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THE STRUCTURES AND ABSOLUTE STEREOCHEMISTRY OF CYCLOGRANDISOLIDE AND EPICYCLOGRANDISOLIDE, NOVEL TRITERPENE LACTONES FROM ABIES GRANDIS

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In a continuing investigation of some of the neutral components of bark extractives (1,2) we have examined the petroleum ether extract of the bark of grand fir (Abies grandis (Dougl) Lindl.). We wish to report the isolation of several novel triterpene lactones for which complete structures and absolute stereochemistry can be assigned.

Column chromatography of the crude bark extract on alumina followed by preparative layer chromatography on silica gel and crystallization gave cyclograndisolide (Ia) as a white solid, m.p. 191-193°. The molecular formula established by elemental analysis and high resolution mass spectrometry was $C_{31}H_{48}O_3$ (3). The IR bands at 1745 and 1660 cm^{-1} and the UV absorption, λ_{max}^{MeOH} 209 (log ε 4.33), suggested an α,β-unsaturated-γ-lactone. The NMR spectrum (4) had a one proton apparent quintet at 3.02 ($J = 1.7$ Hz), a one proton multiplet (5.05), a three proton singlet (6.70, OCH_3), a one proton triplet (7.18, $J \doteq 1.8$ Hz, equatorial H geminal to OCH_3), a triplet for a vinylic methyl (8.10, $J = 1.7$ Hz), signals for five C-methyl groups (8.98, 9.02, 9.07, 9.14), and two doublets at 9.50 and 9.68 ($J = 4.0$ Hz) characteristic of cyclopropane protons.

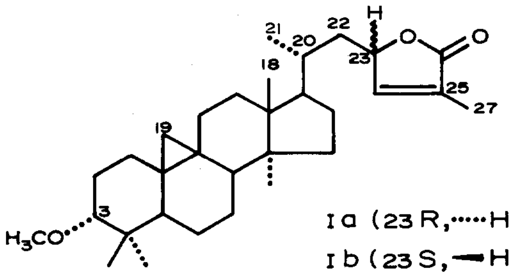
By analogy with abieslactone (5,6) the vinylic methyl was assigned to the α position of the unsaturated lactone while the protons at 3.02 and 5.05 were assigned to the β and γ positions in this system.

The CD curve (dioxane) of cyclograndisolide revealed a weak peak at 250 nm ($[\theta] = +377°$) and a strong negative value at lower wavelengths ($[\theta]_{220} = -31{,}500°$). The ORD curve (dioxane) of this compound had a trough, $[\phi]_{223} = -26{,}700°$. Again by analogy with abieslactone (6) we felt justified in assigning the R configuration about C_{23} of the lactone.

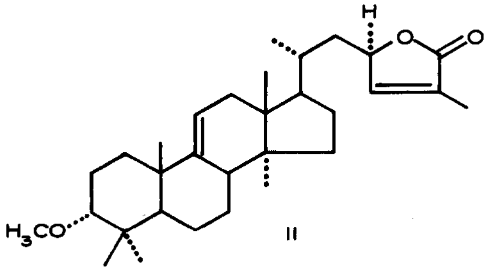
The cyclopropane ring in cyclograndisolide was assigned initially by intuition to the 9,19 position as found in the cycloartane family of triterpenes (7) and in the Buxus alkaloids (8). In agreement with other 9,19-cyclopropanoid triterpenes (9,10) an even mass ion (m/e 314) was observed. The elemental composition of this ion as determined by high resolution mass spectrometry was $C_{31}H_{30}O_2$ and was in complete agreement with the postulated loss of ring A.

It is well known that 9,19-cyclopropanoid triterpenes undergo ring opening under acidic conditions and convert to C_9-C_{11} unsaturated systems. On this basis cyclograndisolide should yield in accord with the implied relationships already noted above, the known triterpene lactone, abieslactone, for which structure II had been advanced (5,6). However treatment of our compound with hydrogen chloride in chloroform resulted in formation of a new substance which we name grandisolide, m.p. 212-214°, and which was <u>not</u> identical with abieslactone. All of our spectral data for grandisolide was in accord with structure II.

