Extractives from *Cedrela odorata* L. The Structure of Methyl Angolensate

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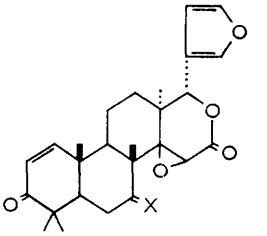
The constituents of the heartwood of *Cedrela odorata* are variable. The structure of methyl angolensate, one of the components, is elucidated on the basis of spectroscopic evidence and chemical transformations. It is a seco-ring-B tetranortriterpenoid closely related biogenetically to gedunin and deacetyl-7-keto-gedunin, which are also found in the heartwood.

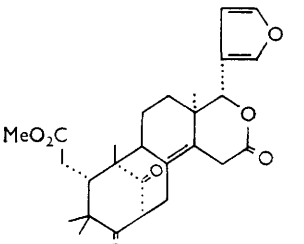
THE West Indian cedar, *Cedrela odorata* L. (*Meliaceae*), is native to the Caribbean islands and tropical continental America. The timber is one of the most valuable in this region, being fairly resistant to termite attack, and is extensively used in the furniture and building industry. Examination of the benzene extractive from the heartwood of this tree has given extremely variable results depending at least in part on the age and location of the specimen. The percentage of total benzene extractive from different specimens (based on dry weight of wood) varied from almost nil to about 5 and the nature and proportions of crystalline material isolable by chromatography of the extract were also variable. The benzene extractive of a cedar specimen obtained from the parish of St. Elizabeth, after removal of the components soluble in light petroleum, gave methyl angolensate in about 1% yield. Chromatography of the mother-liquor afforded minor amounts of gedunin (I) and deacetyl-7-ketogedunin (II) together with two triterpenoids, $C_{30}H_{46}O_4$, m. p. 236—239°, and $C_{30}H_{48}O_4$, m. p. 247—248°. Extraction of a West African specimen of *C. odorata* has given deacetyl-7-ketogedunin and *Cedrela odorata* substance B [1] [identical with mexicanolide (III) isolated from *C. mexicana* [2]]. Methyl angolensate has also been isolated from the heartwood of other *Meliaceae* species—*Entandrophragma angolense* and *E. utile* [3] and *Guarea thompsonii*.[4] We now wish to report the result of our structural investigations on methyl angolensate.*

Bevan and his co-workers [3] had established the presence of a methoxycarbonyl group. The now accepted molecular formula, $C_{27}H_{34}O_7$, was proposed by Housley *et al.*[4] and they also confirmed the presence of an unhindered carbonyl group by the preparation of an oxime and a 2,4-dinitrophenylhydrazone. For clarity in exposition, the evidence will be presented in terms of the structure (IVb) for methyl angolensate.

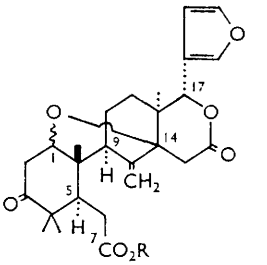
The ultraviolet (u.v.) spectrum of methyl angolensate had a maximum at 204 mμ (ε 6000) while in the infrared (i.r.) region three bands at 3106, 1504, and 877 cm.$^{-1}$ were characteristic of the furan ring. That this was a β-substituted furan was clearly indicated by the nuclear magnetic resonance (n.m.r.) spectrum with multiplets at 7·39 † (2H) and 6·38 (1H).[5] Ozonolysis of



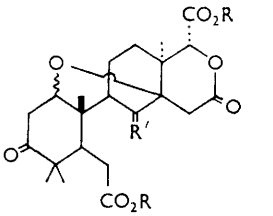
(I: X = ∝-OAc, H)
(II: X = O)



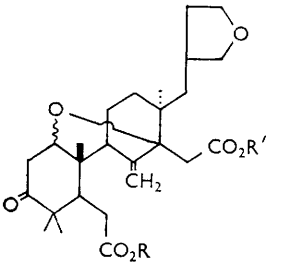
(III)



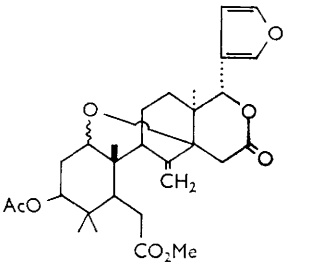
(IVa: R = H)
(IVb: R = Me)



(Va: R = Me, R′ = CH_2)
(Vb: R = H, R′ = CH_2)
(Vc: R = Me, R′ = O)



(VIa: R = Me, R′ = H)
(VIb: R = R′ = Me)
(VIc: R = R′ = H)



(VII)

* In the later stages of this work, we learnt that structural work was also under way at Oxford and at Ibadan and information was exchanged. The work of these groups is presented in the preceding Paper. A preliminary Communication on part of this work has already appeared (C. W. L. Bevan, J. W. Powell, D. A. H. Taylor, P. Toft, M. Welford, W. R. Chan, B. S. Mootoo, and T. G. Halsall, *Chem. and Ind.*, 1964, 1751.).

† Values are δ in p.p.m. from tetramethylsilane.

[1] C. W. L. Bevan, J. W. Powell, and D. A. H. Taylor, *J. Chem. Soc.*, 1963, 980.

[2] J. D. Connolly, R. McCrindle, and K. H. Overton, *Chem. Comm.*, 1965, 162; C. W. L. Bevan, J. W. Powell, and D. A. H. Taylor, *ibid.*, p. 281; S. A. Adeoye and D. A. Bekoe, *ibid.*, p. 301.

[3] A. Akisanya, C. W. L. Bevan, J. Hirst, T. G. Halsall, and D. A. H. Taylor, *J. Chem. Soc.*, 1960, 3827.

[4] J. R. Housley, F. E. King, T. J. King, and P. R. Taylor, *J. Chem. Soc.*, 1962, 5095.

[5] E. J. Corey, G. Slomp, Sukh Dev, S. Tobinaga, and E. R. Glazier, *J. Amer. Chem. Soc.*, 1958, **80**, 1204.

