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# VERTICILLOL, A NOVEL TYPE OF CONIFER DITERPENE

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The wood of Sciadopitys verticillata Sieb. et Zucc. has previously been investigated by Kawamura[1] and the occurrence of "cedrene", cedrol, phyllocladene, and a "diterpene-X" ($C_{20}H_{32}O$, m.p. 133-135°, $[\alpha]_D$ + 179.4°) has been reported. The neutral part of a petroleum ether soluble extract of the wood has now been reinvestigated and the following components have been isolated: isoeugenol methylether, cedrol, sciadin[2], methyl sciadopate[3] and a new diterpene alcohol named verticillol, $C_{20}H_{34}O$, m.p. 104-105°, $[\alpha]_D$ + 168° (c 1.5), M.W. 290 (mass spectrometry), 1 active-H.[xx]

Verticillol exhibits hydroxyl absorption at 3630 and 1161 $cm^{-1}$ (KBr). Attempts to acetylate the compound failed. Verticillol was recovered unchanged after treatment with chromic acid in glacial acetic acid for 10 h at 20°. It must therefore be a tertiary alcohol. Verticillol gives a positive tetranitromethane test but does not show any ultraviolet absorption above 220 mμ ($\epsilon_{208}$ mμ 9500). It consumes two moles of monoperphthalic acid affording a diepoxide ($C_{20}H_{34}O_3$,

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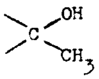
[xx] Unless otherwise stated all new compounds cited in the text gave correct analysis. Rotations were measured in chloroform.

m.p. 160°, $[\alpha]_D$ + 68.7° (c 1.8), $\epsilon_{205}$ mμ 150) which gives no colour reaction with tetranitromethane. Verticillol therefore contains two non-conjugated double bonds and is bicyclic.

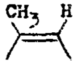
Verticillol can be dehydrated with phosphoryl chloride in pyridine to give "anhydroverticillol-A". This compound after purification by chromatography on alumina was crystalline and could be sublimed under reduced pressure, m.p. 122-132°, $[\alpha]_D$ + 200° (c 1.6). Despite these purification processes the analysis of the compound indicated the presence of small amounts of oxygen. When kept in air at room temperature the compound rapidly adsorbed oxygen. The infrared spectrum of "anhydroverticillol-A" did not exhibit any hydroxyl bands but showed bands characteristic of a vinylidene grouping ( $>C = CH_2$; 1664 and 880 $cm^{-1}$ in KBr), the presence of which was confirmed by the liberation of formaldehyde on ozonolysis. The double bonds of "anhydroverticillol-A" are not conjugated (no ultraviolet absorption above 220 mμ). The compound rapidly consumes 2 equivalents of monoperphthalic acid yielding anhydroverticillol diepoxide, $C_{20}H_{32}O_2$, m.p. 160°, $[\alpha]_D$ + 30.3° (c 2.0). This compound is also obtained on dehydration of verticillol diepoxide with phosphoryl chloride in pyridine. Anhydroverticillol diepoxide exhibits infrared bands characteristic of a vinylidene group (1643 and 910 $cm^{-1}$ in KBr). On ozonolysis it furnishes formaldehyde and verticillol norketodiepoxide, $C_{19}H_{30}O_3$, m.p. 152.5°, $[\alpha]_D$ + 170.3° (c 2.2), $\nu_{max}^{CCl_4}$ 1710 $cm^{-1}$. These dehydration experiments prove that verticillol contains a  $>C(OH)CH_3$ -group.

On dehydration with potassium bisulphate or alcoholic sulphuric acid verticillol gave "anhydroverticillol-B", m.p. 123-130°,

$[\alpha]_D$ + 188.5°, which, like "anhydroverticillol-A", could not be obtained in pure oxygen-free state. Its infrared spectrum did not show the presence of a hydroxyl group or of a vinylidene group and its ultraviolet spectrum did not exhibit any absorption above 220 mμ. Ozonolysis gave no formaldehyde. It readily gave an anhydroverticillol triepoxide, $C_{20}H_{32}O_3$, m.p. 134°, $[\alpha]_D$ -41.1° (c 1.8).

The relationship between verticillol and Kawamura's "diterpene-X" has not been ascertained. However, Kawamura's compound might be identical with "anhydroverticillol-A" or -"B". The compound may be an artefact formed during the isolation process, since, for example, "anhydroverticillol-A" is formed on chromatography of verticillol on activated alumina.

