

Chemical Shift of the Tertiary Methyl Groups in the Nuclear Magnetic Resonance Spectra of Some Limonoids

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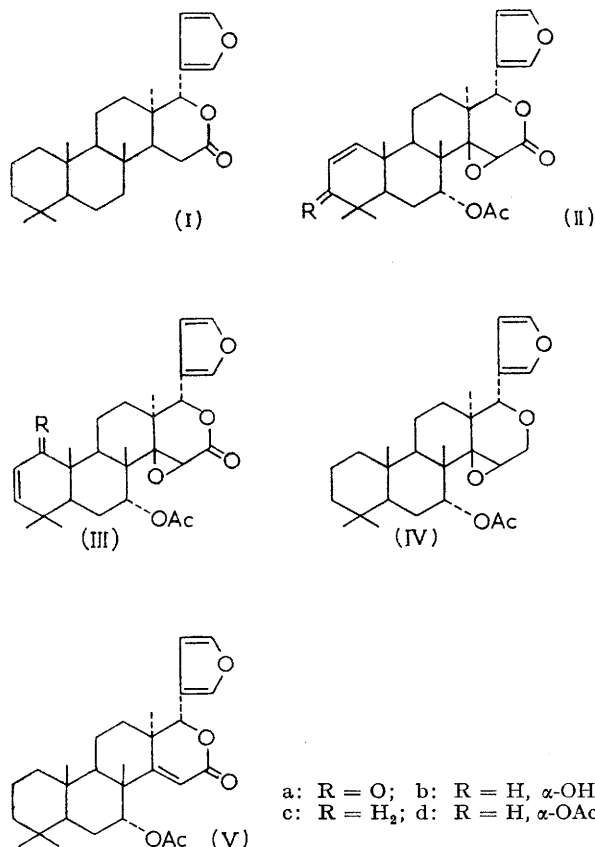
Comparison of the n.m.r. spectra of a series of related limonoids has made it possible to assign the tertiary methyl group resonances. The results are of use in the structural elucidation of new compounds.

It has been shown by Zürcher¹ that the n.m.r. resonance frequency of methyl groups in steroids can be calculated as the sum of a number of incremental terms, dependent on the position and nature of substituents in the molecule. The method has been extended to 4,4-dimethyl

steroids with similar results.^{2,3} In the course of other work we have built up a considerable collection of the n.m.r. spectra of limonoids, some of which have been described by Powell in a recent paper.⁴ It seemed of interest to try to assign the methyl group frequencies in these spectra, and to aid this, a number of new derivatives have been prepared.

In order to facilitate reference to the large number of compounds involved, we wish to use a systematic nomenclature, based on the nucleus (I) which we propose should be known as meliacolide. We had earlier⁵ proposed the name meliacin for this nucleus, but this is unsatisfactory as the same name has also been used as a generic term for limonoids from species of the order Meliaceae.

We wished first to obtain derivatives with no oxygen atoms in ring A. This was accomplished by the reduction of gedunin (IIa) with aluminium isopropoxide to the corresponding 3 α -alcohol (IIb), which was then treated with thionyl chloride to give an allylic chloride. Reduction of this with zinc in acetic acid gave a halogen-free olefin, which on catalytic hydrogenation gave the required 7 α -acetoxy-14 β ,15 β -epoxymeliacolide (IV), which has previously been prepared by Housley, King, King, and Taylor by another method.⁶ Desulphuration of dihydrogedunin ethylene dithioacetal with deactivated Raney nickel gave, unexpectedly, not (IV) but an olefin. The preparation of olefins in this way has previously been reported by Djerassi and Williams,⁷ and from their results it follows that this olefin is the known 2,3-unsaturated compound (IIIc).⁶ Hence the first olefin is the 1(2)-ene (IIc), and we assume that the intermediate halide has the corresponding structure. The stereochemistry of the allylic alcohol (IIb) was proved by hydrogenation of its acetate to the known 3 α ,7 α -di-



¹ R. F. Zürcher, *Helv. Chim. Acta*, 1963, **46**, 2054.

² N. S. Bhacca and D. H. Williams, 'Application of N.M.R. Spectroscopy in Organic Chemistry,' Holden-Day, San Francisco, 1964, p. 168.

³ M. Fetizon, M. Golfier, and P. Raszlo, *Bull. Soc. chim. France*, 1965, 3206.

⁴ J. W. Powell, *J. Chem. Soc. (C)*, 1966, 1794.

⁵ C. W. L. Bevan, J. W. Powell, and D. A. H. Taylor, *J. Chem. Soc.*, 1963, 980.

⁶ J. R. Housley, F. E. King, T. J. King, and P. R. Taylor, *J. Chem. Soc.*, 1962, 5095.

⁷ C. Djerassi and D. H. Williams, *J. Chem. Soc.*, 1963, 4046.

TABLE 1

N.m.r. spectra of ring A unsaturated meliacolides, in p.p.m. relative to SiMe₄, in deuteriochloroform. Coupling constants in c./sec. d = doublet, t = triplet, q = quintuplet

