SECTION C
Organic Chemistry

Limonoids from *Khaya anthotheca* (Welw.) C.DC.

By **E. K. Adesogan, D. A. Okorie,** and **D. A. H. Taylor,*** Department of Chemistry, University of Ibadan, Nigeria

Khaya anthotheca occurs in two distinct chemical varieties. The timber of one, indigenous to East Africa, yields khivorin and a new compound identified as methyl 3β-isobutyryloxy-1-oxomeliacate, while the seeds yield khivorin, 3-deacetylkhivorin, and a new compound identified as 14β,15β-epoxy-16-oxo-1α,3α,7α-triacetoxymeliacan. The second, indigenous to West Africa, lacks the characteristic lactones of other *Khaya* species. The timber contains anthothecol, while the seeds contain havanensin, deoxyhavanensin, and their acetates. An investigation has been made of the influence of the C-7 substituent on the course of the known acid catalysed isomerisation of havenensin.

Khaya anthotheca (Welw.) C.DC. is a large African tree, which furnishes a valuable mahogany. Its distribution is discontinuous and it is rare in Nigeria, occurring only near the Cameroun border. We have already described the chemistry of anthothecol (I),[1] obtained from the timber of a Nigerian specimen † and we have given a preliminary account of the seed chemistry of an East African specimen.[2] We now report the examination of specimens from other parts of Africa. We have isolated anthothecol from timber specimens from Sierra Leone, Ghana, Nigeria, and Cameroun, and the species appears to be homogenous over this area. Anthothecol can be readily detected on a thin-layer chromatogram by its characteristic ferric chloride colour; by this test, it appears to be absent from timber samples from Uganda, the Congo, and Angola. We have made a detailed examination of a tree from Wiawso, in Ghana, and of specimens from Budongo, in Uganda. The timber of the Ghanaian tree gave anthothecol and a small amount of deacetylanthothecol. The root gave only anthothecol; the bark and root bark gave anthothecol and cedrelone. The seeds gave a mixture of which the main consistent was havanensin triacetate (II).[3] Another constituent was the non-crystalline havanensin 1,7-diacetate, identified by oxidation with chromic acid in pyridine, followed by alkaline hydrolysis to give the known trichilenone (IIIa).[3] A second crystalline product, m.p. 178—182°, was resolved on chromatography into the known havanensin 3,7-diacetate,[3] and a new compound $C_{33}H_{42}O_6$, m.p. 200—204°. This was identified as a deoxyhavanensin diacetate by comparison of the spectra of samples of the noncrystalline triacetate made by acetylation of this diacetate and also by chromous chloride reduction of havanensin triacetate. Oxidation of the diacetate with chromium trioxide in acetone followed by alkaline hydrolysis gave a noncrystalline unsaturated ketone. The n.m.r. spectrum of this showed a pair of doublets at δ *ca.* 6·34, 5·68 (*J ca.* 10 c./sec.). Although both of these were partially obscured, the lower field one by the furan β-proton, and the high field one by the vinyl 15-H, they correspond to a $\Delta^{2,3}$-1-ketone and not to a $\Delta^{1,2}$-3-ketone; and hence the natural diacetate is 3α,7α-diacetoxy-1α-hydroxymeliac-14,15-ene (IV) (nomenclature, *cf.* ref. 5). The n.m.r. spectrum agreed with this structure.

We have examined two timber samples from Budongo forest in Uganda, bark from the same trees, and two seed samples collected by the Uganda Forest Department in the same area. The results were consistent. The timber samples gave mainly khivorin, the one of which more was available also gave a small amount of a crystalline solid, m.p. 130°. The seed gave khivorin, 3-deacetylkhivorin and, a new compound, m.p. 220°; $[\alpha]_D^{20}$ −47°. The spectral properties of this were very similar to those of khivorin; the molecular formula had one oxygen atom less. The n.m.r. spectrum lacked the characteristic 17-H singlet of khivorin, and had instead a broad singlet at δ 3·89 p.p.m. Chromous chloride reduction gave a deoxy-compound, with an intense u.v. maximum at 238 nm. (ε 11,000) and i.r. bands at 1680 and 1590 cm.$^{-1}$ appropriate to an αβ-unsaturated ketone. The natural product shows a singlet at δ 3·50 p.p.m. which suggests an epoxide proton; the reduction product has instead a vinyl proton singlet at δ 5·91 p.p.m. On this basis we proposed the structure of 14β,15β-epoxy-16-oxo-1α,3α,7α-triacetoxymeliacan (V) (nomenclature, *cf.* ref. 4), for this compound which we had provisionally named khayanthone.[2] Connolly, Handa, McCrindle, and Overton,[5] have isolated the corresponding 7-hydroxy-compound; Dr. Connolly informs us the acetate is identical with our material.

† This has probably been responsible for dermatitis among cabinet makers (J. W. W. Morgan and D. S. Wilkinson, *Nature*, 1965, **207**, 1101).

[1] C. W. L. Bevan, A. H. Rees, and D. A. H. Taylor, *J. Chem. Soc.*, 1963, 983.

[2] E. K. Adesogan and D. A. H. Taylor, *Chem. Comm.*, 1967, 379.

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

[4] D. A. Okorie and D. A. H. Taylor, *J. Chem. Soc.* (*C*), 1968, 1828.