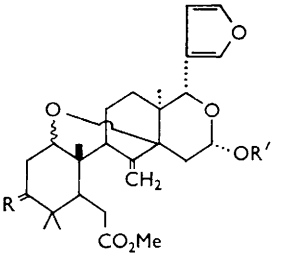
methyl angolensate in ethyl acetate solution gave a trisnor acid isolated as the methyl ester (Va) ($\lambda_{max.}$ 204 mμ, ε 2600). The same ester was also isolated from ozonolysis of angolensic acid followed by esterification with diazomethane. Mild hydrolysis of the dimethyl ester gave the corresponding diacid (Vb).

The presence of a saturated δ-lactone inferred from i.r. spectral data on methyl angolensate and its derivatives was supported by titration. Evidence for the furan–lactone relationship was provided in the following way. The n.m.r. spectrum of methyl angolensate shows a sharp singlet at 5·66 attributable to the proton at C-17 allylicly situated to the furan ring and further deshielded by the oxygen atom on the same carbon atom. The position of this signal is closely similar to that found in the model compounds (I) and (II) (5·60 and 5·50, respectively) indicating an identical environment. This was confirmed by hydrogenation of an ethanolic solution of methyl angolensate with a palladium–charcoal catalyst which furnished a hexahydro-acid, $C_{27}H_{40}O_7$ (VIa). The n.m.r. spectrum of the methyl ester (VIb) showed the disappearance of the signals associated with the furan and the C-17 protons, and the reaction can be interpreted as hydrogenolysis of the lactone followed by saturation of the furan ring. Such behaviour finds a parallel in the chemistry of columbin [6] and limonin.[7]

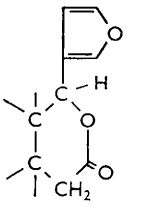
The further substitution of the lactone was defined as follows. Reduction of methyl angolensate with sodium borohydride in pyridine solution gave the alcohol expected from reduction of the C-3 carbonyl function. This compound could not be induced to crystallise but was homogeneous as judged by thin-layer chromatography (t.l.c.) and was characterised as the crystalline monoacetate (VII). In ethanolic solution with sodium borohydride, methyl angolensate afforded a mixture of two diols (VIIIa) and (VIIIb), easily separable by recrystallisation. Chromium trioxide oxidation of (VIIIa), the major product, regenerated methyl angolensate, thus indicating that the reduction must have involved the carbonyl and lactone functions and that the methoxycarbonyl group was unaffected. Such reduction of a lactone to the corresponding hemiacetal by sodium borohydride is not common but there is precedent.[8] The n.m.r. spectra of the diacetates showed in both cases one proton appearing as a low-field quartet at 6·18 ($J_{app.}$ = 8·3 c./sec.). The chemical shift indicated that this signal is generated by a proton attached to a carbon atom bearing both an acetate group and another oxygen atom, while the splitting pattern clearly indicates that it is coupled to two non-equivalent protons on the adjacent carbon atom.[9] The identity in shift and multiplicity of this proton indicates that the two diols have the same configuration at C-16 and hence must be epimeric at C-3. The results described so far could be embodied in the partial structure (IX) for methyl angolensate.

[6] D. H. R. Barton and D. Elad, *J. Chem. Soc.*, 1956, 2085.
[7] D. H. R. Barton, S. K. Pradhan, S. Sternhell, and J. F. Templeton, *J. Chem. Soc.*, 1961, 255.

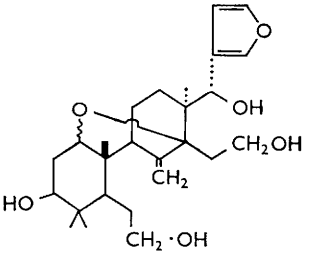
The i.r. ($\nu_{max.}$ 1653 cm.$^{-1}$) and u.v. ($\lambda_{max.}$ 204 mμ, ε 2600) spectral properties of (Va) and (VIb) were indicative of the presence in these compounds of an isolated double bond. Two singlets near δ 5 suggested that this



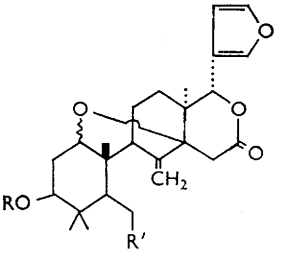
(VIIIa: R = β-OH, H; R′ = H)
(VIIIb: R = α-OH, H; R′ = H)



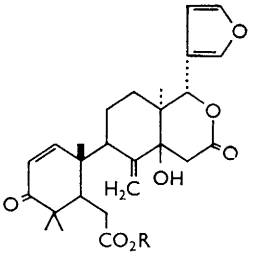
(IX)



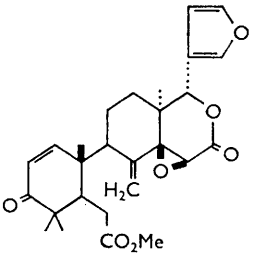
(X)



(XIa: R = H, R′ = CH_2·OH)
(XIb: R = H, R′ = CHO)



(XIIa: R = H)
(XIIb: R = Me)



(XIII)

chromophore was an exocyclic methylene group. These singlets were also present in methyl angolensate and other appropriate derivatives.

The low reactivity of this double bond, already implicit in the reactions so far described, was further supported by the inertness of compound (VIb) to osmium tetroxide in pyridine and to monoperphthalic acid over 2 days. Chemical evidence for the exocyclic methylene group was obtained by ozonolysis of compound (Va), which gave formaldehyde, isolated as the 2,4-dinitrophenylhydrazone, and a neutral compound, $C_{24}H_{32}O_9$, m. p. 213—216°, formulated as (Vc). In conformity, it showed absorption in the i.r. region at 1750 and 1715

[8] D. Lavie, E. Glotter, and Y. Shvo, *Tetrahedron*, 1963, **19**, 1377, and references therein.
[9] R. U. Lemieux, R. K. Kullnig, H. J. Bernstein, and W. G. Schneider, *J. Amer. Chem. Soc.*, 1958, **80**, 6098.