Substituents in epoxymeliacolide	H(1)	H(2)	H(3)	H(7)	H(15)	H(17)	Furan
$\Delta^{2,3}$ -7 α -OAc	—	5.45 complex		4.53 $J^* 4$	3.51	5.61	6.35 7.40 7.43
$\Delta^{2,3}$ -1 α ,7 α -(OH) ₂	ca. 3.5	5.59 complex		ca. 3.5	3.89	5.59	6.30 7.30 7.35
$\Delta^{2,3}$ -1 α -OH-7 α -OAc	3.53 $J^* 7$	5.59 complex		4.51 $J^* 4$	3.51	5.59	6.26 7.31 7.33
$\Delta^{2,3}$ -1 α ,7 α -(OAc) ₂	4.75 $J^* 7$	5.66br s		4.55 $J^* 4$	3.55	5.60	6.30 7.38 7.40
$\Delta^{2,3}$ -1 β ,7 α -(OAc) ₂	5.05 $J^* 10$	5.63 complex		4.75 $J^* 5$	3.68	5.50	6.30 7.36 7.36
$\Delta^{1,2}$ -7 α -OAc	5.9 d of t $J^* 10$ W/2 3	5.4q W/2 20	—	4.53 $J^* 5$	3.53	5.58	6.30 7.36 7.38
$\Delta^{1,2}$ -3 β -Cl-7 α -OAc	5.48d $J^* 10$	5.75 d of d $J^* 10, 5$	4.98d $J^* 5$	4.50 $J^* 5$	3.55	5.60	6.35 7.36 7.38
$\Delta^{1,2}$ -3 α -OH-7 α -OAc	5.3 d of d $J^* 1.4, 10$	5.8 d of d $J^* 2.4, 10$	3.90 $J^* 3.8$	4.50 $J^* 5.2$	3.46	5.55	6.20 7.37 7.35
$\Delta^{1,2}$ -3 α ,7 α -(OAc) ₂	5.21 d of d $J^* 1.5, 11$	5.9 d of d $J^* 3, 11$	5.15 $J^* 4.5$	4.51 $J^* 4$	3.49	5.57	6.30 7.34 7.36

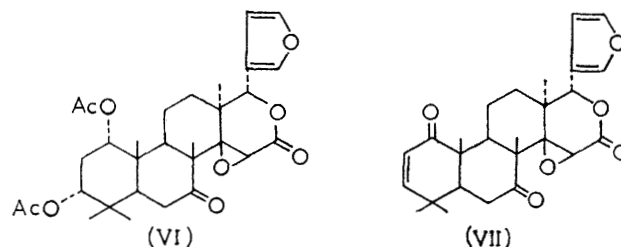
acetoxymeliacolide.⁶ In the allyl alcohol (IIb) the coupling constants are H(2),H(3) 2.4 c./sec., H(1),H(3) 1.4 c./sec. In the allyl chloride the coupling constants are H(1),H(3) 0 c./sec., H(2),H(3) 5 c./sec.; we thus suppose that this is the 3 β -chloro-compound, the hydroxy-group having been replaced with inversion, but without allylic shift.

Desulphuration of dihydrogedunin ethylene dithioacetal with less deactivated Raney nickel gave 7 α -acetoxymeliac-14(15)enolide (V), which is presumably derived by further reduction of the intermediate (IIc). Solvolysis of the allylic halide with potassium acetate in acetic acid proceeded with allylic rearrangement to give the known 1 α ,7 α -diacetoxymeliac-14 β ,15 β -epoxymeliac-2(3)-enolide (IIIId).⁸ A convenient new synthesis of the interesting isogedunin (IIIa) was realised by solvolysis of the halide with formic acid, mild hydrolysis to the mono-alcohol (IIIb), and oxidation.

An alternative synthesis of 1-oxo-compounds was made possible by the discovery of a variety of *Khaya senegalensis* in the timber of which the main extractive was 1 α ,3 α -diacetoxymeliac-14 β ,15 β -epoxy-7-oxomeliacolide (VI), previously only available as a minor constituent. Hydrolysis of this gave the corresponding diol, which on oxidation with a limited amount of chromic acid in acetone as described by Akisanya *et al.*⁸ gave a good yield of the 3-hydroxy-1-oxo-compound, separated from the accompanying isomer by its much lower solubility in methanol. Treatment of the hydroxy-ketone with either acid or alkali caused dehydration to 14 β ,15 β -epoxy-1,7-dioxomeliac-2(3)-enolide (VII).

⁸ A. Akisanya, E. O. Arene, C. W. L. Bevan, D. E. U. Ekong, M. N. Nwaji, J. I. Okogun, J. W. Powell, and D. A. H. Taylor, *J. Chem. Soc. (C)*, 1966, 506.

In the n.m.r. spectra the vinyl protons of compounds with a 1,2 double bond form a much wider pattern than those of compounds with a 2,3 double bond, and we believe this difference is diagnostic. The details of the spectra are collected in Table 1.



A number of derivatives were prepared from the above compounds by standard methods of reduction or oxidation, hydrolysis, or acetylation, which have been fully described in earlier papers and which do not call for further comment. The melting points and rotations of new compounds are collected in Table 2. Carbon and hydrogen analyses and infrared, mass, and n.m.r. spectra have also been recorded.

The introduction of a substituent can affect the chemical shift of protons already present in a molecule in two ways: by altering the local field, the shielding or deshielding effect, or by producing conformational changes. If only the first of these effects operates, the result should be a series of additive increments, as found by Zürcher, while if the second effect operates there may be large and random changes. In fact we have found for the most part a series of increments constant to within 1–2 c./sec., with only a few compounds where conformational changes appear to take place. We list the

TABLE 2

Methyl group shifts in derivatives of meliacolide (I) in c./sec. from SiMe₄, in deuteriochloroform, at 60 Mc./sec.

