (m, H-3), 5·41, 5·48, and 5·62 (all 1H, s, exomethylene protons and H-17)]. This is the acetate of the structure ascribed to mahoganin.[16,17]

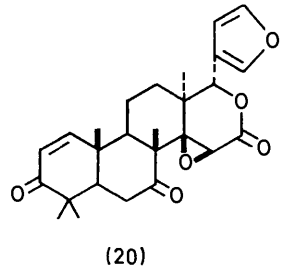
We return now to consider the minor product obtained in formation of the diol (14c). The n.m.r. spectrum of this showed two resonances at δ 3·33 (m) and 4·60br (s) due to protons adjacent to hydroxy-groups (both sharpened on addition of D_2O), and we ascribe these to H-3 and H-15 in the structure (13; R = H). The resonance for H-1, adjacent to the ether bridge, appeared at δ 3·78 (m); in the corresponding diacetate (13; R = Ac) this signal moved to δ 3·51 ,while the H-3 and H-15 signals shifted downfield to δ 4·75 and 5·84 respectively. This assignment of the H-1 and H-3 signals was supported by the result of irradiation at δ 1·7, (H-2) when both were reduced to singlets. The chemical shift of H-15 agrees well with the values reported by Ekong and Selema for compounds of similar type produced by rearrangement of the 14,15 oxide ring in derivatives of 7-deacetylgedunin and 7-deacetylkhivorin.[19] In addition the i.r. spectrum of (13; R = Ac) showed a band at 1770 cm^{-1}. This value, unusually high for a δ-lactone, is consistent with the presence of an α-acetoxy-substituent.

The hydroxy-ether (13; R = H) cannot be produced directly from the diol (14) by attack of the C-1 alkoxide ion on the oxide ring at C-14, since the stereochemistry is wrong. The oxide is originally 14β, and the bridge in (13) is only possible if it is also β at C-14.

A possible mode of formation of (13; R = H) could involve β-elimination of the 14,15-epoxide followed by addition of the 1α-hydroxy- group to the αβ-unsaturated lactone system (*cf.* formation of methyl angolensate).

A similar type of product was obtained by prolonged basic hydrolysis of the ε-lactone (6c). In addition to the triol acid (10c) this gave, after methylation, a by-product to which we ascribed the structure (9; R = H). This had an n.m.r. spectrum showing a singlet at δ 4·48 (H-15) and multiplets of δ 3·56 (H-3) and 3·93 (H-1), which both collapsed to singlets on irradiation at δ 2·14 (C-2 methylene). In this spectrum the H-17 resonance is unusually far downfield at δ 6·21. Acetylation of the methyl ester gave the diacetate (9; R = Ac) ($\nu_{max.}$ 3610, 1770, and 1740 cm^{-1} in CCl_4), whose n.m.r. spectrum showed the expected downfield shifts of the H-15 and H-3 resonances to δ 5·64 and 4·65. Unfortunately dehydration of (9; R = Ac) with thionyl chloride did not give the related exomethylene compound (13; R = Ac), but instead a complex mixture which was not resolved.

We were also interested to prepare the 1-deoxy-derivative (25) to see what effect the 1-oxo-group has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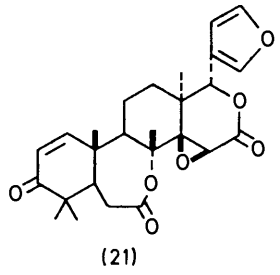
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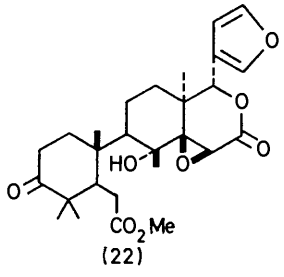

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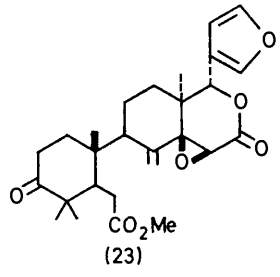

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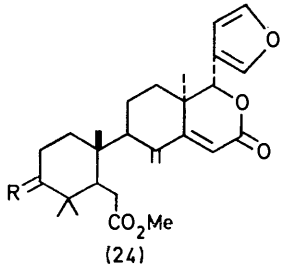

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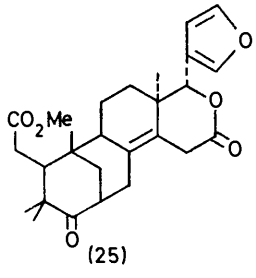

