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THE CRYSTAL STRUCTURE OF 3-EPICARYOPTIN

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ABSTRACT

The crystal structure of 3-epicaryoptin has been determined from single-crystal X-ray data. The crystals are monoclinic, with unit-cell dimensions a = 7.876 (1), b = 17.278 (1), c = 9.697(1) Å, $\beta = 100.24(1)^\circ$, space group $P2_1$, and z = 2. The structure was solved by direct methods and refined by full-matrix least squares. For the correct enantiomer, R = 0.053 for the 2605 independent diffractometer measured reflections. $R^- / R^+ = 1.0056$ which gives a probability against the assignment of $< 6 \times 10^{-5}$.

INTRODUCTION

3- epicaryoptin is one of the most potent natural insect antifeedants known. Insect antifeedants are chemicals that inhibit feeding but do not kill the insect directly, the insect remaining near the treated food and dying through starvation (Kubo et al. 1976). Natural antifeedants are superior to synthetic ones because they do not lose their activity after a given period of time, are more effective at smaller concentrations and are less likely to be toxic. Antifeedant activity is related to the crystal structure (Kato et al. 1972) so the structure determination of the antifeedant is important.

Before we began the work some details of the molecular stereochemistry of 3-epicaryoptin were uncertain and there was a serious division of opinion about its absolute configuration. In view of this conflict an x-ray study of the title compound has been carried out at Imperial College. A preliminary account of this work has been published as a short communication. Using the data obtained and the IBM 4361 computer of University of Çukurova some missing details of the structure have been completed.

This is the full paper reporting the reviewed and completed results of x-ray crystallographic determination of the crystal structure of the title compound.

EXPERIMENTAL

The specimen of 3-epicaryoptin used in this work was extracted from the leaves of verbenaceae which is a plant widely grown in India (Chopra, 1965) and kindly supplied by Professor Donald Rogers.

A single crystal ca. $0.3 \times 0.2 \times 0.4$ mm^3 was selected. Oscillation and Weissenberg photographs showed the crystal to be monoclinic with systematic absences 0k0 $k=2n+1$ consistent with space group $P2_1$.

Accurate until-cell dimensions were obtained by measurement of 20 high-angle α_1 reflections on a diffractometer and performing a least-squares calculation.

Crystal Data: $C_{26}H_{36}O_9$, M=492, Monoclinic, space-group $P2_1$ a=7.876 (1)Å, b=17.278(1)Å, c=9.697 (1)Å, β=100.24(1), V=1298.56 Å^3, Z=2, D_c=1,258 g. cm^{-3}, F(000)=528.00, Cu–K_α radiation, λ= 1.54178Å.

Intensity data were collected for the crystal mounted about its b-axis on a Siemens off-line automatic four-circle diffractometer. A five-value measuring procedure (one side of peak, back-ground, full peak, back-ground on other side of peak, other side of peak) was employed (Allen et. al., 1971). Cu-K_α radiation at a take-off angle of 4,5°, a nickel β filter and a Na (T1)I scintillation counter were used.

A total of 2605 independent reflections (to $\theta < 71°$) were measured by use of the θ-2θ scan technique, and 109 of these were judged to be 'unobserved' since their net count was less than 2.58σ. The net count of the 105 reflection, measured as a reference every 50 reflections, did not alter significantly during the data collection (ca. 4 days) indicating that no deterioration of the crystal had occured. The data were brought to a uniform arbitrary scale by use of these reflections (Allen et. al, 1971) and Lorentz and polarization corrections were applied. (McIntyre and Stansfield, 1988). No absorption corrections were applied.

