Tetrahedron Letters No. 13, pp. 1095-1098, 1970. Pergamon Press. Printed in Great Britain.

CHETTAPHANIN-I, A NOVEL FURANODITERPENOID

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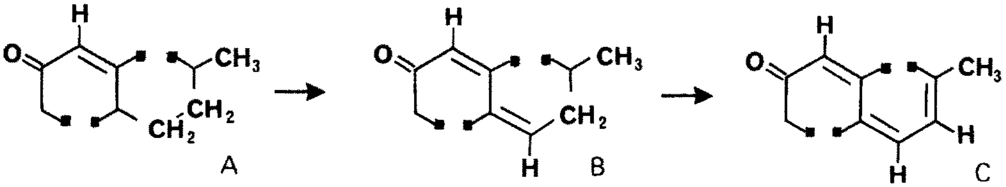
(Received in Japan 28 January 1970; received in UK for publication 17 February 1970)

'Chettaphangkhi' is a indigenous drug applied for stomachics in Thailand and is obtained from the roots of Adenochlaena siamensis Ridl. (Euphorbiaceae)1). From a methylene chloride extract, we have isolated several crystalline furanoditerpenoids by careful repeated column chromatography. We report here the structural elucidation of chettaphanin-I (1) designated as the most abundant component of the extract.

Chettaphanin-I (1), mp. 158-159°, $[\alpha]_D$ -72.7° (c=2.0, acetone), has the molecular formula of $C_{21}H_{26}O_6$ from elemental analysis and the mass spectrum with a parent peak at 374.174 (Calcd. 374.173). In the nmr spectrum of 1, one secondary and two tertiary methyl groups resonate at δ 0.90 (3H, d, J=6.5 Hz) and at δ 1.20 and 1.37 (3H, s, respectively). The signals appearing at δ 6.65 (1H, q), 7.42 (1H, q), and 8.00 (1H, q) are characteristic of a 3-substituted furan2) (ν^{nujol} 3120, 1555, 1500, 1040, and 878 cm^{-1})3). The three proton singlet at δ 3.71 is ascribed to a carbomethoxy hydrogens, the presence of which is confirmed from the IR (1725 and 1155 cm^{-1}) and mass spectral data4) (various abundant peaks arising from the α-cleavage of a bond adjacent to the methyl ester carbonyl group, $C_{21}H_{26}O_6^{+} \rightarrow C_{19}H_{23}O_4^{+}$, $C_{21}H_{24}O_5^{+} \rightarrow C_{19}H_{21}O_3^{+}$, $C_{15}H_{21}O_4^{+} \rightarrow C_{13}H_{18}O_2^{+}$ etc.), and the spectroscopic investigation of the tetraol (2), $C_{20}H_{30}O_5$, mp. 178-179°, obtained by lithium aluminium hydride reduction of 1. Since the nmr signals of the hydroxymethylene of the primary alcohol 2a (δ 3.68 and 4.13, q, J=12 Hz), and acetoxymethylene of its acetate 2b (δ 4.03 and 4.17, q, J=11 Hz) do not show coupling with any other protons, the carbomethoxy group of 1 must be attached to a quarternary carbon atom. The two AB-type quartets of 1 at δ 2.45 and 2.79 (J=17 Hz) and at δ 3.20 and 3.31 (J=19 Hz) are assigned to the isolated geminal methylene hydrogens adjacent to carbonyl groups, because these signals shift upfield in the nmr of 2. In addition, one proton singlet at δ 5.83 suggests the presence of a trisubstituted α,β-unsaturated ketone (ν^{nujol} 1665 cm^{-1}, λ_{max}^{EtOH} 247 mμ: ε=13,000) and the one proton singlet at δ 2.27, which is absent in D_2O, suggests that there is a tertiary hydroxyl group (ν^{nujol} 3650 cm^{-1}).

Dehydration of 1 with acid led to an $\alpha,\beta,\gamma,\delta$ -unsaturated ketone (3), $C_{21}H_{24}O_5$, mp. 165-166° (no OH band in IR, λ_{max}^{EtOH} 283 mμ: ε=13,500). In the nmr of 3, one of the two olefinic protons resonates at δ 5.90 as a doublet and the other at δ 6.05 as a multiplet. Since irradiation of the former signal changes the latter signal into a quartet, these protons undergo long-range coupling with each other and with this, the partial structures shown in Fig. 1 (A ⟶ B) are established.



The symbol ■ refers a carbon atom bearing no proton.

Fig. 1

The dienone (3) was refluxed with N-bromosuccinimide and catalytic amount of dibenzoyl peroxide in CCl_4. Chromatography of the product on silica gel yielded the trienone (4), $C_{21}H_{22}O_5$, mp. 152-154° (λ_{max}^{EtOH} 252 and 372 mμ: ε=8,900 and 10,500)$^{5)}$. The nmr of 4 (Fig. 2) clarified the skeletal arrangement of the nine carbon atoms containing the secondary methyl group in chettaphanin-I (1) as shown in Fig. 1 (C). The remaining structural features to be accommodated are two tertiary methyl groups, a tertiary carbomethoxy group, and a furano-keto-methylene group. These fragments account for the all carbon, hydrogen and oxygen atoms in 4.

