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THE LIMONOID CHEMISTRY OF THE GENUS *KHAYA* (MELIACEAE)

G. A. ADESIDA, E. K. ADESOGAN, D. A. OKORIE and D. A. H. TAYLOR
Department of Chemistry, University of Ibadan, Nigeria

and

B. T. STYLES
Department of Forestry, Commonwealth Forestry Institute, Oxford

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Abstract—The six species of the genus *Khaya* have been examined, and tables are given showing the limonoids isolated. The results are discussed in relation to the taxonomy of the genus.

THE GENUS *Khaya* A. Juss. (Meliaceae) occurring in Africa and Madagascar, is the most important source of African mahogany. It is taxonomically difficult, especially in East Africa and the Congo, and one of us (B.T.S.) is revising it for a monograph on the Meliaceae. The chemistry has been studied in Ibadan, and we have combined to see how far these studies can illuminate the taxonomic problems. Currently, six species, *K. anthotheca* (Welw.) C.DC., *K. grandifoliola* C.DC., *K. ivorensis* A. Chev., *K. madagascariensis* Jumelle et Perrier, *K. nyasica* Stapf ex Bak.f. and *K. senegalensis* (Desr.) A. Juss. are accepted, but they are poorly defined, the morphological differences being slight and inconstant.

In our opinion, *K. senegalensis* is a good species. It can be readily recognized by several botanical characters, particularly the small, narrow leaflets and the small four-valved capsule; and it is ecologically distinct, occupying the sub-Saharan savannah area from Senegal to Uganda.

K. nyasica occurs in Central and Southern East Africa, mainly in rain forest, but also beside rivers in drier areas. This is probably also a good species, being distinguished by the small four-valved capsule, which is unlike that of any other species except *K. senegalensis*. Sterile specimens however are not characteristic.

K. madagascariensis grows along watercourses in N.E. Madagascar. The mature tree is distinct, having thicker leaves, rougher bark, and a much larger and thicker shelled fruit than *K. nyasica*. The size and shape of the leaflets is very similar, and some of the differences may reflect the environment.

The high forest species *K. anthotheca* and *K. ivorensis* both occur in W. Africa; the former extends to Uganda. In the forest they are easily distinguished by the pale smooth bark of the first and the dark brown, flaking bark of the latter. Harms[1] has noted that they are difficult to distinguish in the herbarium; the timber cannot be distinguished microscopically. A form of *K. anthotheca* common in Budongo Forest in Uganda differs from West African material in leaf and fruit morphology, while specimens from Congo and Angola are intermediate. In spite of the similarity of these species we accept that the constancy of the distinctions, especially in the forest, are sufficient to maintain them.

[1] H. HARMS, *Die Natuerlichen Pflanzenfamilien*, Vol. 19B1. p. 49 *et seq.*, Duncker & Humblot, Berlin (1940).

K. grandifoliola is a tree of forest outliers, extending along watercourses into the savannah zone, and sometimes penetrating into the high forest, particularly in West Africa. It is principally distinguished by the very large leaflets, generally longer in proportion than *K. anthotheca* and more often with an abruptly acuminate apex. The fruit is large, similar to that of *K. anthotheca,* but with very much thicker valves. In West Africa *K. grandifoliola* appears to be quite distinct, but in Uganda sterile specimens of *K. anthotheca* can be very similar and have been confused. A number of specimens from fringing areas have been called hybrids,[2] and certain planted trees also appear intermediate (DAHT 228). The latter have the characteristic seed chemistry and seedling leaf shape of *K. anthotheca,* so there seems no doubt they belong to this species.

Chemically, we find that the most characteristic extractive is khivorin (Ia).[3] This or its 3-deacetyl derivative (Ib)[4] or the related 7-ketone (Id)[5] are found in all species, but not so far in any other genus. Derivatives of methyl angolensate (IIa)[6] and of mexicanolide (III)[7]

