Crystal and Molecular Structure of Viridin

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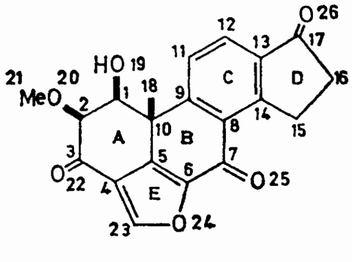
The title compound crystallises in the orthorhombic system, space group $P2_12_12_1$, with a = 16·090, b = 16·162, c = 6·195 Å. The crystal structure has been determined by statistical methods from a three-dimensional X-ray study based on 1580 visually estimated reflection intensities, and refined to a final R value of 0·092. The method of structure solution, and the conformation and geometry of the molecule are discussed in some detail, especially the unique combination of an aromatic ring C and an unsaturated ring E.

THE highly active antifungal metabolite, viridin, was first isolated from *Gliocladium virens*.[1a] On the basis of extensive chemical and spectroscopic data, structure (I) was suggested.[1b] Labelling studies suggested [1c] a steroidal rather than a diterpenoid biogenetic pathway; hence the angular methyl group C(18)H_3 was assigned the β absolute configuration, in accordance with that for all natural steroids.



(I)

The mould *Trichoderma viride* is known to produce as its major metabolite the compound gliotoxin,[2a] $C_{13}H_{13}O_4N_2S_2$. In support of the chemical studies on gliotoxin then in progress at Imperial College, it was decided to determine its crystal and molecular structure (this was before the publication of the structure of gliotoxin by Fridrichsons and Mathieson [2b]). On recrystallising the crude extract from various solvents, several 'polymorphs' of gliotoxin were obtained. One solution gave three excellent crystals and an X-ray study was commenced on them in the belief that they were a polymorph of gliotoxin. The density was 10% high, but this was tentatively attributed to the inclusion of solvent molecules. However, the Patterson function revealed no sulphur–sulphur vectors; in fact the map was indicative of an all-light-atom structure. One of the crystals was used to obtain a mass-spectrum, which suggested the material might be viridin, for which single-crystal cell constants had recently been published:[3] they agreed well with ours, and also removed the density anomaly. The compound was easily separated in the solid phase from gliotoxin by flotation in a liquid of suitable density and was found to represent approximately 25% of the solid extract. This represents a new source of supply of viridin. The structure of the recently isolated metabolite, viridiol, also from *Trichoderma viride* is based on that of viridin.[4] There is considerable current interest in the properties and synthesis of aromatic ring C steroids.[5]

We have performed a full three-dimensional X-ray analysis on viridin, and have confirmed the structure and relative configuration suggested by Grove *et al.*

EXPERIMENTAL

The crystals were grown from acetone–methyl iodide as yellowish prisms, with extinction directions parallel to the morphological faces. Oscillation and Weissenberg photographs revealed the Laue symmetry *mmm*. The crystals were stable to X-rays and gave excellent Weissenberg photographs.

Cell dimensions were initially obtained from Weissenberg photographs; precise values were later obtained from axial θ-values measured on a diffractometer.

Crystal Data.—$C_{20}H_{16}O_6$, M = 352·0, Orthorhombic, a = 16·090(1), b = 16·162(1), c = 6·195(1) Å, U = 1611·0 Å^3, D_m = 1·44(2) (by flotation), Z = 4, D_c = 1·45, $F(000)$ = 736·0. Space group $P2_12_12_1$ (No. 19, D_2^4) from systematic absences: $h00$, $0k0$, and $00l$ for $h,k,l \neq 2n$. Cu-K_α radiation (λ_{mean} = 1·54178 Å); μ(Cu-K_α) = 6·30 cm^{-1}.

The layers $hk0$—7 were photographed with nickel-filtered Cu-K_α radiation by use of the multiple-film equi-inclination Weissenberg method from a crystal of dimensions *ca.* 0·6 × 0·5 × 0·5 mm^3; errors due to absorption were considered to be negligible. 1580 reflection intensities were visually estimated and placed on an arbitary common scale by comparison with common data from the $h0l$ and $h1l$ layers.[6a] A further 250 reflections were treated as accidental absences and were included in the data list.

The data were put on an absolute scale and normalised structure factors (E values) were computed by means of the DATFIX program.[7]

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[1] (*a*) P. W. Brian and J. C. McGowan, *Nature*, 1945, **156**, 144; (*b*) J. F. Grove, P. McCloskey, and J. S. Moffatt, *J. Chem. Soc.* (*C*), 1966, 743; (*c*) M. M. Blight, J. J. W. Coppen, and J. F. Grove, *Chem. Comm.*, 1968, 1117.

