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STRUCTURE OF LINDERENE

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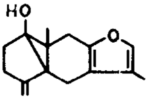
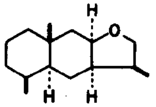
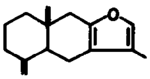
IN 1953, K. Takeda(1) tentatively proposed the structure I for linderene, $C_{15}H_{18}O_2$, m.p. 143-145°, a crystalline component of *Lindera Strychinifolia* Vill., from the results of dehydrogenation of linderene itself and of octahydrodehydroxylinderene, $C_{15}H_{26}O$, b.p. 5 mm. 135°, m.p. 27°,(2),* the reduction product of linderene.

Recently, however, the structure of octahydrodehydroxylinderene (II) has been clarified by H. Hikino et al.(3) as a result of the structural elucidation of atractylone (III). We also have succeeded in the synthesis of II from tetrahydroalantolactone (IV) directly.(4) Further, the structure of linderazulene (V),(5) the dehydrogenation


(I)


(II)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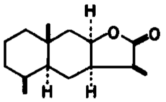
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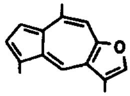
(V)

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* This compound was isolated as crystallines, m.p. 27°, by careful chromatographic separation.

product of linderene, was also established by synthesis from guaiol by our group.(6)

The ultraviolet spectra of linderene (VIa) and dihydrolinderene (VII) respectively show a maximum at 206.1mμ (ε 10,950) and at 219.8mμ (ε 7,400), and these results indicate the presence of a conjugated chromophore besides the furan ring in linderene. This was further confirmed by the NMR spectra of these two compounds VIa and VII; in the former the proton signal corresponding to the cyclopropane ring appears at 8.52 τ and in the latter this signal is shifted to 9.47 τ.

Some interesting information was obtained by further studies on the NMR spectra of linderene (VIa) and its acetate (VIb).** The doublet signal at 5.53τ (J=9.7 c.p.s.) corresponding to one proton in the spectrum of linderene shows the presence of a hydrogen atom attached to a carbon bearing hydroxyl group, and this signal is shifted to the lower field (τ=4.05, J=10.0 c.p.s.) in the spectrum of linderene acetate. The data mentioned above indicate that the hydroxyl group in linderene is not a tertiary but a secondary one and that a hydrogen atom is present on the adjacent carbon. These NMR studies show that the structure I is untenable for linderene and, together with other chemical evidences, support structure VIa for it.

All attempts to isolate the pure linderene acetate or dihydrolinderene acetate by acetylation with acetic anhydride in pyridine under various conditions were unsuccessful. Manganese dioxide oxidation of linderene or dihydrolinderene also gave only a resinous substance.

Catalytic hydrogenation of dihydrolinderene (VII) with PtO_2 in alcohol gave a fully saturated tetracyclic derivative, hexahydrolinderene (VIII), $C_{15}H_{24}O_2$, m.p. 120-121.5°, $[\alpha]_D^{22}$ -30.5°, ν_{max}^{Nujol} 3405 cm^{-1}; NMR 9.52τ (cyclopropane). The

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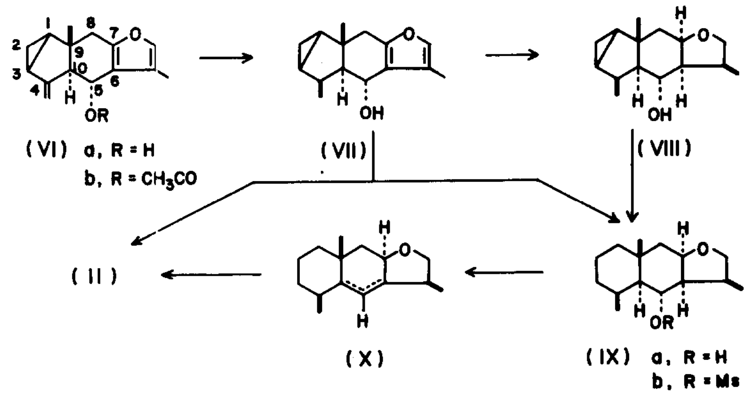
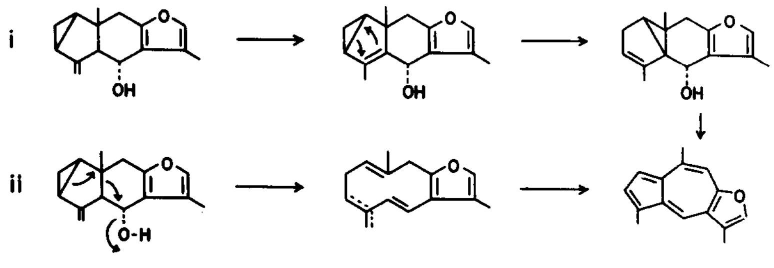
** Linderene acetate (VIb), $C_{17}H_{20}O_3$, m.p. 82°, was obtained from the same plant.