TABLE 1. EXTRACTIVES FROM *Khaya anthotheca*

Origin and herbarium reference	Part of plant and reference (if any)	Compound isolated (% yield)							
		Anthothecol	Cedrelone	Dihydrokhayasin	Khivorin and 3-deacetylkhivorin	Havanensin acetates	Deoxyhavanensin acetates	Khayanthone	Unidentified compound m.p. 128°
Ghana DAHT 200	timber[8]	0·18							
Ghana —	timber	0·07							
Ghana —	timber	0·025							
Sierra Leone —	timber	0·02							
Nigeria FHI 24, 333	timber[5]	0·03							
Congo Dubois 498	timber	—							T
Congo IF 950	timber	—							T
Angola	timber	—							T
Uganda —	timber	—			T				
Uganda DAHT 224	timber[8]	—		T	0·064				
Uganda DAHT 225	timber	—			0·005				
Uganda DAHT 244	timber	—			T				
Ghana DAHT 200	root	0·4							
Ghana DAHT 200	bark	0·08	0·02						
Uganda DAHT 224	bark	No limonoids found							
Ghana DAHT 200	root bark	0 08	0 02			2·8	0·18		
Ghana DAHT 200	seed					2·4			
Ghana —	seed				0·55			0·7	
Uganda —	seed				0·5			0·7	
Uganda —	seed								
Uganda DAHT 228	seed				0·5			0·7	

T = Trace.

[2] B. T. STYLES, unpublished data.
[3] C. W. L. BEVAN, T. G. HALSALL, M. N. NWAJI and D. A. H. TAYLOR, *J. Chem. Soc.* 768, (1962).
[4] E. K. ADESOGAN, J. W. POWELL and D. A. H. TAYLOR, *J. Chem. Soc.* (c) 554 (1967).
[5] C. W. L. BEVAN, J. W. POWELL and D. A. H. TAYLOR, *J. Chem. Soc.* 980 (1963).
[6] C. W. L. BEVAN, J. W. POWELL and D. A. H. TAYLOR, T. G. HALSALL, P. TOFT and M. WELFORD, *J. Chem Soc.* (c) 163 (1967).
[7] E. K. ADESOGAN, C. W. L. BEVAN, J. W. POWELL and D. A. H. TAYLOR, *J. Chem. Soc.* (c) 2127 (1966).
[8] E. K. ADESOGAN, D. A. OKORIE and D. A. H. TAYLOR, *J. Chem. Soc.* (c) 205 (1970).

TABLE 2. EXTRACTIVES FROM *Khaya grandifoliola*

Origin and herbarium reference	Part of plant and reference (if any)	Compounds isolated (% yield)										
		Methyl angolensate	Methyl 6-hydroxy angolensate and acetate	7-Ketokhivorin	Grandifoliolone	Mexicanolide	Khivorin	Deoxyandirobin	20β-Dihydro progesterone acetate	Deacetylgedunin	Fissinolide	Khayasin
Ghana —	timber[9]	0·001	0·0006	0·1	0·002							
Ghana —	timber	0·02	0·002									
Nigeria Aponmu No. 1	timber	0·007	0·02			0·02						
Nigeria DAHT 220	timber	0·016	T	0·001								
Nigeria FHI 42, 782	timber[5]						0·015					
Nigeria FHI 54, 740	timber	0·01				0·004		0·02				
Nigeria —	timber[7]	0·02				0·005						
Uganda DAHT 230	timber	0·005					0·02					
Uganda DAHT 239	timber	T				0·01	0·03					
Uganda DAHT 243	timber	T					0·05					
Nigeria DAHT 157	root	0·08										
Nigeria DAHT 157	bark	0·03	0·03						0·9			
Uganda DAHT 230	bark	0·04										
Uganda DAHT 239	bark	0·02										
Nigeria DAHT 157	root bark		0·01	0·01						0·03		
Nigeria DAHT 157	seed					0·02					1·5	
Nigeria DAHT 220	seed					0·12					1·4	0·12
Uganda DAHT 243*	seed					0·30					0·52	0·16

T = Trace.
* Also 2-hydroxy fissinolide, 0·16; and 2-acetoxy fissinolide, 0·22%.

TABLE 3. EXTRACTIVES FROM *Khaya ivorensis*

Origin and herbarium reference	Part of plant and reference (if any)	Compound isolated (% yield)			
		Khivorin	Methyl angolensate	2-Hydroxyfissinolide	Mexicanolide
Ghana —	timber	0·005			
Nigeria FHI 42, 796	timber[3]	0·05			
Nigeria —	timber[10]	0·05	0·003		*
Nigeria —	root	0·01			
Nigeria —	bark	No limonoids found			
Nigeria —	root bark		0·1	0·01	*
Nigeria —	seed		0·03		0·02
Nigeria —	seed		0·05		

* Minor compounds also isolated.

[9] J. D. CONNOLLY and R. MCCRINDLE, *Chem. Commun.* 1193 (1967).
[10] E. K. ADESOGAN and D. A. H. TAYLOR, *J. Chem. Soc.* (c) 1710 (1970).