[2] (*a*) J. A. Elvidge and F. S. Spring, *J. Chem. Soc.*, 1949, *S*, 135; (*b*) J. Fridrichsons and A. McL. Mathieson, *Acta Cryst.*, 1967, **23**, 439.

[3] J. F. Grove, J. S. Moffatt, and E. B. Vischer, *J. Chem. Soc.*, 1965, 3803.

[4] J. S. Moffatt, J. D. Bu'lock, and Tse Hing Yuen, *Chem. Comm.*, 1969, 839.

[5] See *e.g.*, (*a*) L. A. Chatterjee and B. G. Hazra, *Chem. Comm.*, 1970, 618; (*b*) J. Meney, Y.-H. Kim, R. Stevenson, and T. N. Margulis, *ibid.*, 1970, 1706.

[6] (*a*) POLO, an interlayer scaling program by M. G. B. Drew; (*b*) M. G. B. Drew, D. H. Templeton, and A. Zalkin, *Acta Cryst.*, 1969, *B*25, 261.

[7] This, and all subsequent calculations (except where stated otherwise), were performed by use of the 'X-Ray '63' system of programs, by J. M. Stewart, University of Maryland Technical Report TR 64 6.

Structure Solution and Refinement

The structure was solved by statistical methods, based on those of Karle and Karle,[8] using the symbolic-addition procedure followed by tangent refinement. A modified version of the PHASEM program [6b] was used. The origin- and enantiomorph-defining phases, together with three symbolic ones, were chosen from the 182 reflections whose E values were $>1·6$, and are listed in Table 1.

TABLE 1

h			E_h	Phase (mcycles)	
6	13	0	3·23	0	define origin
1	14	0	2·97	250	
0	17	1	2·24	250	
15	0	1	2·02	250	defines enantiomorph
10	18	0	3·20	a	
9	9	3	3·08	b	
5	8	4	3·00	c	

The 10,18,0 reflection is an invariant and its phase must be zero or 500. Both b and c were varied between 0 and 1000 mcycles, in steps of 125 mcycles. Thus, 128 different starting-set combinations were investigated. For each set, the first 29 reflections, derived from the symbolic addition, were refined for five cycles, then the top eighty, including these 29, were refined for 20 more cycles, and finally the top 150 reflections for 25 more. (The restriction to the largest 150 E values was dictated by program capacity.) All sets of signs except one showed some oscillatory behaviour from cycle to cycle: the exception was $a = 500$, $b = 250$, $c = 625$ mcycles. This set had the lowest Karle R factor (by 1·3%) of the seven ' best ' sets, but there were among these several with the same lowest Drew R factor; indeed these had slightly higher average consistencies than the set with the lowest Karle R factor.

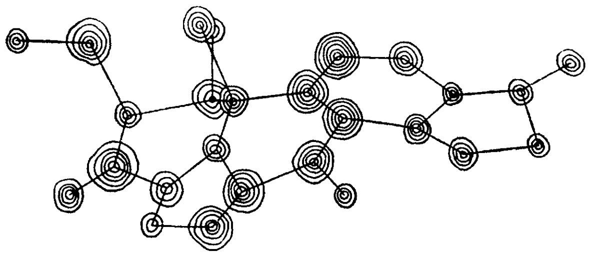

FIGURE 1 The c axis projection of the E-map for viridin. The contours are at equal, arbitrary intervals

An E-map was then computed using these 150 phases as coefficients (Figure 1). It contained the correct number (104) of peaks per cell, and all were well shaped. Their peak heights, however, were no reliable guide to chemical identity. There were a few other maxima, but all were ill-shaped and had very low peak heights, hardly significant above the background level. The 26 peaks that comprise one molecule were selected with ease, and inclusion of these as carbon atoms in a structure-factor calculation, followed by four cycles of BLOKLS block-diagonal least-squares refinement,[7] resulted in a conventional R factor of 0·185. A difference map was also computed and the absence of any major features confirmed the correctness of the structure model.