[5] J. D. Connolly, K. L. Handa, R. McCrindle, and K. H. Overton, *Chem. Comm.*, 1966, 867.

The substance, m.p. 130°, obtained from the timber was not a pure compound. The main molecular ion in the mass spectrum was at 542, which corresponds to a dihydro-derivative of khayasin (VI);[6] this was confirmed by taking the spectrum of a mixture of the new substance and khayasin. There were also satellite peaks at 556 and 514; these three peaks could represent the isobutyrate, α-methyl butyrate, and acetate of the same alcohol. We were unable to separate these esters with probable that the main constituent was 8,14-dihydrokhayasin (VIIa).

Hydrolysis with alkali and re-esterification with diazomethane gave an alcohol, m.p. 234°, which appeared to be pure. This had spectral properties similar to the original, and so was not the product of a fission reaction similar to that undergone by khayasin.[6] Acetylation gave an acetate, not obtained crystalline, in the n.m.r. spectrum of which the doublet at δ 5·01 p.p.m.

N.m.r. spectra recorded at 60 Mc./sec. in deuteriochloroform, in p.p.m. from tetramethylsilane

Substituents in meliacan	1-H	3-H	7-H	15-H	2-H	4α-Me	4β-Me	8-Me	10-Me	13-Me	Furan
3α,7α-Di-OAc-1α-OH-$\Delta^{14,15}$ (IV)	3·48	4·9	5·3	5·2							6·25 7·21
		*J** 5·5	*J** 5	*J** 5		0·8	0·84	1·17	0·92	0·92	7·31
1α,3α,7α-Tri-OAc-$\Delta^{14,15}$	4·62	4·68	5·36	5·2							6·25 7·23
			*J** 4·5	*J** 5		0·82	0·82	1·17	0·98	0·92	7·34
3,7,15-Trioxo-$\Delta^{1,2}$ (XII)	7·05				5·84	1·15	1·13	1·35	1·36	0·85	6·21 7·20
	J 10				*J* 10						7·34
Substituents in 14β,15β epoxymeliacan											
3β,7β-Di-OAc		4·45 *J** 15	5·1 *J** 15	3·26							6·1 7·02
						0·85	0·85	0·98	0·91	0·91	7·25
3,7-Dioxo				3·56		1·10	1·10	1·16	1·16	0·78	6·1, 7·04, 7·26
1,7-Dioxo				3·56		0·93	1·13	1·18	1·47	0·82	6·1, 7·06, 7·30
7α-OAc-3-oxo-$\Delta^{1,2}$	7·12 *J* 10		4·75 *J** 5	3·44	5·81 *J* 10	1·08	1·08	1·13	1·21	0·98	6·1, 7·06, 7·32
3,7-Dioxo-$\Delta^{1,2}$ (IIIb)	7·20 *J* 10			3·68	5·91 *J* 10	1·13	1·13	1·2	1·35	0·8	6·15, 7·11 7·31
1,7-Dioxo-$\Delta^{2,3}$ (XIVb)		6·34 *J* 10		3·58	5·71 *J* 10	1·07	1·15	1·2	1·41	0·8	6·16, 7·07 7·30
					17-H						
1α,3α,7α-Tri-OAc-16-oxo (V)	4·75	4·75	4·75	3·45	3·92	0·83	0·95	1·12	1·05	1·15	6,25, 7·41, 7·60
Substituents in methyl meliacate											
3-Isobutyryloxy-1-oxo (VIIa)		4·96 *J* 10			5·88	0·82	0·83		1·1	1·03	6·42, 7·36, 7·52
3α-OH-1-oxo (VIIb)					5·82	0·68	1·02		1·02	1·02	6·42, 7·37, 7·55
1,3-Dioxo					5·60	0·85	1·12		1·15	0·95	6·43, 7·42, 7·56
1β-OH-$\Delta^{14,15}$-3-oxo (VIIId)	3·62 *J* 2·5			5·78	5·05	1·17	1·08		1·30	1·05	6·4, 7·47, 7·47
1β-OAc-$\Delta^{14,15}$-3-oxo (VIIIc)	4·82 *J* 2·5			5·80	5·05	1·22	0·98		1·27	1·07	6·41, 7·47, 7·47

the small amount of material available. The occurrence of such mixtures is very common, and khayasin itself is difficult to obtain pure.[6] The u.v. spectrum showed a maximum at 214 nm. (ε 5000), attributable to a furan ring. The i.r. spectrum showed carbonyl peaks very similar to those in khaysin. The n.m.r. spectrum was similar to that of khayasin except that the tertiary methyl resonances were shifted, and the 17-H signal was moved downfield from δ 5·63 to 5·86 p.p.m. The 3-H doublet was similar to that in khayasin, except that it had a satellite slightly downfield, probably due to 3-H in the homologous α-methyl butyrate. It appeared (*J* 10 c./sec.) representing 3-H in the original was replaced by a broad singlet at δ 4·70 p.p.m. This suggests epimerisation at C-3 on hydrolysis, as with swietenine,[7] to give the alcohol (VIIb).

