The Molecular Structure of Gutierolide, a Novel Chloro-diterpenoid Lactone

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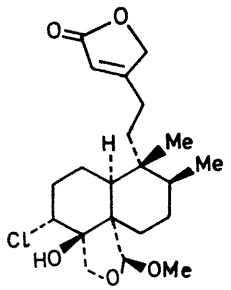
Summary The molecular structure of the first naturally occurring chloro-diterpene, gutierolide, as determined by *X*-ray crystallographic analysis, is presented.

THE first naturally occurring chloro-diterpene, gutierolide (I) was isolated from the alcoholic percolate of the above-ground part of the annual herb, *Gutierrezia dracunculoides* (DC) Blake (family Compositae), without the use of chloride salts or chlorine-containing solvents and in the following manner. The alcoholic residue was extracted with dilute acetic acid and then partitioned between ethyl acetate and water. The nonpolar fraction was distributed between petroleum and 10% aqueous methanol, and the residue from the latter phase was chromatographed on a silicic acid column. Elution was by a sequence of solvent systems composed of petroleum with increasing proportions of ethyl acetate, and the gutierolide fraction was crystallized from ethanol or methanol.

Gutierolide (I) $C_{21}H_{31}O_5Cl$,† m.p. 207—209°, $[\alpha]_D^{21}$ — 103° (methanol), showed an absorption maximum in the u.v. region at 210 nm (log ϵ 4·11), and gave a positive Kedde



(I)

test,[1] both features characteristic of a butenolide moiety.[2] The i.r. spectrum ($CHCl_3$) exhibited peaks at ν 3480 (hydroxyl), 1780 and 1750 (medium and strong intensity, respectively, for the carbonyl of the α,β-unsaturated-γ-lactone),[3] and 1640 cm^{-1} (olefin).

The mass spectrum ‡ obtained by the electron impact or chemical ionization method did not show a molecular-ion peak but instead gave peaks at *m/e* 367 (3·8%) and 366 (2·77%) (M — OCH_3 and M — $HOCH_3$, respectively) and a chlorine-containing fragment at *m/e* 228·1269 (80%) ($C_{13}H_{22}O^{35}Cl$ requires *m/e* 228·1281) with the ^{37}Cl isotope peak at *m/e* 230 (28%). The base peak was at *m/e* 111 ($C_6H_7O_2$) and was assigned to the fragment containing the lactone and its side-chain.

The relatively low yields of this compound during isolation precluded a classical chemical determination of its structure and it was decided to use crystallographic techniques. Gutierolide was recrystallized slowly from a methanolic solution and preliminary X-ray diffraction patterns indicated an orthorhombic lattice with space group $P2_12_12_1$. The cell dimensions were measured on a Picker four-angle diffractometer and were found to be a = 15·217, b = 17·397, c = 7·353 Å. On the basis of four molecules per unit cell, the crystal density is 1·32 g/cm³. The three dimensional intensity data were collected on the Picker FACS-1 diffractometer out to 2θ = 128° using graphite monochromatized Cu-K radiation and the θ–2θ scan technique. A total of 1554 reflections were considered significant above background.

The chlorine atom was located on a sharpened Patterson synthesis and the six atoms of the ring to which the chlorine is bonded were found on a symmetry minimum map,[4] which used the chlorine position as the point of superposition. The remaining non-hydrogen atoms were located on an E-map based on the tangent formula[5] refined phases of 216 reflections using the seven-atom partial structure for the starting phases. All hydrogen atoms in the structure were located on a difference Fourier computed at R = 13·0%. The atomic parameters (anisotropic thermal ellipsoids for the non-hydrogen atoms, positional parameters for all atoms) were refined by block-diagonal least-squares computations to the present R factor of 0·036. The absolute configuration of gutierolide (Figure) was determined by the

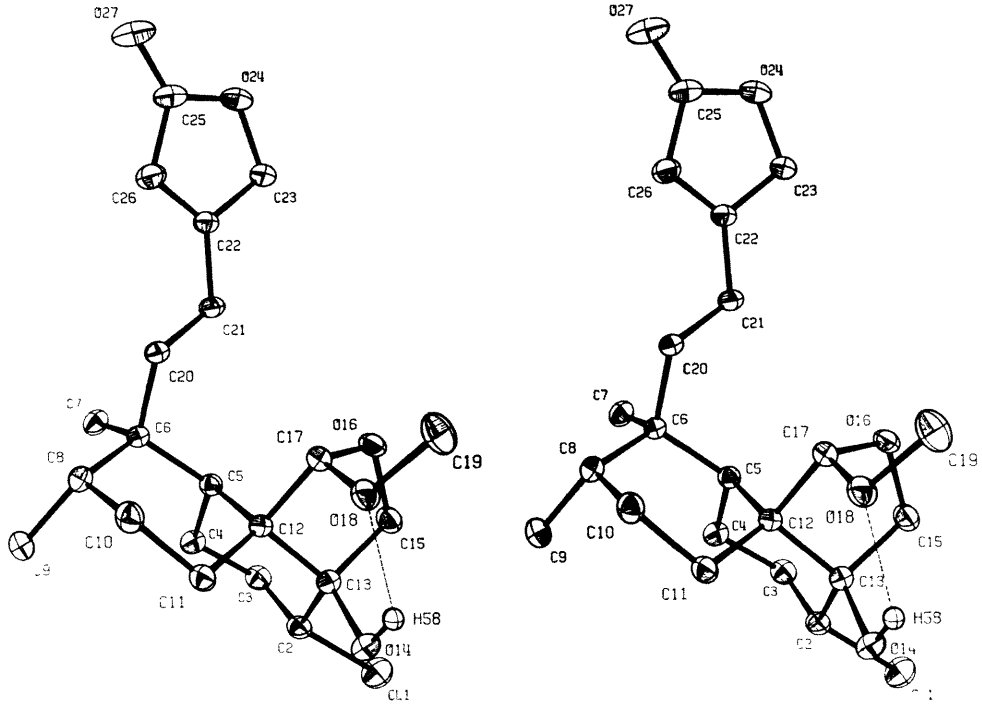


FIGURE. *Stereoscopic view of gutierolide as found in the crystals and showing the absolute stereochemistry determined by this study. This is a computer-drawn diagram using the program ORTEP.*[6]

† Satisfactory elemental analyses were obtained.
‡ Mass spectra were determined *via* the direct inlet method on an A.E.I. MS-9 double-focussing instrument.

correction of the chlorine scattering curve for the real and imaginary parts of anomalous scattering. Further refinement will be continued following the correction of the data for extinction effects.

Gutierolide contains a five-membered acetal ring in the standard envelope conformation, and two six-membered rings in the normal chair conformation. The ring containing the chlorine atom is *cis*-fused to each of the two aforementioned rings. In addition to these three rings there is a butenolide ring which contains the double bond C(23)–C(26) and the carbonyl moiety C(25)–O(27). There is an intramolecular hydrogen-bond between the hydroxyl oxygen O(14) and the ether oxygen O(18) of the acetal moiety.

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