It had not been possible to distinguish between oxygen and carbon atoms by their peak heights in the E-map, but the six oxygen atoms were readily identified partly by the bond lengths and partly by their somewhat lower temperature factors. After three more cycles of BLOKLS refinement in which they were given appropriate scattering factors,[9] R fell to 0·148; however, the overall scale-factor was oscillating slightly. Individual layer scale-factors were now included and after four more cycles of refinement R reached 0·141. A difference map revealed all the hydrogen atoms in their expected positions. Their observed positions were included in a structure-factor calculation, each being assigned an isotropic temperature factor 0·5 Å^2 greater than the atom to which it was bound. After four cycles R was 0·131 and all parameter shifts were $<0·04\,\sigma$. The hydrogen parameters were not refined.

The non-hydrogen temperature factors were converted into their anisotropic β_{ij} equivalents. Six cycles of least-squares with fixed layer scale-factors and a 0·5 damping factor, gave an R factor of 0·106. A Hughes-type weighting scheme was suggested for the zero and first layers by an analysis of the observed and calculated structure factors over ranges of $|F_o|$ and $\sin^2\theta$. It took the form $\sqrt{w} = 1$ for $F_o < F^*$ and $\sqrt{w} = F^*/F_o$ for $F_o > F^*$, where w is the weight to be applied in least-squares refinement and F^* is a constant. The latter was set at 410 and 610 for the zero and first layers respectively; unit weights were used for the other layers as the analysis indicated that this was the most appropriate scheme.

TABLE 2

Final positional parameters for the non-hydrogen atoms, as fractions of the unit-cell edges; standard deviations are in parentheses

Atom	x	y	z
C(1)	0·50626(39)	−0·01541(44)	−0·09978(109)
C(2)	0·56680(41)	0·05810(46)	−0·10534(131)
C(3)	0·54435(48)	0·13332(44)	0·02935(145)
C(4)	0·49528(43)	0·11424(41)	0·21749(137)
C(5)	0·46106(37)	0·03375(36)	0·24983(109)
C(6)	0·40357(41)	0·03954(38)	0·40735(119)
C(7)	0·34568(40)	−0·02463(41)	0·46805(117)
C(8)	0·34637(36)	−0·09417(37)	0·30985(110)
C(9)	0·40425(35)	−0·10129(38)	0·14162(112)
C(10)	0·48037(34)	−0·04386(37)	0·13018(105)
C(11)	0·39813(40)	−0·16609(42)	−0·00963(126)
C(12)	0·33547(44)	−0·22370(45)	0·00228(145)
C(13)	0·27865(40)	−0·21675(43)	0·16964(128)
C(14)	0·28193(36)	−0·15434(39)	0·32443(112)
C(15)	0·21088(42)	−0·16010(47)	0·48036(136)
C(16)	0·16340(47)	−0·23819(49)	0·41328(156)
C(17)	0·20637(43)	−0·27063(46)	0·21378(145)
C(18)	0·55187(38)	−0·08892(41)	0·24901(117)
O(19)	0·53962(32)	−0·08077(35)	−0·22526(85)
O(20)	0·64604(28)	0·02763(34)	−0·03080(107)
C(21)	0·71692(60)	0·07225(86)	−0·11571(258)
O(22)	0·56654(45)	0·20228(37)	−0·02232(139)
C(23)	0·45750(51)	0·16348(45)	0·36988(159)
O(24)	0·40178(31)	0·11977(28)	0·49161(95)
O(25)	0·30043(34)	−0·01988(33)	0·62742(89)
O(26)	0·18674(37)	−0·33112(40)	0·10811(124)

A few mis-punchings of intensity data were corrected and five low-angle intense reflections with $F_c > F_o$ were removed for suspected extinction. R was now 0·103. The β_{ij} values were converted back to their isotropic B-factors and these were refined together with the non-hydrogen positional parameters and layer scale-factors for a further six cycles of BLOKLS, by which time the scale-factors were judged to have settled down completely. For the final

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[8] I. L. Karle and J. Karle, *Acta Cryst.*, 1966, **21**, 849.

[9] ' International Tables for X-Ray Crystallography,' vol. III, Kynoch Press, Birmingham, 1962.

stage of refinement, the B values were reconverted to β_{ij} values and six cycles of least-squares were performed on all non-hydrogen parameters, with the new layer scale-factors kept fixed. All parameter shifts were now $<0{\cdot}01\ \sigma$ and refinement was judged to be complete with R now 0·0916 for the 1580 non-zero reflections. The final structure factors, listed in Supplementary Publication No. SUP 20332 (11 pp., 1 microfiche),* were calculated with the final parameters listed in Tables 2 and 3, where their estimated standard deviations (σ) are also given. The observed hydrogen positions are listed in Table 4. The atom numbering system used is given in (I).