We sought confirmation of the proposed structure in a partial synthesis. Catalytic hydrogenation of khayasin and its 14 : 15 and 8 : 30 double-bond isomers was unsuccessful; at least under conditions which left the furan ring intact. It is often possible to reduce unsaturated acids successfully with Raney alloy in sodium hydroxide solution, and this can be done under conditions which do not reduce a furan ring.[8] The reduction of carapin itself (VIIIa) under these conditions would not be possible since carapin is unstable to alkali.[9] In the

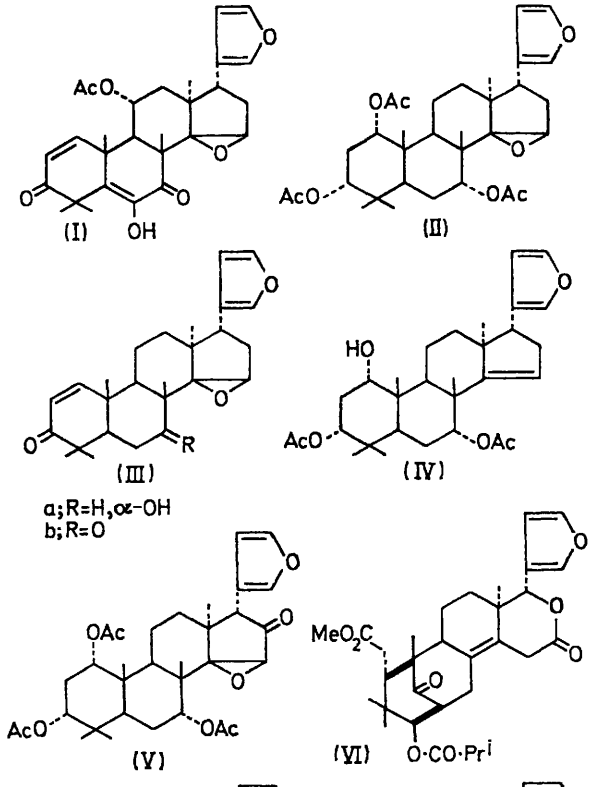
[6] E. K. Adesogan, C. W. L. Bevan, J. W. Powell, and D. A. H. Taylor, *J. Chem. Soc.* (*C*), 1966, 2127.

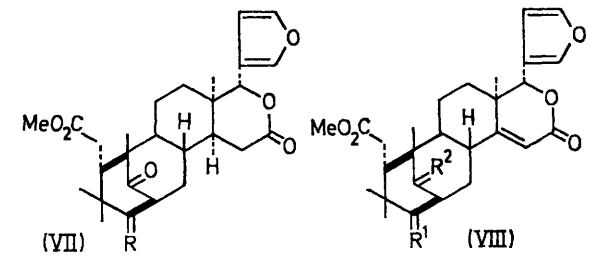
[7] J. D. Connolly, R. Henderson, R. McCrindle, K. H. Overton, and S. Bhacca, *J. Chem. Soc.*, 1965, 6935.

[8] D. A. H. Taylor, *J. Chem. Soc.*, 1959, 2767.

[9] E. O. Arene, C. W. L. Bevan, J. W. Powell, and D. A. H. Taylor, *Chem. Comm.*, 1965, 302.

parallel case of mexicanolide, the derived 3β-alcohol is stable.[10] Although we have obtained the 3β-alcohol related to carapin as a natural product,[11] the amount was small, and thus we investigated the borohydride





a; R = H,β-O·CO·Pr^i
b; R = H,αOH

a; R^1 = O; R^2 = O
b; R^1 = H, β·OAc; R^2 = O
c; R^1 = O; R^2 = H,β-OAc
d; R^1 = O; R^2 = H,β-OH

reduction of carapin. This gave an alcohol, m.p. 238—242° (acetate m.p. 209—212°), which was re-oxidised to carapin, but was quite different from the 3β-alcohol and its acetate.[12] We return later to the structure of this alcohol.

The alcohol, dissolved in methanolic alkali and treated with Raney alloy, gave a product which after re-methylation and oxidation with chromic acid in acetone, appeared to be a mixture of carapin and a new compound. After mild alkaline treatment to destroy carapin,[9] the product was chromatographed on alumina, giving a new compound, m.p. 196—198°, having the formula of dihydrocarapin. The method of preparation leaves little room for doubt of the identity of this substance. Oxidation of the alcohol, m.p. 234°, obtained by hydrolysis of dihydrokhayasin, gave the same dihydrocarapin thereby confirming the structure (VIIa) which we assign to the natural product. The stereochemistry at C-8 follows from that of carapin,[12] that at C-14 is uncertain, but we consider hydrogenation on the α-face of the molecule to be more likely.

We have recently assigned the tertiary methyl resonances at 49, 45, 70, and 64 c./sec.* in deuteriochloroform in the 60 Mc./sec. n.m.r. spectrum of khayasin to the 4α-, 4β-, 10-, and 13-methyl groups respectively.[13] We would expect the 10- and 13-methyl groups to be shifted slightly downfield in khayasin, with respect to the saturated compound, as they are in the plane of the double bond, while the geminal methyl groups at C-4 should be shifted slightly upfield. In dihydrokhayasin the methyl resonances were at 50, 48, 65, and 61 c./sec., showing shifts in accordance with expectation.