SOLUTION AND REFINEMENT OF THE STRUCTURE

The structure was solved by direct methods. The literature on the 'direct methods' is very extensive and details on the subject may be found in standart texts such as (Woolfson, 1963) and numerous reviews and articles (Hauptman and Karle, 1959); (Karle and Karle, 1966); (Hauptman, 1986); (Woolfson, 1988); (Giacovazzo et al, 1988), (Debaerdemaeker, 1988). The structure of the compound was solved by application of the program MULTAN (Main, 1978) to 300 reflections with normalized structure factors (E's)$>$1.50. An E map calculated for the phase solution with the highest 'combined figure of merit' gave plausible positions for the non-hydrogen atoms of the structure. The structure was refined isotropically and then anisotropically by full-matrix least squares to give a residual R=0.090. A difference map contained sharp peaks corresponsing to all of the hydrogen atoms. These were, for subsequent refinements, fixed at calculated positions 1.0Å from their parent carbon atoms.

Further refinement, hydrogens isotropically, the remaining non-hydrogen atoms anisotropically, reduced R to a final value of 0.053 for the correct enantiomer. Allowance for the anomalous scattering from its nine oxygen atoms gave $\frac{R^-}{R^+} = \frac{0.0541}{0.0538} = 1{,}0056$ which gives a probability against the assignment of $<6 \times 10^{-5}$ (Hamilton, 1965); (QuanHai-Fu, 1988). The maximum residual electron density in the final difference map was 0.2 e $Å^{-3}$ Unit weights were used throughout the refinements. Atomic scattering factors were taken from (Doyle-Turner, 1968) with the exception of those for hydrogen which were taken from (Stewart et al., 1965). The computations were carried out on the Imperial College CDC 6400, the University of London CDS 6600 and 7600, and the University of Çukurova IBM 4361 computers using, in the main, programs belonging to the X-ray 72 System (Stewart et al., 1972).

RESULTS AND DISCUSSION

The final fractional atomic coordinates and anisotropic thermal parameters for the non-hydrogen atoms together with their estimated standard deviations, are listed in Tables 1 and 2. Those for the hydrogen atoms with their isotropic temperature factors are given in Table 3.

Figure 1 shows a view fo the molecule (Jognson, 1965).

The bond lengths and angles together with their estimated standard deviations are listed in Tables 4 and 5. Most of the bond lengths and angles are around the normal values; however few of them deviate from the

Table 1. Fractional coordinates for the non-hydrogen atoms with estimated standart deviations in parentheses

Atom	x	y	z
C (1)	.2753 (6)	.5400 (0)	.7041 (4)
C (2)	.1797 (6)	.4631 (3)	.6738 (5)
C (3)	.1403 (5)	.4272 (3)	.8068 (5)
C (4)	.3095 (6)	.4158 (3)	.9065 (5)
C (5)	.3974 (6)	.4939 (2)	.9540 (4)
C (6)	.5697 (6)	.4817 (3)	1.0545 (4)
C (7)	.6732 (6)	.5559 (3)	1.0806 (5)
C (8)	.7214 (6)	.5872 (2)	.9450 (4)
C (9)	.5563 (5)	.6053 (2)	.8337 (4)
C (10)	.4422 (5)	.5306 (2)	.8154 (4)
C (11)	.6260 (5)	.6254 (2)	.6991 (4)
C (12)	.7068 (7)	.5621 (3)	.6224 (5)
C (13)	.7013 (7)	.5976 (3)	.4778 (5)
C (14)	.8523 (8)	.6500 (4)	.4621 (7)
C (15)	.7942 (8)	.7200 (4)	.4414 (7)
C (16)	.5530 (7)	.6555 (3)	.4639 (5)
C (17)	.4079 (6)	.3444 (3)	.8949 (5)
C (18)	.2736 (6)	.5427 (3)	1.0239 (5)
C (19)	.4612 (6)	.6769 (2)	.8748 (5)
C (20)	.8465 (6)	.6557 (3)	.9841 (5)
C (21)	.1628 (7)	.5018 (4)	1.2273 (5)
C (22)	.0755 (9)	.4348 (5)	1.2810 (7)
C (23)	.6124 (8)	.3889 (3)	1.2427 (6)
C (24)	.5616 (11)	.3702 (4)	1.3792 (7)
C (25)	−.1056 (6)	.3459 (3)	.7871 (5)
C (26)	−.1736 (7)	.2663 (3)	.7551 (6)
O (1)	.3133 (4)	.3552 (2)	1.0090 (3)
O (2)	.1681 (4)	.4929 (2)	1.0920 (3)
O (3)	.2264 (7)	.5551 (3)	1.2956 (4)
O (4)	.5337 (5)	.4561 (2)	1.1901 (3)
O (5)	.7055 (5)	.3521 (2)	1.1846 (5)
O (6)	.4915 (4)	.6564 (2)	.5904 (3)
O (7)	.6240 (5)	.7302 (2)	.4394 (4)
O (8)	.0583 (4)	.3523 (2)	.7741 (3)
O (9)	−.1885 (5)	.3982 (2)	.8139 (7)