TABLE 4. EXTRACTIVES FROM *Khaya madagascariensis*

Origin and herbarium reference	Part of plant and reference (if any)	Compounds isolated (% yield)								
		11β-Acetoxykhivorin	2-Hydroxy-8(14)-dihydrofissinolide	Fissinolide	3-Deacetylkhivorin	Khayasin	Mexicanolide	Khivorin	2-Hydroxykhayasin	6-Deoxyswietenolide
Madagascar DAHT 251	timber and root[11]	0·1	0·07							
Madagascar DAHT 251	bark and root bark	No limonoids isolated								
Madagascar DAHT 251	seed			0·05	0·5					
Madagascar —	seed			0·66	0·12	0·05	0·03	0·14	0·18	0·45

are common. We have also isolated a number of minor components which seem to occur in most species, and a few which only occur in one. Gedunin derivatives are very rare, though common elsewhere in the family.

We have found the timber chemistry variable; not only may trees from the same area differ, but different parts of one trunk may give different extractives. We find qualitative differences, where they occur, take place horizontally and so may depend on age. The seed chemistry is much less variable. In Tables 1–6 we list the specimens we have examined and the results obtained.

K. senegalensis shows considerable variation. The timber usually contains khayasin (IVa)[7] or 7-keto khivorin (Id) as the major extractive; the first of these is characteristic and

TABLE 5. EXTRACTIVES FROM *Khaya nyasica*

Origin and herbarium reference	Part of plant and reference (if any)	Compounds isolated (% yield)									
		3-Deacetylkhivorin	Khivorin	11β-Acetoxy-khivorin	Khayanthone	6-Deoxyswietenine isobutyrate	Deoxykhayanthone	Swietenine esters	Nyasin	Fissinolide	Methyl 3β-acetoxy-1-oxomeliac-14(15)-enate
Tanzania DAHT 257	timber[12]		0·04	0·025	0·004	0·006	0·0009	0·003			
Tanzania DAHT 258	timber		0·02								
Tanzania Semsei 943	timber			0·013					0·001		
Tanzania Semsei 1025	timber		0·004								
Malawi —	timber		No limonoids obtained								
Tanzania DAHT 257	bark		No limonoids obtained								
Rhodesia	seed	0·06	0·16							0·14	0·06
Malawi	seed			Similar to above sample							
Tanzania DAHT 257	seed			Similar to above sample							

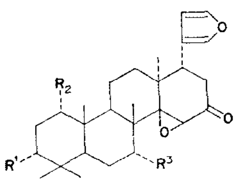
[11] D. A. H. Taylor, *J. Chem. Soc.* (c) 336 (1970).
[12] D. A. H. Taylor, *J. Chem. Soc* (c) 2439 (1969).

TABLE 6. EXTRACTIVES FROM *Khaya senegalensis*

Origin and herbarium reference	Part of plant and reference (if any)	Compounds isolated (% yield)														
		7-ketokhivorin	Khivorin	3-Deacetylkhivorin	7-Deacetylkhivorin	3:7-Dideacetyl khivorin	3-Deacetyl-7-Ketokhivorin	7-Ketogedunin	Methyl angolensate	Mexicanolide	6-Deoxyswietenine esters	6-Hydroxy-mexicanolide	6-Deoxyswietenolide esters	Methyl 6-hydroxy-angolensate	11β-Acetoxy-6-deoxyswietenine acetate	Khayasin
Nigeria FHI 51, 590	timber	0·04														
Nigeria —	timber															0·05
Nigeria 060, 689	timber[13]								0·08							0·1
Nigeria DAHT 208	timber	0·2	0·03													
Nigeria DAHT 209	timber	Qualitatively similar to above														
Nigeria DAHT 210	timber															A
Nigeria DAHT 211	timber															A
Nigeria DAHT 212	timber	A														
Nigeria DAHT 213																A
Nigeria DAHT 214	timber	A														
Nigeria DAHT 215	sap wood									0·03						
Nigeria DAHT 215	heart wood	0·1														
Nigeria DAHT 216	timber	A														
Nigeria DAHT 217	timber															A
Nigeria DAHT 218	timber															A
Uganda DAHT 233	timber															A
Uganda DAHT 234	timber	0·01														
Uganda DAHT 235	timber															A
Nigeria FHI 060, 689	root[13]								Trace							
Nigeria FHI 060, 689	bark[13]													0·015		
Nigeria DAHT 206	timber													0·01		
Nigeria DAHT 208	timber								0·01							
Uganda DAHT 233												0·005		0·005		
Nigeria FHI 060, 689	root bark							0·02						0·02		
Nigeria DAHT 129	seed[4]	0·1	0·4	0·2												
Nigeria DAHT 164	seed[13]			0·7					1·2							
Nigeria DAHT 206	seed			0·3							0·15					
Nigeria DAHT 208	seed	0·36	0·075	0·04	0·04	0·06					0·02				0·02	
Nigeria DAHT 210	seed	0·12	0·12	0·03	0·06		0·12			0·03	0·24					
Nigeria DAHT 211	seed	0·3		0·1	0·21	0·12					0·25					
Nigeria DAHT 215	seed	0·38	0·2	0·21	0·1		0·4				0·28					
Nigeria DAHT 216	seed	0·06	0·06		0·09		0·06			0·03	0·24					
Uganda DAHT 234	seed	0·04			0·4	0·3				0·16			0·3			
Uganda DAHT 235	seed	0·07			0·2								0·3			
Uganda DAHT 238	seed		0·04		0·1				0·01							