(25)

on the methyl shifts in mexicanolide.[20] Baeyer–Villiger oxidation of 7-deacetoxy-7-oxogedunin[21] (20) gave the corresponding ε-lactone (21). Attempts to hydrolyse the lactone ring led to the addition of methanol to the conjugated double bond, so this was reduced

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[17] D. A. H. Taylor, *Chem. Comm.*, 1969, 58.
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first. Sodium borohydride gave the saturated alcohol, which was reoxidised with Jones reagent to give the saturated keto-lactone. This was hydrolysed with 4M-sodium hydroxide, and the resultant acid characterised as its methyl ester (22) [$\nu_{max.}$ (CCl_4) 3600 and 3500 cm^{-1}]. Dehydration with thionyl chloride gave the exomethylene derivative (23) [δ 5·27, 5·30, and 5·40 (=CH_2 and H-17)], which was reduced with chromium(II) chloride to the required diene lactone (24; R = O). This lactone was much more stable than the corresponding β-diketone (11a), being only partially cyclised by refluxing 10% methanolic potassium hydroxide. However, treatment with sodium methoxide in methanol for 24 hours effected complete cyclisation, giving 1-deoxymexicanolide (25), which could not be induced to crystallise. The alcohol (24; R = H,βOH) was stable under the cyclisation conditions thus excluding the formation of products involving anion formation at C-6, α to the ester function. The n.m.r. spectrum of 1-deoxymexicanolide (25) was very similar to that of mexicanolide. A small shielding (~0·2 p.p.m.) of one methyl signal and H-17 was observed. Attempts to reduce the 3-oxo-group of (25) led to a complex mixture involving reduction of the lactone ring, as in mexicanolide, and this was not pursued.

EXPERIMENTAL

For general experimental details see Part I.[2]

The Deoxy-derivative (3).—7-Deacetoxy-7-oxokhivorin (2) (5 g) in acetone (140 ml) and glacial acetic acid (50 ml) was treated with excess of chromium(II) chloride solution at 45° for 24 h under nitrogen. Dilution with water and extraction with chloroform gave the deoxy-derivative (3) (4·4 g) which was purified by preparative t.l.c. (p.l.c.) and crystallised from ethanol as fine needles, m.p. 253—257°, $\nu_{max.}$ 1735 and 1715 cm^{-1}, δ 0·8, 1·0, 1·15, 1·22, and 1·53 (tertiary methyls), 1·97 and 2·08 (2 × AcO), 4·7 (m, H-1 and H-3), 4·97 (s, H-17), 6·53 (s, H-15), and 6·4 and 7·42 (furan protons) (Found: C, 68·2; H, 7·15. Calc. for $C_{30}H_{38}O_8$: C, 68·4; H, 7·3%).

The ε-Lactone (7b).—Excess of peracetic acid was added dropwise to a cooled solution of the deoxy-derivative (3) (1·8 g) in methylene chloride (10 ml) containing anhydrous disodium hydrogen phosphate (2 g) and the reaction was left for 15 h. The crude product, obtained by addition of water and extraction with ethyl acetate, was purified by p.l.c. and crystallisation from benzene to give the *ε-lactone* (7b) as plates, m.p. 294—296°, $\nu_{max.}$ ($CHCl_3$) 1730 cm^{-1}, δ 0·87, 0·93, 1·08, 1·14, and 1·63 (tertiary methyls), 1·92, (2 × AcO), 4·64 (m, H-1 and H-3), 4·9 (s, H-17), 6·41 (s, H-15), and 6·29 and 7·35 (furan protons) (Found: C, 66·5; H, 7·0. $C_{30}H_{38}O_9$ requires C, 66·4; H, 7·1%).

The Unsaturated Ester (11b).—The ε-lactone (7b) (320 mg) was refluxed overnight in dry benzene (20 ml) containing toluene-*p*-sulphonic acid (20 mg). The product consisted of unchanged starting material and an acid (116 mg) which was separated by p.l.c. and methylated with ethereal diazomethane. Crystallisation from ethanol furnished the *ester* (11b) as needles, m.p. 119—124°, δ 0·84, 1·0, 1·07, and 1·14 (tertiary methyls), 2·0 and 2·06 (2 × AcO), 4·78 (m, H-1 and H-3), 5·22, 5·28 (CH_2=), 5·22 (s, H-17), 5·82 (s, H-15), and 6·47, 7·43, and 7·53 (furan protons) (Found: C, 64·4; H, 7·6. $C_{31}H_{40}O_9,H_2O$ requires C, 64·8; H, 7·4%).