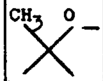
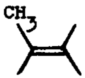
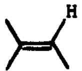
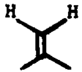
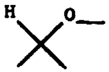
Low temperature ozonolysis (-70°) of verticillol followed by decomposition of the ozonides with water yields levulinic aldehyde isolated as its bis-2,4-dinitrophenylhydrazone. The high boiling fraction from this reaction was a complex mixture of neutral and acidic components from which none has yet been isolated. From a similar ozonolysis experiment conducted at room temperature or an ozonolysis at low temperature followed by oxidation with neutral hydrogen peroxide a small amount of a $C_{13}$-lactone acid ($C_{13}H_{20}H_4$, m.p. 153-154°, $\nu_{max}^{KBr}$ 1735 (broad) and 1705 $cm^{-1}$) could be obtained. This lactone acid was also obtained by oxidation[4] of verticillol with an aqueous solution of potassium permanganate and sodium periodate. On treatment with ethereal diazomethane the lactone acid gave the corresponding methyl ester, $C_{14}H_{20}O_4$, m.p. 69.5-72° and 107.5-108° (dimorphous), $\nu_{max}^{CCl_4}$ 1777 (γ-lactone) and 1735 $cm^{-1}$ (ester).

The NMR-spectrum of verticillol (Table 1) clearly demonstrates that the two double bonds are trisubstituted and of the type .

# TABLE 1

Characteristic NMR-signals in the spectra of verticillol and some of its derivatives.[x]

Chemical shifts (δ-units, ppm)

| Compound |  |  |  |  |  |  | Other groups |
|---|---|---|---|---|---|---|---|
| Verticillol | 1.21 s<br>(3H) | 1.48 sb<br>(3H)<br>1.50 sb<br>(3H) | 0.69 s<br>(3H)<br>0.77 s<br>(3H) | 4.89 d(J 7 cps)b<br>(1H)<br>5.64 d(J 12 cps)b<br>(1H) | - | - | -OH;<br>2.00 s<br>(1H)[xx] |
| Verticillol diepoxide | 1.27 s<br>(9H) | - | 0.85 s<br>(3H)<br>0.96 s<br>(3H) | - | - | 2.93 d(J 7 cps)b<br>(1H)<br>3.45 t(J 6 cps)<br>(1H) | - |
| Anhydro-verticillol diepoxide | 1.26 s<br>(6H) | - | 0.78 s<br>(3H)<br>1.00 s<br>(3H) | - | 4.53 sb<br>(1H)<br>4.90<br>(1H) | 2.5 u<br>3.20 q($J_1$ 7.5 cps;<br>$J_2$ 4.5 cps) (1H) | - |
| γ-Lactone ester (2) | 1.38 s<br>(3H) | - | 0.89 s<br>(3H)<br>1.03 s<br>(3H) | - | - | - | -COOCH$_3$;<br>3.63 s<br>(3H) |

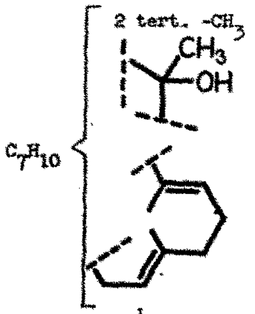
[x] The chemical shifts are given in ppm from tetramethylsilane (internal standard). The spectra were recorded in carbon tetrachloride solutions on a Varian A-60 instrument (60 Mc/s). The abbreviations are: s, singlet or overlapping singlets; d, doublet; t, triplet; q, quartet; b, each line is slightly split due to further small couplings; u, the peak position is uncertain since it is close to a more intense band.

[xx] The signal disappeared after treatment of the solution with deuterium oxide.

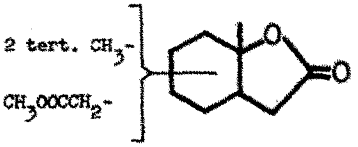
The signal patterns of the two olefinic protons of verticillol and of the oxiran protons of verticillol diepoxide reveal couplings to adjacent $CH_2$-groups. Furthermore, it is clear that verticillol possesses two tertiary methyl groups. Therefore, taking the levulinic aldehyde formation into account part structure (1) can be proposed for verticillol.

