The Crystal and Molecular Structure of Citrinin

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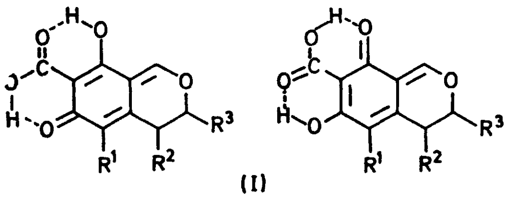
Summary A single-crystal X-ray diffraction study of citrinin has shown that it is a p-quinone methide in which intramolecular repulsion between the methyl groups has resulted in a marked distortion of the molecule.

FOR some time, naturally occurring quinone methides have been implicated as important intermediates in certain biological processes such as lignan and lignin biosyntheses and the oxidative phosphorylation processes, as well as in the chemistry of Vitamins E and K and the ubiquinones. The fungal metabolites, citrinin, pulvilloric acid, and ascochitine have been assumed to be p-quinone methides (Ia), although available evidence has not unequivocally ruled out the o-quinone formulation (Ib) for these substances. The constitution of citrinin has been determined by synthetic and degradative methods.[1,2] The presence of intramolecular hydrogen bonding has been confirmed by an i.r. study[3] and the quasiaxial conformation of the methyl groups, R^2 and R^3, has been established by a ^{1}H n.m.r. investigation.[4] The absolute configurations of the asymmetric centres have been determined.[5,6] None of these methods was able to distinguish between the p- and the o-quinone structures, although the former is intuitively preferable.[7] Since the results of a recent X-ray structure determination of cordeauxiaquinone have indicated that an unexpected tautomer is present in the crystalline state,[8] it was of particular interest to determine the structures of the compounds (I). We report the results of an X-ray structure determination of citrinin in which $R^1 = R^2 = R^3 =$Me.



(I)

(a) (b)

Yellow needle-shaped crystals of $C_{13}H_{14}O_5$ suitable for X-ray work were obtained by the slow evaporation of a solution of the compound in 95% ethanol. The crystals were orthorhombic in the space group $P2_12_12_1$, $a = 13{\cdot}455(2)$, $b = 7{\cdot}300(1)$, $c = 12{\cdot}261(2)$, $Z = 4$. The 919 independent reflections, for which $F_0^2/\sigma(F_0^2) \geqslant 3{\cdot}0$, were measured with Cu-$K_\alpha$ radiation on a Picker FACS-I automatic diffractometer equipped with a graphite crystal monochromator. An examination of a Patterson synthesis indicated that most of the atoms in the molecule should lie in a plane perpendicular to the b-axis. The very strong 020 and 040 reflections supported this assumption. The phases were determined by the symbolic addition method with the program MULTAN. Eight sets of 102 phases for reflections ($E \geqslant 1{\cdot}5$) were obtained from which the correct structure was deduced. The positional and anisotropic temperature parameters of the carbon and oxygen atoms were refined by a full-matrix least-squares method and the inclusion of the hydrogen atoms with isotropic temperature factors reduced the conventional *R*-value to 6·7%. No corrections were made for extinction or absorption effects. A perspective view of the molecule is shown in the Figure.

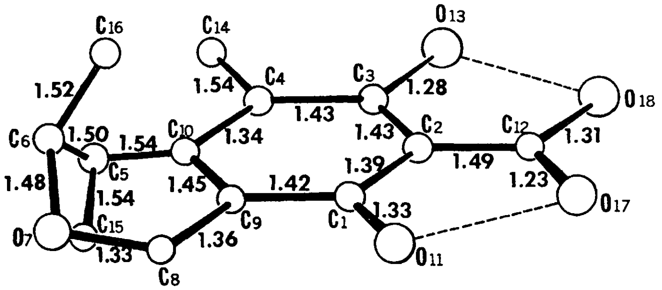


FIGURE. *A perspective view of the molecule of citrinin,* $C_{13}H_{14}O_5$. *The e.s.d.'s of the bond distances lie between* 0·007 *and* 0·010 Å. *The broken lines represent hydrogen bonds.*

The bond distances in the Figure clearly show that citrinin is a *p*-quinone methide. The two C–O distances in the molecule are both 1·33 Å, whereas the C=O distances are 1·23 and 1·28 Å. The estimated standard deviation of all these bond distances is 0·008 Å. The C(15) and C(16) methyl groups are *trans* to each other; this agrees with the quasi-axial conformation of the methyl groups in deuteriochloroform solutions that was found by the ^1H n.m.r. method.[4] There are two intramolecular hydrogen bonds in the molecule, O(11)–H–O(17) and O(18)–H–O(13). It was postulated from an i.r. study that in CCl_4 solution, citrinin exists as an equilibrium mixture of the form in which both hydrogen bonds are present and the form in which only one of the intramolecular hydrogen bonds, O(11)–H–O(17) is present.[3]

In the quinone ring, the atoms C(1), C(2), C(3), C(4), and C(10) lie in a plane whose equation with respect to the crystallographic axes is: $0{\cdot}0046X + 0{\cdot}9975Y - 0{\cdot}0701Z = 1{\cdot}617$. The atom C(4) has a maximum deviation of −0·009 Å from this plane. Atoms C(8), C(9), and O(13) show deviations of 0·113, 0·026, and 0·092 Å respectively, from this plane. The equation of the least-squares plane formed by C(1), C(8), C(9), and C(10) is: $0{\cdot}0508X + 0{\cdot}9938Y - 0{\cdot}0987Z = 1{\cdot}731$. The atoms C(5), C(6), and O(7) show deviations of −0·214, 0·524, and 0·134 Å, respectively, from this plane. The dihedral angle between the two planes whose equations are given above is approximately 3°. Hence, the quinone ring is not planar and the ring containing the heterocyclic oxygen atom is in the half-chair form. These distortions in the molecule may be attributed to the interatomic repulsions between the C(14), C(15), and C(16) methyl groups.

(*Received, September* 21*st*, 1971; *Com.* 1659.)

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