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MALLOTUCIN C AND D, TWO DITERPENIC LACTONES FROM MALLOTUS REPANDUS

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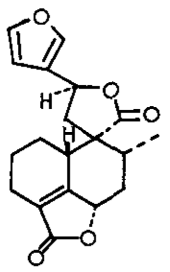
Abstract— Investigation on the constituents of the titled plant collected in June resulted in the isolation of mallotucin B and mallotucins C and D (as acetates). Mallotucin A (≡teucvin), which is the only diterpenic constituent in the plant collected in December, was not detected. Structures of mallotucins C and D were elucidated on the basis of their chemical correlation with mallotucin A and the detailed spectral analyses of their acetates. Mallotucin A is suggested to be biosynthesized from chettaphane-type precursors, mallotucins B, C and/or D.

In the previous paper[1], we have described the structure elucidation of mallotucin A (1), a norditerpenic dilactone, and mallotucin B (2), a diterpene lactone with chettaphane carbon skeleton, isolated from *Mallotus repandus* (Euphorbiaceae) collected in Sarawak, Malaysia. The former was found to be identical with teucvin isolated from *Teucrium viscidum* (Labiatae)[2], and the latter was conformed to the first diterpenoid with carboxyl groups at both 18- and 19-carbons. Further investigation revealed that, while the plant material collected in December contained only 1, the same species collected in June in the same area contained in addition to 2 two more diterpenic lactones, which are named mallotucin C and D, (3 and 4). This paper deals with the structure elucidation of these new compounds, 3 and 4.



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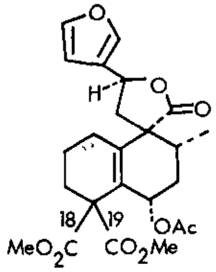

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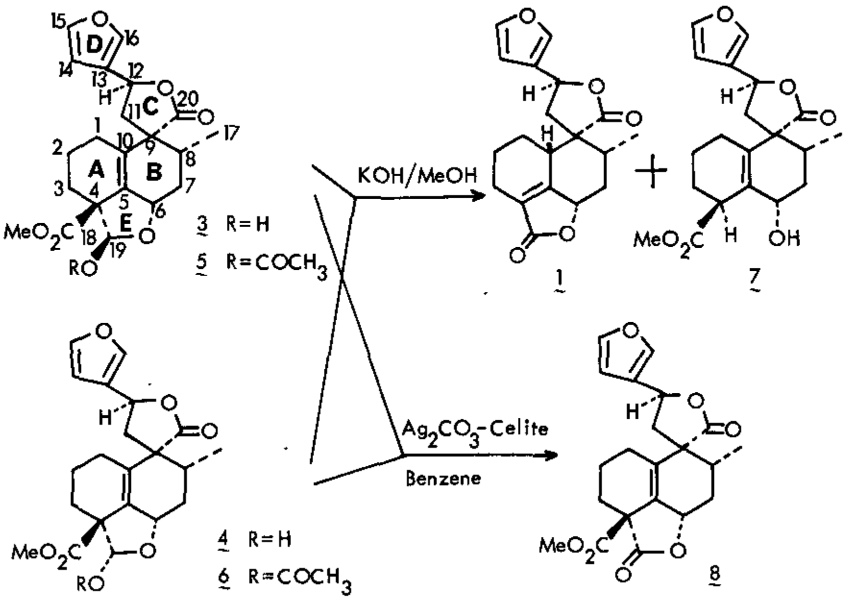


3 R=H
5 R=COCH3
1
7
4 R=H
6 R=COCH3
8

Careful SiO_2 column chromatography of the chloroform extract of the bark resulted in the isolation of 2[1] and the inseparable 1:2 mixture (^{1}H-NMR) of 3 and 4. Acetylation of the mixture and crystallization from EtOAc-hexane afforded the corresponding acetates of different crystalline form. They were mechanically separated and recrystallized from the same solvent system to mallotucin C acetate (5), colorless plates, mp 184-186°C, $[\alpha]_D$+75.7°($CHCl_3$), and mallotucin D acetate (6), colorless granules, mp 195-197°C (dec.), $[\alpha]_D$+71.4°($CHCl_3$)[3].