We return now to the structure of the alcohol obtained by borohydride reduction of carapin. The methyl groups in the 3β-acetate (VIIIb) resonate at 50, 50, 63, and 65 c./sec. at 60 Mc./sec.; we have assigned these to 4α-, 4β-, 10-, and 13-Me respectively.[13] The methyl groups in the reduction product acetate resonate at 60, 65, 73, and 77 c./sec. Several 3α-acetates are known; the changes in the methyl resonance frequencies compared to the corresponding 3β-acetates are small; consequently we do not think the present compound is a 3α-acetate. The alternative is that it is a 1-acetoxy-3-oxo-compound; very few of these are known. Recently, we have described a 1α-hydroxy-3-oxo-compound, obtained stereospecifically by hydride transfer from the 3β-hydroxy-1-oxo-isomer.[14] Our experience [13] suggests that methyl shifts calculated from this single case should provide a rough estimate at least of the resonance positions to be expected in a related compound; on this basis we calculate that the methyl resonances of the 1α-acetoxy-3-oxo-compound (VIIIc) should be near 57, 63, 59, and 64 c./sec. The observed values are not close to this, and seem to exclude this structure. Therefore, we conclude that the borohydride reduction product of carapin is the only remaining isomer, the 1β-alcohol (VIIId). Stereochemically, this is the most probable product from the reduction of a 1-ketone. Examination of a model predicts a rather small coupling constant for $J_{1,2}$, in line with the observed 2·5 c./sec. The model also shows that the 1β-acetate is close to 10-Me and very close to 4α-Me. Therefore, we expect large shifts of the resonances of these methyl groups, as observed.

Chan, Gibbs, and Taylor [3] have shown that havanensin isomerises when heated or upon treatment with dilute

* All resonances taken from tetramethylsilane.

[10] J. D. Connolly, R. McCrindle, and K. H. Overton, *Chem. Comm.*, 1965, 162.
[11] E. K. Adesogan, Ph.D. Thesis, Ibadan, 1968.
[12] D. A. H. Taylor, *J. Chem. Soc.* (*C*), 1969, 2439.
[13] N. S. Ohochuku and D. A. H. Taylor, *J. Chem. Soc.* (*C*), 1969, 864.
[14] D. A. H. Taylor, *J. Chem. Soc.* (*C*), in the press.

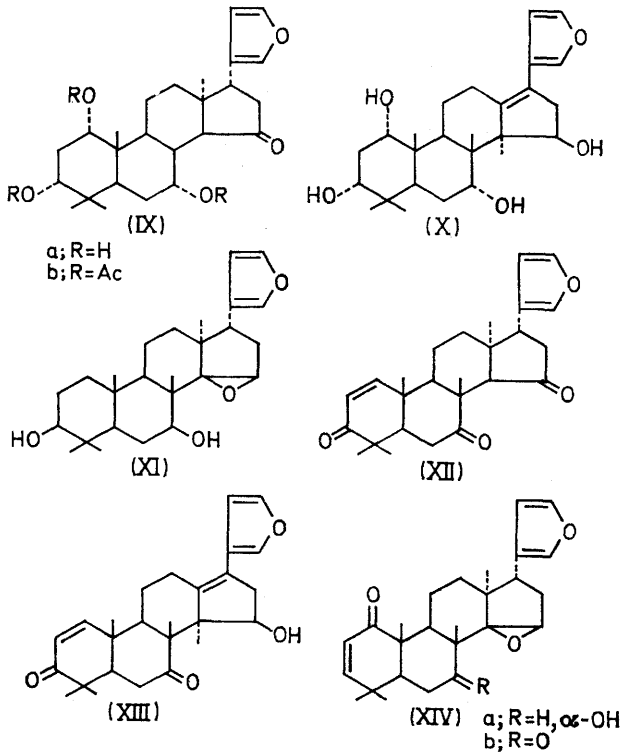
acid to give neohavanensin (IXa). It has been shown that the epoxide rearrangement of limonin involves the 7-substituent,[15] and we were interested to know if the 7-substituent influenced this reaction as well. We confirmed that havanensin with 0·05N-acid gives neohavanensin. However, under similar conditions we found that havanensin triacetate gives a mixture of neohavanensin acetate and a second compound. This was isolated, after hydrolysis, as a gum showing a strong u.v. maximum at 242 nm. (ε 13,600). We attribute this to a vinyl-furan chromophore in the structure (X). Similar products have been obtained by isomerisation of cedrelone and anthothecol.[1]

Since neighbouring group assistance is possible from both the 7α-hydroxy- and 7α-acetoxy-compounds, we prepared a 7β-hydroxy-compound, where this participation is impossible. The known trichilenone (IIIa)[3] was oxidised with chromic acid in pyridine to the 7-ketone (IIIb). Borohydride reduction of this reduced the two carbonyl groups and the double bond to give a diol. This was shown to be the required 3β,7β-dihydroxy-14β,15β-epoxymeliacan (XI) (nomenclature, *cf.* ref. 4), by the n.m.r. spectrum of the derived diacetate, in which the 3-H and 7-H signals appear as multiplets [δ 4·43, J^* (= $J_{AX} + J_{BX}$ in an ABX system) 15; δ 5·1, J^* 15 c./sec.]. The large coupling constants show that both protons are axial, so that the two acetoxy-groups are β-oriented.