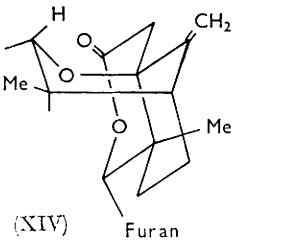
cm.$^{-1}$ while the bands in the u.v., i.r., and n.m.r. spectra which were ascribed to the C=CH_2 group had disappeared.

Reduction of methyl angolensate with lithium aluminium hydride in ether afforded a mixture of products. One compound, m. p. 230—232°, was the expected tetrol (X). In agreement, it showed no carbonyl absorption in the i.r. region while acetylation with acetic anhydride and pyridine gave an amorphous product recognised as a tetra-acetate from its n.m.r. spectrum. A second compound, m. p. 168—172°, had a single carbonyl band in the i.r. region at 1742 cm.$^{-1}$ (δ-lactone) and on oxidation with chromium trioxide afforded angolensic acid (IVa). Clearly this must be the diol (XIa). This diol was also obtained from the reduction of methyl angolensate with lithium and liquid ammonia. Oppenauer oxidation of the diol (XIa) gave the hydroxyaldehyde (XIb) with i.r. bands at 3425, 1742, and 1709 cm.$^{-1}$. The n.m.r. spectrum showed a signal for one proton as a triplet at 9·92 (J = 1 c./sec.), a position characteristic for aldehydic protons. The multiplicity demands a system of the type $-CH_2CHO$ in (XIb) and hence of $-CH_2CO_2Me$ in methyl angolensate itself.

Of the two remaining oxygen atoms in methyl angolensate, one is involved in a carbonyl function (*vide supra*) while the other in view of its unreactivity must be ethereal. The presence in the n.m.r. spectrum of a one proton quartet as the X part of an ABX system at 3·54 ($J_{app.}$ = 6·0, 4·2 c./sec.) is consistent with the presence of an oxide ring of the type $-CH_2-CH-O-C-$. Compelling evidence for the relationship of this group with the carbonyl function was obtained as follows. Treatment of methyl angolensate or angolensic acid with sodium isobutoxide in isobutanol at room temperature furnished a crystalline acid (XIIa), $C_{26}H_{32}O_7$, m. p. 216—219°, further characterised as the neutral monomethyl ester (XIIb), $C_{27}H_{34}O_7$, m. p. 192—193·5° by treatment with diazomethane. The spectral data for this ester were in accord with the assigned structure. Thus it had bands in the u.v. region at 204 and 235 mμ (ε 11,500 and 8500) while the i.r. spectrum in addition to bands associated with the δ-lactone and methyl ester (1745 and 1735) now showed a hydroxyl band (3425) and a new carbonyl band at 1664 cm.$^{-1}$ characteristic of an αβ-unsaturated ketone. In the n.m.r. spectrum, the major difference from that of methyl angolensate was the appearance of an AX system at 5·97 and 7·75 (J = 10 c./sec.) which is associated with the conjugated enone chromophore. In addition a singlet at 3·83 (1H) disappeared on shaking the sample with deuterium oxide. There was no signal which could be attributed to a proton on the carbon atom bearing the hydroxyl group. The downfield shift of the signal for the C-1 proton (7·75), compared the values obtained for gedunin (I) (7·10), deacetyl-7-ketogedunin (II) (7·13), and andirobin [10] (XIII) (7·20), must be due to the proximity of the hydroxyl group.

[10] W. D. Ollis, A. D. Ward, and R. Zelnik, *Tetrahedron Letters*, 1964, 2607.

The chemistry of (XIIb) is characterised by a facile recyclisation under a variety of conditions to regenerate methyl angolensate (see Experimental section). No isomer could be detected by t.l.c. using a variety of solvent systems. The direction of addition of the hydroxyl group to the ring A enone could lead to a boat (XIV) or chair (XV) conformation of the oxide ring and has a direct bearing on the configuration at C-1. This point is discussed more fully by Bevan and his co-workers in the preceding Paper. In contrast to the



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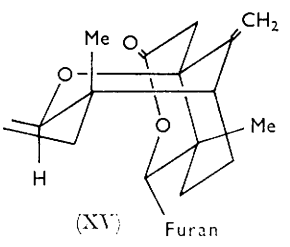
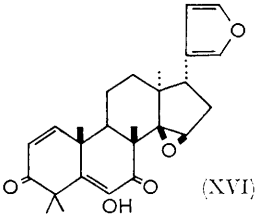
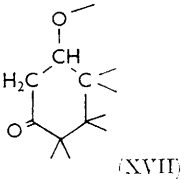


(XV)



(XVI)



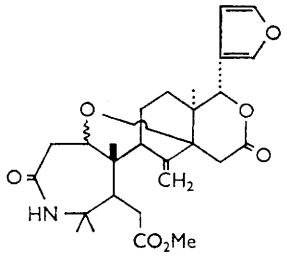
(XVII)

behaviour of cedrelone [11] (XVI) with hydroxylamine, the unsaturated ketone (XIIb) gave a normal oxime, as evidenced by the n.m.r. spectrum of its acetate. This still showed a pair of doublets [at 6·62 and 7·13 (J = 10·5 c./sec.)].

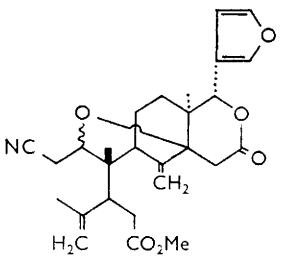
The formation of (XIIa) could best be interpreted as involving a β-elimination of the oxide ring generating the conjugated enone and a tertiary hydroxyl group. The n.m.r. spectrum in particular clearly indicated the system (XVII) in methyl angolensate. This could only be incorporated in ring A of a triterpenoid precursor with the carbonyl group either at C-1 or C-3. A decision in favour of the latter was made by treatment of methyl angolensate oxime with thionyl chloride at −20°. Two compounds were isolated by chromatography of the product. The major component, $C_{27}H_{35}O_7N$, had spectral properties consistent with its formulation as the expected lactam (XVIII). The minor product, $C_{27}H_{33}O_6N$, had i.r. bands at 2247 (C≡N), 1748 (ester and lactone), 1667 and 914 cm.$^{-1}$ (C=CH_2). The n.m.r. spectrum showed the presence of two tertiary methyl groups (0·91, 0·97) and a methyl attached to a double bond (1·87). In addition, there were now four protons in the olefinic region of the spectrum at 4·96 (3H) and 5·20 (1H). This compound must be formulated as the nitrile (XIX) arising from the "abnormal" Beckmann rearrangement involving a *gem*-dimethyl group at C-4 with a carbonyl at C-3. There is excellent

[11] R. Hodges, S. G. McGeachin, and R. A. Raphael, *J. Chem. Soc.*, 1963, 2515.