Both acetates contain a secondary methyl group [5: δ^H 1.09 ppm (3H, d, J=6.0), 6: δ^H 1.10 ppm (3H, d, J=6.0)], γ-lactone [5: ν 1750 cm^{-1}, 6: 1745 cm^{-1}], a methoxycarbonyl [5: ν 1710 cm^{-1}, δ^H 3.71 ppm (3H, s), 6: ν 1725 cm^{-1}, δ^H 3.77 ppm (3H, s)] and a β-substituted furan ring [5: ν 3025, 1505, 1230, 1210, 865, 795 cm^{-1}, δ^H 6.38 (1H, m), 7.43 ppm (2H, m), 6: ν 3100, 1505, 1240, 870, 775 cm^{-1}, δ^H 6.39 (1H, m), 7.49 ppm (2H, m)], in addition to an acetoxyl group [5: ν 1725 cm^{-1}, δ^H 2.03 ppm (3H, s), 6: ν 1725 cm^{-1}, δ^H 2.07 ppm (3H, s)]. Furthermore, NMR spectra of 5 and 6 are very similar to those of 1 and 2. The similarity of their structure was also demonstrated by their ^{13}C-NMR spectra shown in Table 1 and verified by their chemical correlation. On heating with KOH in methanol, 5 and 6, as well as the mixture of 3 and 4, afforded 1 (~30%) and the alcohol 7, mp 55-57°C (~45%) [ν 3380, 1750, 1720 cm^{-1}, δ^H 1.06 (3H, d, J=6.0), 3.70 (3H, s), 4.30 (1H, br.s), 5.44 (1H, t, J=9.0), 6.39 (1H, m), 7.42 ppm (2H, m)].

The substitution pattern in 3 and 4 was secured in the following ways. 1) ^{13}C-NMR spectra of 5 and 6 indicate the presence of two quaternary sp^3-type carbons (5: 55.8, 52.7 ppm, 6: 58.4, 53.0 ppm). 2) The

Table 1 ^{13}C-NMR spectra

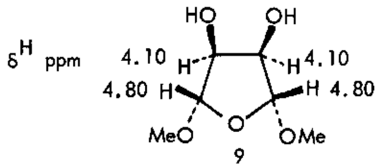
C-No.	1	2	5	6**
1	21.6 (t)	26.5 (t)	23.8 (t)	24.9
2	19.7 (t)	18.9 (t)	19.8 (t)	19.7
3	24.7 (t)	32.1 (t)	27.9 (t)	25.5
4	126.1 (s)	57.0 (s)	56.3 (s)	57.6
5	162.1 (s)	130.3 (s)	136.3 (s)	134.2
6	78.3 (d)	70.0 (d)	77.5 (d)	77.6
7	35.3 (t)	32.6 (t)	33.4 (t)	35.5
8	35.7 (d)	35.7 (d)	35.4 (d)	36.5
9	53.5 (s)	53.9 (s)	52.6 (s)	52.9
10	41.9 (d)	136.3 (s)	131.1 (s)	132.7
11	40.6 (t)	40.8 (t)	40.2 (t)	40.0
12	71.9 (d)	72.3 (d)	72.3 (d)	72.4
13	124.9 (s)	125.3 (s)	124.8 (s)	125.0
14	108.0 (d)	108.1 (d)	108.1 (d)	108.2
15	144.2*(d)	144.2* (d)	144.3*(d)	144.3*
16	139.6*(d)	139.4*(d)	139.6*(d)	139.7*
17	17.0 (q)	16.6 (q)	16.2 (q)	16.4
18	173.0 (s)	170.9 (s)	171.2 (s)	172.6
19	—	171.5 (s)	102.0 (d)	98.6
20	175.9 (s)	176.4 (s)	176.6 (s)	176.6
$-CO_2\underline{C}H_3$	—	52.3 (q) 52.7 (q)	52.3 (q)	52.4
$-OCOCH_3$	—	21.0 (q) 170.2 (s)	21.1 (q) 169.4 (s)	21.4 170.1

*These signals may be reversed. **Off resonance experiment was not carried out.