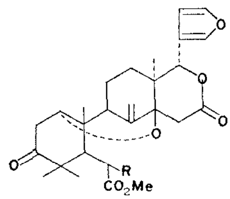
(A) Obtained crystalline, but not examined quantitatively.

[13] E. K. ADESOGAN and D. A. H. TAYLOR, *J. Chem. Soc.* (c) 1947 (1968).



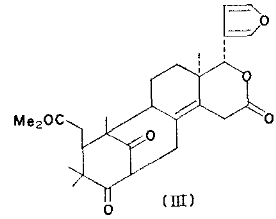
(I)

(a) $R^1 = R^2 = R^3 = OAc$
(b) $R^1 = OH$, $R^2 = R^3 = OAc$
(c) $R^3 = OH$, $R^1 = R^2 = OAc$
(d) $R^3 = O$, $R^1 = R^2 = OAc$

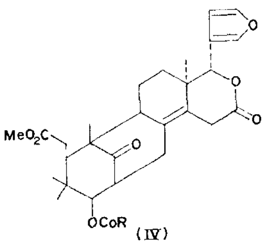


(II)

(a) R = H
(b) R = OH

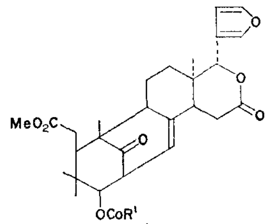


(III)

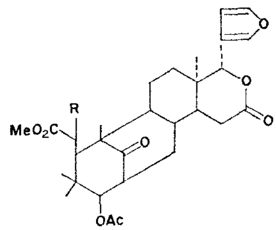


(IV)

(a) R = Pr^i
(b) R = Me

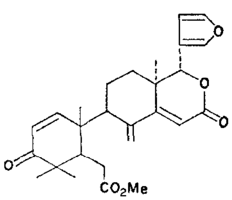


(V)



(VI)

(a) R = H
(b) R = OH



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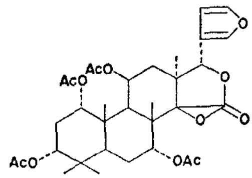

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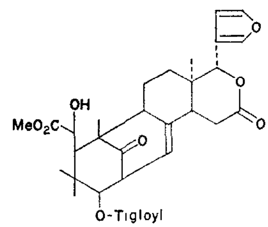
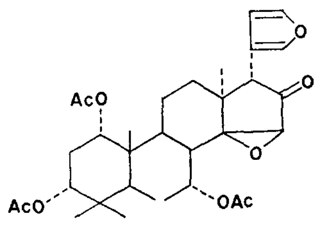


(IX)

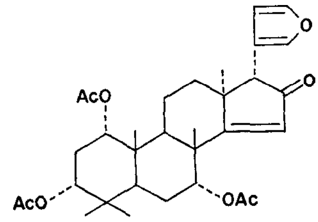
we have found it in the timber of no other species. The bark usually contains methyl angolensate with a variable amount of the 6-hydroxy derivative (IIb). The seed contains the khivorin derivatives (Ib) and (Ic), 6-deoxyswietenine isobutyrate (V), a double bond isomer of khayasin; and minor compounds. It is curious that the isomers (IVa) and (V) occur one in the timber and one in the seed of the same plant. An investigation was made of a group of 1-yr-old saplings. The timber of the parent tree contained mainly 7-ketokhivorin, but this was only found in two out of 20 saplings. Eleven contained methyl 3β-acetoxy-6-hydroxy-1-oxomeliac-14(15)-enate (VIb), not previously found elsewhere. Four of the remainder contained 7-ketogedunin, which again has not been found in mature trees.