Treatment of the 7-ketone (IIIb) with acid gave equal amounts of two crystalline isomers. The first showed three carbonyl absorption bands in the i.r. region, at 1740, 1700, and 1670 cm.$^{-1}$, as expected for the cyclopentanone (XII), which is the neo-isomer. The second product showed a broad carbonyl absorption band at 1690 cm.$^{-1}$, and a hydroxy-band at 3450 cm.$^{-1}$. In the u.v. region there was a strong maximum at 237 nm. (ε 18,200) which we attribute to the unsaturated ketone and a vinyl furan; we assign structure (XIII) to this. Acid treatment of the 3β,7β-diol similarly gave equal amounts of two isomers, the first showed a carbonyl group in the i.r. region at 1715 cm.$^{-1}$ (hydrogen bonded cyclopentanone), and thus had a structure analogous to (XII); the second had no carbonyl group, but showed absorption in the u.v. region at 242 nm. (ε 12,800), and thus was a vinyl-furan analogous to (XIII).

Opening of the oxide ring therefore proceeds readily whatever the substituent at C-7. However, while the 7α-hydroxy-compound gives only the 15-ketone, the 7α-acetate gives some of the isomeric 15-hydroxy-vinyl-furan, and the 7-ketone and 7β-hydroxy-compound give equal amounts of the two isomers. We suggest that the initial stage is always an opening of the oxide ring to give a 15-hydroxy-14-carbonium ion. Subsequently, either the 13-Me group migrates, or a proton is lost to give a ketone, either *via* the enol formed by elimination of the 15-proton, or after hydride transfer from the hydroxy-group. We suggest that the exclusive formation of the ketone from the 7α-hydroxy-compound is due to stabilisation of the intermediate ion by electron donation from the 7α-hydroxy-group, which protects the carbonium ion from attack by the α-oriented methyl group. The increasing amounts of the methyl shift product in other cases then result from the lower capacity for electron release of other C-7 substituents. In the absence of this stabilising factor, the two possible products are formed in roughly equal amounts.

In the borohydride reduction of the 7-ketone (IIIb), we obtained as well as the saturated diol, a saturated monohydroxy-ketone, m.p. 185—188°, not altered by further treatment with borohydride. The saturated 3,7-diketone, prepared by catalytic hydrogenation of (IIIb), gave this hydroxy-ketone as the only product of borohydride reduction, while trichilenone (IIIa) with borohydride gave only dihydrotrichilenone, identical with the product of catalytic hydrogenation. Similar reduction of an unsaturated to a saturated ketone with borohydride has been noticed in the case of



cedrelone.[16] It seemed probable that the hydroxy-ketone, m.p. 185—188°, was the 7β-hydroxy-isomer of dihydrotrichilenone. This is supported by the optical rotations of gedunin derivatives,[13] which although not closely parallel, are likely to be of the same order. Reduction of a 3-ketone to either epimeric alcohol produces a small laevorotatory change of *ca.* 15° in the specific rotation, whereas reduction of a 7-ketone produces a much bigger dextrotatory change of *ca.* 140°.

[15] A. D. Cross, *Quart. Rev.*, 1960, **14**, 317.
[16] R. Hodges, S. G. McGeachin, and R. A. Raphael, *J. Chem. Soc.*, 1963, 2515.

The specific rotation of the saturated 3,7-diketone is −93°, that of the 3β,7β-diol is −30°. The specific rotation of the hydroxy-ketone is −30°; this is consistent with it being a 7-hydroxy-3-oxo-compound, and since it is not dihydrotrichilenone, it must be the 7β-hydroxy-isomer. It seems that the saturated 3-keto-group is not normally reduced by borohydride; but that reduction of a $\Delta^{1,2}$-3-ketone may give either a saturated ketone or a saturated alcohol, in the latter case the saturated ketone is not an intermediate.

Reduction of isotrichilenone (XIVa), of which more was available, with nascent hydrogen was normal. Isotrichilenone with lithium and methanol in liquid ammonia gave the saturated 1β,7α-diol; the related 7-ketone (XIVb) with lithium in liquid ammonia gave the saturated diketone, while with lithium and methanol in liquid ammonia, it gave the 1β,7β-diol.

EXPERIMENTAL

Optical rotations are for solutions in chloroform, determined at 20° with a Perkin-Elmer 141 polarimeter; mass spectra are recorded on a Perkin-Elmer Hitachi RMU 6E instrument and n.m.r. spectra in deuteriochloroform on a Varian A56/60.

Extraction of Timber.—(a) *From Ghana.* A timber sample (1·25 kg.) from the Mpesetum concession of Gliksten W.A. Limited, near Sefwi Wiawso in Ghana,* was pulverized and extracted with refluxing light petroleum (b.p. 60—80°). The extract was evaporated and the residue was stirred with ether; the insoluble portion crystallized from methanol to give anthothecol (I) (2·25 g.), identical with an authentic sample.[1] Chromatography of the crystallisation mother liquor gave deacetylanthothecol (20 mg.), the n.m.r. spectrum of which was identical with an authentic sample.[1]

(b) *From Uganda.* A timber sample (5 kg.) from the Budongo Forest in Uganda † was pulverized and extracted with refluxing light petroleum (b.p. 60—80°). Solid which separated from the extract was filtered off, dissolved in methylene chloride–pentane, and chromatographed over alumina. All fractions eluted with methylene chloride–pentane crystallised from methanol to give khivorin (total yield 5·25 g.); the combined mother liquors gave a second crop of crystals (300 mg.), m.p. 130—200°. This was re-chromatographed to give first a solid (95 mg.) crystallising from methanol in needles, m.p. 130°, which is mainly *methyl* 3β-*isobutyryloxy*-1-*oxomeliacate* (VIIa) (M^+ 542, subsidiary homologous peaks at 556 and 514; $[\alpha]_D^{20}$ −116°) and then khivorin.