chemical shift and splitting pattern of methylene signals (H_{11}) of both 5 [δ^H 2.23 (dd, J=13.5, 8.2) and 2.68 ppm (dd, J=13.5, 8.2)] and 6 [δ^H 2.27 (dd, J=13.5, 9.0) and 2.77 ppm (dd, J=13.5, 8.2)] are similar to those of 2 [δ^H 2.40 (dd, J=13.6, 7.5) and 2.70 ppm (dd, J=13.6, 8.6)][1] and different from those of 1 [δ^H 2.56 (2H, d, J=8.5)].[1] These observations, together with the absence of a conjugate system except furan ring (end absorption in UV) allocate a double bond at C_5-C_{10} position, and therefore a missing substituent at C_4 must form a ring (ring E) with C_6-oxygen. That the ring E is a lactol was revealed by the presence of an one-proton singlet in 3 (δ^H 5.24 ppm) and 4 (δ^H 5.50 ppm) which showed acetylation shifts (5: δ^H 6.07 ppm, 6: 6.43 ppm) and further by Ag_2CO_3-Celite oxidation of the mixture of 3 and 4 to the dilactone ester 8, mp 188-189°C [ν 1765, 1735 cm^{-1}, δ^H 1.13 (3H, d, J=6.0), 3.76 (3H, s), 5.17 (1H, br.t, J=9.0), 5.46 (1H, t, J=9.0), 6.40 (1H, m), 7.42 (2H, m)]. Thus the planer structures for 3 and 4 were established.

The stereochemistry to be clarified concerns only C_4 and C_{19} on ring E, as the conversion of **3** and **4** to **1** established the stereochemistry at the other chiral centers. The conversion of **3** and **4** to **8** demonstrated that these are epimeric only at C_{19} having the same configuration at C_4.

H_6 which is in β-configuration is axially oriented from its coupling constant [**5**: J=11.0, 6.0, **6**: J=8.0 (br.t)]. There is considerable difference in its chemical shift between **3** and **4**, and **5** and **6** ($\delta^{H}_{\mathbf{3}}$=4.82, $\delta^{H}_{\mathbf{4}}$=4.55, $\Delta\delta^{H}_{\mathbf{3}-\mathbf{4}}$=0.27, $\delta^{H}_{\mathbf{5}}$=4.89, $\delta^{H}_{\mathbf{6}}$=4.59, $\Delta\delta^{H}_{\mathbf{5}-\mathbf{6}}$=0.30) and the precedences in the sugar derivatives **9** and **10**[4] suggest the trans relationship of H_6 and H_{19} in **3** and **5** and cis in **4** and **6**. Therefore H_{19} is α in **3** and **5**, and β in **4** and **6**. The chemical shift differences for H_{19} ($\delta^{H}_{\mathbf{3}}$=5.24, $\delta^{H}_{\mathbf{4}}$=5.50, $\Delta\delta^{H}_{\mathbf{3}-\mathbf{4}}$=-0.26, $\delta^{H}_{\mathbf{5}}$=6.07, $\delta^{H}_{\mathbf{6}}$=6.43, $\Delta\delta^{H}_{\mathbf{5}-\mathbf{6}}$=-0.36) have opposite sign to those for H_6 due to the methoxycarbonyl in the vicinity. The configuration of the ester group, though undetermined on this basis, was established to be β by the chemical shift differences in carbon; the carbonyl carbon (C_{18}) in **3** (and **5**) shows the gauche (γ-) effect[5] ($\Delta\delta^{C}_{\mathbf{3}-\mathbf{4}}$= -1.3 ppm, $\Delta\delta^{C}_{\mathbf{5}-\mathbf{6}}$=-1.3 ppm) due to the substituents at C_{19}. Thus the entire stereochemistry of **3** and **4** was established.



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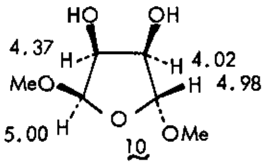

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Fujita has suggested the elimination of one-carbon unit from ent-clerodane for the biogenesis of **1** *in* Teucrium species. However, in view of the isolation of the congeners **2**, **3**, **4** of chettaphane carbon skeleton and their facile conversion to **1**, **1** is more likely formed, at least in Mallotus species, by the loss of one-carbon unit from chettaphane-type precursor(s). The seasonal difference in the constituents would support the view.

References and Note

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2. E. Fujita, I. Uchida and T. Fujita, J. Chem. Soc., Chem. Comm., 1973, 793. Idem, J. Chem. Soc., Perkin I, 1974, 1547.
3. Molecular formulas were confirmed by high-resolution mass spectra for all new compounds. Unless otherwise stated, the spectra were measured under the following conditions: UV in methanol, IR in KBr disk, ^{1}H-NMR and ^{13}C-NMR in $CDCl_3$.
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