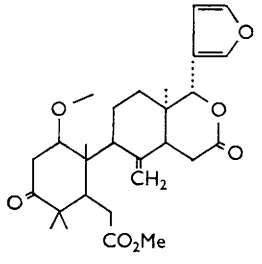
analogy for such elimination reactions.[12] When account is taken of probable stereoelectronic requirements of the reaction,[12] then the formation of the nitrile (XIX), rather than the more heavily substituted double-bond isomer, indicates that the proton at C-5 is axial.



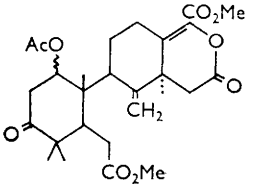
(XVIII)



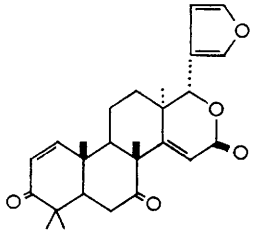
(XIX)



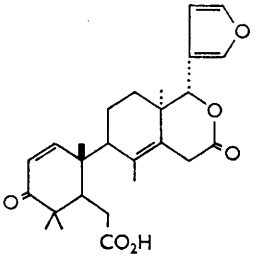
(XX)



(XXI)



(XXII)



(XXIII)

The co-occurrence of methyl angolensate with gedunin and deacetyl-7-ketogedunin suggests a biogenetic relationship between these compounds. The evidence presented for the nature and relationships of the functional groups, taken in conjunction with the molecular formula, shows that methyl angolensate is bicarbocyclic. When account is also taken of the presence of only four *C*-methyl groups (δ 0·86, 0·94, 1·04, 1·19) and an exocyclic methylene group, then a consideration of biogenetically acceptable structures from a euphol-type precursor leads directly to the partial formula (XX) for methyl angolensate.

Of the possible tertiary positions available for the attachment of the other end of the oxide link, C-14 is favoured biogenetically, since in all known limonoids, C-14 is either the terminus of a double bond or bears oxygen. Chemical support for the correctness of this postulate was forthcoming in the following way. Methyl angolensate in ethereal solution was recovered unchanged after treatment with boron trifluoride etherate for 17 hr. However, in acetic anhydride the same reagent converted the trisnor ester (Va) to a crystalline compound $C_{27}H_{36}O_9$. The n.m.r. spectrum showed the presence of an acetate group, while a new low-field proton at 5·29 could be assigned to the proton on carbon bearing the acetate. An ultraviolet subtraction curve of the trisnor ester (Va) from the product (XXI) had $\lambda_{max.}$ 204 mμ (ε 5800), which is the contribution of the αβ-unsaturated ester chromophore to the total u.v. absorption. These values are consistent with those obtained for such systems.[13] As expected from the structure (XXI), mild treatment with alkali generated a substance containing an αβ-unsaturated ketone ($\lambda_{max.}$ 233 mμ, ε 7200).

The absolute stereochemistry already written into the structure (IVa) follows from its assumed biogenesis. The relative configurations at C-13, C-14, and C-17 are in agreement with the probable concerted nature of the Lewis acid-catalysed rearrangement.[11] The configuration at C-5 has already been discussed.

Methyl angolensate thus belongs to the increasing group of tetranortriterpenoids characterised by a cleavage between C-7 and C-8. This group now includes andirobin,[10] swietenolide,[14] swietenine,[15] carapin,[16] mexicanolide,[2] and a low-melting compound from *Khaya senegalensis*.[17] Its genesis from a precursor such as deacetyl-7-ketogedunin is straightforward. Models indicate that the cleavage of ring B and inversion of ring C from boat to chair must precede the formation of the oxide ring. Such cleavage could be either by photochemical [18] or chemical [7] means. Indeed, conversion of deacetyl-7-ketogedunin (II) to the deoxy-compound (XXII) with chromous chloride, followed by treatment with alkali, afforded a crystalline acid, $C_{26}H_{32}O_6$, the spectral properties of which (see Experimental section) were in accord with the structure (XXIII).

EXPERIMENTAL

Melting points were determined on a Kofler hot-stage apparatus. Rotations were taken in chloroform solution at room temperature unless otherwise specified. Light petroleum used for recrystallisation is the fraction of b. p. 60—80°. Alumina used for column chromatography was Merck, grade III—IV according to the Brockmann scale. Thin-layer chromatography (t.l.c.) was done on 0·25 mm. thick layers of silica with ethyl acetate as solvent, and the chromatoplates were developed with iodine vapour. Ultraviolet spectra were recorded on a Unicam spectrophotometer (S.P. 700) and are for ethanol solutions.

[12] G. H. Whitham, *J. Chem. Soc.*, 1960, 2016; J. Klinot and A. Vystrčil, *Coll. Czech. Chem. Comm.*, 1962, **27**, 377; C. W. Shoppee, R. E. Lack, and S. K. Roy, *J. Chem. Soc.*, 1963, 3767.
[13] A. T. Neilsen, *J. Org. Chem.*, 1957, **22**, 1539.
[14] J. D. Connolly, R. McCrindle, K. H. Overton, and W. D. Warnock, *Tetrahedron Letters*, 1965, 2937.
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Infrared spectra, as Nujol mulls, were obtained on a Perkin-Elmer spectrophotometer (model 137). Nuclear magnetic resonance (n.m.r.) spectra were recorded on a Varian Associates A60 spectrometer and are for *ca.* 7% deuterochloroform solutions which also contained tetramethylsilane as internal reference at $\delta = 0{\cdot}00$.