Extraction of Root.—Root wood (3 kg.) from Sefwi Wiawso was extracted as described above, giving recrystallised anthothecol (12·25 g.).

Extraction of Bark. (a) *From Ghana.* Bark (3 kg.), extracted as above, gave a gum (12 g.) which was chromatographed over neutral alumina. Methylene chloride–pentane eluted cedrelone (70 mg.) identical with an authentic sample from *Toona ciliata.* Methylene chloride eluted anthothecol (250 mg.). Root bark gave a similar result.

(b) *From Uganda.* Bark of DAHT224 gave no crystalline product.

* Herbarium specimens are preserved in the Forest Herbarium, Oxford, as DAHT 200.

† Herbarium specimens are preserved in Oxford as DAHT 224.

Extraction of Seeds.—(a) *From Ghana.* Seed of DAHT 200 (380 g.) was minced and extracted with light petroleum (b.p. 60—80°) in a Soxhlet apparatus. A solid (5·45 g.) separated, m.p. *ca.* 180° (from methanol). The oily fraction of the extract was chromatographed over neutral alumina. Pentane eluted a fatty oil; increasing concentrations of methylene chloride gave: (1) havanensin triacetate (6·65 g.) (II), m.p. 188—191°, $[\alpha]_D^{20}$ −63° (from methanol–methylene chloride), and (2), havanensin 1,7-diacetate (4 g.) (a noncrystalline oil). The combined mother liquors were hydrolysed with sodium hydroxide, giving havanensin (5·35 g.), m.p. 235—237°. The solid fraction, m.p. *ca.* 180°, was chromatographed over alumina, to give two pure compounds and a residual unresolved mixture. The first, m.p. 204—208° (0·70 g.), was identified as *deoxyhavanensin 3,7-diacetate* (IV) (Found: C, 72·0; H, 8·5. $C_{30}H_{42}O_6$ requires C, 72·3; H, 8·5%), $[\alpha]_D$ −18°]; the second, m.p. 180°, $[\alpha]_D^{20}$ −41° (2·4 g.) was havanensin 3,7-diacetate (lit.,[3] m.p. 174—175°).

(b) *From Uganda.* A sample of seed (900 g.), collected by the Uganda Forest Department, was extracted as above; the extract was chromatographed on alumina. Pentane eluted a fatty oil and methylene chloride–pentane eluted: (1) 14β,15β-*epoxy*-16-*oxo*-1α,3α,7α-*triacetoxymeliacan* (V) (6·55 g.), m.p. 220° (from methylene chloride–hexane) (Found: C, 67·4; H, 7·4. $C_{32}H_{42}O_9$ requires C, 67·35; H, 7·4%), $[\alpha]_D^{20}$ −47°; (2) khivorin) 2·75 g.), m.p. 250—254°; (3) 3-deacetylkhivorin (2·45 g.), m.p. 245°.

A second sample of seed gave similar results.

Hydrolysis of Methyl 3β-*Isobutyryloxy*-1-*oxomeliacate.*—The ester (80 mg.) was hydrolysed by refluxing methanolic potassium hydroxide during 1 hr. The product, isolated with methylene chloride, had m.p. 320°. Re-esterification with diazomethane gave *methyl* 3α-*hydroxy*-1-*oxomeliacate* (VIIb), m.p. 234° (Found: C, 68·5; H, 7·5. $C_{27}H_{36}O_7$ requires C, 68·6; H, 7·7%). The acetate did not crystallise.

Borohydride Reduction of Carapin.—Carapin (VIIIa) (1·0 g.) was dissolved in methylene chloride (10 ml.) and methanol (20 ml.) and treated with potassium borohydride (0·5 g.) in a little water. After 3 hr. the solution was diluted with acid and the product was extracted with methylene chloride. After evaporation of the solvent, the residue was dissolved in methanol. *Methyl* 1β-*hydroxy*-3-*oxomeliac*-14,15-*enate* (VIIIa) (250 mg.) rapidly crystallised, m.p. 238—242° (from methanol–methylene chloride) (Found: C, 69·0; H, 7·3. $C_{27}H_{34}O_7$ requires C, 68·9; H, 7·3%); $[\alpha]_D^{20}$ +100°; the mass spectrum showed a weak molecular ion at 470 and an intense peak at 374). The *acetate* had m.p. 209—212° (Found: C, 67·7; H, 7·2. $C_{29}H_{36}O_8$ requires C, 67·95; H, 7·1%); $[\alpha]_D^{20}$ +71°).

Methyl 1,3-*Dioxomeliacate.*—(*a*) The above 1β-ol (200 mg.) was dissolved in methanol (50 ml.) and potassium hydroxide (5 g.) in water (50 ml.) was added. After addition of Raney alloy (10 g.) the whole was stored overnight at 25°. The solution was then filtered and the filtrate was diluted with water, methylene chloride, and dilute hydrochloric acid; the organic layer was then separated. Evaporation of solvent left a residue which was esterified with diazomethane and then oxidised with chromic acid in acetone. The product from this was dissolved in methanol (50 ml.) and treated with potassium hydroxide (0·5 g.) in a little water. Aliquots were removed for u.v. analysis every 0·5 hr. After 1·5 hr., the intensity of the absorption at 290 nm. remained constant; after 3 hr., the solution was

acidified and extracted with methylene chloride. The residue in methylene chloride–pentane was chromatographed over neutral alumina (5 g.; grade III); methylene chloride eluted *methyl* 1,3-*dioxomeliacate* (45 mg.), m.p. 196—198° (from methanol–methylene chloride) (Found: C, 68·8; H, 7·0%); M^+ 470; $[\alpha]_D^{20}$ −79°.