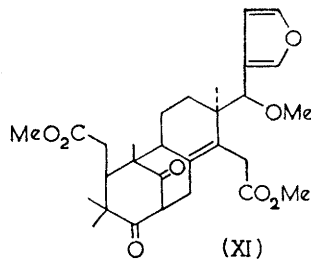
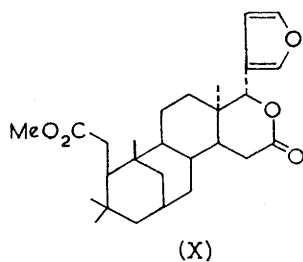
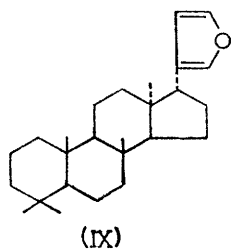
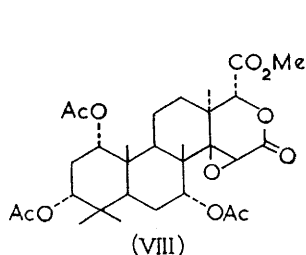
Substituents in 14 β ,15 β - epoxymeliacolide	Calculated					Found					M.p.	[α] _D ²⁰	Ref.
	4 α	4 β	8	10	13	4 α	4 β	8	10	13			
7 α -OAc	47	49	63	57	75	47	49	65	57	76	180—183°	—20°	6
7 α -OH	51	51	60	56	75	50	50	60	55	74	250—258	+4	6
7 β -OAc	51	50	61	53	75	—	—	—	—	—	—	—	—
7 β -OH	55	47	63	54	72	—	—	—	—	—	—	—	—
7-oxo	52	54	65	64	69	52	52	67	65	68	205—208	—110	6
3 α ,7 α -(OAc) ₂	46	54	64	59	77	45	53	65	58	77	243—246	—55	6
3 β ,7 α -(OAc) ₂	47	51	66	60	75	46	51	64	58	75	134—136	—7	6
3 β ,7 β -(OAc) ₂	51	52	64	56	75	53	53	65	59	75	128—130	+25	—
7 α -OAc-3 α -OH	49	51	64	56	75	50	50	64	57	75	190—192	—17	6
7 α -OAc-3 β -OH	45	54	63	58	74	45	52	63	56	74	209—211	—15	a
3 β -OAc-7 α -OH	51	53	63	59	75	52	52	61	57	74	—	—	4
7 α -OAc-1 β -OH	46	49	65	60	75	46	49	65	60	75	223—225	—	—
7 α -OAc-3-oxo	61	62	67	67	76	61	62	65	67	75	237—238	+4	b
7 α -OAc-1-oxo	51	61	67	79	77	50	63	65	80	80	205—207	+6	—
3 β ,7 α -(OH) ₂	49	56	60	57	74	48	56	61	58	74	137—139	0	6
7 α -OH-3-oxo	65	64	64	66	76	62	62	62	64	74	264	+43	6
7 α -OH-1-oxo	55	63	64	78	77	55	62	63	78	77	255—258	—	—
3,7-dioxo	66	67	69	74	70	66	66	68	72	72	236—238	—90	6
1,7-dioxo	56	66	69	86	71	56	68	68	87	69	224	—81	—
3 α ,7 α ,12 β -(OAc) ₃	49	53	85	81	74	48	57	85	80	74	302	—44	c
1 α ,3 α ,7 α -(OAc) ₃	49	56	66	63	75	49	56	66	62	76	256—262	—42	d
1 α ,3 α ,7 β -(OAc) ₃	53	57	64	59	75	55	55	63	59	76	307—309	—129	—
1 α ,3 α -(OAc) ₂ -7 α -OH	53	58	63	62	75	54	56	61	60	75	not crystalline	—	—
1 α ,3 α -(OAc) ₂ -7 β -OH	57	54	66	60	72	56	56	66	61	73	258—260	+31	—
1 α ,7 α -(OAc) ₂ -3 α -OH	52	53	66	60	73	51	56	65	60	74	245	—38	13
1 α ,7 α -(OAc) ₂ -3-oxo	64	64	69	71	74	63	63	68	71	72	216—218	—18	13
1 α ,3 α -(OAc) ₂ -7-oxo	54	61	68	70	69	54	60	70	70	70	228—230	—100	5
7 α -OAc-1 α ,3 α -(OH) ₂	51	52	66	54	77	50	53	65	55	77	268—275	—19	8
3 α -OAc-1 α ,7 α -(OH) ₂	52	57	63	56	79	52	56	62	56	77	not crystalline	—	—
7 α -OAc-1 α -OH-3-oxo	63	63	69	65	78	64	65	70	66	79	not crystalline	—	—
1 α -OAc-3 α -OH-7-oxo	57	58	68	67	67	56	60	68	68	68	240	—	13
3 α -OAc-1,7-dioxo	55	71	70	88	73	54	72	70	88	71	215—217	—100	—
1 α ,3 α -(OH) ₂ -7-oxo	56	57	68	61	71	59	54	69	63	69	282—284	—	8
3 α -OH-1,7-dioxo	58	68	70	85	71	58	69	69	87	69	274—277	—	8
1 α ,3 α ,7 α ,11 β -(OAc) ₄	49	56	78	75	74	48	55	78	77	75	258	—20	9
$\Delta^{1,2}$ -7 α -OAc	51	52	66	66	73	52	54	67	67	75	215—218	—	—
$\Delta^{1,2}$ -3 α ,7 α -(OAc) ₂	50	53	67	68	75	50	55	67	69	74	138—140	+50	—
$\Delta^{1,2}$ -7 α -OAc-3 α -OH	50	54	67	67	73	50	54	65	67	73	215—218	+53	—
$\Delta^{1,2}$ -3 α -OAc-7-oxo	55	58	69	75	69	54	56	71	76	66	not crystalline	—	—
$\Delta^{1,2}$ -7 α -OAc-3-oxo	65	65	70	76	74	63	63	69	74	73	218	—44	a
$\Delta^{1,2}$ -7 β -OAc-3-oxo	69	66	68	72	74	68	65	68	71	74	not crystalline	—	—
$\Delta^{1,2}$ -7 α -OH-3-oxo	69	67	67	75	74	69	67	67	75	74	250—272	+75	a
$\Delta^{1,2}$ -7 β -OH-3-oxo	73	63	70	73	71	71	65	69	71	69	227	+100	—
$\Delta^{1,2}$ -3 α ,7 β -(OH) ₂	58	52	67	62	70	60	49	68	65	70	149—150	+105	—
$\Delta^{1,2}$ -3 α -OH-7-oxo	55	59	69	74	67	53	59	71	74	67	not crystalline	—	—
$\Delta^{1,2}$ -3,7-dioxo	70	70	72	83	68	69	69	74	82	69	262	—55	5
$\Delta^{1,2}$ -7 α ,11 β -(OAc) ₂ -3-oxo	65	65	82	88	73	66	66	79	84	72	—	—	e
$\Delta^{1,2}$ -3-oxo-6 α ,7 α ,11 β -(OAc) ₃	68	66	82	87	73	68	66	82	87	73	—	—	e
$\Delta^{2,3}$ -7 α -OAc	54	52	65	58	76	54	53	66	59	76	184	+33	6
$\Delta^{2,3}$ -1 α ,7 α -(OAc) ₂	55	56	66	60	74	54	56	67	60	75	230—235	+105	—
$\Delta^{2,3}$ -1 β ,7 α -(OAc) ₂	54	58	63	61	77	54	58	63	61	77	not crystalline	—	—
$\Delta^{2,3}$ -7 α -OAc-1 α -OH	51	56	64	56	77	52	55	66	55	77	not crystalline	—	—
$\Delta^{2,3}$ -7 α -OAc-1-oxo	58	64	69	80	78	59	64	68	79	77	208—212	+46	8
$\Delta^{2,3}$ -1 α ,7 α -(OH) ₂	55	58	61	55	77	54	59	62	55	75	241—244	—	8
$\Delta^{2,3}$ -7 α -OH-1-oxo	62	66	66	79	78	65	65	64	78	76	230—235	+71	—
$\Delta^{2,3}$ -1,7-dioxo	63	69	71	87	72	65	68	70	87	72	249	—34	—
Substituents in 1 α ,2 α -14 β ,15 β - diepoxymeliacolide													
3 α ,7 α -(OAc) ₂	43	54	64	57	79	45	50	65	69	76	—	—	4
7 α -OAc-3-oxo	58	62	67	65	78	59	61	66	64	77	217—219	+80	8
7 α -OH-3-oxo	62	64	64	64	78	59	60	64	66	77	285—291	—	8
3,7-dioxo	63	67	69	72	73	61	67	70	72	72	—	—	4
Substituents in meliac-14(15)- enolide													
7 α -OAc	48	51	75	57	71	47	49	75	56	70	not crystalline	—	—
7 β -OAc	53	50	78	57	70	—	—	—	—	—	—	—	—
7 α -OH	51	54	72	54	71	50	53	70	55	73	not crystalline	—	—
7 β -OH	54	49	72	54	69	—	—	—	—	—	—	—	—
7-oxo	53	54	90	67	70	53	53	90	67	70	260—264	—	—
3 α ,7 α -(OAc) ₂	47	56	76	59	73	46	55	77	59	72	240—242	+6	—
3 β ,7 β -(OAc) ₂	53	52	81	60	70	53	54	81	60	70	178—180	—	—
7 α -OAc-3 α -OH	50	53	76	56	71	51	51	76	57	70	238—240	+61	—
7 α -OAc-3-oxo	62	64	79	67	72	61	62	78	65	70	219—222	+64	d

