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DITERPENIC LACTONES OF MALLOTUS REPANDUS

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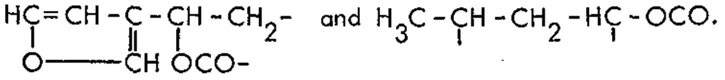
From the title plant obtained in Sarawak, two lactones were isolated and characterized in addition to lupeol and taraxerol. Mallotucin A, 1, m.p. 201-202°, was found to be identical with teucvin isolated from Teucrium viscidum var. Miquelianum: The present result reinforces the previous structure assignment. Mallotucin B, 2, m.p. 131.5-132.5°, was found to be the first diterpenoid with geminal methoxycarbonyl groups.

Mallotus species (Euphorbiaceae) have been subjected to chemical investigation which resulted in the isolation of various constituents[1] because of their biological activities[2]. We have isolated several compounds from the neutral extract of the title plant (local name: Akar charak) obtained in Sarawak, Malaysia. The present paper describes the structure determination of two lactones, mallotucin A which turned out to be identical with teucvin,[3] and mallotucin B, the first diterpene with geminal methoxycarbonyl groups.

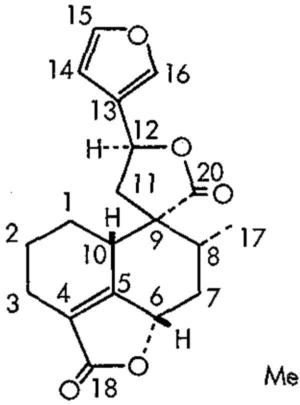
Extraction of the bark by hot water and/or chloroform, followed by silica gel chromatography yielded two compounds, mallotucin A, 1, colorless plates, $C_{19}H_{20}O_5$,[4] m.p. 201-202° (dec.), $[\alpha]_D$ +191° ($CHCl_3$), (0.2% of dry bark) and mallotucin B, 2, colorless needles, $C_{24}H_{28}O_9$, m.p. 131.5-132.5° (3×10^{-3}%), in addition to lupeol and taraxerol.

The presence of furan ring in 1 was suggested by Ehrich color reaction, IR bands (3100, 1505, 1020, 857 cm^{-1}) and by mass spectral peaks (m/e 95, 94, 81), while that of two γ-lactone groups, one saturated and the other unsaturated, was indicated by the IR bands (1760, 1745 and 1690 cm^{-1}), and the positions of UV maximum (λmax 217 nm (ϵ 17800))[5] and the Cotton effect ($[\phi]$ +2850 (240 nm), -4440 (220)). PMR spectrum (Table) was analysed in various solvents with the aid of the shift reagent $Eu(fod)_3$, NMDR experiments and NOE measurements ($H_{11} \longleftrightarrow H_{14}$ 6% in $CDCl_3$) revealing the groupings

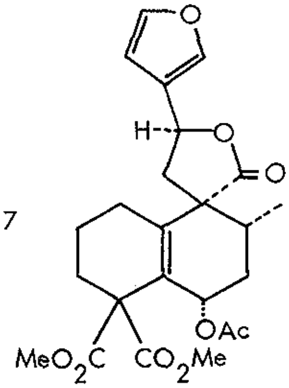


$$\begin{array}{l}\mathrm{H\underset{|}{C}{=}CH{-}\underset{\|}{C}{-}\underset{|}{C}H{-}CH_2{-}}\\ \mathrm{O{-\!-\!-\!-}CH\;\;OCO{-}}\end{array} \quad \text{and} \quad \mathrm{H_3C{-}\underset{|}{C}H{-}CH_2{-}H\underset{|}{C}{-}OCO.}$$

CMR spectrum (Table) is consistent with the findings.



1



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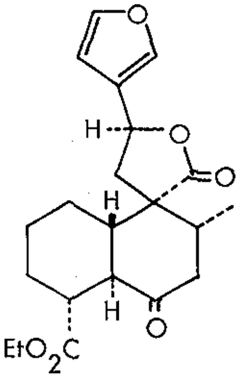

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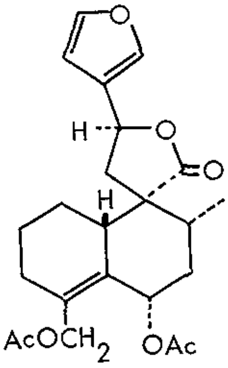

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TABLE NMR Spectral Data (δ)