K. grandifoliola is also variable. We have examined a number of specimens from different places and usually find methyl angolensate and mexicanolide as the main extractives, although khivorin and 7-ketokhivorin sometimes occur in quantity. From one specimen[14] we obtained deoxyandirobin (VII), not otherwise known as a natural product. The bark usually contains methyl angolensate, while the seeds, characteristically, contain fissinolide (IVb),[15] the acetate corresponding to khayasin.

[14] E. K. Adesogan and D. A. H. Taylor, *Chem. & Ind.* 1365 (1967).
[15] E. K. Adesogan and D. A. H. Taylor, *Chem. Commun.* 225 (1967); R. Zelnik and C. M. Rosito, *Tetrahedron Letters* 6441 (1966).



(X)



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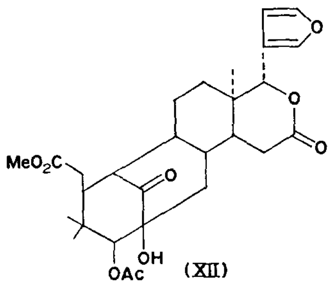

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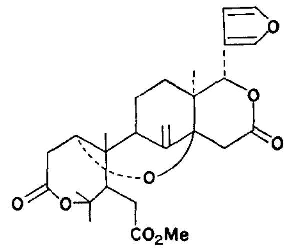

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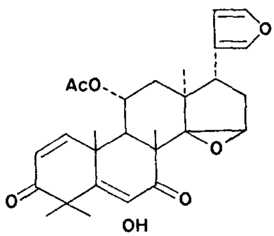

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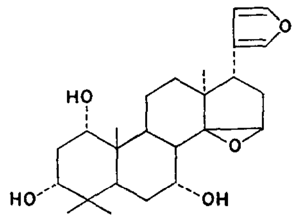

(XV)

There seems to be a clear distinction from *K. senegalensis* in that the wood of *K. grandifoliola* does not contain khayasin, while the seeds contain fissinolide. Both these points seem to be characteristic. It is also interesting that we have not found 3-deacetylkhivorin in the seed of *K. grandifoliola*.

K. nyasica is again variable, some timber samples give very little extract. We have not seen sufficient to chart the variation completely, but there seem to be very few ring B-seco limonoids present. The main extractives are khivorin and 11β-acetoxykhivorin (VIII).[16] We also found a minor amount of swietenine (IX),[17] and of khayanthone (X) and deoxykhayanthone (XI) which may be biosynthetic intermediates to khivorin. We have not found any of these in the timber of any other *Khaya*. The seed gave consistent results, containing 3-deacetylkhivorin, fissinolide, and the conjugated isomer of this (VIa).[12]

We have been able to examine only one complete specimen of *K. madagascariensis*. The timber contained 11β-acetoxykhivorin as the main limonoid, only found otherwise in *K.*

[16] D. A. H. Taylor, *Chem. Commun.* 1172 (1968).

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

nyasica. There was also an interesting compound, methyl 3β-acetoxy-2-hydroxy-1-oxo-meliacate (XII),[11] which is unusual in not having a nuclear double bond, and also in having a 2-hydroxy group. The seeds contained mainly 3-deacetylkhivorin and fissinolide.

K. ivorensis gives khivorin as the main timber limonoid; chromatography of the residue gives methyl angolensate and many minor compounds, including derivatives of swietenolide, but not swietenine. One is methyl ivorensate (XIII),[18] the only ring A-seco limonoid so far found in the Meliaceae. The root bark is a particularly rich source of these minor compounds. The seed contains mainly methyl angolensate together with mexicanolide and the alcohol corresponding to khayasin.

The timber of *K. anthotheca* from Uganda gives very little extract, such as there is, is mainly khivorin, together with a small amount of dihydrokhayasin. The seed contains khayanthone, khivorin and 3-deacetylkhivorin, but apparently no ring B-seco derivatives. *K. anthotheca* from West Africa is unique in containing none of the characteristic ring D lactones; the timber contains anthothecol (XIV)[19] and the seed havanensin (XV) and related compounds.[20] Samples from Angola and the Congo gave little extract and may resemble those from Uganda.