TABLE 2 (Continued)

Substituents in 14 β ,15 β -epoxymeliacolide	Calculated					Found					M.p.	[α] ²⁰	Ref.
	4 α	4 β	8	10	13	4 α	4 β	8	10	13			
7 α -OH-3-oxo	65	67	76	64	72	64	66	75	63	71	—	—	4
3,7-dioxo	67	67	94	77	71	66	66	94	77	68	234—236	—	4
1 α ,3 α ,7 α -(OAc) ₃	50	58	78	63	71	50	56	78	62	71	243—245	+16	d
1 α ,3 α ,7 β -(OAc) ₃	55	57	81	60	70	55	55	81	61	70	336—337	+69	—
1 α ,3 α -(OAc) ₂ -7 α -OH	53	61	75	60	71	57	61	75	57	71	—	+66	—
1 α ,3 α -(OAc) ₂ -7 β -OH	56	56	75	60	69	56	56	75	60	69	290—292	—	—
1 α ,3 α -(OAc) ₂ -7-oxo	55	61	93	73	70	57	61	94	74	71	240—242	—22	—
7 α -OAc-1 α ,3 α -(OH) ₂	52	54	78	54	73	52	56	78	56	72	140—145	+42	—
3 α -OAc-1,7-dioxo	56	71	95	91	72	57	73	93	93	76	255	—31	—
3 α -OH-1,7-dioxo	59	68	95	88	72	61	68	91	90	74	310—315	—	—
$\Delta^{1,2}$ -7 α -OAc-3-oxo	66	67	82	76	70	65	66	81	74	70	209—214	+105	d
$\Delta^{1,2}$ -7 α -OH-3-oxo	69	70	79	73	70	67	71	78	73	71	—	—	4
$\Delta^{1,2}$ -3,7-dioxo	72	70	97	86	69	70	70	95	84	68	—	—	4
$\Delta^{2,3}$ -1 α ,7 α -(OAc) ₂	56	58	78	60	70	55	57	78	60	70	295—300	+182	—
$\Delta^{2,3}$ -1 α ,7 α -(OH) ₂	55	61	73	53	73	54	60	71	53	74	184—185	—	—
$\Delta^{2,3}$ -1,7-dioxo	64	69	96	90	71	66	69	95	87	72	330—335	+28	—
Substituents in 1 α ,2 α -epoxy-meliac-14(15)-enolide													
7 α -OAc-3-oxo	59	64	79	65	74	62	65	81	65	75	—	—	—
7 α -OH-3-oxo	62	67	76	62	74	61	66	75	61	73	—	—	—
3,7-dioxo	64	67	94	75	73	62	67	94	74	72	—	—	—
Substituents in the etio-ester (VIII)													
7 α -OAc-3-oxo	60	61	66	66	82	61	61	65	66	80	188—190	—23	a
1 α ,3 α ,7 α -(OAc) ₃	48	55	65	62	81	48	55	64	61	80	—	—	f
1 α ,3 α -(OAc) ₂ -7-oxo	53	60	67	69	75	53	59	68	69	76	—	—	f
1 α ,3 α ,7 α -(OAc) ₃ -14,15-deoxy	49	57	77	62	77	49	57	78	62	73	256—259	—5	d
1 α ,3 α -(OAc) ₂ -7-oxo-14,15-deoxy	54	60	92	72	76	54	59	90	72	75	—	—	f