expected values. The O(7)–C(15) bond is 1.349 Å and significantly shorter than O(7)–C(16) bond which is 1.443 Å. This is caused by the C(15) = C(14) double bond due to partial parallel overlap of the unhybridized p-orbital of C(5) with the non-bonding orbital of O(7). This interaction should also be the cause of longer length of C(16)–O(7) bond. The bond C(16)–O(6) is shorter than the bond C(16)–O(7) with the values of 1.397 Å and 1.443 Å respectively. This is due to increased electropositivity of C(16) under the influence of O(7), thus the bond C(16)–O(6) becomes shorter. The interaction between C(5)–C(6) is increased due to the increased electropositivty of C(6) because of the linkage with O(4). C(5) is also under the influence of C(4) which is quite electropositive due to

Table 2. Anisotropic thermal parameters* (x10^3 Å^2) for the non-hydrogen atoms with standard deviations in parentheses

Atom	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C(1)	54(2)	51(2)	51(2)	– 0(2)	3(2)	3(2)
C(2)	54(3)	59(3)	53(2)	– 3(2)	7(2)	– 6(2)
C(3)	51(2)	39(2)	68(3)	– 6(2)	11(2)	–12(2)
C(4)	55(2)	41(2)	51(2)	– 6(2)	10(2)	– 2(2)
C(5)	54(2)	37(2)	47(2)	– 3(2)	7(2)	– 3(2)
C(6)	65(3)	41(2)	48(2)	–10(2)	3(2)	2(2)
C(8)	70(3)	46(2)	51(2)	–11(2)	1(2)	– 1(2)
C(8)	58(3)	35(2)	54(2)	– 7(2)	6(2)	– 2(2)
C(9)	55(2)	30(2)	50(2)	2(2)	9(2)	– 0(2)
C(10)	48(2)	34(2)	45(2)	1(2)	6(2)	1(2)
C(11)	52(2)	38(2)	57(2)	7(2)	11(2)	9(2)
C(12)	87(3)	50(3)	65(3)	15(3)	30(3)	12(2)
C(13)	99(4)	53(3)	63(3)	– 6(3)	32(3)	1(2)
C(14)	86(4)	90(4)	104(4)	6(3)	46(3)	32(4)
C(15)	94(4)	69(4)	104(4)	– 7(3)	37(4)	24(3)
C(16)	74(3)	64(3)	62(3)	– 6(3)	11(2)	15(2)
C(17)	60(3)	37(2)	78(3)	– 2(2)	8(2)	– 2(2)
C(18)	67(3)	48(2)	58(3)	–10(2)	20(2)	– 9(2)
C(19)	67(3)	33(2)	68(3)	5(2)	16(2)	– 2(2)
C(20)	71(3)	48(3)	76(3)	–19(2)	5(3)	– 1(2)
C(21)	91(4)	105(5)	58(3)	–36(4)	24(3)	– 9(3)
C(22)	119(6)	154(7)	80(4)	–60(5)	25(4)	20(5)
C(23)	106(5)	62(3)	75(3)	–35(3)	–23(3)	23(3)
C(24)	187(8)	93(5)	84(4)	–41(5)	–14(5)	45(4)
C(25)	55(3)	42(2)	79(3)	1(2)	13(2)	3(2)
C(26)	58(3)	49(3)	114(5)	–14(2)	2(3)	– 4(3)
O(1)	76(2)	38(2)	68(2)	–11(2)	14(2)	5(2)
O(2)	76(2)	62(2)	55(2)	–21(2)	25(2)	–13(2)
O(3)	163(5)	152(5)	76(3)	–72(4)	48(3)	–61(3)
O(4)	97(3)	57(2)	51(2)	–22(2)	– 1(2)	12(2)
O(5)	104(3)	60(2)	128(3)	– 9(2)	–12(3)	35(3)
O(6)	70(2)	52(2)	62(2)	8(2)	12(2)	16(2)
O(7)	101(3)	65(2)	100(3)	12(2)	36(2)	36(2)
O(8)	52(2)	48(2)	90(2)	–12(2)	19(2)	–28(2)
O(9)	70(3)	54(2)	270(7)	– 4(2)	62(4)	–25(3)