The Alcohol (16; R = H, αOH).—Treatment of the ester (11b) (70 mg) in methanol (5 ml) with 4M-NaOH (0·4 ml) at room temperature for 20 h, gave, after acidification and methylation with diazomethane, the *alcohol* (16; R = H, αOH) (61 mg) which was recrystallised from ethanol as needles, m.p. 209—212°, $\nu_{max.}$ 3550 and 1740 cm^{-1}, δ 0·89, 0·95, 0·97, and 1·03 (tertiary methyls), 3·74 (-CO_2CH_3), 4·91, 5·17 (CH_2=), 5·54 (s, H-17), and 6·45, 7·43, and 7·5 (furan protons) (Found: C, 68·5; H, 7·6. $C_{27}H_{36}O_7$ requires C, 68·6; H, 7·7%).

Methyl Angolensate (16; R = O).—The alcohol (16; R = H,αOH) (30 mg), in acetone (3 ml), was oxidised with Jones reagent (6 drops) at 0°. The product (24 mg) was crystallised from ethanol as needles, m.p. 201—205°, $[\alpha]_D$ −41°, and was identical (t.l.c. and n.m.r.) with methyl angolensate (m.p. 203—208°, $[\alpha]_D$ −43°).

The Ester (12; R = H).—The ε-lactone (7b) (53 mg), in methanol (5 ml), was treated with 4M-NaOH (2 ml) for 12 h at room temperature. The acidic product (46 mg) was methylated with diazomethane and recrystallised from aqueous methanol to give the *ester* (12; R = H) as prisms, m.p. 280°, $\nu_{max.}$ 3610, 3530, and 1735 cm^{-1}, δ 0·93 (6H), 1·02, 1·18, and 1·62 (tertiary methyls), 3·43 and 3·67 (m, H-3 and H-1), 3·7 (-CO_2CH_3), 5·8 (s, H-17), and 6·4 and 7·4 (2H), (furan protons) (Found: C, 64·1; H, 7·7. $C_{27}H_{38}O_8,H_2O$ requires C, 63·8; H, 7·9%). The corresponding *acetate* (12; R = Ac) was crystallised from ethanol as small prisms, m.p. 258—260°, $\nu_{max.}$ 3610 and 1740 cm^{-1}, δ 0·8, 0·97, 1·0, 1·07, and 1·57 (tertiary methyls), 1·92 (AcO), 3·63 (-CO_2CH_3), 3·95 (m, H-1), 4·63 (m, H-3), 5·8 (s, H-17), and 6·27 and 7·37 (2H) (furan protons) (Found: *m/e*, 532·2665. $C_{29}H_{40}O_9$ requires *m/e*, 532·2672).

The Exomethylene Derivative (16; R = H,αOAc).—The acetate (12; R = Ac) (14 mg), in dry pyridine (1 ml), was treated with several drops of thionyl chloride. Water was added almost immediately. Purification of the product by preparative t.l.c. and subsequent recrystallisation from methanol gave the *exomethylene derivative* (16; R = H,αOAc) (11 mg) as cubes, m.p. 224—226°, $\nu_{max.}$ 1740 cm^{-1}, δ 0·79 (9H) and 0·97 (tertiary methyls), 2·06 (AcO), 3·65 (m, H-1), 3·65 (-CO_2CH_3), 4·68 (m, H-3), 4·83, 5·08 (CH_2=), 5·74 (s, H-17), and 6·38 and 7·4 (2H) (furan protons). This compound was also prepared by acetylation of the alcohol (16; R = H,αOH).

The ε-Lactone (6b).—Treatment of 7-deacetoxy-7-oxokhivorin (8 g) with excess of peracetic acid, as previously described, and p.l.c. of the crude product yielded the *ε-lactone* (6b) (2·5 g), recrystallised from methanol as prisms, m.p. 308°, δ 0·9, 1·03, 1·08, 1·33, and 1·47 (tertiary methyls), 1·97 and 2·03 (2 × AcO), 3·73 (s, H-15), 4·73 and 4·58 (m, H-1 and H-3), 5·37 (s, H-17), and 6·33 and 7·38 (2H) (furan protons) (Found: C, 64·4; H, 7·0. $C_{30}H_{38}O_{10}$ requires C, 64·5; H, 6·9%).