^a A. Akisanya, C. W. L. Bevan, T. G. Halsall, J. W. Powell, and D. A. H. Taylor, *J. Chem. Soc.*, 1961, 3705. ^b A. Akisanya, Ph.D. Thesis, London, 1963. ^c D. A. H. Taylor, *Chem. Comm.*, 1967, 500. ^d C. W. L. Bevan, T. G. Halsall, M. N. Nwaji, and D. A. H. Taylor, *J. Chem. Soc.*, 1962, 768. ^e J. D. Connolly, R. McCrindle, K. H. Overton, and J. Feeney, *Tetrahedron*, 1966, **22**, 891. ^f K. O. Jibodu and D. A. H. Taylor, unpublished work.

methyl group shifts of the compounds we have studied in Table 2 with our assignments. The shifts are recorded in deuteriochloroform in c./sec., from tetramethylsilane at 60 Mc./sec., and are to the nearest c./sec. We do not find the increments sufficiently constant to justify a greater accuracy of measurement.



In assigning the methyl groups, we started with khivorin (1 α ,3 α ,7 α -tri-acetoxy-14 β ,15 β -epoxymeliacolide). This has methyl group resonances at 49, 56, 62, 66, and

76 c./sec. Ozonolysis to the corresponding etio-ester (VIII) gave a compound in which only one methyl group, that at 76 c./sec., was shifted, being moved downfield to 80 c./sec. On the principle that changes affect mainly groups which are sterically close, we therefore assigned this band to the methyl group at C(13). In 11 β -acetoxykhivorin, the main limonoid of *Khaya nyasica* and *Khaya madagascariensis*,⁹ the methyl resonances are at 48, 55, 77, 75, and 80 c./sec. We assign the 75 c./sec. band to the methyl at C(13), of the others, the two which are strongly shifted will be those at C(8) and C(10), which are close to the new acetoxy-group, while the 48 and 55 c./sec. resonances will be those at C(4 α) and C(4 β), not necessarily respectively. Of the bands in khivorin at 62, 66 c./sec. which we assign to the C(8) and C(10) methyl groups, one, that at 66 c./sec., is unaffected by the loss of the 1 α -acetoxy-group in 14 β ,15 β -epoxy-3 α ,7 α -diacetoxy-meliacolide, while the other is shifted upfield from 62 to 58 c./sec. This we assign to Me(10), adjacent to the oxygen atom at C(1). It remains to decide which of the methyl groups we assign to 4 α and 4 β is which. We have seen that introduction of the axial 1 α -acetoxy-group produces a downfield shift of 4 c./sec. in the *trans*-axial methyl group at C(10). It is reasonable to suppose that a similar increment would be produced in the axial 4 β -methyl group by a *trans*-axial 3 α -acetoxy-group. In fact the two methyl groups concerned resonate at 45, 53 c./sec. in 3 α ,7 α -di-

⁹ D. A. H. Taylor, *Chem. Comm.*, 1968, 1172.

acetoxy-14 β ,15 β -epoxymeliacolate, and at 47, 49 c./sec. in 7 α -acetoxy-14 β ,15 β -epoxymeliacolate. We assign the bands at 45, 47 c./sec. to the 4 α -methyl group, and the bands at 53, 49 c./sec. to the 4 β -methyl group, giving a downfield increment of -2 and +4 c./sec. at Me(4 α) and Me(4 β) respectively, for the introduction of the 3 α -acetoxy-group. In this way we have assigned all the bands in khivorin, and obtained a first set of incremental values. Using these on further compounds, we have been able to assign more bands, and we have treated other substituents in a similar manner. Thus we obtain incremental values for a 3-oxo-group by comparing 1 α ,7 α -diacetoxy-14 β ,15 β -epoxy-3-oxomeliacolate and 7 α -acetoxy-14 β ,15 β -epoxy-3-oxomeliacolate, and using the 1 α -acetoxy-increment to identify Me(10). We have also checked the assignment of Me(13) in several cases by ozonolysis to the corresponding etio-acid. We consider that the overall consistency of the increments obtained in this way justifies the assumptions used. A number of minor discrepancies occur, most often in hydroxy-compounds. These probably relate to stereochemical change, which may be consequent on hydrogen-bonding. Since we have not yet been able to prepare 7-deoxy-compounds or 14,15-saturated compounds, we have not been able to find increments for changes at these positions. To obtain useful tables, we base our calculations on the known 7 α -hydroxy-, 7 α -acetoxy-, and 7-oxo-derivatives of 14 β ,15 β -epoxymeliacolate and meliac-14,15-enolide; a better overall agreement is obtained by using values for these compounds which differ slightly from those found. The increments that we use are listed in Table 3.

