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SIX GROUPS OF ω-ETHYL-, ω-ETHENYL- AND ω-ETHYNYL-α-ALKYLIDENE-γ-LACTONES (1)

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Several compounds belonging to the γ-lactone types 1 and 2 were isolated from two japanese Lauraceae, Lindera obtusiloba Blume (first 4 entries, Table 1) and Litsea japonica (Thunb.) Jus. (first 6 entries, Table 2). We wish to report the occurrence of 18 novel representatives in the amazonian Lauracea Licaria mahuba (Samp.) Kosterm. While the 6 mahubenolides, the 6 mahubynolides and 2 mahubanolides were obtained in pure state, the existence of 4 additional mahubanolides was so far only inferred by PMR spectral examination of mixtures. Isolation and structure elucidation of the compounds belonging to series 1 had to be performed speedily, since the pure compounds decompose spontaneously in a few days.

All mahuba lactones possess identical carbon skeletons, as ascertained by defunctionalization to 4-methyleicosane performed as follows. Hydrogenation (Pd/C, C_6H_6) led to saturated γ-lactones of very similar spectral characteristics. The spectra were not perfectly identical in all cases, of course, for stereochemical reasons. Reduction ($LiAlH_4$, THF), first of these lactones and then of the mesylate of the resulting triol, gave the hydrocarbon. Its identity was established by synthesis involving initially Grignard reaction between 1-n-hexadecyl magnesium bromide and 2-pentanone, followed by dehydration (TsOH, PhMe) of the resulting alcohol and hydrogenation (Pd/C, PhMe) of the olefin mixture.

UV, IR and PMR spectra reported for the obtusilactones and the litsenolides (Tables 1,2) were compatible with the corresponding spectra of the mahuba lactones belonging to series 1 (ν_{max}^{film} 1780 cm^{-1}) and 2 ($\nu_{max}^{CHCl_3}$ 1755 cm^{-1}) respectively. As in the case of the previously reported compounds (2,3), the PMR spectra were helpful in the characterization not only of the side chain terminals (δ: $=CH_2$ 4.7-5.2, ≡CH 1.93, $-CH_3$ 0.88) and the exocyclic methylene (δ 4.7 & 4.9) or methyl (δ A series 1.35, B series 1.46) and hydrogen (δ A series 4.53, B series 4.36 ± 0.01) at the γ-carbons, but also of the geometry of the trisubstituted double bonds at the α-carbons of the lactones (δ Z-H 6.63 ± 0.05, E-H 6.99 ± 0.03).

TABLE 1. NATURAL γ-LACTONES OF TYPE 1

	REF.	C-β	CONFIG. OH	R^1	R^2	n	mp	$\|\alpha\|_D$	YIELD
OBTSUSILACTONE	2			H	b	9	oil	-53°	
ISOOBTUSILACTONE	2			b	H	9	oil	-56°	
OBTUSILACTONE A	2			H	a	11	oil	-46°	
ISOOBTUSILACTONE A	2			a	H	11	oil	-54°	
MAHUBENOLIDE		R	α	H	b	13	oil	+ 6.2°	1.1
ISOMAHUBENOLIDE		R	α	b	H	13	oil	+22.0°	11.6
MAHUBYNOLIDE		R	α	H	c	13	oil	+ 8.0°	0.7
ISOMAHUBYNOLIDE		R	α	c	H	13	oil	+23.1°	3.5
MAHUBANOLIDE[m]				H	a	13			
ISOMAHUBANOLIDE[n]				a	H	13			

TABLE 2. NATURAL γ-LACTONES OF TYPE 2

	REF.	C-β,γ	CONFIG.		R^1	R^2	n	mp	$\|\alpha\|_D$	YIELD
			Me	OH						
LITSENOLIDE A_1	3	S,R	α	β	H	b	9	oil	- 2.4°	
LITSENOLIDE A_2	3	S,R	α	β	b	H	9	oil	-40.4°	
LITSENOLIDE B_1	3	S,R	α	β	H	c	9	40-41°	- 5.9°	
LITSENOLIDE B_2	3	S,R	α	β	c	H	9	42-43°	-44.9°	
LITSENOLIDE C_1	3	S,R	α	β	H	a	11	60-62°	- 9.4°	
LITSENOLIDE C_2	3	S,R	α	β	a	H	11	44-45°	-45.2°	
DIHYDROMAHUBENOLIDE A		R,S	β	α	H	b	13	48-50°	+ 8.5°	0.6
ISODIHYDROMAHUBENOLIDE A		R,S	β	α	b	H	13	45-46°	+37.1°	3.3
DIHYDROMAHUBYNOLIDE A		R,S	β	α	H	c	13	61-63°	+ 9.0°	0.6
ISODIHYDROMAHUBYNOLIDE A		R,S	β	α	c	H	13	64-65°	+42.4°	4.6
DIHYDROMAHUBANOLIDE A[o]					H	a	13			
ISODIHYDROMAHUBANOLIDE A		R,S	β	α	a	H	13	49-50°	+36.6°	0.6
DIHYDROMAHUBENOLIDE B		S,S	β	β	H	b	13	46-47°	-35.1°	0.5
ISODIHYDROMAHUBENOLIDE B		S,S	β	β	b	H	13	66-67°	-96.5°	1.9
DIHYDROMAHUBYNOLIDE B		S,S	β	β	H	c	13	55-56°	-32.6°	0.2
ISODIHYDROMAHUBYNOLIDE B		S,S	β	β	c	H	13	79-80°	-90.2°	1.1
DIHYDROMAHUBANOLIDE B[p]					H	a	13			
ISODIHYDROMAHUBANOLIDE B		S,S	β	β	a	H	13	70-71°	-93.3°	0.4

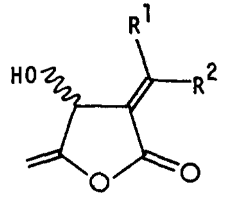
Notes to Tables:

$|\alpha|_D$... all measurements at 24 ± 2°; for solvents see text.