We differentiate seven chemical types, five being accepted species plus the Eastern and Western forms of *K. anthotheca*. Several are variable, but all can be distinguished chemically, and we provide a key for this. They fall into three groups, each homogenous and clearly distinct from the others. The first, characterized by lack of ring D lactones, contains only the Western form of *K. anthotheca*; the second, characterized by the presence of relatively large amounts of ring B-seco limonoids and the relative absence of khivorin, contains *K. grandifoliola* and *K. senegalensis*; while the third, characterized by major amounts of khivorin and the relative absence of ring B-seco limonoids, contains the remainder. In the last group, *K. nyasica* and *K. madagascariensis* are more similar than the others, since both contain 11β-acetoxykhivorin and they have similar seed chemistry. A case might be made for combining these as a single species.

The two chemical types of *K. anthotheca* do not appear to warrant description as separate taxa, even though some morphological differences exist. *K. anthotheca* has a discontinuous distribution, and it seems probable that the West and East African types represent populations of the same species which have been separated for some time. *K. ivorensis* is certainly very closely related, especially to the Eastern type, but there are consistent chemical and botanical distinctions.

EXPERIMENTAL

The analyses have been performed by chromatography of extracts on alumina or on silica gel, and isolation of the crystalline components. The technique has been described in our earlier papers; new com-compounds are described below In all cases the samples were adequate to give results from a normal specimen of material; timber samples were not smaller than 1 kg, so in the cases where no products are recorded the content of limonoid was very low.

It is probably possible to identify the species of a *Khaya* timber sample by the pattern of spots present in a thin layer chromatogram, but the identification of individual substances from unknown samples in this way is not reliable, as too many substances give similar R_fs.

3:7-*Dideacetylkhivorin.* This was obtained in minor amounts from some samples of *K. senegalensis* seed. It had m.p 273–276°; $[\alpha]_D^{21}$ −26° (Found: C, 66·8; H, 7·7. $C_{28}H_{38}O_{10}$ requires C, 66·9; H, 7 6) The structure followed from oxidation to 7-ketogedunin (cf Ref. 4).

[18] E. K. Adesogan and D. A. H. Taylor, *J. Chem. Soc.* (c) 1710 (1970).
[19] C. W. L. Bevan, A. H. Rees and D. A. H. Taylor, *J. Chem. Soc.* 983 (1963).
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Methyl 3β-acetoxy-6-hydroxy-1-oxomeliac-14:15-enate. Obtained from saplings of *K. senegalensis*, this had m.p. 310–312°, $[\alpha]_D^{21}$ −21°. (Found: C, 65·6; H, 7·0. $C_{29}H_{30}O_9$ requires C, 65·9; H, 6·9.) The structure followed from the NMR spectrum. [14-H, δ 5·76, *J* 2·5 c/sec; 17-H, δ 5·1 (s); 3-H, δ 4·81, *J* 10 c/sec; 6-H, δ 4·57 (b.s.), sharpens with D_2O. C-Me, 81, 65, 62, 52 c/sec; Calc. 82, 67, 65, 51 c/sec (cf. Ref. 21).]

Key for the Chemical Identification of Khaya *Species*

(1)	Timber contains no detectable limonoids in a 100 g sample	2
	Timber contains limonoids	3
(2)	Seeds contain fissinolide and 3-deacetylkhivorin	*K. nyasica*
	Seeds contain khayanthone and 3-deacetylkhivorin	*K. anthotheca* (Eastern form)
(3)	Timber contains anthothecol, seeds contain havanensin	*K. anthotheca* (Western form)
	Timber does not contain anthothecol	4
(4)	Timber contains 11β-acetoxykhivorin	5
	Timber does not contain 11β-acetoxykhivorin	6
(5)	Timber contains khivorin but not methyl 3β-acetoxy-2-hydroxy-1-oxomeliacate	*K. nyasica*
	Timber contains methyl 3β-acetoxy-2-hydroxy-1-oxomeliacate but no khivorin	*K. madagascariensis*
(6)	Timber contains khayasin	*K. senegalensis*
	Timber contains khivorin	7
	Timber does not contain khivorin or khayasin	8
(7)	Seeds contain mainly methyl angolensate	*K. ivorensis*
	Seeds contain mainly khivorin and khayanthone	*K. anthotheca* (Eastern form)
	Seeds contain mainly fissinolide	*K. grandifoliola*
(8)	Timber contains 7-ketokhivorin	*K. senegalensis*
	Timber contains methyl angolensate and/or mexicanolide	9
(9)	Seeds contain fissinolide	*K. grandifoliola*
	Seeds do not contain fissinolide	*K. senegalensis*

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