We have also attempted to relate the resonance bandwidth of the methyl groups to their position in the molecule. In a number of cases this is rendered impossible by the overlapping of signals, but in many limonoids such as khivorin we find a pattern of two narrow bands, two of intermediate width, and one wide band. The two narrow bands appear to be often, but not always, those due to Me(8) and Me(13), the wider band appears to be consistently upfield of the others and to be consistently that due to Me(4 α), which is the only equatorial methyl group in the molecule. We have recorded the spectra of many of the compounds in benzene in the hope of correlating the solvent shifts, but these are very complex owing to the large number of polar groups in most of the compounds, and we have not made much progress with this.

We have applied the same increments to a number of derivatives of meliacan (IX) (nomenclature, see ref. 10) and obtained satisfactory agreement; the figures are included as Table 4. We have also examined a number of derivatives of methyl meliacate¹¹ (X) and of C.O.C.¹² (XI). The results, included as Table 5,* appear encouraging, but not sufficient compounds are known for

us to be very confident of them. The increments used are listed in Table 6. We have already made a somewhat similar treatment of methyl angolensate derivatives.¹¹

TABLE 3

Calculated increments in derivatives of meliacolate (I)					
	4 α	4 β	8	10	13
1 β -OH	-1	0	+2	+3	0
1 α -OH (ring A sat.)	+2	+1	+2	-2	+2
1 α -OAc (ring A sat.)	+3	+2	+2	+4	-2
1 α -OH ($\Delta^{2,3}$)	-3	+4	-1	-2	+1
1 α -OAc ($\Delta^{2,3}$)	+1	+4	+1	+2	-2
1 β -OAc	0	+6	-2	+3	+1
1-oxo	+4	+12	+4	+22	+2
3 β -OH	-2	+5	0	+1	-1
3 β -OAc	0	+2	+3	+3	0
3 α -OH (ring A sat.)	+2	+2	+1	-1	0
3 α -OAc (ring A sat.)	-1	+5	+1	+2	+2
3 α -OH ($\Delta^{1,2}$)	-1	+2	+1	+1	0
3 α -OAc ($\Delta^{1,2}$)	-1	+1	+1	+2	+2
3-oxo	+14	+13	+4	+10	+1
6 α -OAc	+3	+1	0	-1	0
11 β -OAc	0	0	+12	+12	-1
12 β -OAc	+3	-1	+21	+22	-3
$\Delta^{1,2}$	+4	+3	+3	+9	-2
$\Delta^{2,3}$	+7	+3	+2	+1	+1
1 α ,2 α -epoxy	-3	0	0	-2	+2
Increment for 17-furan \rightarrow					
17-COOCH ₃	-1	-1	-1	-1	+6

As an example of the use of these tables, we have obtained a monoacetate in small yield from the acetylation of 14 β ,15 β -epoxy-1 α ,3 α ,7 α -trihydroxymeliacolate. This was not the known 7 α -acetate, but could be either the 3- or the 1-acetyl derivative. The figures calculated from our tables for these two compounds are respectively

TABLE 4

Methyl group shifts in derivatives of meliacan (IX)¹⁰ in c./sec. from SiMe₄ in deuteriochloroform at 60 Mc./sec.

Substituents in 14 β ,15 β -epoxy-meliacan.	Calculated					Found					Ref.
	4 α	4 β	8	10	13	4 α	4 β	8	10	13	
7 α -OAc	47	48	60	55	60	—	—	—	—	—	—
7 α -OH	51	50	58	54	60	—	—	—	—	—	—
7-oxo	52	53	66	62	48	—	—	—	—	—	—
3,7-dioxo	66	66	70	72	49	66	66	70	70	47	a
1,7-dioxo	56	65	70	84	48	56	68	71	88	49	a
1 α ,3 α ,7 α -(OAc) ₃ ...	49	55	63	61	60	48	54	63	60	60	b
3 α ,7 α -(OAc) ₂ -1 α -OH	48	54	63	55	64	48	55	63	56	65	b
3 α ,7 α -(OAc) ₂ -1-oxo	50	65	65	79	62	50	64	67	79	62	a
1 α ,7 α -(OAc) ₂ -3 α -OH	52	52	63	58	58	52	56	64	59	59	b
$\Delta^{1,2}$ -7 α -OAc-3-oxo	65	64	67	74	59	65	65	68	73	59	a
$\Delta^{1,2}$ -7 α -OH-3-oxo ...	69	66	65	73	59	68	65	64	71	58	b
$\Delta^{1,2}$ -3,7-dioxo	70	69	73	81	47	69	69	72	81	48	a
$\Delta^{2,3}$ -7 α -OH-1-oxo ...	62	65	64	77	61	64	65	65	76	62	b
$\Delta^{2,3}$ -1,7-dioxo	63	68	72	85	49	64	69	72	85	48	a

^a D. A. Okorie and D. A. H. Taylor, unpublished work.

^b W. R. Chan, J. A. Gibbs, and D. R. Taylor, *Chem. Comm.*, 1967, 720.

52, 57, 63, 56, 79 and 56, 55, 63, 59, 72 c./sec. The values found are 52, 56, 62, 56, 77 c./sec., from which it appears that the compound is the 3-acetate. Another example is provided by a compound isolated from the

* This table supersedes that in reference *e* reported in Table 5.