Extraction of Cedrela odorata.—Dried, finely ground heartwood (3·4 kg.) was extracted by percolation with benzene (11 l.). After evaporation of the solvent, the oily residue (165 g.) was washed twice with boiling light petroleum (400, 100 ml.). The gummy residue was crystallised from ethyl acetate–light petroleum to give methyl angolensate (40·5 g.). An analytical sample, needles from methanol, had m. p. 204—205° (lit.,[3] 197°), $[\alpha]_D$ −44°, $\lambda_{max.}$ 204 mμ (ε 6000), $\nu_{max.}$ 3106, 1504, and 877 (furan), 1745 (δ-lactone and methyl ester), 1720 (cyclohexanone), 1653 and 911 cm.$^{-1}$ (exocyclic methylene) (Found: C, 69·0; H, 7·5; O, 23·6. $C_{27}H_{34}O_7$ requires C, 68·9; H, 7·3; O, 23·8%).

The *oxime* prepared in the usual way with hydroxylamine and pyridine crystallised from methanol as plates, m. p. 235—236° (lit.,[4] 228—229°) (Found: C, 66·7; H, 7·3; N, 3·05. $C_{27}H_{35}O_7N$ requires C, 66·8; H, 7·3; N, 2·9%).

A portion (12·0 g.) of the residue obtained by evaporation of the mother-liquor after crystallisation of methyl angolensate was chromatographed on alumina. Elution with benzene gave *gedunin* (I), 2·10 g., m. p. (prisms from ethyl acetate–light petroleum) 196—198° (lit.,[3] needles from methanol, 218°), $[\alpha]_D$ +44° (*c* 1·2), $\nu_{max.}$ 1734, 1725 (lactone and acetate), 1660 (cyclohexenone), 3106, 1500, 876 cm.$^{-1}$ (furan). N.m.r.: 7·30 (2H, multiplet, α-furan H); 7·10 (1H, doublet, $J = 10$ c./sec., H-1); 6·33 (1H, multiplet, β-furan H); 5·83 (1H, doublet, $J = 10$ c./sec. H-2); 5·60 (1H, singlet, H-17), 4·52 (1H, multiplet, H-7); 3·52 (1H, singlet, H-15); 2·05 (3H, singlet, OAc); quaternary methyls at 1·25 (3H), 1·22 (3H), 1·15 (3H), 1·05 (6H) (Found: C, 68·9; H, 7·05. $C_{28}H_{34}O_7$ requires C, 69·7; H, 7·1%). Elution with ethyl acetate–benzene (1 : 5) gave *methyl angolensate*, identified by comparison with an authentic sample. Elution with ethyl acetate–benzene (1 : 1) afforded *triterpenoid X* (200 mg.), m. p. (needles from methanol) 236—239°, $[\alpha]_D$ −90°, $\nu_{max.}$ 3333, 1700 cm.$^{-1}$ (Found: C, 76·4; H, 10·1; O, 13·6. $C_{30}H_{46}O_4$ requires C, 76·55; H, 9·85; O, 13·6%). Elution with ethyl acetate gave *triterpenoid Y* (850 mg.), m. p. (prisms from benzene) 247—248°, $[\alpha]_D$ −45°, $\nu_{max.}$ 3333 cm.$^{-1}$ (Found: C, 76·2; H, 10·2; O, 13·5. $C_{30}H_{48}O_4$ requires C, 76·2; H, 10·2; O, 13·5%). Elution with methanol–ethyl acetate (1 : 10) afforded *deacetyl-7-ketogedunin* (II), 110 mg. (identical with material prepared from gedunin by hydrolysis followed by oxidation), m. p. (plates from methanol) 264—266° (lit.,[1] 262°) $[\alpha]_D$ −52° (*c* 1·3), $\nu_{max.}$ 1504, 876 (furan), 1734 (δ-lactone), 1710 (cyclohexanone), 1669 cm.$^{-1}$ (conjugated enone). N.m.r.: 7·36 (2H, multiplet, α-furan H); 7·13 (1H, doublet, $J = 10$ c./sec., H-1); 6·39 (1H, multiplet, β-furan H); 5·50 (1H, singlet, H-17); 3·90 (1H, singlet, H-15); quaternary methyl δ at 1·37 (3H), 1·23 (3H), 1·13 (9H).

Angolensic Acid (IVa).—This was prepared as described earlier.[3] It had m. p. (needles from aqueous methanol) 245, 265—267° (decomp.), $[\alpha]_D$ −43°; $\nu_{max.}$ 1730 (δ-lactone), 1710 cm.$^{-1}$ (cyclohexanone and carboxylic acid) (Found: C, 68·6; H, 7·1; O, 24·55. $C_{26}H_{32}O_7$ requires C, 68·4; H, 7·1; O, 24·5%).

The *methyl ester* prepared in the usual way with diazomethane was identical with methyl angolensate (m. p., mixed m. p., and i.r. spectrum).

Ozonolysis of Methyl Angolensate.—Methyl angolensate (4·98 g.) in ethyl acetate (125 ml.) was ozonised at −78° for 3 hr. Water (30 ml.) was added and the mixture heated under reflux for 30 min. The aqueous layer was removed and the organic layer was washed with 10% sodium hydrogen carbonate solution (3 × 20 ml.). The combined hydrogen carbonate extract was acidified to Congo Red with 2N-sulphuric acid and extracted with ethyl acetate. The acidic product (3·4 g.) obtained on evaporation of the solvent *in vacuo* was dissolved in methanol and treated with ethereal diazomethane. Crystallisation from ethyl acetate–hexane afforded the *trisnor ester* (Va) as needles, m. p. 177—178°, $[\alpha]_D$ −59°, $\lambda_{max.}$ 204 mμ (ε 2600); $\nu_{max.}$ 1754, 1740, 1718, 1653, 917 cm.$^{-1}$ (Found: C, 65·0; H, 7·3; O, 27·8. $C_{25}H_{34}O_8$ requires C, 64·9; H, 7·4; O, 27·7%).