TABLE 3

Final anisotropic thermal parameters ($\times 10^5$) * for the non-hydrogen atoms, with standard deviations in parentheses

Atom	β_{11}	β_{22}	β_{33}	β_{12}	B_{13}	β_{23}
C(1)	160(22)	301(27)	294(187)	−6(21)	123(55)	4(59)
C(2)	175(24)	290(29)	1320(229)	16(22)	35(66)	169(69)
C(3)	265(28)	231(27)	2050(265)	−36(24)	119(81)	195(72)
C(4)	181(23)	197(23)	1746(244)	−31(21)	−19(66)	75(67)
C(5)	145(20)	156(21)	625(178)	19(18)	−110(54)	21(54)
C(6)	200(23)	144(21)	1258(206)	12(19)	23(63)	−235(56)
C(7)	187(23)	222(24)	759(190)	37(21)	−51(58)	15(58)
C(8)	113(19)	158(21)	694(181)	2(17)	−82(50)	−84(49)
C(9)	95(18)	196(22)	714(178)	9(17)	−49(54)	−112(54)
C(10)	108(19)	170(21)	381(167)	23(17)	−125(51)	−63(51)
C(11)	173(23)	236(25)	1123(200)	−20(21)	43(66)	−170(63)
C(12)	240(27)	270(28)	1581(232)	−37(23)	−22(75)	−267(75)
C(13)	152(22)	239(26)	1463(221)	−80(21)	−56(62)	−25(64)
C(14)	92(19)	193(22)	966(189)	6(18)	38(52)	−2(55)
C(15)	179(24)	317(30)	1463(224)	−51(23)	188(68)	−92(74)
C(16)	233(28)	290(30)	2540(296)	−90(25)	160(78)	−11(82)
C(17)	185(26)	272(29)	2156(263)	−82(23)	−91(72)	27(75)
C(18)	150(22)	241(24)	733(194)	67(20)	−157(59)	37(59)
O(19)	269(20)	390(23)	581(142)	−54(20)	200(49)	−182(49)
O(20)	111(16)	375(23)	2706(201)	−21(17)	147(51)	230(64)
C(21)	270(37)	888(77)	6493(647)	−160(46)	770(142)	582(200)
O(22)	589(36)	276(24)	4310(297)	−99(243)	719(96)	294(77)
C(23)	316(31)	190(26)	2699(291)	−27(25)	116(92)	−130(78)
O(24)	278(19)	162(16)	1835(165)	25(16)	143(57)	−274(48)
O(25)	339(22)	311(22)	970(147)	−35(19)	393(54)	−219(51)
O(26)	326(25)	429(28)	3509(255)	−222(23)	−23(73)	−353(78)

* The thermal parameters are defined by the equation $f_i = f_i^0 \exp - (\beta_{11}h^2 + \beta_{22}k^2 + \beta_{33}l^2 + 2\beta_{12}hk + 2\beta_{13}hl + 2\beta_{23}kl)$.

TABLE 4

Observed but unrefined positional parameters for the hydrogen atoms, as fractions of the cell edge

	x	y	z
H(1)[C(1)]	0·452	0·001	−0·181
H(2)[C(2)]	0·570	0·078	−0·267
H(3)[C(11)]	0·441	−0·170	−0·134
H(4)[C(12)]	0·331	−0·271	−0·110
H(5)[C(15)]	0·233	−0·165	0·637
H(6)[C(15)]	0·173	−0·109	0·471
H(7)[C(16)]	0·165	−0·281	0·537
H(8)[C(16)]	0·102	−0·224	0·383
H(9)[C(18)]	0·567	−0·154	0·130
H(10)[C(18)]	0·587	−0·052	0·270
H(11)[C(18)]	0·529	−0·112	0·380
H(12)[O(19)]	0·607	−0·118	−0·160
H(13)[C(21)]	0·760	0·030	−0·205
H(14)[C(21)]	0·709	0·060	−0·240
H(15)[C(21)]	0·770	0·070	0·044
H(16)[C(23)]	0·470	0·226	0·391

Each hydrogen atom was given a B-factor 0·5 Å^2 greater than that of the atom to which it is attached. Mean C–H distance is 1·06 Å.

