

ON THE STRUCTURE OF PROSTRATIN: AN X-RAY STUDY

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The characterisation of prostratin, a compound of *Pimelea Prostrata*, proved to be a complicated task¹ and it was felt that additional structural evidence would be helpful. An X-ray diffraction study was therefore undertaken on the MnO_2 oxidation product with crystals of very poor quality, after the failure of many efforts to produce heavy atom derivatives.

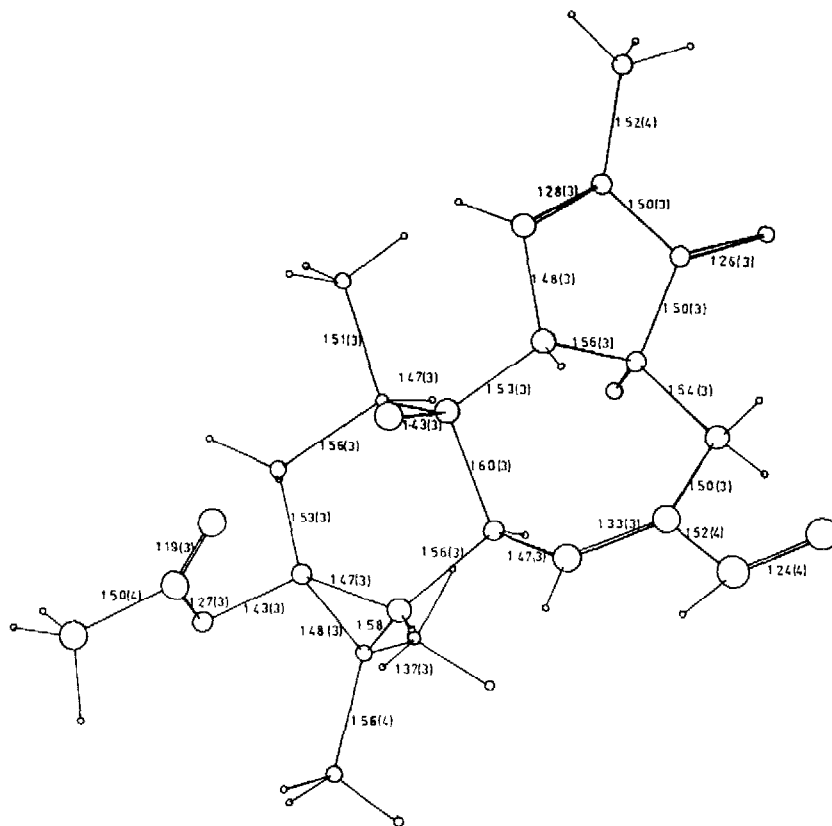
Crystal data. $C_{22}H_{28}O_6$, $M = 388.6$; orthorhombic, $a = 9.901(2)$, $b = 11.739(3)$, $c = 17.879(3)$ Å, $V = 2078$ Å³, space group = $F2_12_12_1$, $\rho = 1.23(1)$ g cm⁻³ by flotation in aqueous $CdCl_2$, $Z = 4$; $Cu-K\alpha = 1.5418$ Å, $\mu = 7.45$ cm⁻¹, crystal size $ca.$ 0.3 x 0.18 x 0.12 mm.

The $2\theta/\omega$ step-scan technique was used in diffractometer measurements and gave 715 reflexions with an intensity $>3\sigma$ ($880 >2\sigma$). Absorption corrections were not applied. Solutions of the phase problem proved extremely difficult and occupied us, at intervals, for a number of years but eventually an approach based on the prior modification of the intensity data proved successful. This assumed starting phases and the conventional application of "direct" methods using the program MULTAN² but data were first adjusted so as to reduce the importance of the large maxima in the Patterson function. Before solving the structure in this way we had applied standard probability procedures and computer packages as well as Patterson methods - including the vector verification procedure which we had previously used successfully.³

The current R -factor is 11.5% for isotropic refinement of the non-hydrogen atoms. The number of data does not allow a description in terms of anisotropic thermal parameters and this fact, together with the poor quality of the intensity data, indicates that although the molecular structure is clearly revealed bond lengths and angles will have only moderate accuracy.

The diagram shows the structure of the molecule together with bond distances and their calculated standard deviations. The analysis confirms that the structure of prostratin is very closely related to that of phorbol found in an X-ray study of bromo-derivatives^{4,5} and a solvate.⁶ There are no configurational differences and the observed bond lengths confirm the presence of the C(1) - C(2) and C(6) - C(7) double bonds, the carbon-to-oxygen distances are also as expected, within the limits of accuracy. There are, however, conformational differences in the six- and seven-membered rings. That in the latter is the most surprising since prostratin shows a bond rotation of 14.4° about the C(6) - C(7) double bond, from the data published for the phorbol derivative⁴ we calculate a rotation of only 1.5°. The reasons for this are not clear. There is an intermolecular hydrogen bond ($O \cdots O = 2.65$ Å) in the prostratin crystal involving the aldehydic oxygen atom and the hydroxyl group on C(4) but this is not positioned so as to explain the rotation. The other conformational change is less unexpected and is seen in the six-membered ring which more closely approximates in prostratin to the ideal envelope or sofa form. The discrepancy is most obvious in the C(9), C(11), C(12), C(13) region, where calculated bond

rotations for prostratin and the published phorbol structure differ by 17.3, 19.3 and 15.2° for the three sequential links between these atoms. This is consistent with the omission of the equatorial hydroxyl group from C(12) in prostratin and with the substitution of an acetyl group in place of an hydroxyl at C(13) and the consequent formation of an intramolecular hydrogen bond ($O \cdots O = 2.68\text{\AA}$) between the acetyl group and the hydroxyl on C(9) at the ring junction.



The Molecular Structure of Prostratin

(Bond lengths are in \AA units, the atom numbering is that of reference 1.)

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