

THE STRUCTURE OF DENDROPANOXIDE

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Abstract. The structure of dendropanoxide, otherwise known as campanulin, has been shown to be 3:10-epoxy-D: β -friedo-oleanane. The NMR and mass spectra show conclusively that it contains a 5-membered oxide ring.

The isolation of the unusual triterpene oxide dendropanoxide, or campanulin, has been reported from several plant species¹⁻⁵ of which the primary source appears to be the *Rhododendron* family. There are at present two structures (I) and (II) which have been put forward for dendropanoxide differing only in the attachment of one end of the oxide ring. Kimura, Hashimoto and Agata¹ favoured the 4-membered oxide (I) on the basis of the reactivity of the compound. Cleavage of the oxide with 0.6% sulphuric acid or hydrochloric acid in ethanol gave a compound found to be identical with alnus-5-(10)-en-3 β -ol (III) while reduction of I with zinc dust in acetic acid and sodium acetate followed by CrO₃-pyridine yielded a mixture of alnusenone (IV) and alnus-5-(10)-en-3-one (V). The oxide did not react with lithium aluminium hydride. Comparison of these reactions with those of 5,8-epoxy-5-ergosta-9,22-dien-3 β -ol acetate,⁶ 5,8-epoxy-5-ergosta-22-en-3 β -ol acetate⁷ and 3,5-epoxy-5-cholestane⁸ as well as two unsaturated products having C₅ as a common atom led them to conclude that the 3 β ,5 β -epoxy structure (I) was to be preferred.

On the other hand, Rangaswami and Sambamurthy, who have named the compound campanulin, favoured the 5-membered oxide structure (II).⁹ Their preference is based solely on their report of an IR band at 1099 cm⁻¹ and the absence of a band at 990-971 cm⁻¹. The former absorption band is characteristic of tetrahydrofurans whereas the latter is associated with oxetanes. In contrast to this, Arthur, Lee and Ma have reported that this triterpene oxide has strong IR bands at 970-980 cm⁻¹.

We have isolated this same triterpene oxide along with friedelin (VI) and a number of other compounds from *Rhododendron collettianum* (Aitch and Hemsell)⁵. Examination of the IR spectrum shows it is similar to that reported by Arthur, Lee and Ma in that there is a family of significant bands between 1024 and 966 cm⁻¹, but no significant absorption at all between 1050 and 1100 cm⁻¹. This would seem to favour the 4-membered oxide (I). However, examination of the IR spectrum of a more pertinent model,¹¹ namely, 7-oxabicyclo[2.2.1]heptane (VII) shows that this system has strong characteristic ether bands at 935, 980 and 1002 cm⁻¹ which suggests that the 5-membered oxide (II) is more than likely correct.

Further spectral evidence supports the 5-membered oxide ring. Examination of a 100 MHz NMR spectrum of dendropanoxide shows a single downfield proton at δ 3.73 (doublet, *J* 5.5). Comparison of this value with that of the proton at C₃ in farnesiferol¹² (VIII) which is found at δ 3.69 shows that it corresponds much better to this system than that of the 4-membered oxide ring where this proton is usually found¹³ in the vicinity of δ 4.7. The NMR signals for the methyl groups in dendropanoxide are found in two areas, three being found at δ 1.139, 1.164 and 1.182, the latter of which is a doublet with *J* 0.8 Hz. The remaining five methyl groups are found between δ 0.90 and 1.01. The three downfield methyl signals are undoubtedly due to the *gem*-dimethyl group at C₄ and the methyl attached to C₉. The doublet signal at δ 1.182 is probably due to the methyl group at C₉ because this group sits full in the deshielding cone of the ether oxygen atom. In addition, it is the only one of these three methyl groups which has *trans* hydrogen atoms in relation to it which are located at C₈ and C₁₁. The long range splitting of this methyl group is another example of *w* coupling across four single bonds. This is primarily found when the methyl group is coupled with a *trans* hydrogen atom and is normally observed as a broadening of the methyl signal.¹⁴ Cases have been recorded of clearly observed splitting.¹⁵

The mass spectrum of dendropanoxide (II) is quite different from that of friedelin (VI) in spite of the obvious relationship of the two compounds (Fig. 1a dendropanoxide; 1b friedelin). The base peak of dendropanoxide occurs at *m/e* 137, whereas the corresponding peak in friedelin is only moderately strong. A prominent metastable peak occurs at *m/e* 45.8 which corresponds to the decomposition 411 \rightarrow 137. The molecular ion at *m/e* 426 is exceeded in intensity only by the 137 peak and the peak at *m/e* 411 corresponding to the loss of CH₃ from the molecular ion. A metastable peak at *m/e* 396.9 corresponds to this decomposition. We suggest that the fragment at *m/e* 137 results from the fragmentation pattern in chart I. It is difficult to rationalize an ion corresponding to *m/e* 137 from structure (I).