DISCUSSION

Description of the Molecule.—The structure of the molecule is shown in c axis projection in Figure 2.[10] The relative stereochemistry suggested by Grove [1b] has been confirmed. Tables 5(a) and 6 detail the intramolecular bonded distances and valence angles, together with their estimated standard deviations. The latter are probably low estimates since block-diagonal least-squares refinement was used to optimise the parameters.

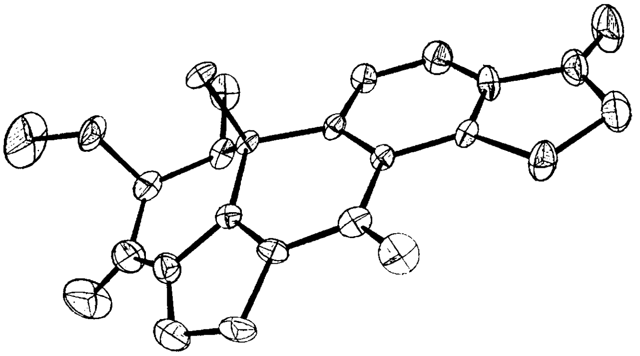

FIGURE 2 The c axis projection of a single molecule of viridin. The thermal ellipsoids are scaled to include 50% probability

The various types of bonds present in the molecule can be classified in a straightforward manner as shown in Table 5(b). The bond lengths show no significant deviations from their accepted values.[11]

Many of the conformational features of the viridin molecule are due to the strain induced by the unique

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* For details of Supplementary Publications see Notice to Authors No. 7 in *J. Chem. Soc.* (*A*), 1970, No. 20.

[10] C. K. Johnson, ORTEP, A Thermal Ellipsoid Plotting Program, ORNL 3794, Oak Ridge National Laboratory, 1965.

[11] *Chem. Soc. Special Publ.*, No. 18, 1965.

unsaturated ring E, on the A and B rings. Ring A is buckled and the most difficult to describe. Ring B is a slightly flattened boat, with both bow and stern deflected β to the main plane of the molecule. Ring C is benzenoid and ring D is flat and essentially co-planar with C. Ring E is also flat.

Table 5

(*a*) Intramolecular bonded distances (Å) and their estimated standard deviations in parentheses

C(1)–C(2)	1·527(10)	C(8)–C(9)	1·402(9)
C(1)–C(10)	1·554(9)	C(8)–C(14)	1·424(8)
C(1)–O(19)	1·417(9)	C(9)–C(10)	1·538(8)
C(2)–C(3)	1·518(11)	C(9)–C(11)	1·409(10)
C(2)–O(20)	1·443(8)	C(10)–C(18)	1·548(9)
C(3)–C(4)	1·441(12)	C(11)–C(12)	1·374(10)
C(3)–O(22)	1·213(10)	C(12)–C(13)	1·387(11)
C(4)–C(5)	1·427(9)	C(13)–C(14)	1·393(10)
C(4)–C(23)	1·376(12)	C(13)–C(17)	1·478(10)
C(5)–C(6)	1·348(9)	C(14)–C(15)	1·500(10)
C(5)–C(10)	1·490(9)	C(15)–C(16)	1·533(11)
C(5)–C(7)	1·444(9)	C(16)–C(17)	1·510(12)
C(6)–O(24)	1·398(8)	C(17)–O(26)	1·218(10)
C(7)–C(8)	1·491(9)	O(20)–C(21)	1·448(13)
C(7)–O(25)	1·229(9)	C(23)–O(24)	1·368(10)

(*b*) Bond group assignments

(i) C–C bonds

sp^3–sp^3	C(1)–C(2)	1·537	⟨1·543(8)⟩
	C(1)–C(10)	1·554	
	C(10)–C(18)	1·538	
	C(15)–C(16)	1·533	
sp^3–sp^2	C(2)–C(3)	1·518	⟨1·511(16)⟩
	C(5)–C(10)	1·490	
	C(16)–C(17)	1·510	
	C(14)–C(15)	1·500	
	C(9)–C(10)	1·538	
sp^2–sp^2 (Non-aromatic and non-double bond)			
	C(3)–C(4)	1·441	⟨1·437(7)⟩
	C(4)–C(5)	1·427	
	C(6)–C(7)	1·444	
sp^2–sp^2			
(External to aromatic ring)	C(7)–C(8)	1·491	⟨1·485(7)⟩
	C(13)–C(17)	1·478	
(Aromatic ring)	C(8)–C(9)	1·402	⟨1·398(16)⟩
	C(9)–C(11)	1·409	
	C(11)–C(12)	1·374	
	C(12)–C(13)	1·387	
	C(13)–C(14)	1·393	
	C(14)–C(8)	1·424	
(True double bond)	C(4)–C(23)	1·376	⟨1·362(14)⟩
	C(5)–C(6)	1·348	