¹⁰ D. A. Okorie and D. A. H. Taylor, *J. Chem. Soc. (C)*, 1968, 1828.

¹¹ E. K. Adesogan and D. A. H. Taylor, *J. Chem. Soc. (C)*, 1968, 1974.

¹² E. K. Adesogan, C. W. L. Bevan, J. W. Powell, and D. A. H. Taylor, *J. Chem. Soc. (C)*, 1966, 2127.

TABLE 5

Methyl shifts in derivatives of methyl meliacate (X) ¹¹ in c./sec. from SiMe₄ in deuteriochloroform at 60 Mc./sec.

Substituents in methyl meliac-14(15)-enate	Calculated				Found				Ref.
	4 α	4 β	10	13	4 α	4 β	10	13	
1-oxo	40	54	63	63	—	—	—	—	—
3 β -OAc-1-oxo	50	51	64	67	50	50	63	65	11
3 β -OH-1-oxo	45	55	63	65	45	56	63	65	11
1,3-dioxo	53	67	69	63	53	68	68	61	a
6 α -OAc-1,3-dioxo	69	73	71	63	71	74	71	64	c
6 α -OH-1,3-dioxo	70	67	87	61	70	65	87	62	c
Substituents in methyl meliac-8(14)-enate...									
1-oxo	39	47	69	62	—	—	—	—	—
3 β -OAc-1-oxo	49	44	70	66	49	44	70	65	b
3 β -OH-1-oxo	44	48	69	64	44	49	69	63	11
1,3-dioxo	52	60	75	62	52	60	75	60	12
6 α -OAc-1,3-dioxo	68	66	76	62	68	65	76	60	e
6 α -OH-1,3-dioxo	69	60	93	60	70	60	93	62	e
3 β ,6 α -(OAc) ₂ -1-oxo ...	65	50	72	66	64	52	70	65	c
Substituents in methyl meliac-8(30)-enate									
1-oxo	38	53	69	62	—	—	—	—	—
3 β -OAc-1-oxo	48	50	70	66	50	50	70	66	11
3 α -OAc-1-oxo	47	52	69	65	48	50	69	65	11
3 β -OH-1-oxo	43	54	69	64	44	49	67	65	11
3 α -1-oxo	47	52	69	65	48	50	69	65	11
1,3-dioxo	51	66	75	62	51	66	75	61	11
3 β ,6 α -(OH) ₂ -1-oxo ...	60	54	87	62	59	53	86	61	d
3 α ,6 α -(OH) ₂ -1-oxo ...	61	57	88	62	60	60	87	60	d
3 β -OH-1,6-dioxo	59	53	73	64	58	54	72	65	d
3 α -OH-1,6-dioxo	60	56	74	64	62	55	76	65	d
3 β ,11 β -(OAc) ₂ -1-oxo...	47	47	77	61	47	47	76	60	11*
3 α ,11 β -(OAc) ₂ -1-oxo...	46	49	76	60	46	49	76	60	11*
3 α ,11 β -(OH) ₂ -1-oxo ...	42	53	83	66	42	53	83	66	11*
1,3,6-trioxo	67	65	80	62	68	65	77	60	d
Substituents in C.O.C. (XI)									
1-oxo	40	54	69	59	—	—	—	—	—
3 β -OAc-1-oxo	50	51	68	63	50	50	70	65	b
3 β -OH-1-oxo	45	55	67	61	45	56	68	60	12
3 α -OH-1-oxo	46	58	68	61	46	58	66	62	12
1,3-dioxo	53	67	73	59	54	67	75	57	12

* Structure revised on the basis of double resonance n.m.r. experiments, to be described.

^a E. O. Arene, C. W. L. Bevan, J. W. Powell, and D. A. H. Taylor, *Chem. Comm.*, 1965, 302. ^b E. K. Adesogan and D. A. H. Taylor, *Chem. Comm.*, 1967, 225. ^c Personal communication from Dr. J. D. Connolly. ^d J. D. Connolly, R. Henderson, R. McCrindle, K. H. Overton, and N. S. Bhacca, *J. Chem. Soc.*, 1965, 6935. ^e D. A. Stone and D. A. H. Taylor, *Phytochemistry*, 1968, 1683.

seed of *Khaya senegalensis*.¹³ This was shown to be a monoacetate of 14 β ,15 β -epoxy-3 α ,7 α -dihydroxy-7-oxo-meliacolide, and it was considered on the basis of biological analogy to be probably the 1-acetate. Insufficient material was available to confirm this. The

TABLE 6

Calculated increments in derivatives of methyl meliacate (X) ¹¹ and C.O.C. (XI) ¹²

	4 α	4 β	10	13
3 β -OAc	+10	-3	+1	+4
3 α -OAc	+9	-1	0	+3
3 β -OH	+5	+1	0	+2
3 α -OH	+6	+4	+1	+2
3-oxo	+13	+13	+6	0
6 α -OAc	+16	+6	+2	0
6 α -OH	+17	0	+18	-2
6-oxo	+16	-1	+4	0
11 β -OAc	-2	-3	+7	-5
11 β -OH	-2	-3	+13	+2

calculated values for the 3- and the 1-acetates are 53, 60, 68, 64, 73; 57, 58, 68, 67, 67 c./sec., while the found values are 56, 60, 68, 68, 68 c./sec., agreeing with the proposed formula. A third example is provided by an oxidation product of 7 α -acetoxy-14 β ,15 β -epoxy-1 α ,3 α -dihydroxymeliacolide. It was known that the major oxidation product of this compound, using 2 equivalents of oxidising agent, was the 3 α -hydroxy-1-oxo-compound, but the spectrum of this had not been recorded.⁸ A further sample was prepared, the spectrum of this showed methyl groups at 64, 65, 70, 66, 79 c./sec., against the calculated values of 53, 63, 68, 78, 75 c./sec. The calculated values of the 1 α -hydroxy-3-oxo-compound, 63, 63, 69, 65, 78 c./sec., made it clear that the unexpected minor product had in fact been isolated.