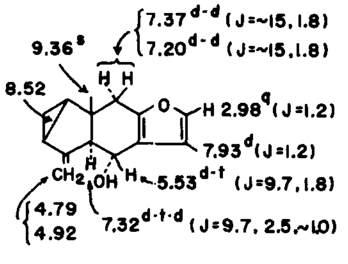
absorption bands at 3076 and 3009 cm^{-1} (in CCl_4) in the IR spectrum of this compound show the presence of a $-CH_2-$ group in the cyclopropane ring.$^{(7)}$ Reductive cleavage of the cyclopropane ring in VIII was achieved by catalytic hydrogenation with PtO_2 in alcohol containing acetic acid and gave IXa, $C_{15}H_{26}O_2$, m.p. 115°, $[\alpha]_D^{25}$ -44.1°, ν_{max}^{Nujol} 3407 cm^{-1}, in a quantitative yield. This octahydrolinderene (IXa) showed neither the bands at 3076 and 3009 cm^{-1} (cyclopropane ring methylene) in the IR nor a proton signal due to a cyclopropane ring in the NMR spectra. IXa was also obtained directly by catalytic hydrogenation of VII with PtO_2 in acetic acid with a small amount of II. It is now assumed from these results that the position of the hydroxyl group in linderene is limited to C-5.

Since the CrO_3 oxidation of VIII under mild conditions gave unchanged starting material and under drastic conditions it gave only a resinous substance, dehydration of IX was next attempted. When octahydrolinderene mesylate (IXb), m.p. 112°, obtained from IXa by the usual manner, was heated at ca. 100° for 5 hrs. in dimethylsulfoxide, it gave an oily unsaturated compound X. X was easily converted to octahydrodehydroxylinderene, m.p. 27°, by catalytic hydrogenation. The NMR spectrum of this unsaturated compound shows the following signals: one methyl signal at 8.57 τ as a singlet, one methyl signal at 8.85τ as a doublet (J=7.5 c.p.s.), and one vinyl proton signal at 4.78τ as a doublet (J=2.8 c.p.s.). The only structure of this unsaturated compound which would satisfy the NMR data must be represented by X. Therefore, the position of the hydroxyl group in linderene is C-5 and the cyclopropane ring is also located between C-1 and C-3. The nature of the proton signal (doublet J=9.7 c.p.s.) of the C-5 hydrogen atom shows the *trans*-diaxial relationship between C-5 and C-10 hydrogens. This assignment (α-hydroxyl group) was also consistent with the fact that the hydroxyl group in hexahydrolinderene (VIII) was resistant to CrO_3 oxidation. The β-configuration of the C-9 methyl group was also confirmed by the convertion of IV to II.

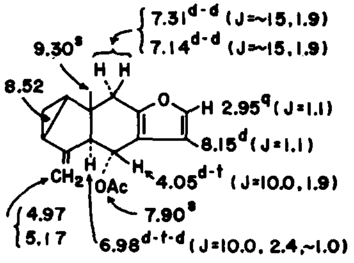
The formation of linderazulene from linderene (VIa) can be rationalized by the following two routes:



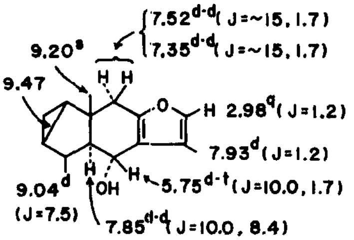
The NMR data of linderene, linderene acetate and dihydrolinderene are shown in the following figures:



(VIa)



(VIb)



(VII)

s = singlet
d = doublet
t = triplet
q = quartet

Chemical Shifts (τ) and Coupling Constants (J = c.p.s.)

The proton spin decoupling experiments of dihydrolinderene (VII) at 100 MC. show homoallylic spin-spin coupling (J=ca. 1.8 c.p.s.) between the C-5 proton and C-8 protons.(8)

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All the compounds mentioned here gave satisfactory elementary analyses.

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