This compound was recovered unchanged after refluxing in benzene with toluene-*p*-sulphonic acid.

Alkaline Hydrolysis of the ε-Lactone (6b).—The ε-lactone (6b) (1·29 g) and K_2CO_3 (1 g) were dissolved in aqueous methanol and the solution was left at room temperature overnight. The resulting mixture of diacetoxy-acid and methyl ester was converted completely into the *methyl ester* (10b) with diazomethane. Crystallisation from methanol yielded pure *methyl ester* (10b) (1·12 g) as prisms,

m.p. 274—277°, $\nu_{max.}$ ($CHCl_3$) 3590 and 1735 cm^{-1}, δ 0·92, 1·06 (6H), and 1·25 (6H) (tertiary methyls), 2·07 (2 × AcO), 3·6 ($-CO_2CH_3$), 3·63 (s, H-15), 4·76 and 5·22 (m, H-1 and H-3), 5·41 (s, H-17), and 6·39 and 7·44 (2H) (furan protons) (Found: C, 63·2; H, 7·1. $C_{31}H_{42}O_{11}$ requires C, 63·0; H, 7·2%).

Brief treatment of the ε-lactone (6b), in methanol, with 4M-NaOH gave a mixture of the *dihydroxy-lactone* (6c) and, after methylation with diazomethane, the methyl ester (10b). The dihydroxy-lactone (6c) was recrystallised from aqueous methanol in fine needles, m.p. 250—253°, $\nu_{max.}$ ($CHCl_3$) 3620, 3480, and 1740 cm^{-1}, δ 0·82, 0·96, 1·11, 1·3, and 1·34 (tertiary methyls), 3·66 and 3·74 (m, H-1 and H-3), 3·71 (s, H-15), 5·4 (s, H-17), and 6·4 and 7·42 (2H) (furan protons) (Found: C, 63·6; H, 6·9. $C_{26}H_{34}O_8,H_2O$ requires C, 63·4; H, 7·4%). Longer reaction times transformed the ε-lactone (6b) into a mixture, after methylation, of the *triol ester* (10c) and the *ether* (9; R = H). The triol ester (10c) was recrystallised from methanol, m.p. 236—240°, $\nu_{max.}$ (KBr) 3520, 3460, and 1730 cm^{-1}, δ 0·95, 0·98, 1·10, and 1·21 (6H) (tertiary methyls), 3·56 ($-CO_2CH_3$), 3·62 (s, H-15), 3·68 and 4·13 (m, H-1 and H-3), 5·41 (s, H-17), and 6·39 and 7·42 (2H) (furan protons) (Found: C, 63·8; H, 7·45. $C_{22}H_{38}O_9$ requires C, 64·8; H, 7·55%). The ether (9; R = H) was recrystallised from benzene as small needles, m.p. 235—238°, $\nu_{max.}$ ($CHCl_3$) 3460 and 1735 cm^{-1}, δ 0·88, 0·91, 0·96, 1·14, and 1·33 (tertiary methyls), 3·56 (m, H-3), 3·93 (m, H-1), 3·64 ($-CO_2CH_3$), 4·45 (s, after D_2O exchange, H-15), 6·21 (s, H-17), and 6·51, 7·44, and 7·48 (furan protons) (Found: C, 64·0; H, 7·5. $C_{27}H_{38}O_9$ requires C, 64·0; H, 7·6%). The corresponding *diacetate* (9; R = Ac), prepared in the usual way was recrystallised from chloroform–ether in cubes, m.p. 173—176°, $\nu_{max.}$ 3610, 3490, 1770, and 1740 cm^{-1}, δ 0·8, 0·96, 1·08, 1·27, and 1·49 (tertiary methyls), 1·82 and 2·19 (2 × AcO), 3·67 ($-CO_2CH_3$), 3·98 (m, H-1), 4·65 (m, H-3), 5·64 (s, H-15), 5·88 (s, H-17), and 6·59, 7·44, and 7·98 (furan protons) (Found: C, 62·9; H, 7·0. $C_{31}H_{42}O_{11}$ requires C, 63·0; H, 7·2%).