(*b*) The natural 3α-ol (VIIb) (35 mg.), oxidised with chromic acid in acetone, gave the ketone (m.p. 195—198°) which showed no depression of m.p. when mixed with the previous sample; its n.m.r. spectrum was identical with that of the above sample.

Trichilenone.—Havanensin 1,7-diacetate (1·7 g.) in pyridine (17 ml.) was mixed with the complex prepared from chromium trioxide (1·7 g.) and pyridine (17 ml.) and was then set aside overnight. The solution was diluted with water and ether, and filtered through Celite. The ether layer was evaporated, and the noncrystalline residue was dissolved in methanol (100 ml.) and heated under reflux with aqueous sodium hydroxide (100 ml.; 2N) for 2 hr. The product, isolated with ether, crystallised to give trichilenone (IIIa) (1·1 g.), m.p. 198—200° (lit.,[3] m.p. 199—201°).

Deoxyhavanensin Triacetate.—Havanensin triacetate (II) (0·5 g.) in pyridine (100 ml.) was placed in a 250-ml. flask, which was then completely filled with aqueous chromous chloride solution and stoppered. After 36 hr. the reaction mixture was diluted with chloroform and dilute sulphuric acid. The product was purified by dissolution in ether–pentane (1 : 2) and filtration through Kieselgel. Evaporation gave a noncrystalline product, which had the same n.m.r. spectrum as a sample produced by acetylation of the above diacetate with pyridine and acetic anhydride.

Deoxyisotrichilenone.—The product from the oxidation of deoxyhavanensin 3,7-diacetate (IV) (150 mg.) with an excess of chromic acid (8N) in acetone was hydrolysed with aqueous methanolic potassium hydroxide; the reaction mixture was diluted with methylene chloride and water. The methylene chloride layer was concentrated and the residue was acetylated with acetic anhydride (2 ml.) and toluene-*p*-sulphonic acid (100 mg.). The product in ether was filtered through alumina. Evaporation gave the unsaturated ketone as a gum.

Isotrichilenone.—Havanensin 3,7-diacetate (2·3 g.) was oxidised overnight with chromium trioxide (1·0 g.) in pyridine (100 ml.). The solution was diluted with chloroform and water, and the organic layer was evaporated to dryness. The product was heated under reflux with aqueous methanolic potassium hydroxide to give isotrichilenone (1·45 g.), m.p. 245° (lit.,[3] m.p. 205—207°; the spectral data agree, and it seems these are two polymorphic forms).

Deoxykhayanthone.—Khayanthone (V) (40 mg.) was dissolved in acetic acid (25 ml.) in a 50-ml. flask; the flask was then filled with aqueous chromous chloride solution, stoppered, and set aside overnight. The product ($\lambda_{max.}$ 237 nm., ε 17,000), extracted with chloroform, could not be crystallised, although its n.m.r. spectrum was identical with that of a crystalline specimen of deoxykhayanthone subsequently isolated from *Khaya nyasica*.[12]

Neohavanensin.—Havanensin (250 mg.) in methanol (30 ml.) was treated with hydrochloric acid (20 ml.; 0·05N aqueous) at room temperature for 0·5 hr. The product, isolated with ether and crystallised from methanol, gave neohavanensin (IXa) (200 mg.), m.p. 286—288° (Found: C, 72·7; H, 9·2. Calc. for $C_{26}H_{38}O_5$: C, 72·5; H, 8·9%); $[\alpha]_D^{21}$ −29° (in methanol). The properties correspond with those given by Chan *et al.*[3]

Isomerisation of Havanensin Triacetate.—Havanensin triacetate (II) (500 mg.), dissolved in methanol (60 ml.), was treated with hydrochloric acid (60 ml.; 0·05N aqueous) for 0·5 hr. The product, isolated with ether, was crystallised from methylene chloride–methanol to give neohavanensin triacetate (IXb) (220 mg.), m.p. 233—236° (Found: C, 69·0; H, 7·9%. Calc. for $C_{32}H_{44}O_8$: C, 69·0; H, 8·0%); $[\alpha]_D^{21}$ −68°. The mother liquor was hydrolysed with methanolic sodium hydroxide and chromatographed on alumina to give neohavanensin (IXa) and the noncrystalline vinyl-furan isomer (X) ($\lambda_{max.}$ 242 nm.; ε 13,600).

3,7-*Dioxo*-14β,15β-*epoxymeliac*-1,2-*ene*.— Trichilenone (IIIa) (1·1 g.) in pyridine (11 ml.) was oxidised with chromium trioxide (1·1 g.). The product crystallised from chloroform–methanol to give the 7-ketone (IIIb) (750 mg.), m.p. 179—181° (Found: C, 76·3; H, 7·9. $C_{26}H_{32}O_4$ requires C, 76·4; H, 7·9%); $[\alpha]_D^{20}$ −73·4°.

