

The Autoxidation of the Conjugated Triene Side-chain of Ebelin Lactone

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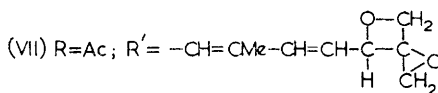
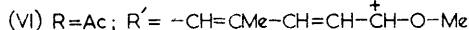
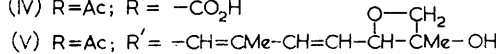
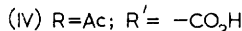
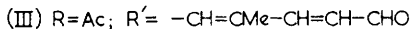
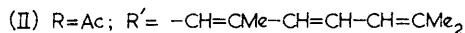
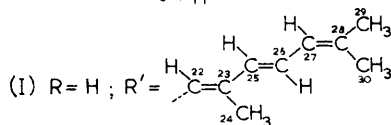
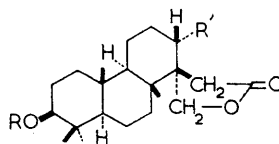
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EXPOSURE of ebelin lactone (I) in crystalline form to the air in diffuse daylight brings about autoxidation of the conjugated side chain, and after four weeks hardly any ebelin lactone is left. Such sensitivity to aerial oxidation is a feature of polyenes, and relevant solid-state (film) oxidations have been studied using the conjugated trienes allo-ocimene¹ and eleostearic acid;² the products of the solid-state autoxidation of ebelin lactone differ markedly in type from the products of these autoxidations. Acetyebelin lactone (II) is quite stable in the crystalline state, and samples have been recovered practically unchanged after six months' exposure.

When a sample of ebelin lactone after four weeks' exposure was acetylated and examined chromatographically (thin layer), two major products, two minor products, and at least one more in very small yield, were evident; three of these products were readily separable by column chromatography.

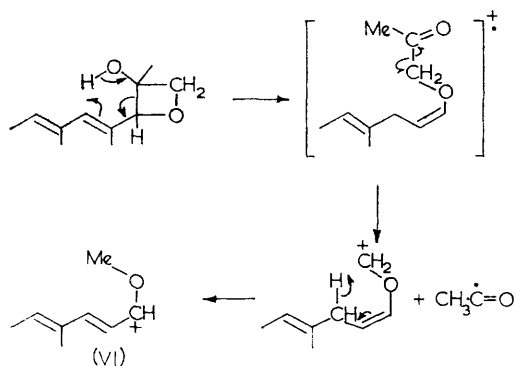
Spectroscopic methods indicated that one of the major products was the dienal (III). This was confirmed by its oxidation with permanganate to the same octanor-acid (IV) as obtained by permanganate oxidation of acetyebelin lactone³ and by its synthesis from acetyebelin lactone by osmium tetroxide oxidation. The other major component, for which we suggest the structure (V), analysed for $C_{32}H_{48}O_6$ with $M = 528$ (confirmed by

mass-spectral analysis). It possessed typical conjugated diene absorption in the ultraviolet with λ_{max} 233, 238, and 247 (sh) $m\mu$ (ϵ 32,900, 34,300,



21,400) and the position of the diene system was indicated by oxidation to the same octanor-acid (IV) above. The presence of a hydroxyl group was shown by its infrared spectrum (ν_{max} 3440 cm^{-1})

and the tertiary nature of this hydroxyl group, inferred from its resistance to acetylation, was confirmed from its n.m.r. signal which appeared as a singlet of unit area at δ 3.90 (dimethyl sulphoxide),⁴ disappearing on exchange with deuterium oxide. In the absence of any rearrangements, this tertiary hydroxyl can only be located on C-28. In the n.m.r. spectrum of (V), the proton of the trisubstituted double bond gave a doublet (δ 5.33, $J = 10.0$ c./sec.) which was superimposed on the signals of the *trans*-disubstituted double bond protons. The latter protons [δ 6.19 (1H; doublet) and δ 5.46 (1H; doublet of doublets)] formed part of an ABX system with $J_{AB} = 15.6$ c./sec. and $J_{BX} = 7.2$ c./sec.; the H_X proton appeared as a doublet at δ 3.29, indicative of a proton on carbon bearing oxygen. (The ABX system was confirmed by spin decoupling experiments). This same oxygen atom was also linked to a methylene group as evidenced by a two-proton singlet at δ 3.18. A singlet at δ 2.00 (3H) is due to the methyl of the acetyl group, while a singlet (3H) at δ 1.77 is ascribed to the methyl group attached to the double bond system; there are signals corresponding to $5 \times CH_3$ in the δ 0.7—1.1 region. In the absence of skeletal rearrangements, formula (V) becomes the only possible structure for this autoxidation product. The presence of a prominent ion in its mass spectrum at m/e 485 is ascribed to the ion (VI) which is considered to arise in the manner outlined in Scheme 1.



SCHEME 1

In both compounds (III) and (V) the stereochemistry about the C-25-C-26 double bond has been maintained in the *trans*-configuration as

evidenced by the coupling constant of the protons concerned. The stereochemistry about the C-22-C-23 double bond has not been determined for either (III) or (V) but it seems probable that the configuration originally present in ebelin lactone (which has been assigned the all-*trans*-configuration on the basis of its ultraviolet absorption) would be retained. The very high extinction coefficients of the ultraviolet maxima of (III) and (V) support this assignment.

A third compound (VII) isolated in very low yield had molecular weight 526 (mass spectrum) and analysed for $C_{33}H_{46}O_6$. Its ultraviolet absorption [λ_{max} 233, 238, and 247 (sh) $m\mu$ (ϵ 19,250, 19,250, 11,000)] indicated a conjugated diene; the wavelengths of the maxima suggested a substitution pattern similar to that in (V) but the considerably diminished extinction coefficient suggests the possibility of some change in the geometry about the double bonds. Its infrared spectrum showed the expected carbonyl bands due to the γ -lactone and acetyl groups (at 1774 and 1739 cm^{-1} respectively) but no other carbonyl bands and no hydroxyl bands. The two introduced oxygen atoms must therefore be present as peroxide or ether linkages; the former could be excluded on chemical grounds. The n.m.r. spectrum showed the presence of five protons on carbon also bearing oxygen* and three olefinic protons. Significantly, in its mass spectrum it gave an equally prominent ion at m/e 485 as that given by (V). The strength of the signal at m/e 485 indicates a particularly stable ion, and considering the similar genesis of (V) and (VII) indicates the probability that the signal has been given by the same species. It is necessary that any formula advanced for (VII) should be able to accommodate the formation of an ionic species of m/e 485 also derivable from the known structure of (V). Formula (VII) which we advance for this compound fits all these requirements and in particular can give rise to the ion (VI) as in Scheme 2.

The formation of (III), (V), and (VII) can be satisfactorily accounted for by the mechanisms given in Scheme 3; variations of these mechanisms to give the same products are clearly possible. It is of interest that, unlike allo-ocimene and eleostearic acid,^{1,2} the triene system of the crystalline ebelin lactone appears to be attacked exclusively at the terminal double bond or the methyl groups terminating the chain. This may be due to the steric hindrance associated with the polycyclic system at the other end of the chain, but may be

* In the discussions on the n.m.r. of (III), (V), and (VII) the various signals described have been in addition to those given by the four protons in the γ -lactone ring and the proton on the carbon in ring-A bearing the acetoxy group; all five protons gave clearly distinguishable signals in the three spectra.