The β-*Diketone* (6a).—The dihydroxy-lactone (6c) (50 mg) was oxidised with excess of Jones reagent in acetone at 0°. Purification by p.l.c. and crystallisation from ethanol afforded the β-*diketone* (6a), m.p. 280—284°, $\lambda_{max.}$ 260 nm (ε 10,000) changing to $\lambda_{max.}$ 289 nm (ε 21,500) on addition of two drops of 0·1M-NaOH, δ 1·21, 1·25, 1·32 (6H), and 1·40 (tertiary methyls), 3·45br (s, 2 × H-2), 3·67 (s, H-15), 5·38 (s, H-17), and 6·36 and 7·41 (2H) (furan protons) (Found: *m/e*, 470. $C_{26}H_{30}O_8$ requires *m/e*, 470).

Chromium(II) chloride reduction of the β-diketone (6a) gave an inseparable mixture of products.

The Exomethylene-derivative (14b).—The diacetoxy methyl ester (10b) (840 mg) was dehydrated as usual with thionyl chloride in pyridine. The major product, obtained by p.l.c. and crystallisation from methanol, was the *exomethylene derivative* (14b) (732 mg), m.p. 197—199°, δ 0·85, 0·93, 1·03, and 1·23 (tertiary methyls), 2·08 (2 × AcO), 3·63 ($-CO_2CH_3$), 3·87 (s, H-15), 4·72 and 4·93 (m, H-1 and H-3), 5·07 and 5·4 (CH_2=), 5·47 (s, H-17), and 6·35 and 7·37 (2H) (furan protons) (Found: C, 65·4; H, 6·9. $C_{31}H_{40}O_{10}$ requires C, 65·0; H, 7·0%).

Alkaline Hydrolysis of (14b).—Treatment of the exomethylene derivative (14b) (447 mg) in methanol (10 ml) with 4M-NaOH (5 ml) at room temperature for 6 h gave, after methylation, a mixture of two products which were separated by p.l.c. The more polar component, which was not obtained crystalline, was the *diol* (14c) (213 mg), *m/e* 488, $\nu_{max.}$ 3600, 3500, and 1745 cm^{-1}, δ 0·95, 0·97 (6H), and 1·01 (tertiary methyls), 3·44 ($-CO_2CH_3$), 3·57 and 3·74 (m, H-1 and H-3), 3·92 (s, H-15), 5·24 and 5·36 (CH_2=), 5·42 (s, H-17), and 6·37 and 7·42 (2H) (furan protons).

The less polar component, the *ether* (13; R = H) (53 mg), was recrystallised from chloroform–ether as needles, m.p. 182—186°, $\nu_{max.}$ 3540 and 1740 cm^{-1}, δ 0·83, 0·88, 0·95, and 1·0 (tertiary methyls), 3·33 (m, after D_2O exchange, H-3), 3·67 ($-CO_2CH_3$), 3·78 (m, H-1), 4·6 (s, after D_2O exchange, H-15), 5·1, 5·27, and 5·37 (s, H-17 and CH_2=), and 6·33 and 7·33 (2H) (furan protons) (Found: *m/e*, 488·2411. $C_{27}H_{36}O_8$ requires *m/e*, 488·2410). The corresponding *diacetate* (13; R = Ac) was recrystallised from methanol as small needles, m.p. 296°, $\nu_{max.}$ 1770 and 1745 cm^{-1}, δ 0·8 (6H) and 0·96 (6H) (tertiary methyls), 2·05 and 2·12 (2 × AcO), 3·51 (m, H-1), 3·65 ($-CO_2CH_3$), 4·75 (m, H-3), 4·79 and 5·12 (CH_2=), 5·66 (s, H-17), 5·84 (s, H-15), and 6·37 and 7·39 (2H) (furan protons) (Found: *m/e*, 572·2622. $C_{31}H_{40}O_{10}$ requires *m/e*, 572·2621).

The β-*Diketone* (14a) *and the Hydroxy-ketone* (14f).—The diol (14c) (170 mg), in acetone, was oxidised with Jones reagent at 0° to give two products. The β-*diketone* (14a) (91 mg) was recrystallised from methanol as fine needles, m.p. 188—192°, $\nu_{max.}$ ($CHCl_3$) 1735 and 1707 cm^{-1}, $\lambda_{max.}$ 261 nm (ε 9300) changing to $\lambda_{max.}$ 289 nm (ε 22,600) on addition of two drops of 0·1M-NaOH, δ 0·9, 0·96 (6H), and 1·02 (tertiary methyls), 3·66 ($-CO_2CH_3$), 3·73 (s, H-15), 3·9 (s, 2H-2), 5·32 and 5·54 (CH_2=), 5·54 (s, H-17), and 6·36 and 7·42 (2H) (furan protons) (Found: C, 66·8; H, 6·7. $C_{27}H_{32}O_8$ requires C, 66·9; H, 6·7%).