The Diacid (Vb).—A mixture of the above-mentioned methyl ester (54 mg.), 5% potassium hydroxide (5 ml.), water (4 ml.), and ethanol (1 ml.) was left to stand at room temperature overnight. Acidification and extraction with ethyl acetate gave, after removal of the solvent, a product which crystallised from ethyl acetate as prisms, m. p. 264—266°, $[\alpha]_D$ −42° (EtOH), $\nu_{max.}$ 3125, 1754, 1739, 1709, and 920 cm.$^{-1}$ (Found: C, 63·7; H, 7·2; O, 29·8. $C_{23}H_{30}O_8$ requires C, 63·6; H, 7·0; O, 29·5%).

The same diacid was also obtained in *ca.* 50% yield from ozonolysis of angolensic acid using conditions similar to those described above.

Ozonolysis of the Trisnor Ester (Va).—The ester (298 mg.) in ethyl acetate (40 ml.) was ozonised at −25° for 2 hr. and the reaction mixture worked up as already described. Distillation of the aqueous solution into a saturated solution of 2,4-dinitrophenylhydrazine in 2N-sulphuric acid gave formaldehyde 2,4-dinitrophenylhydrazone, 12 mg., identified by m. p., mixed m. p., and i.r. spectrum.

The ethyl acetate layer was washed free of acids with 10% sodium hydrogen carbonate solution and then evaporated to give a neutral product (247 mg.). This after chromatography over alumina and crystallisation from ethyl acetate–light petroleum afforded compound (Vc) as prisms, m. p. 213—216°, $[\alpha]_D$ −47°, $\lambda_{max.}$ 208 mμ (ε 290), $\nu_{max.}$ 1745 (δ-lactone and methyl ester), 1715 cm.$^{-1}$ (cyclohexanone) (Found: C, 62·15; H, 7·2; O, 31·1. $C_{24}H_{32}O_9$ requires C, 62·05; H, 6·9; O, 31·0%).

Methyl Hexahydroangolensate (VIa).—A solution of methyl angolensate (1·03 g.) in 95% ethanol (25 ml.) was shaken, in an atmosphere of hydrogen, with pre-reduced palladised charcoal (5% w/w; 1·00 g.); *ca.* 3·1 mol. of hydrogen was absorbed. Filtration, evaporation of the solvent *in vacuo*, and crystallisation of the residue from ethyl acetate–hexane gave *methyl hexahydroangolensate* (460 mg.) as needles, m. p. 196—198·5°, $[\alpha]_D$ +32·5°, $\lambda_{max.}$ 204 mμ (ε 2500), $\nu_{max.}$ 1733 (methyl ester), 1718 cm.$^{-1}$ (cyclohexanone and carboxyl) (Found: C, 68·2; H, 8·6; O, 23·6. $C_{27}H_{40}O_7$ requires C, 68·0; H, 8·5; O, 23·5%).

Hexahydroangolensic Acid (VIc).—2·5% Aqueous sodium hydroxide (10 ml.) was added to a solution of the above-mentioned ester (128 mg.) in ethanol (1 ml.) and the mixture left to stand at room temperature overnight. Acidification gave a product which crystallised from ethyl acetate–hexane as needles, m. p. 240—246° (decomp.), $[\alpha]_D$ +28° (EtOH), $\nu_{max.}$ 1733, 1712, 1656, and 888 cm.$^{-1}$ (Found: C, 67·8; H, 8·5. $C_{26}H_{38}O_7$ requires C, 67·5; H, 8·2%).

Methylation with ethereal diazomethane in the usual

way yielded the *dimethyl ester* (VIb), prisms from ethyl acetate–hexane, m. p. 158—165°, $[\alpha]_D$ +55°, $\nu_{max.}$ 1739, 1715, and 911 cm.$^{-1}$ (Found: C, 68·3; H, 8·5. $C_{28}H_{42}O_7$ requires C, 68·5; H, 8·6%).

Reduction of Methyl Angolensate with Sodium Borohydride.—(*a*) A mixture of sodium borohydride (124 mg.) in water (1 ml.) and methyl angolensate (480 mg.) in pyridine (10 ml.) was left to stand at room temperature for 5 hr. The product after acidification (522 mg.) was acetylated in the usual way with acetic anhydride and pyridine to give an *acetate* (VII), which crystallised from aqueous methanol as prisms, m. p. 118—120°, $[\alpha]_D$ −56°, $\nu_{max.}$ 1740, 1718, 1634, and 879 cm.$^{-1}$ (Found: C, 67·1; H, 7·6. $C_{29}H_{38}O_8$ requires C, 67·7; H, 7·5%).

(*b*) A solution of sodium borohydride (290 mg.) and methyl angolensate (1·00 g.) in 95% ethanol (38 ml.) was left to stand at room temperature for 10 hr. Examination of the product by t.l.c. showed the presence of two components. Crystallisation from methanol afforded the diol (VIIIb), prisms, 120 mg., m. p. 211—214°, $[\alpha]_D$ +61·5°, $\nu_{max.}$ 3424, 3300, 1739, 1647, and 876 cm.$^{-1}$ (Found: C, 68·7; H, 7·8; O, 23·7. $C_{27}H_{38}O_7$ requires C, 68·3; H, 8·1; O, 23·6%). The diol (VIIIa) present in major amount was obtained from the mother-liquor of the above crystallisation. It crystallised from methanol as prisms and had m. p. 192—197°, $[\alpha]_D$ −42°, $\nu_{max.}$ 3280, 1739, 1653, and 877 cm.$^{-1}$ (Found: C, 67·1; H, 7·8. $C_{27}H_{38}O_7,\frac{1}{2}H_2O$ requires C, 67·2; H, 8·1%).

Acetylation of the diol (VIIIa) with acetic anhydride–pyridine in the usual way gave the *diacetate*, short rods from methanol, m. p. 192—195°, $[\alpha]_D$ −39°, $\nu_{max.}$ 1754, 1733, 1655, and 1230 cm.$^{-1}$ (Found: C, 66·8; H, 7·4. $C_{31}H_{42}O_9$ requires C, 66·65; H, 7·6%).

The corresponding *diacetate* from the diol (VIIIb) crystallised from methanol, needles, m. p. 208—212°, $[\alpha]_D$ +29·5°, $\nu_{max.}$ 1742, 1647, 1497, 1235, and 877 cm.$^{-1}$ (Found: C, 66·3; H, 7·5. $C_{31}H_{42}O_9$ requires C, 66·65; H, 7·6%).