Although one might expect, *a priori*, that acidic opening of the oxide ring might initiate the further

backbone rearrangement to friedelin, only the two unsaturated ketones (IV) and (V) were found.^{1,5,9} This fact was part of the argument used by the Japanese workers¹ to justify the 4-membered oxide structure (I). The lack of formation of friedelin and the production of the unsaturated ketones can be explained if one looks at a model of dendropanoxide (IX). If one assumes that the eliminations and migrations only take place in a concerted manner and require

the *trans*-coplaner conformation, it can be seen that the hydrogen atom at C₈ can readily participate in an elimination or migration. However, neither of the methyl groups at C₄ are in a proper relationship to this migrating hydrogen atom to participate further and only the hydrogen atom at C₆ takes part in the reaction leading to the Δ structure (IV).

All of this data conclusively prove that dendropanoxide is 3 β :10 β -epoxy-D: β -friedo-oleanane (II).

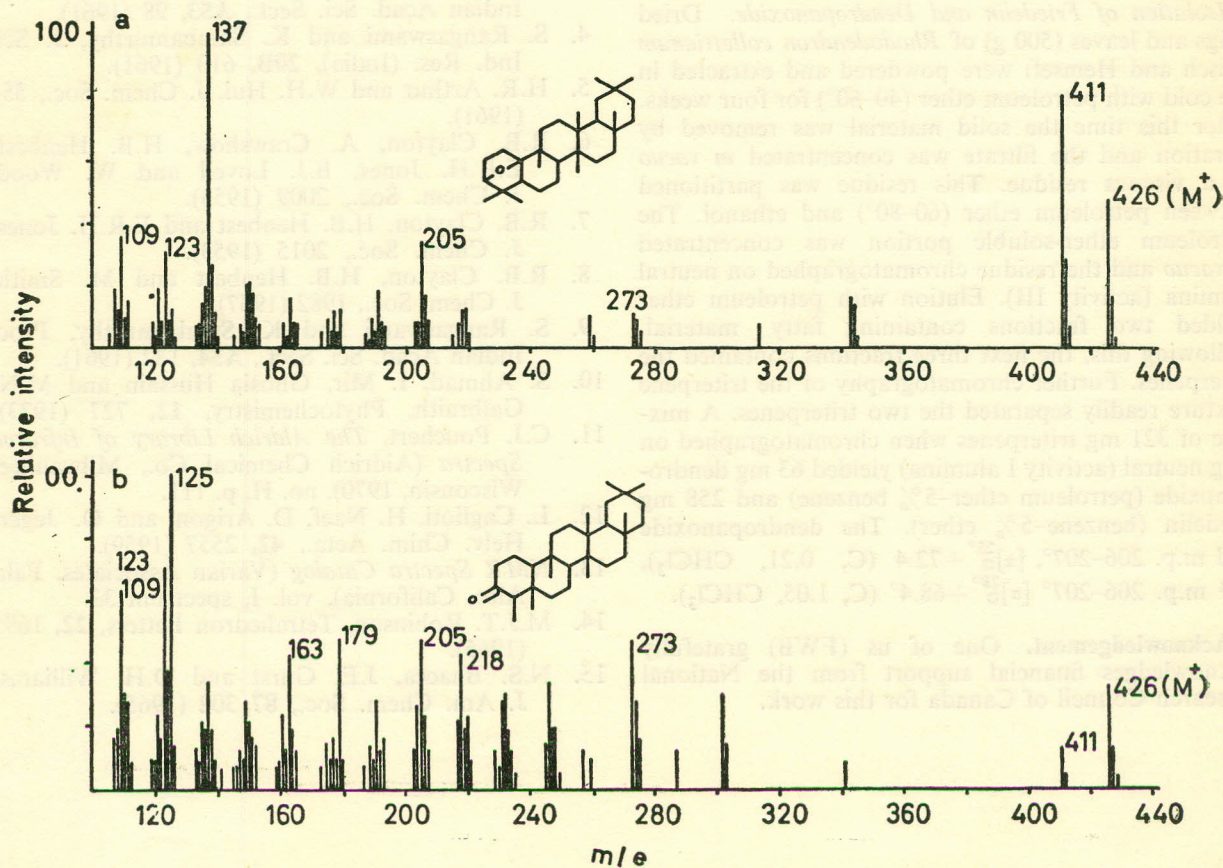
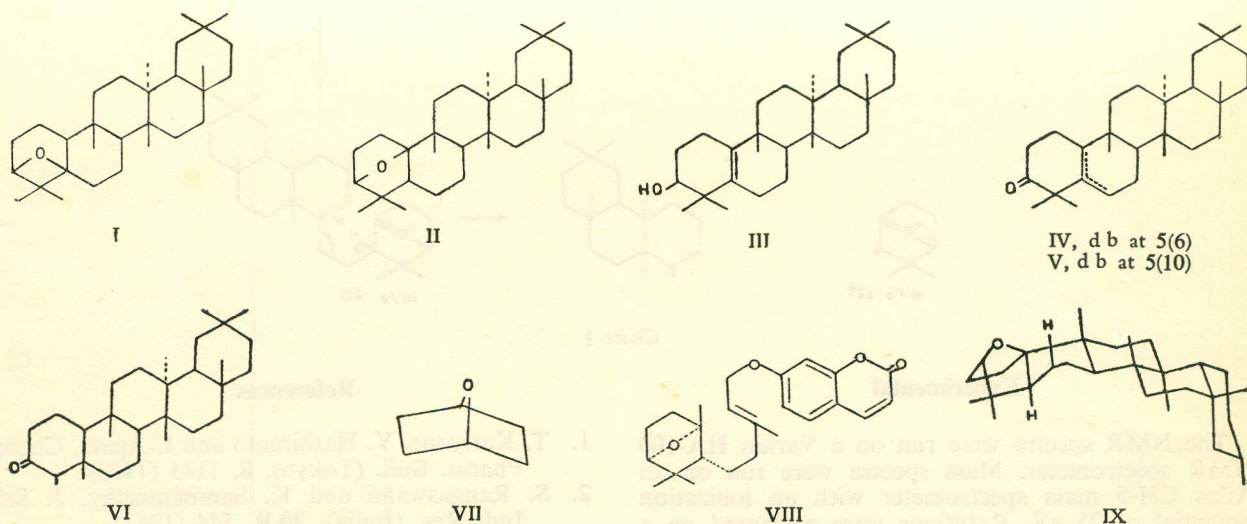