The *hydroxy-ketone* (14f) (20 mg) was recrystallised from chloroform–ether as cubes, m.p. 196—199°, $\nu_{max.}$ 3610, 3525, 1745, and 1710 cm^{-1}, δ 0·95, 1·12 (6H), and 1·17 (tertiary methyls), 3·67 ($-CO_2CH_3$), 3·94 (s, H-15), 4·05 (m, H-3), 3·36 (2H) and 3·51 (s, H-17 and CH_2=), and 6·36 and 7·42 (2H) (furan protons) (Found: C, 66·6; H, 7·0. $C_{27}H_{34}O_8$ requires C, 66·7; H, 7·0%).

Andirobin (17).—Dehydration of the hydroxy-ketone (14f) with thionyl chloride in pyridine yielded andirobin (17), m.p. 193—196°, identical (t.l.c., n.m.r., i.r.) with natural material.

The Diene-lactone (11a).—The β-diketone (14a) (43 mg) was reduced with chromium(II) chloride in the usual way. The *diene-lactone* (11a) (22 mg) was separated by p.l.c. and crystallised from chloroform–ether as needles, m.p. 204—210°, $\lambda_{max.}$ 259 nm (ε 22,800) changing to $\lambda_{max.}$ 286 nm (ε 29,100) on addition of two drops of 0·1M-NaOH, δ 0·92, 0·98, 1·05, and 1·16 (tertiary methyls), 3·32 and 3·72 (ABq, *J* 16 Hz, 2 × H-2), 3·68 ($-CO_2CH_3$), 5·15, 5·33, and 5·44 (each 1H, s, CH_2= and H-17), 5·96 (s, H-15), and 6·42 and 7·42, 7·49 (furan protons) (Found: C, 69·1; H, 6·8. $C_{27}H_{32}O_7$ requires C, 69·2; H, 6·9%).

Mexicanolide (18).—The diene-lactone (11a) (15 mg) was stirred in chloroform in the presence of a few drops of aqueous $NaHCO_3$ for 24 h. The sole product was mexicanolide (18) which was crystallised from methanol in cubes, m.p. 221—226, $[\alpha]_D$ −85° (identical n.m.r., i.r., and u.v. with natural material, m.p. 222—227°, $[\alpha]_D$ −90°) (Found: C, 69·0; H, 6·8. Calc. for $C_{27}H_{32}O_7$; C, 69·2; H, 6·9%).

Oxidation of the Triol Ester (10c).—The triol ester (10c) (313 mg) was oxidised with Jones reagent in acetone at 0°. The two major products were separated by p.l.c. The β-*diketone* (10a) (124 mg) was not obtained crystalline

and had $\nu_{max.}$ (CCl_4) 3600, 1740, and 1705 cm^{-1}, $\lambda_{max.}$ 260 nm (ε 9800) changing to $\lambda_{max.}$ 288 nm (ε 20,000) on addition of two drops of 0·1M-NaOH, δ 1·00, 1·13, 1·15, 1·28, and 1·31 (tertiary methyls), 3·38br (s, 2 × H-2), 3·64 (s, H-15), 3·67 ($-CO_2CH_3$), 5·38 (s, H-17), and 6·36 and 7·40 (2H) (furan protons) (Found: *m/e*, 502.2201. $C_{27}H_{34}O_9$ requires *m/e*, 502.2203).

The gummy *hydroxy-ketone* (10e) (92 mg) had $\nu_{max.}$ ($CHCl_3$) 3600, 3510, 1735, and 1715sh cm^{-1}, δ 0·97, 1·09, 1·21 (6H), and 1·38 (tertiary methyls), 3·65 ($-CO_2CH_3$), 3·69 (s, H-15), 3·79 (m, H-3), 4·47 (s, H-17), and 6·41 and 7·46 (2H) (furan protons) (Found: *m/e* 504.2332. $C_{27}H_{36}O_9$ requires *m/e*, 504.2359).