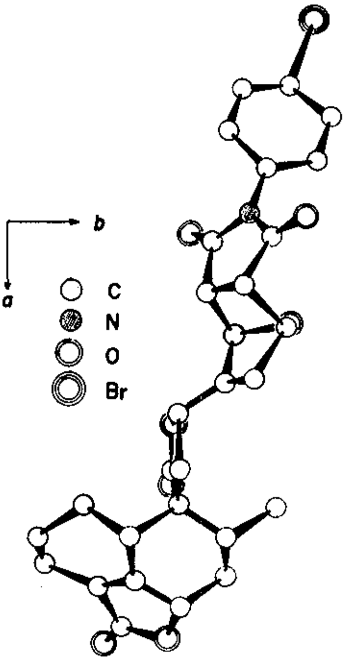
Compound numbering	**1**		**2**	
	PMR	CMR	PMR	CMR
1	?	21.6(t)	?	40.8(t)
2	?	24.7(t)	?	26.5(t)
3	?	40.6(t)	?	32.1 or 32.6(t)
4	-C=	124.9 or 126.1(s)	-C-	57.0(s)
5	-C=	162.1(s)	-C=	136.3(s)
6	4.74(ddt, 9.0, 8.0, 2.5)	71.9 or 78.3(d)	5.47(br. t, ~8)	70.0(d)
7	2.17(2H, d, 8.5)	35.3(t)	?	32.6 or 32.1(t)
8	~2.1	35.7(d)	~1.85	35.7(d)
9	-C-	53.5(s)	-C-	53.9(s)
10	?	41.9(d)	-C=	130.3(s)
11	2.40(2H, d, 8.5)	19.7(t)	2.77(dd, 13.6, 8.6), ~2.4	18.9(t)
12	5.45(t, 8.5)	78.3 or 71.9(d)	5.47(br. t, ~8)	72.3(d)
13	-C=	126.1 or 124.9(s)	-C=	125.3(s)
14	6.38(t, 1.0)	108.0(d)	6.40(t, 1.0)	108.1(d)
15	7.45(compl. 1.0)	144.2(d)	7.45(compl)	144.2(d)
16	7.45(compl. 1.0)	139.6(d)	7.45(compl)	139.4(d)
17	1.06(d, 6.3)	17.0(q)	1.08(d, 6.1)	16.6(q)
18	CO	173.0(s)	CO	170.9 or 171.5(s)
19	——	——	CO	171.5 or 170.9(s)
20	CO	175.9(s)	CO	176.4(s)
AcO	——	——	1.94(s)	21.0(q), 170.2(s)
CH_3O	——	——	3.70(s), 3.75(s)	52.3(s), 52.7(s)

Figures in parentheses are coupling constants.

? : broad complex groups of signals δ 1.8–2.4

A few reactions were carried out. On heating with KOH in ethanol, 1 gave the ketoester 3, colorless needles, m.p. 159-160°, ν 1758, 1716 cm^{-1} (br), in which only α,β-unsaturated lactone was cleaved. The presence of a saturated carbonyl group in 3 was verified by the CD maximum ($[\theta]$ +2510 (284 nm)). The inertness of the second lactone group was also demonstrated by LAH reduction. The reduction followed by acetylation afforded the diacetate 4, colorless viscous oil, ν 1760, 1730 cm^{-1}. The chemical shift and coupling pattern of the carbinyl hydrogens, δ_{18} 4.66, 5.16 (each d, J=12) and $\delta_6 \sim 5.4$ (br. m), established the double bond at C_4.

For the final proof of the structure, X-ray crystallographic analysis was carried out, using p-bromophenylmaleimide adduct. Heating 1 with p-bromophenylmaleimide in chloroform afforded two adducts, 5, colorless microcrystals, m.p. 214-215° and 6, orthorhombic prisms, m.p. 130-132°. Single crystal of 6, $C_{29}H_{26}O_7NBr\cdot 2CHCl_3$ (from $CHCl_3$) belongs to space group $P2_12_12_1$, Z=4, $\underline{a}$=17.674, $\underline{b}$=19.122, $\underline{c}$=10.293Å. Three dimensional intensity data were collected by 4-circle automatic diffractometer (Picker) using Cu-Kα raddiation. A total of 983 reflections were collected and analysed by the heavy atom method. After refinement by a block-diagonal least squares method, R-factor was reduced to 8.3%. The absolute configuration of 6 was determined from the anomalous X-ray dispersion of heavy atoms. The perspective view of molecular structure along the $\underline{c}$-axis is shown in the Figure. The structure thus deduced is



identical with that proposed recently by Fujita, *et al.* for teucvin isolated from *Teucrium viscidum var. Miquelianum* (Labiatae).[3] Since their structure assignment was based primarily on X-ray analysis of the derivative of 3, in which the chirality at C_6 is lost, the present result provides the direct support for the structure of teucvin.

Structure of 2 was determined as follows. Elemental analysis and mass spectrum (m/e 460, 431, 400, 384, 340, 323 (base peak), 95, 81) confirmed its molecular formula $C_{24}H_{28}O_9$. Spectral analysis suggested the presence of a furan (m/e 95, 81, ν 1595, 1505, 875 cm^{-1}, δ 6.40 (1H, t, J=1), 7.45 (2H, m)), a lactone (ν 1750 cm^{-1}, δ 5.47 (t, J=~8)), two methoxycarbonyls (ν 1720 cm^{-1} and δ 3.70, 3.75 (both 3H, s)), a secondary acetoxyl (ν 1720 cm^{-1}, δ 1.94 (3H, s), 5.47 (t, J=~8) and a secondary methyl group (δ 1.08 (3H, d, J=6.1)). PMDR experiments disclosed exactly the same carbon sequence (*vide supra*) as in 1. CMR spectrum of 2 (Table) is also similar to that of 1, but chemical shift difference disclosed that 1) a tetra-substituted double bond is also present in 2 but not in conjugation with any carbonyl group unlike in 1, and therefore 2) two methoxycarbonyl groups attach to the same carbon. These observations indicate the planer structure 2, when cooccurrence of 1 is taken into consideration. In fact, when 2 was treated with KOH in aqueous methanol at room temperature for a week, 1 was obtained in 35% yield along with the methyl ester corresponding to 3 (30% yield). This experiment also established the absolute stereochemistry of 2.

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3 E. Fujita, I. Uchida and T. Fujita, *JCS Chem. Comm.*, 1973, 793. *Idem*, *JCS Perkin I*, 1974, 1547.

4 Molecular formulas were established by elemental analyses and by mass spectrum (Found: 328.1314. Calcd: 328.1311). All the compounds described shows the correct elemental analyses. Spectral data refer to the following conditions unless otherwise stated. UV (λ) and ORD ([Φ]): EtOH solution, CD: MeOH solution, IR (ν): KBr pellet, PMR (δ) and CMR: $CDCl_3$ solution.

5 The differencial UV curve between **1** and crotonin[6] shows λ_{max}^{EtOH} 220 nm (ε 10000).

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