X-Ray Crystal Structure of (+)-Crispatanolide, a Novel Eudesmane-type Sesquiterpene δ-Lactone from *Makinoa crispata* (Liverwort)

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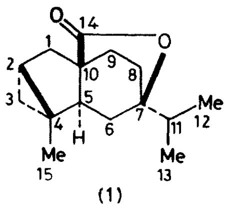
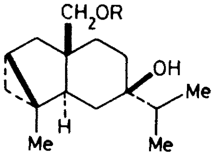
Summary From the liverwort, *Makinoa crispata* (Dilaenaceae), a novel eudesmane-type sesquiterpene δ-lactone, crispatanolide, was isolated and its structure was established to be 2,4-cycloeudesman-14,7-olide (**1**) by *X*-ray analysis

IN our continuing search for biologically active terpenoids of the liverworts, we have investigated *Makinoa crispata* which proved to be a rich source of sesquiterpene lactones and diterpene dialdehydes We now report the isolation and the structure of crispatanolide (**1**), a novel eudesmane-type sesquiterpene δ-lactone The ether extract of *M crispata* was chromatographed on silica gel to afford crispatanolide (**1**) (0·1% of total extract) together with the previously known cinnamolide (**4**)[1] (0·05%) and perrottetianal (**5**)[2] (0·4%)

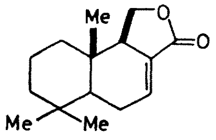
Crispatanolide (**1**), m p 109—110 °C, $[\alpha]_D$ + 68·7° (*c*, 0·8 in $CHCl_3$), had the molecular formula $C_{15}H_{22}O_2$ (M^+, 234·1614, calc 234·1619) Its i r spectrum showed the presence of a δ-lactone group (1740 cm^{-1}) which was further confirmed by the ^{13}C n m r signals at δ 178·3 (s) and 86·3 (s) p p m The ^1H n m r spectrum showed isopropyl (δ 0·98 and 1 00, each d, *J* 8 Hz) and tertiary methyl signals (δ 1·05, s), 3 cyclopropane ring protons (δ 0·33, 1H,



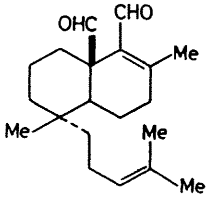
(1)



(2) R = H
(3) R = Ac



(4)



(5)

and 0·73, 2H; each m), and one proton (2·72, dd, J 12 and 8 Hz) on an sp^3 carbon atom. The ^{13}C n.m.r. spectrum also showed the presence of 3 methyl (δ 17·1, 17·1, and 19·1 p.p.m.), 5 methylene (δ 26·2, 27·8, 30·8, 32·4, and 34·9 p.p.m.) and 3 methine groups (δ 28·3, 35·6, and 50·3 p.p.m.), together with 2 tetrasubstituted sp^3 carbon atoms (δ 26·2 and 58·6 p.p.m.). The above spectral data together with the molecular formula indicated that (**1**) was a tricyclic sesquiterpene with a δ-lactone group. Reduction of (**1**) with $LiAlH_4$ gave a diol (**2**), [$C_{15}H_{26}O_2$ (M^+ 238); ν_{max} 3500 cm^{-1} (OH); δ 3·62 (1H, d, J 11 Hz) and 4·08 (1H, dd, J 11 and 2 Hz)], acetylation of which with acetic anhydride in pyridine afforded a monoacetate (**3**), [$C_{17}H_{28}O_3$ (M^+ 280); ν_{max} 3500 (OH) and 1730 cm^{-1} (OAc); δ 4·08 (1H, d, J 11 Hz) and 4·57 (1H, dd, J 11 and 2 Hz); ^{13}C n.m.r. δ 73·8 (s) p.p.m.]. The detailed structure of crispatanolide (1) was established by X-ray crystallography. Recrystallization from n-hexane afforded a thin needle-like crystal of dimensions 0·1 × 0·2 × 2·0 mm. *Crystal data:* $C_{15}H_{22}O_2$, orthorhombic, space group $P22_12_1$, a = 6·175(7), b = 12·148(10), c = 17·742 (16) Å, D_c = 1·169 g cm^{-3}, Z = 4. The diffraction intensities were collected in the θ–2θ scan mode using graphite-monochromated Mo-K_α radiation on a Syntex R3 diffractometer, and corrected for Lorentz, polarization, and background effects. The structure was solved by direct methods using the Multan program[3] and refined by full-matrix least-squares calculations. The final R-value is 0·142 for 1008 reflections. The relative stereochemistry of the crispatanolide molecule is shown in the Figure.† As expected from the spectral and chemical evidence, crispatanolide is an eudesmane-type sesquiterpene δ-lactone containing a cyclopropane ring; 2,4-cycloeudesman-14,7-olide (**1**). The absolute configuration shown of (**1**) was tentatively assigned by its positive Cotton effect {$[\phi]_{222}$ (MeOH) + 1383}.[4]

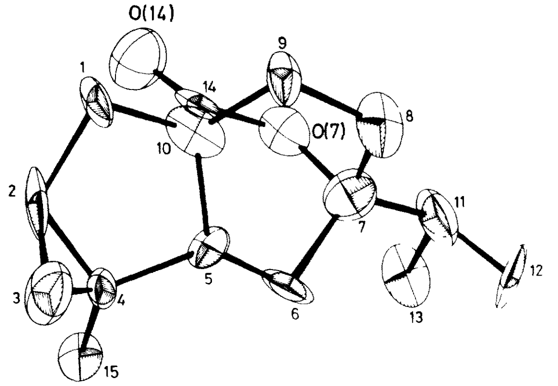


FIGURE. X-Ray structure of crispatanolide (**1**).

Crispatanolide (**1**) is the first known naturally occurring eudesmane-type sesquiterpene having a δ-lactone ring between C-14 and C-7 and a cyclopropane unit in the A-ring, which is interesting from not only the structural but also the biogenetic viewpoint.

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† The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

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[4] V. I. Minkin, M. Legrand, and M. J. Rougier, 'Determination of Configurations by Dipole Moments, C.D., or O.R.D.' in 'Stereochemistry, Fundamental and Methods,' vol. 2, ed. H. B. Kagan, Georg Thieme, Stuttgart, 1977.