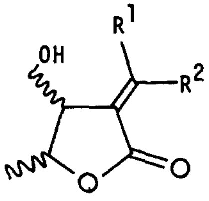
YIELD... in pure compound $^0/_{000}$ of trunk wood.

m,n,o,p... detected in less pure samples of mahubenolide, isomahubenolide and dihydromahubenolides A and B, respectively.

All new compounds showed correct HRMS and PMR peak intensities and multiplicities.



1

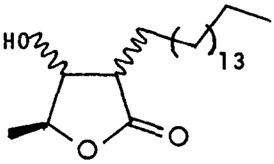


2

a $(CH_2)_nCH_2\text{-}CH_3$

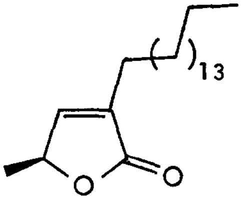
b $(CH_2)_nCH=CH_2$

c $(CH_2)_nC\equiv CH$



3a α-OH

3b β-OH



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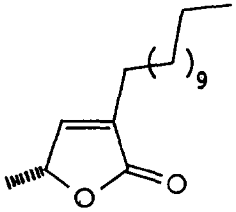

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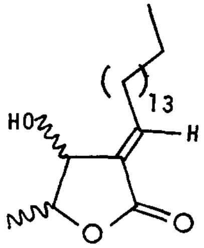

6a α-OH, α-Me

6b β-OH, β-Me

The trans or cis relationship of the β,γ-substituents in the dihydro-mahuba lactones of series A and B respectively was ascertained by the LIS PMR technique. $Eu(fod)_3$ complexes with the hydroxyl at C-β causing a greater shift of the signals due to cis than to trans entities, viz. $\Delta\delta_{H-\gamma}$ 10.0 vs 5.4 and $\Delta\delta_{Me-\gamma}$ 4.8 vs 2.9 . Hydrogenation (Pd/C, C_6H_6) of the compounds of the trans (A) and cis (B) series gave, respectively, 3a and 3b, which, though different, gave by successive acetylation (Ac_2O, C_5H_5N) and elimination of AcOH (Al_2O_3, C_5H_{12}) the same endocyclic α,β-unsaturated γ-lactone 4. This is dextrorotatory, $|\alpha|_D$ +27°, in opposition to the levorotatory 5, $|\alpha|_D$ -29.8°, of known absolute stereochemistry (3). The absolute configurations of the dihydromahubenolides and dihydromahubynolides of both series are, thus, as shown in Table 2.

Among these compounds isodihydromahubenolide B proved important for the determination of the absolute configuration of the mahuba lactones of series 1. Indeed, hydrogenation ($Pd/CaCO_3$, C_6H_6) of both, isomahubenolide and isomahubynolide, gave isomahubanolide as principal product, accompanied by 6a for which PMR indicated the cis relationship of the substituents at C-β,γ. Its optical rotation, $|\alpha|_D$ + 77°, revealed it to be enantiomeric with the analogous hydrogenation product of isodihydromahubenolide B 6b, $|\alpha|_D$ -93°. This defines the absolute configuration of the mahubenolides and mahubynolides (Table 1). In contrast to the mahuba lactones, the obtusilactones are all levorotatory. If these data, obtained in MeOH and $CHCl_3$ while all other $|\alpha|_D$ -values cited were obtained in dioxane, are considered, the S-configuration prevails in the obtusilactones.

The obtusilactones and the litsenolides were considered to be synthesized in the plant from C_{14}- or C_{16}-fatty acids and pyruvate (2,3). This requires the vinyl and ethynyl terminals to represent the starter unit in the acetate-malonate chain extension process. As suggested previously (4,5), however, the biosynthesis of these terminals may involve decarboxylation, the starter unit of the carbon chain being represented, consequently, by the carbon pair at the opposite terminal. This postulate is the most reasonable rationalization of the biosynthesis of all previously isolated groups of alkane-alkene-alkyne constituents of Lauraceae (5). Thus, unless it is admitted that the alkane, alkene and alkyne terminals represent in some constituents starter units and in others termination units, the lactones here described may be formed in the same way as postulated for rubrenolide and rubrynolide (6), by extrusion of a C-atom from a normal polyketide precursor (5).

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REFERENCES AND NOTE

1. Part LIII in the series "The Chemistry of Brazilian Lauraceae". For part LII see C.J. Aiba, O.R. Gottlieb, J.G.S. Maia, F.M. Pagliosa and M. Yoshida, Phytochemistry 17, 2038 (1978).
2. M. Niva, M. Iguchi and S. Yamamura, Tetrahedron Lett., 1539 (1975); Chem. Lett., 655 (1975).
3. K. Takeda, K. Sakurawi and H. Ishii, Tetrahedron 28, 3757 (1972).
4. J.D. Bu'Lock, in Comparative Phytochemistry (T. Swain ed.), p. 79, Academic Press, London.
5. O.R. Gottlieb, Phytochemistry, 11, 1537 (1972).
6. N.C. Franca, O.R. Gottlieb and D.T. Coxon, Phytochemistry, 16, 257 (1977).

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