Acetylation of the Hydroxy-ketone (10e).—The hydroxy-ketone (10e) (61 mg) was acetylated in the usual way. Two products were obtained which were separated only with difficulty by repeated p.l.c. The more polar component was the *acetate* (10d) (14 mg) which was not crystalline, *m/e* 546, $\nu_{max.}$ 3600, 3520, 1740, and 1710 cm^{-1}, δ 0·87, 1·27 (9H), and 1·4 (tertiary methyls), 2·02 (AcO), 3·65 (4H) ($-CO_2CH_3$ and H-15), 4·93 (m, H-3), 5·4 (s, H-17), and 6·35 and 7·37 (2H) (furan protons).

The *enone* (15) (35 mg), the less polar component, was recrystallised from ether–light petroleum as plates, m.p. 193—194°, $\nu_{max.}$ 3600, 3525, 1740, and 1675 cm^{-1}, δ 1·0, 1·12, 1·21, 1·28, and 1·36 (tertiary methyls), 3·6 (4H) ($-CO_2CH_3$ and H-15), 5·39 (s, H-17), 5·86 and 6·59 (ABq, *J* 10 Hz, H-2 and H-3), and 6·36 and 7·39 (2H) (furan protons) (Found: C, 66·6; H, 7·0. $C_{27}H_{34}O_8$ requires C, 66·7; H, 7·0%).

Iso-andirobin (19).—The enone (15) (15 mg) was dehydrated in the usual way with thionyl chloride in pyridine. P.l.c. of the crude product yielded *iso-andirobin* (19) (7 mg) as a gum, $[\alpha]_D$ +22°, $\nu_{max.}$ 1745 and 1675 cm^{-1}, δ 0·4, 1·04 (6H), and 1·23 (tertiary methyls), 3·67 ($-CO_2CH_3$), 3·88 (s, H-15), 5·26, 5·29, and 5·62 (each 1Hs, H-17 and CH_2=), 5·91 and 6·62 (ABq, *J* 10 Hz, H-2 and H-3), and 6·35 and 7·4 (2H) (furan protons) (Found: *m/e*, 468·2097. $C_{27}H_{32}O_7$ requires *m/e*, 468·2147).

The Acetate (14d) (*'Mahoganin' Acetate*).—The acetate (10d) (10 mg) was dehydrated as above. The major product, separated by p.l.c. was the *acetate* (14d) (6 mg) which was not obtained crystalline, $\nu_{max.}$ 1740 and 1705 cm^{-1}, δ 0·82, 0·92, and 1·26 (6H) (tertiary methyls), 2·11 (AcO), 3·61 ($-CO_2CH_3$), 3·9 (s, H-15), 4·9 (m, H-3), 5·41, 5·48, and 5·62 (each 1H, s, CH_2= and H-17), and 6·36 and 7·42 (2H) (furan protons) (Found: *m/e*, 528.2357. $C_{29}H_{36}O_9$ requires *m/e*, 528.2359).

The ε-*Lactone* (21).—7-Deacetoxy-7-oxogedunin (20) (2 g) was oxidised under normal Baeyer–Villiger conditions with peracetic acid. P.l.c. of the crude product followed by crystallisation from methanol gave the ε-*lactone* (21) (870 mg), m.p. 244—246°, $\nu_{max.}$ ($CHCl_3$) 1745 and 1677 cm^{-1}, δ 1·07, 1·22, 1·26, 1·31, and 1·4 (tertiary methyls), 3·75 (s, H-15), 5·43 (s, H-17), 5·96 and 7·09 (ABq, *J* 11 Hz, H-2 and H-1), and 6·41 and 7·46 (2H) (furan protons) (Found: C, 68·55; H, 6·7. $C_{26}H_{30}O_7$ requires C, 68·7; H, 6·65%). Attempted hydrolysis of the ε-lactone (21) with methanolic KOH resulted in addition of methanol to the enone double bond.

*The Dihydro-*ε*-lactone*.—The ε-lactone (21) (271 mg), in ethyl acetate, was treated with excess of $NaBH_4$ at room temperature for 4 h. The crude product was immediately oxidised with Jones reagent in acetone at 0°. P.l.c. and crystallisation from chloroform–methanol gave the *dihydro-*ε*-lactone* (580 mg), m.p. 287—291°, $\nu_{max.}$ ($CHCl_3$) 1740 and 1710 cm^{-1}, δ 1·03, 1·1, 1·18, 1·31, and 1·48 (tertiary methyls), 3·72 (s, H-15), 5·4 (s, H-17), and 6·4 and 7·44 (2H) (furan protons) (Found: C, 68·2; H, 7·1. $C_{26}H_{32}O_7$ requires C, 68·4; H, 7·1%).