The methyl ester of the γ-lactone acid which analyzed for $C_{14}H_{20}O_4$ must be bicyclic. Its NMR-spectrum exhibits a well separated signal group at δ 2.10-2.37 ppm with an integrated intensity corresponding to 4 protons. This signal group is assigned to protons in α-positions to the two carbonyl groups. The γ-lactone ester should therefore have two $-CH_2-CO$-groups.. Other characteristic NMR-signals of this compound are given in Table 1. The fourteen carbon atoms of the compound can be accounted for as follows: four carbon atoms by the γ-lactone ring; one by a tertiary methyl group attached to the γ-carbon of this ring (NMR-singlet at δ 1.37 ppm); three by a $-CH_2 \cdot COOCH_3$ group; two by two tertiary methyl groups (NMR-singlets at δ 0.88 and 1.02 ppm). The remaining four carbon atoms must be part of a 6-membered ring fused to the γ-lactone ring since the hydroxyl group of verticillol is attached to a 6-membered or larger ring, as is shown by the infrared band at 1710 $cm^{-1}$ of norketoverticillol diepoxide. From the above data the lactone ester can be formulated as in structure (2).

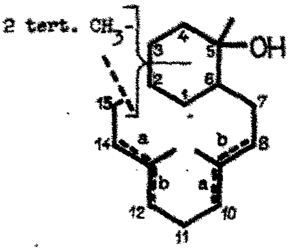
The lactone acid is probably formed via the loss of a $C_2$-fragment originating from a  - $CH_3$ group of verticillol. From the part structures (1) and (2) verticillol can be formulated as (3). The fact that no γ-lactone could be detected in the reaction mixture from a low temperature ozonolysis of verticillol favours alternative "a" for the double bond positions. This double bond alternative also explains the unusual degradation of verticillol to the γ-lactone



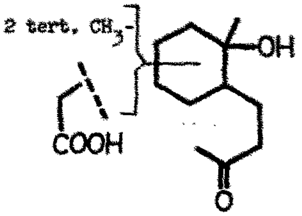
1.



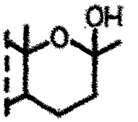
2.



3.



4.



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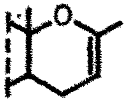

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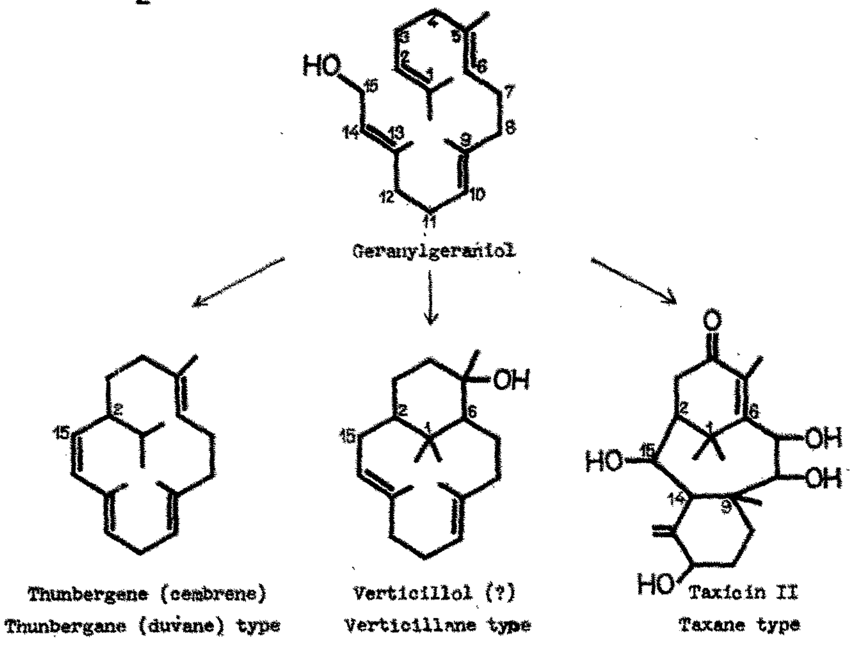

Thunbergene (cembrene)
Thunbergane (duvane) type

Verticillol (?)
Verticillane type

Taxicin II
Taxane type

acid. The originally formed keto-acid (4) may cyclize to a semiacetal (5) which after dehydration to the enol ether (6) is further oxidized. Acetic acid was detected in the reaction mixture by vapour phase chromatography.

According to the isoprene rule the two tertiary methyl groups of verticillol (3) should be located at the C(1)-position as a *gem* dimethyl group. The presence and position of the *gem* dimethyl group can also be explained by the results of Ishikawa *et al.*[4] in which the isolation of isobutyric acid on Kuhn-Roth's oxidation of verticillol is reported. For biogenetic reasons the C(15)-atom should be bonded to the C(2)-atom. This would relate verticillol to both the thunbergane (duvane)[x, 5-8] and the taxane[9] type of diterpenes as is shown in the formula scheme. Further studies on the structure of verticillol are in progress.

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[x] Historically thunbergane would be the correct name for this skeleton.

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