its linkage with O(1). These two effects are the probable sources for the short bond length of C(5)–C(6). The bond between C(11)–O(6) is longer than the bonds C(16)–O(6) and C(16)–O(7) because of the effect of C(12). It seems that C(12) is not on the same plane formed by C(16), O(6), C (11), C(13) and therefore causes the bond C(11)–O(6) to stretch-out.

The ring made up with O(7), C(16), C(13), C(14), C(15) is planar, because the sum of the interior angles is 540.8° which is equal to the theoretical value of 540°.

It was mentioned that before we began the work some details of the molecular stereochemistry of 3-epicaryoptin were uncertain and the-

Table 3. Fractional coordinates (x10^3) of the hydrogen atoms

Atom*	x	y	z
H(11)	306	560	613
H(12)	196	578	737
H(21)	255	426	629
H(22)	70	482	605
H(32)	60	462	848
H(62)	643	442	1017
H(71)	780	547	1153
H(72)	600	596	1120
H(102)	513	487	785
H(111)	719	667	725
H(121)	831	549	670
H(122)	640	511	620
H(131)	813	623	467
H(132)	680	555	400
H(141)	979	632	470
H(151)	875	764	427
H(161)	452	637	384
H(171)	364	307	815
H(172)	536	344	911
H(181)	338	580	1091
H(182)	195	574	947
H(191)	540	722	887
H(192)	358	688	801
H(193)	420	666	966
H(201)	952	639	1055
H(202)	890	676	899
H(203)	789	699	1026
H(221)	68	439	1383
H(222)	-48	426	1226
H(223)	14	383	1269
H(241)	481	415	1405
H(242)	484	322	1372
H(243)	655	364	1461
H(261)	-299	264	765
H(262)	-165	250	657
H(263)	-108	228	823
H(264)	- 80	230	736
H(265)	-222	245	838
H(266)	-270	266	671

* The numbering of the hydrogen atoms is that fheao ttoms to which they are bonded.

re was a serious division of opinion about its absolute configuration. This X-ray study of 3-epicaryoptin has yielded the absolute stereochemistry shown in Figure 2. It is opposite to that assigned to clerodin, despite the fact that 3-epicaryptin and clerodin have been shown physicochemically to share a common absolute stereochemistry (Hosozawa et al., 1974). In view of this conflict a fresh X-ray study of clerodin has been carried out and this has verified that an error occured in the stereoformulae.