EXPERIMENTAL

Light petroleum refers to the fraction b.p. 60–80°; rotations are in chloroform.

7 α -Acetoxy-14 β ,15 β -epoxy-3 α -hydroxymeliac-1(2)-enolide.—Gedunin (IIa) (20 g.) and aluminium isopropoxide (30 g.) were dissolved in propan-2-ol (2 l.) and heated for 2 hr. under partial reflux. The solution was then evaporated, the residue decomposed with dilute sulphuric acid, and organic material isolated with chloroform. Crystallisation from benzene–light petroleum gave the 3 α -hydroxy-compound (8 g.) as needles, m.p. 215–218°, [α]_D²⁰ +53° (Found: C, 69.4; H, 7.7. C₂₈H₃₆O₇ requires C, 69.4; H, 7.5%). The acetate, prepared in the usual way, had m.p. 138–140°, [α]_D²⁰ +50° (Found: C, 67.8; H, 7.7. C₃₀H₃₈O₈ requires C, 68.4; H, 7.3%). Hydrogenation of this over Adams catalyst in methanol gave the known ⁶ 3 α ,7 α -diacetoxy-14 β ,15 β -epoxymeliacolide, m.p. 253–256°, [α]_D²⁰ -55°.

7 α -Acetoxy-3 β -chloro-14 β ,15 β -epoxymeliac-1(2)-enolide.—The alcohol (IIb) (8.0 g.) was dissolved in benzene (400 ml.) and thionyl chloride (10 ml.) added. After keeping overnight the solution was washed with dilute alkali and acid, and evaporated. The residue was chromatographed over kieselgel, and the product eluted with 15% of ether in light petroleum. Crystallisation from benzene–light petroleum gave the 3 β -chloro-compound (6 g.), m.p. 275–285°, [α]_D²⁰ +115°.

1 α ,7 α -Diacetoxy-14 β ,15 β -epoxymeliac-2(3)-enolide (IIIId).—The above chloro-compound (6 g.) and potassium acetate (10 g.) were refluxed in acetic acid (100 ml.) for 3 hr. The product was isolated from water with chloroform; the diacetoxy-compound (4.8 g.), m.p. 230–235°, identical with an authentic sample,⁸ crystallised from methanol.

7 α -Acetoxy-14 β ,15 β -epoxy-1 α -formylmelic-2(3)-enolide.—The chloro-compound (7.5 g.) was dissolved in formic acid (80 ml.) and pyridine (4 ml.) added. After keeping for 24 hr., the solution was diluted with water and the product filtered off. Crystallisation from methanol gave the 1 α -formate, m.p. 207–208°, [α]_D²⁰ +117° (Found: C, 68.1; H, 7.1. C₂₈H₃₆O₈ requires C, 68.0; H, 7.0%). Mild hydrolysis with sodium hydrogen carbonate in cold aqueous methanol gave the 1 α -alcohol, which was not crystalline. Chromic acid oxidation of the alcohol gave isogedunin, identical with a previous sample.⁸

7 α -Acetoxy-14 β ,15 β -epoxymeliac-1(2)-enolide (IIc).—The above chloro-compound (0.5 g.) was refluxed with zinc dust

¹³ E. K. Adesogan, J. W. Powell, and D. A. H. Taylor, *J. Chem. Soc. (C)*, 1967, 554.

(1 g.) in glacial acetic acid (20 ml.) for 10 min. The product was isolated from water with chloroform and chromatographed on keiselgel. Ether-light petroleum (1 : 5) eluted the 7 α -acetoxy-compound (IIc), m.p. 215—218° from methanol. The n.m.r. spectrum indicated that this compound was not quite pure, but mixed with the dihydro-derivative.

7 α -Acetoxy-14 β -15 β -epoxymeliacolide (IV).—The acetate (IIc) was hydrogenated over Adams catalyst in methanol to give the saturated acetate (IV), m.p. 180—183° (from methanol) (Found: C, 71.2; H, 8.45. Calc. for C₂₈H₄₀O₆: C, 71.2; H, 8.5%), $[\alpha]_D^{20}$ -20° (lit.,⁶ m.p. 191—192°, $[\alpha]_D^{20}$ -13.5°).

7 α -Acetoxy-14 β ,15 β -epoxymeliac-2(3)-enolide (IIIC).—Dihydrogedunin (1.5 g.) and ethanedithiol (5 ml.) were dissolved in acetic acid (15 ml.) and hydrobromic acid (0.5

ml.; 48% aqueous) added. After 2 hr. the product was collected, washed with methanol, and dried. The ethylenedithioacetal (1.4 g.) had m.p. 340° (decomp.). Raney alloy (50 g.) was treated with sodium hydroxide solution in the usual way, and the product washed four times with water and twice with methanol. The catalyst thus obtained was then boiled with ethyl acetate for 1 hr., the solvent replaced with fresh ethyl acetate (500 ml.), and the thioacetal added. After refluxing for 8 hr. the solution was filtered from catalyst and the solvent evaporated. Crystallisation from methylene chloride-methanol gave the unsaturated acetate (IIIC), m.p. 178—180° (lit.,⁶ 184°). The n.m.r. and mass spectra indicated that this compound was not quite pure, but contained a small amount of the saturated acetate (IV).

[8/1166 Received, August 12th, 1968]