The framework of 1 was established by the fact that dehydrogenation of 2 with selenium afforded 1,2,5-trimethylnaphthalene (5)$^{6)}$ in high yield.

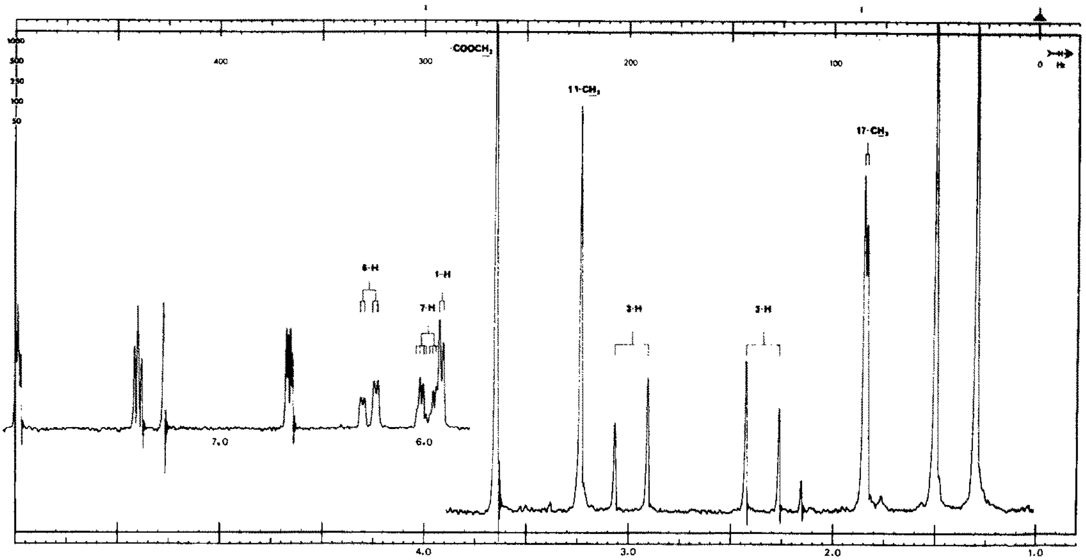
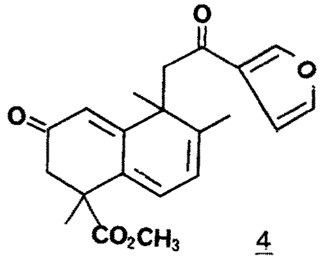
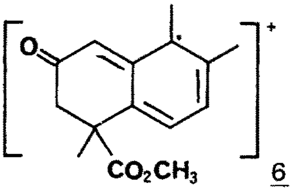


Fig. 2 NMR Spectrum of Trienone (4)

The high resolution IR spectra of 1 and its derivatives showed absence of a gem-dimethyl group. The mass spectrum of 4 supports the absence of a gem-dimethyl group. The dominant fragmentation of the molecular ion (m/e 354, 71%) gives the ion (6) at m/e 245 (85%) ($M-CH_2COC_4H_3O$), from which the loss of CH_3CO_2 and H afforded the ion (7) at m/e 185 as the base peak. The extrusion of methyl from the ions (6 and 7) was not observed. These facts exclude the possibility that the carbomethoxy group is bonded at C-9.

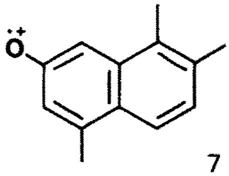


4



6

m/e 245



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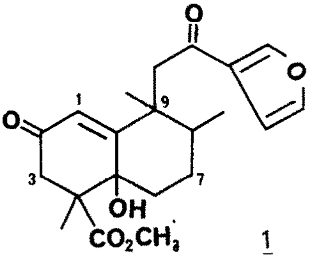
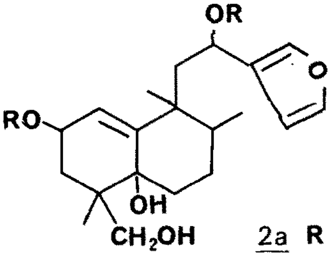
m/e 185

The structure of chettaphanin-I is therefore defined as 1. The structure of chettaphanin-I (1) does not conform to the biogenetic 'isoprene rule' and it is thus a new-type furanoditerpenoid with a rearranged labdane or eperuane skeleton.

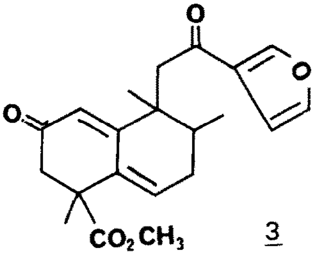
Detailed work to define the stereochemistry of 1 will be published in near future.



1



2a R = H
2b R = Ac



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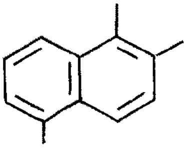

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Acknowledgement. The authors express their thanks to Dr. Komol Pengsritong, Ministry of Public Health, Thailand for his interest in this work.

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