Chromium Trioxide Oxidation of the Diol (VIIIa).—8N-Chromium trioxide reagent[19] (0·15 ml.) was added slowly during 5 min. to a stirred solution of the diol (95 mg.) in acetone (25 ml.) at 0°. The mixture was kept for 5 min. and then the excess oxidant was decomposed by the addition of methanol. Isolation of the product in the usual way and crystallisation from methanol gave methyl angolensate (m. p., mixed m. p., and i.r. spectrum).

Lithium Aluminium Hydride Reduction of Methyl Angolensate.—A mixture of lithium aluminium hydride (570 mg.) and methyl angolensate (2·15 g.) in dry ether (100 ml.) was heated under reflux for 23 hr. After isolation in the usual manner, the product was separated into the *diol* (XIa) and the *tetrol* (X) by fractional recrystallisation from ethyl acetate–light petroleum. The *diol* was obtained as needles, m. p. 168—172°, $[\alpha]_D$ −22° (EtOH), $\nu_{max.}$ 3236, 1742, and 1647 cm.$^{-1}$ (Found: C, 70·0; H, 8·1; O, 21·65. $C_{26}H_{36}O_6$ requires C, 70·2; H, 8·2; O, 21·6%). The *tetrol*, needles from ethyl acetate–light petroleum, had m. p. 230—232°, $[\alpha]_D$ −25° (EtOH) (Found: C, 69·8; H, 8·65; O, 21·6. $C_{26}H_{40}O_6$ requires C, 69·6; H, 9·0; O, 21·4%). There was no carbonyl band in the i.r. spectrum. The tetrol, with acetic anhydride and pyridine, gave an amorphous *acetate* shown to be a tetra-acetate by its n.m.r. spectrum.

Lithium–Liquid Ammonia Reduction of Methyl Angolensate.—A solution of methyl angolensate (503 mg.) in dry dioxan–ether (1 : 1, 20 ml.) was added to a stirred solution of lithium (146 mg.) in liquid ammonia (125 ml.) during 5 min. Methanol was added dropwise until the blue colour was discharged and the ammonia allowed to evaporate. After addition of water (20 ml.), the mixture was extracted with ethyl acetate. Evaporation of the extract *in vacuo* and crystallisation of the residue from ethyl acetate–light petroleum gave the diol (XIa) (315 mg.) described above (m. p., mixed m. p., and i.r. spectrum).

Oxidation of the Diol (XIa).—(*a*) The diol (75 mg.) in acetone (5 ml.) was treated with an excess of the above chromium trioxide reagent for 15 min. at 5°. The mixture was concentrated at room temperature *in vacuo*, diluted with water, and extracted with ethyl acetate. Evaporation of the ethyl acetate gave an acidic product which on crystallisation from aqueous methanol afforded angolensic acid (m. p., mixed m. p., and i.r. spectrum).

(*b*) A solution of the diol (304 mg.) in dry toluene (30 ml.) and freshly distilled cyclohexanone (10 ml.) was distilled and *ca.* 10 ml. distillate collected. Aluminium isopropoxide (657 mg.) in dry toluene (20 ml.) was slowly added to the reaction vessel during 30 min., a slow rate of distillation being maintained. The mixture was heated under reflux for 2½ hr. and then steam-distilled. The residual suspension was acidified to Congo Red and extracted with ethyl acetate. Chromatography of the product on alumina gave the *hydroxyaldehyde* (XIb) (81 mg.), cubes from ethyl acetate–light petroleum, m. p. 224—226°, $[\alpha]_D$ −61°, $\nu_{max.}$ 3425, 1742, 1709, and 1650 cm.$^{-1}$ (Found: C, 70·6; H, 7·9; O, 21·8. $C_{26}H_{34}O_6$ requires C, 70·5; H, 7·7; O, 21·7%). Acetylation of the hydroxyaldehyde with pyridine and acetic anhydride under the usual conditions afforded the *acetate* as an amorphous solid which showed the loss of the hydroxyl band in the i.r. spectrum.

The αβ-Unsaturated Keto-acid (XIIa).—A mixture of sodium (250 mg.), dry toluene (12 ml.), isobutanol (25 ml.), and angolensic acid (306 mg.) was stirred at room temperature for 16 hr. After dilution with water, the toluene layer was removed and the aqueous solution was carefully acidified to Congo Red with 2N-sulphuric acid. The acidic *product* (152 mg.) crystallised from ethyl acetate–light petroleum, prisms, m. p. 216—219°, $[\alpha]_D$ +19° (EtOH), $\lambda_{max.}$ 204 and 237 mμ (ε 8700, 12,000), $\nu_{max.}$ 3390, 1745, 1700, and 1664 cm.$^{-1}$ (Found: C, 68·5; H, 7·2; O, 24·4. $C_{26}H_{32}O_7$ requires C, 68·4; H, 7·1; O, 24·5%). Methylation with diazomethane furnished the corresponding *methyl ester* (XIIb). This recrystallised from aqueous methanol as prisms, m. p. 192—193·5°, $[\alpha]_D$ +15°, $\lambda_{max.}$ 204 and 237 mμ (ε 11,500, 8500), $\nu_{max.}$ 3425, 1745, 1730, and 1664 cm.$^{-1}$ (Found: C, 69·2; H, 7·0; O, 24·0. $C_{27}H_{34}O_7$ requires C, 68·9; H, 7·3; O, 23·8%).

The *oxime* recrystallised from aqueous ethanol as needles, m. p. 178—179°, $[\alpha]_D$ −59° (EtOH) (Found: C, 64·6; H, 7·4; O, 25·3; N, 2·7. $C_{27}H_{35}O_7N,H_2O$ requires C, 64·4; H, 7·4; O, 25·4; N, 2·8%).

Treatment of the oxime with acetic anhydride and pyridine afforded the *oximino-acetate*, rods from ethyl acetate–light petroleum, m. p. 147—152°, $[\alpha]_D$ −87° (Found: C, 64·0; H, 7·0; N, 2·6. $C_{29}H_{37}O_8N,H_2O$ requires C, 63·8; H, 7·2; N, 2·6%).