The Methyl Ester (22).—The dihydro-ε-lactone (327 mg), in methanol (15 ml), was hydrolysed with 4M-NaOH (1 ml). The acidic product (305 mg) was methylated with diazomethane and crystallised from chloroform–methanol to give the *ester* (22), m.p. 198—201°, $\nu_{max.}$ 3610, 3510, 1740, and 1715 cm^{-1}, δ 1·02, 1·14 (6H), 1·22, and 1·32 (tertiary methyls), 3·58 ($-CO_2CH_3$), 3·62 (s, H-15), 5·4 (s, H-17), and 6·37 and 7·42 (2H) (furan protons) (Found: C, 66·4; H, 7·5. $C_{27}H_{36}O_8$ requires C, 66·4; H, 7·4%).

The Exomethylene Derivative (23).—The ester (22) (192 mg) was dehydrated with thionyl chloride in pyridine under the usual conditions. The product was purified by p.l.c. and crystallised from ethanol to give the *exomethylene derivative* (23) (157 mg), m.p. 149—151°, $\nu_{max.}$ ($CHCl_3$) 1735 and 1705 cm^{-1}, δ 0·92, 0·96, 1·07, and 1·11 (tertiary methyls), 3·64 ($-CO_2CH_3$), 3·93 (s, H-15), 5·27, 5·3, and 5·46 (each 1H, s, CH_2= and H-17), and 6·36 and 7·42 (2H) (furan protons) (Found: C, 69·2; H, 7·4. $C_{27}H_{34}O_7$ requires C, 68·9; H, 7·3%).

The Diene-lactone (24; R = O).—The exomethylene-derivative (23) (98 mg) was reduced with chromium(II) chloride as described above. P.l.c. and crystallisation from ether afforded the *diene-lactone* (24; R = O) (87 mg) as fine needles, m.p. 145—146° $\nu_{max.}$ ($CHCl_3$) 1720br cm^{-1}, δ 0·99, 1·04, 1·1, and 1·14 (tertiary methyls), 3·65 ($-CO_2CH_3$), 5·13 and 5·42 (CH_2=), 5·19 (s, H-15), and 6·48, 7·46, and 7·56 (furan protons) (Found: C, 71·2; H, 7·4. $C_{27}H_{34}O_6$ requires C, 71·3; H, 7·5%).

1-*Deoxymexicanolide* (25).—The diene-lactone (24; R = O) (43 mg) was dissolved in sodium methoxide in dry methanol and allowed to stand at room temperature for 24 h. The crude product was methylated with diazomethane. P.l.c. afforded 1-*deoxymexicanolide* (25) (26 mg) as the major product. In spite of repeated p.l.c. it could not be crystallised, $[\alpha]_D$ +75°, *m/e* 454; $\nu_{max.}$ (CCl_4) 1740 and 1708 cm^{-1}, δ 0·92, 0·96, and 1·03 (6H), (tertiary methyls), 3·35br (s, 2 × H-15), 3·65 (s, $-CO_2CH_3$), 5·02 (s, H-17), and 6·44, 7·4, and 7·52 (furan protons) (Found: *m/e*, 454. $C_{27}H_{34}O_6$ requires *m/e*, 454).

Reduction of 1-deoxymexicanolide (25) with sodium borohydride in ethanol gave a multitude of products which were not characterised.

The Alcohol (24; R = H,βOH).—The exomethylene derivative (24; R = O) (30 mg) in methanol (3 ml) was reduced with excess of $NaBH_4$ in the usual way. The *alcohol* (24; R = H,βOH) was purified by p.l.c., δ 0·93, 0·95 (6H), and 1·00 (tertiary methyls), 3·27 (m, H-3), 3·66 ($-CO_2CH_3$), 5·06 and 5·35 (CH_2=), 5·24 (s, H-17), 5·87 (s, H-15), 6·50, 7·46, and 7·57 (furan protons) (Found: *m/e*, 456·2512. $C_{27}H_{36}O_6$ requires *m/e*, 456·2512).

The alcohol (24; R = H,βOH) was recovered unchanged after treatment with sodium methoxide under the above conditions.

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