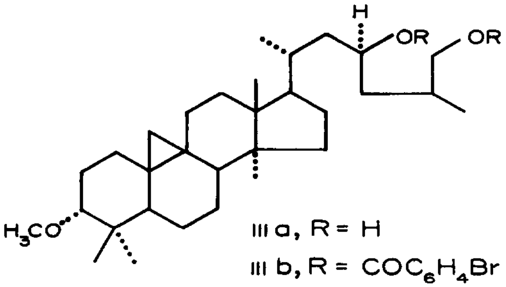
To place the assignment of structures Ia and II for cyclograndisolide and grandisolide respectively on a more firm basis, an appropriate derivative of the former was submitted to X-ray analysis.



Ia (23R,·····H)
Ib (23S,—H)



II



IIIa, R = H
IIIb, R = COC_6H_4Br

Cyclograndisolide could be hydrogenated to give the dihydro derivative ($C_{24,25}$ dihydro Ia), m.p. 198-199°, and the latter was reduced with lithium aluminum hydride to give the diol (IIIa), m.p. 133-134°. Treatment of the diol with p-bromobenzoyl chloride in pyridine gave the bis-p-bromobenzoate (IIIb), m.p. 154-156°.

Crystals of this derivative (IIIb) are orthorhombic, space group $P2_12_12_1$, with $\underline{a}$ = 6.635, $\underline{b}$ = 20.919, $\underline{c}$ = 30.530, four molecules per unit cell. The structure was determined with Cu-K_α diffractometer data by Patterson, electron-density and least-squares methods, the final $\underline{R}$ being 0.096 for 1518 observed reflexions. The absolute configuration was determined by the anomalous disperson method. Full details of the X-ray analysis will be published in due course.

This analysis confirms the presence of the 9,19 cyclopropane ring and cyclograndisolide is established as (23R)-3α-methoxy-9,19-cyclo-9β-lanost-24-en-26,23-lactone (Ia). On this basis grandisolide is II, abieslactone is therefore not II and at present is not assigned a new structure since insufficient data is available as yet.

A second compound, epi-cyclograndisolide (Ib), m.p. 194-195°, $C_{31}H_{48}O_3$, isolated from the petroleum ether extract was shown to be isomeric with Ia. The spectral data (IR, UV, NMR and mass spectrometry) showed marked similarities with cyclograndisolide. An important difference was noted in the ORD and CD measurements. The CD curve (dioxane) showed a shoulder, $[\theta]_{250}$ = +1708° and a strong positive value at lower wavelength, $[\theta]_{220}$ = +39,100° while the ORD curve revealed a peak, $[\phi]_{225}$ = +22,600°, essentially opposite to that of Ia. It was clear that epi-cyclograndisolide has the S configuration at C_{23} and is represented by the structure Ib.

In conclusion the above novel lactones provide an interesting addition to the cycloartenol family which has received recent interest in view of its importance in phytosterol biosynthesis (11,12).

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REFERENCES

1. J.P. Kutney and I.H. Rogers, Tetrahedron Letters, 761 (1968).
2. J.P. Kutney, I.H. Rogers and J.W. Rowe, Tetrahedron, **25**, 3731 (1970).
3. Satisfactory elemental analyses were obtained for all compounds reported. In addition, high resolution mass spectrometry was employed to establish molecular formulae.

4. NMR spectra were determined at 100MHz on a Varian HA100 spectrometer in deuteriochloroform. The values are given in τ units.

5. S. Matsunaga, J. Okada and S. Uyeo, Chem. Comm., 525 (1965).

6. S. Uyeo, J. Okada, S. Matsunaga and J.W. Rowe, Tetrahedron, **24**, 2859 (1968).

7. For a collection of references, see G. Ourisson, P. Crabbe and O. Rodig, "Tetracyclic Triterpenes. The Chemistry of Natural Products", E. Lederer Ed., Holden-Day, San Francisco, California, 1964.

8. V. Cerny and F. Sorm, "The Alkaloids" Vol. IX, R.F. Manske Ed., Academic Press, New York, N.Y., 1967, p. 375.

9. H.E. Audier, R. Bengelmans and B.C. Das, Tetrahedron Letters, 4341 (1966).

10. R.T. Aplin and G.M. Hornby, J. Chem. Soc. (B), 1078 (1966).

11. P. Benveniste, L. Hirth and G. Ourisson, Phytochem. **5**, 31, 45 (1966).

12. L.J. Good, "Terpenoids in Plants", J.B. Pridham Ed., Academic Press, New York, N.Y., 1967.