Cyclisations of Compound (XIIb).—(*a*) A mixture of the ester (XIIb) (60 mg.) in acetone (5 ml.) and 8N-chromic acid (2 drops) was left to stand at room temperature for 10 min. then worked up in the usual way. The product,

[19] K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 1946, 39.

homogeneous on t.l.c., crystallised from methanol to give methyl angolensate (40 mg.).

(*b*) A solution of the ester (XIIb) (55 mg.) in pyridine (1·5 ml.) was added to chromium trioxide (94 mg.) in pyridine (1 ml.) and the mixture left to stand overnight. The product (48 mg.) was methyl angolensate.

(*c*) A solution of the ester (XIIb) (140 mg.) and fused sodium acetate (205 mg.) in freshly distilled acetic anhydride (10 ml.) was heated under reflux for 2½ hr. The product (128 mg.) was methyl angolensate.

(*d*) The ester (XIIb) (42 mg.) in methanol (1·5 ml.) and 2N-sulphuric acid (1 ml.) was left to stand overnight at room temperature. The crystalline precipitate (30 mg.) was identified as methyl angolensate.

Beckmann Rearrangement of Methyl Angolensate Oxime.—Purified thionyl chloride (10 ml.), cooled in dry ice–acetone, was added rapidly to methyl angolensate oxime (1·1 g.) at −78° and the mixture immediately poured into 4N-potassium hydroxide (50 ml.) at 20°. After standing for 15 min. the reaction mixture was filtered and the product, which showed two major spots on t.l.c., was chromatographed over alumina. Elution with benzene–ethyl acetate (3 : 2) afforded the *nitrile* (XIX), needles from methanol, (135 mg.) m. p. 203—205°, $\nu_{max.}$ 2247, 1748, 1667, 914, and 877 cm.$^{-1}$ (Found: C, 70·0; H, 7·2. $C_{27}H_{33}O_6N$ requires C, 69·4; H, 7·1%). Further elution with ethyl acetate gave the *amide* (XVIII). This recrystallised from methanol as rods (340 mg.) m. p. 249—250°, $[\alpha]_D$ −42°, $\nu_{max.}$ 3509, 1718, 1645, 919, and 877 cm.$^{-1}$ δ 5·98 (broad, NH) (Found: C, 67·15; H, 7·3; N, 2·9. $C_{27}H_{35}O_7N$ requires C, 66·8; H, 7·3; N, 2·9%).

The αβ-Unsaturated Ester (XXI).—Freshly distilled boron trifluoride etherate (1 ml.) was slowly added to the *trisnor ester* (Va) (300 mg.) in acetic anhydride (6 ml.). After standing at room temperature for 30 min. with occasional shaking, the reaction mixture was poured into ice–water (50 ml.) with stirring. The resulting precipitate (268 mg.) crystallised from methanol to give the *title compound* as prisms, m. p. 212—215°, $[\alpha]_D$ −11°, $\lambda_{max.}$ 205 mμ (ε 8400), $\nu_{max.}$ 1757, 1733, 1695, 1658, and 909 cm.$^{-1}$ (Found: C, 64·5; H, 7·0; O, 28·5. $C_{27}H_{36}O_9$ requires C, 64·3; H, 7·2; O, 28·5%).

Deoxydeacetyl-7-ketogedunin (XXII).—Excess chromous chloride solution in N-hydrochloric acid was added to a solution of deacetyl-7-ketogedunin (400 mg.) in acetone (50 ml.) and acetic acid (15 ml.). The mixture was stored under carbon dioxide for 4 days. The product (317 mg.) crystallised as needles from ethyl acetate, m. p. 291—294°, $[\alpha]_D$ +47°, $\lambda_{max.}$ 219 mμ (ε 14,100), $\nu_{max.}$ 1718, 1672, 1506, and 872 cm.$^{-1}$. N.m.r.: 7·45 (2H, multiplet, α-furan H), 6·38 (1H, multiplet, β-furan H), 7·07 (1H, doublet, J = 10 c./sec., H-1), 5·91 (1H, doublet, J = 10 c./sec., H-2), 6·63 (1H, singlet, H-15), 5·00 (1H, singlet, H-17), quaternary methyls at 1·59 (3H), 1·38 (3H), 1·17 (6H), 1·12 (3H) (Found: C, 74·0; H, 7·2; O, 19·3. $C_{26}H_{30}O_5$ requires C, 73·9; H, 7·2; O, 18·9%).

Alkaline Treatment of Compound (XXII).—A mixture of the deoxy-compound (XXII) (215 mg.), methanol (30 ml.), and 4N-aqueous sodium hydroxide (25 ml.) was heated under reflux for 1½ hr. Most of the methanol was removed *in vacuo* and the resulting clear solution was acidified with 2N-sulphuric acid and extracted with ethyl acetate (3 × 15 ml.). The acidic product (149 mg.) crystallised from ethyl acetate to give the acid (XXIII), prisms, m. p. 212—214°, $[\alpha]_D$ +19°, $\nu_{max.}$ 1739, 1647, 1506, and 877 cm.$^{-1}$ (Found: C, 68·4; H, 7·4; O, 24·3. $C_{30}H_{40}O_8$, requires C, 68·2; H, 7·6; O, 24·2%).

The n.m.r. spectrum of the amorphous *methyl ester*, prepared with diazomethane, showed signals at 7·30 (2H, multiplet, α-furan H), 6·25 (1H, multiplet, β-furan H), 6·69 (1H, doublet, J = 10 c./sec., H-1), 5·87 (1H, doublet, J = 10 c./sec., H-2), 4·98 (1H, singlet, H-17), 3·62 (OMe), 1·73 (3H, CH_3–C=C–), quaternary methyls at 1·20 (3H), 1·07 (6H), and 0·94 (3H).

We thank Dr. A. W. Sangster for the collection and identification of the cedar sample, and Dr. D. R. Taylor for discussions. An Alcan Jamaica Ltd., Junior Research Fellowship to B. S. M. is gratefully acknowledged.

[6/739 *Received, June 15th,* 1966]