Fig. 1

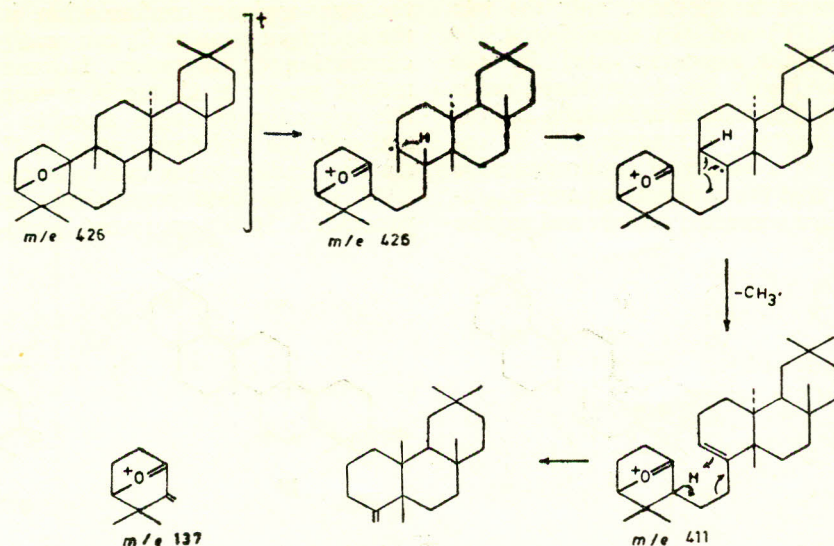


Chart 1

Experimental

The NMR spectra were run on a Varian HA-100 NMR spectrometer. Mass spectra were run on an Atlas CH-5 mass spectrometer with an ionization potential of 25 eV. Rotations were measured on a Jasco ORD/UV-5 spectropolarimeter.

Isolation of Friedelin and Dendropanoxide. Dried twigs and leaves (500 g) of *Rhododendron collettianum* (Aitch and Hemsel) were powdered and extracted in the cold with petroleum ether (40–60°) for four weeks. After this time the solid material was removed by filtration and the filtrate was concentrated *in vacuo* to a viscous residue. This residue was partitioned between petroleum ether (60–80°) and ethanol. The petroleum ether-soluble portion was concentrated *in vacuo* and the residue chromatographed on neutral alumina (activity III). Elution with petroleum ether yielded two fractions containing fatty material. Following this, the next three fractions contained the triterpenes. Further chromatography of the triterpene mixture readily separated the two triterpenes. A mixture of 321 mg triterpenes when chromatographed on 30 g neutral (activity I alumina) yielded 63 mg dendropanoxide (petroleum ether–5% benzene) and 258 mg friedelin (benzene–5% ether). The dendropanoxide had m.p. 206–207°, $[\alpha]_D^{25} +72.4$ (C, 0.21, $CHCl_3$), lit.¹ m.p. 206–207° $[\alpha]_D^{28} +68.4$ ° (C, 1.05, $CHCl_3$).

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