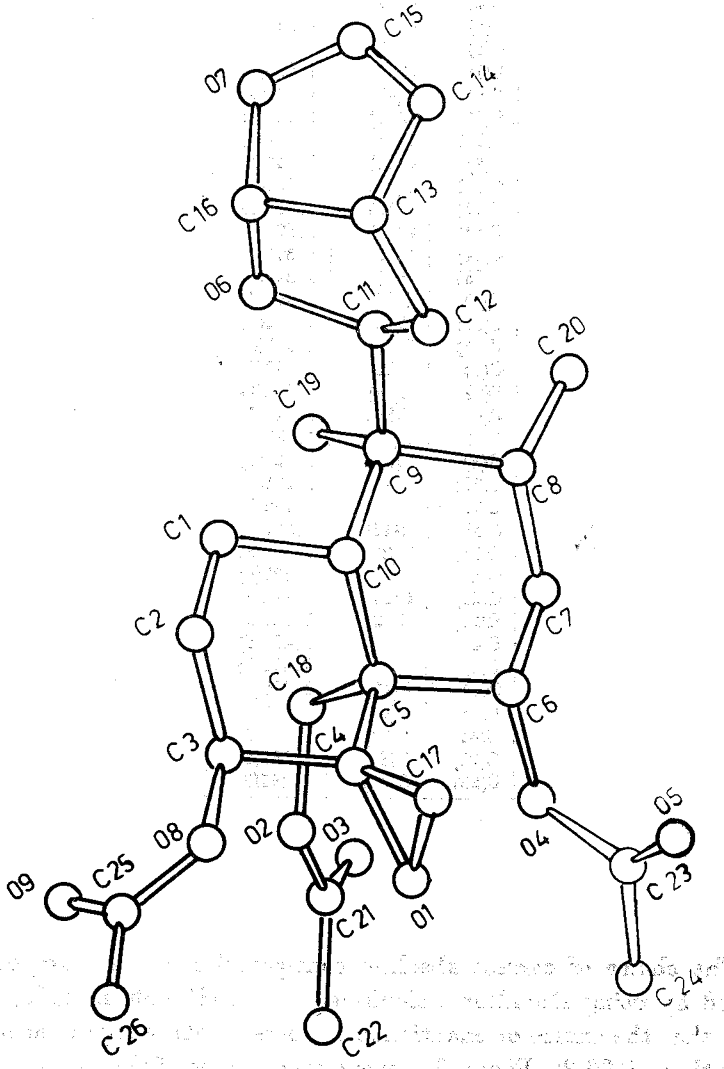

FIGURE 1. The solid state conformation of 3-epicaryoptin.

Table 4. Bond lengths (Å) with standard deviations in parentheses

C(1)	C(2)	1.528(5)
C(2)	C(3)	1.512(5)
C(3)	C(4)	1.511(5)
C(4)	C(5)	1.548(4)
C(5)	C(6)	1.349(4)
C(6)	C(7)	1.522(5)
C(7)	C(8)	1.531(5)
C(8)	C(9)	1.570(4)
C(9)	C(10)	1.548(4)
C(10)	C(5)	1.579(4)
C(9)	C(11)	1.540(4)
C(11)	C(12)	1.521(5)
C(12)	C(13)	1.518(7)
C(13)	C(14)	1.520(7)
C(14)	C(15)	1.304(8)
C(15)	O(7)	1.349(8)
O(7)	C(16)	1.443(7)
C(16)	C(13)	1.532(7)
C(16)	O(6)	1.397(6)
O(6)	C(11)	1.457(5)
C(9)	C(19)	1.542(4)
C(8)	C(20)	1.543(5)
C(3)	O(8)	1.457(5)
O(8)	C(25)	1.323(6)
C(25)	O(9)	1.171(7)
C(25)	C(26)	1.488(7)
C(5)	O(18)	1.532(5)
C(18)	O(2)	1.437(6)
O(2)	C(21)	1.329(6)
C(21)	O(3)	1.192(8)
C(21)	C(22)	1.534(8)
C(4)	O(1)	1.439(5)
C(4)	C(17)	1.473(5)
O(1)	C(17)	1.350(6)
C(6)	O(4)	1.462(6)
O(4)	C(23)	1.372(5)
C(23)	O(5)	1.186(8)
C(23)	C(24)	1.485(8)

The choice of correct absolute configuration of the compound is verified by using Hamilton's significance test (Hamilton, 1965) which shows that the choice of enantiomer is correct with a significance level better than 99.99 %. Figure 3 shows a stereo view of the packing of the molecules in the structure (Johnson 1965).