Isomerisation of the 7-Ketone (IIIb).—The ketone (IIIb) (200 mg.) in methanol (40 mg.) was treated with hydrochloric acid (40 ml.; 0·05N aqueous). The product on fractional crystallisation from methanol gave the *neoketone* (XI) (92 mg.) [m.p. 278—280° (Found: C, 76·65; H, 7·9); $[\alpha]_D^{20}$ −53°; $\nu_{max.}$ 1740, 1700, and 1670 cm.$^{-1}$] and the *vinyl-furan isomer* (XII) (86 mg.) [m.p. 182—185° (Found: C, 76·7; H, 8·0); $[\alpha]_D^{20}$ −59·4°; $\nu_{max.}$ 1690 cm.$^{-1}$, $\lambda_{max.}$ 257 nm. (ε 18,200), $\lambda_{max.}$ *versus* the 7-ketone (IIIb) 240 nm. (ε 12,100)].

Borohydride Reduction of the 7-Ketone (IIIb).—To the ketone (350 mg.), dissolved in chloroform (8 ml.) and methanol (20 ml.) was added sodium borohydride (600 mg.) in methanol (7 ml.); after 3 hr. the product was isolated with chloroform. Crystallisation from methanol gave (i) 3β,7β-*dihydroxy*-14β,15β-*epoxymeliacan* (XI) (150 mg.) [m.p. 185—188° (Found: C, 75·5; H, 9·3. $C_{26}H_{38}O_4$ requires C, 75·3; H, 9·2%); $[\alpha]_D^{20}$ −30° (in methanol)]; and (ii) 7β-*hydroxy*-3-*oxo*-14β,15β-*epoxymeliacan* (50 mg.) [m.p. 185—188° (Found: C, 75·4; H, 8·8. $C_{26}H_{36}O_4$ requires C, 75·7; H, 8·8%); $[\alpha]_D^{20}$ −36° (in methanol)].

The *diacetate* of the above diol (XI) prepared with pyridine and acetic anhydride failed to crystallise (Found: C, 72·1; H, 8·3. $C_{30}H_{42}O_6$ requires C, 72·3; H, 8·5%).

Isomerisation of the Diol (XI).—The diol (100 mg.) in methanol (20 ml.) was treated with acid as above. Chromatography of the product over alumina gave (1) the *neo*-3β,7β-*dihydroxy-compound* (40 mg.) [m.p. 221—224° (Found: C, 75·4; H, 9·2), $\nu_{max.}$ 1715 cm.$^{-1}$] and (2) the *vinylfuran isomer* (35 mg.), m.p. 150—152° (Found: C, 75·3; H, 9·0%; the i.r. spectrum showed no carbonyl absorption, $\lambda_{max.}$ 242 nm. (ε 12,800).

3,7-*Dioxo*-14β,15β-*epoxymeliacan*.— The unsaturated ketone (IIIb) (200 mg.), dissolved in methanol (30 ml.), was hydrogenated over Adams catalyst (25 mg.). The *dihydro-derivative* (150 mg.) had m.p. 175—178° (from methanol) (Found: C, 76·0; H, 8·5. $C_{26}H_{34}O_4$ requires C, 76·1; H, 8·3%); $[\alpha]_D^{20}$ −93°.

Borohydride Reduction of 3,7-*Dioxo*-14β,15β-*epoxymeliacan*.—The above ketone (150 mg.) in chloroform (5 ml.) and methanol (10 ml.) was reduced with sodium borohydride (300 mg.) in methanol (5 ml.). The only product isolated was 7β-hydroxy-3-oxo-14β,15β-epoxymeliacan (80 mg.), identical with the previous sample.

Borohydride Reduction of Trichilenone.—Trichilenone (IIIa), reduced as above, gave as the sole product *dihydro-*

trichilenone, m.p. 203° (Found: C, 75·4; H, 8·7); $[\alpha]_D^{20}$ −24°; $\nu_{max.}$ 1715 cm.$^{-1}$.

1,7-*Dioxo*-14β,15β-*epoxymeliac*-2,3-*ene*.—Oxidation of isotrichilenone (XIVa) (1·45 g.) with chromium trioxide in pyridine and crystallisation of the product from methylene chloride gave the 7-*ketone* (XIVb) (870 mg.), m.p. 254° (Found: C, 76·7; H, 8·0%).

Reduction of 1,7-*Dioxo*-14β,15β-*epoxymeliac*-2,3-*ene*.—(a) *With lithium and methanol in ammonia*. The ketone (XIVb) (200 mg.) in tetrahydrofuran (25 ml.) was added to lithium (0·5 g.) in liquid ammonia (100 ml.). The colour was discharged with methanol, and the product was worked up to give the 3β,7β-*diol* (125 mg.) which crystallised from toluene–methyl cyclohexane as needles, m.p. 228—232° (Found: C, 75·4; H, 9·3%). Similar treatment of isotrichilenone (XIVa) (40 mg.) gave the 3β,7α-*diol* (30 mg.), m.p. 227—230°, mixed m.p. with the 7β alcohol, 205—210° (Found: C, 75·6; H, 9·2%).

(b) *With lithium in ammonia*. The 7-ketone (XIVb) (200 mg.) in tetrahydrofuran (25 ml.) was added to a solution of lithium (500 mg.) in liquid ammonia (100 ml.). After 5 min. the solution was treated with an excess of ammonium chloride. Work up gave the saturated 1,7-*diketone* (110 mg.), m.p. 198—201° (Found: C, 76·1; H, 8·2%).

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