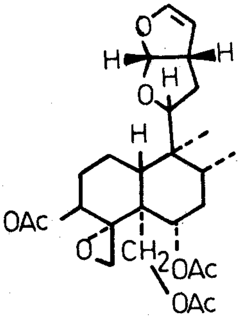

FIGURE 2. The absolute configuration of 3-epicaryoptin

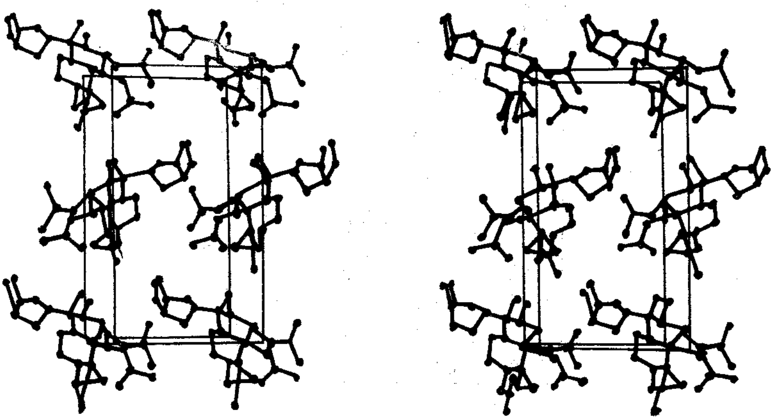

FIGURE 3. Stereoscopic view of the packing of the molecules in the unit cell.

Table 5. Bond angles (°) with standard deviations in parentheses.

C(2)	C(1)	C(10)	111.9(3)
C(1)	C(2)	C(3)	111.1(3)
C(2)	C(3)	C(4)	108.2(3)
C(3)	C(4)	C(5)	111.8(3)
C(4)	C(5)	C(10)	105.1(3)
C(5)	C(10)	C(1)	110.3(3)
C(5)	C(6)	C(7)	34.4(4)
C(6)	C(7)	C(8)	111.2(4)
C(7)	C(8)	C(9)	111.1(3)
C(10)	C(5)	C(6)	74.3(3)
C(8)	C(9)	C(11)	105.0(3)
C(19)	C(9)	C(11)	108.1(3)
C(9)	C(8)	C(20)	115.9(4)
C(7)	C(8)	C(20)	108.2(4)
C(9)	C(11)	C(12)	119.8(4)
C(11)	C(12)	C(13)	102.4(5)
C(12)	C(13)	C(16)	103.8(5)
C(13)	C(16)	O(6)	108.0(5)
C(16)	O(6)	C(11)	108.1(3)
O(6)	C(11)	C(12)	103.2(3)
C(13)	C(14)	C(15)	108.3(5)
C(14)	C(15)	O(7)	117.2(5)
C(15)	O(7)	C(16)	107.1(4)
O(7)	C(16)	C(13)	107.2(5)
C(16)	C(13)	C(14)	102.2(5)
C(12)	C(13)	C(14)	116.4(3)
C(2)	C(3)	O(8)	108.9(3)
C(4)	C(3)	O(8)	108.7(3)
C(3)	O(8)	C(25)	117.1(4)
C(5)	C(4)	C(17)	123.2(3)
C(3)	C(4)	O(1)	116.9(3)
C(4)	O(1)	C(17)	61.3(3)
O(1)	C(17)	C(4)	59.4(3)
C(4)	C(5)	C(18)	109.0(3)
C(6)	C(5)	C(18)	167.8(3)
C(10)	C(5)	C(18)	114.3(3)
C(5)	C(18)	O(2)	109.8(4)
C(18)	O(2)	C(21)	120.5(4)
O(2)	C(21)	O(3)	124.0(5)
C(7)	C(6)	O(4)	108.3(3)
C(6)	C(4)	C(23)	116.3(4)
O(4)	C(23)	O(5)	124.1(4)
O(4)	C(23)	C(24)	110.2(5)
O(5)	C(23)	C(24)	126.8(5)
O(9)	C(25)	C(26)	124.4(5)
O(8)	C(25)	C(26)	112.2(4)
O(8)	C(25)	O(9)	123.3(5)

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