(ii) C–O Bonds

sp^2–sp^2 (Carbonyl)	C(3)–O(22)	1·213	⟨1·220(7)⟩
	C(7)–O(25)	1·229	
	C(17)–O(26)	1·218	
sp^2–sp^2	C(6)–O(24)	1·398	⟨1·383(15)⟩
	C(23)–O(24)	1·368	
sp^3–sp^3	* C(1)–O(19)	1·417	⟨1·445(3)⟩
	C(2)–O(20)	1·448	
	C(21)–O(20)	1·443	

* Excluded from averaging considerations as it is involved in a hydrogen bond.

Ring C has typical benzenoid bond regularity and

Table 6

Valence angles (deg.) in the asymmetric unit, with their estimated standard deviations in parentheses

C(2)–C(1)–C(10)	114·8(6)	C(2)–O(20)–C(21)	114·2(7)
C(2)–C(1)–O(19)	108·9(5)	C(4)–C(23)–O(24)	111·7(6)
C(10)–C(1)–O(19)	112·6(5)	C(6)–O(24)–C(23)	105·1(6)
C(1)–C(2)–C(3)	117·1(6)	C(7)–C(8)–C(9)	123·7(5)
C(1)–C(2)–O(20)	106·8(6)	C(7)–C(8)–C(14)	117·9(6)
C(3)–C(2)–O(20)	107·9(6)	C(9)–C(8)–C(14)	118·3(6)
C(2)–C(3)–C(4)	113·8(6)	C(8)–C(9)–C(10)	120·9(6)
C(2)–C(3)–O(22)	121·4(8)	C(8)–C(9)–C(11)	120·6(6)
C(4)–C(3)–O(22)	124·8(8)	C(10)–C(9)–C(11)	118·3(5)
C(3)–C(4)–C(5)	121·3(7)	C(1)–C(10)–C(5)	105·3(5)
C(3)–C(4)–C(23)	132·3(7)	C(1)–C(10)–C(9)	115·7(5)
C(5)–C(4)–C(23)	105·1(6)	C(1)–C(10)–C(18)	112·1(5)
C(4)–C(5)–C(6)	107·7(6)	C(5)–C(10)–C(9)	108·6(5)
C(4)–C(5)–C(10)	128·1(6)	C(5)–C(10)–C(18)	108·3(5)
C(6)–C(5)–C(10)	124·2(5)	C(9)–C(10)–C(18)	106·6(5)
C(5)–C(6)–C(7)	125·6(6)	C(9)–C(11)–C(12)	121·3(7)
C(5)–C(6)–O(24)	110·4(5)	C(11)–C(12)–C(13)	118·0(7)
C(7)–C(6)–O(24)	123·8(6)	C(12)–C(13)–C(14)	123·3(6)
C(6)–C(7)–C(8)	111·4(6)	C(12)–C(13)–C(17)	127·5(7)
C(6)–C(7)–O(25)	123·1(6)	C(14)–C(13)–C(17)	109·2(6)
C(8)–C(7)–O(25)	125·4(6)	C(8)–C(14)–C(13)	118·6(6)
C(15)–C(16)–C(17)	106·2(6)	C(8)–C(14)–C(15)	129·7(6)
C(13)–C(17)–C(16)	107·9(6)	C(13)–C(14)–C(15)	111·7(6)
C(13)–C(17)–O(26)	125·3(8)	C(14)–C(15)–C(16)	104·9(6)
C(16)–C(17)–O(26)	126·9(7)		

Table 7

(*a*) Equations of the least-squares planes in the form $lx + my + nz = p$, where x, y, and z are expressed in fractional co-ordinates, and p in Å

		l	m	n	p
Plane (*A*1):	C(2), C(3), C(5), C(10)	12·78	−2·55	3·63	6·72
Plane (*A*2):	C(2)—(4), O(22)	13·51	−1·88	3·31	7·18
Plane (*A*3):	C(2)—(5), C(10)	12·91	−2·94	3·51	6·78
Plane (*B*1):	C(5), C(6), C(8), C(9)	10·18	−7·30	3·89	5·42
Plane (*B*2):	C(6)—(8), O(25)	11·43	−7·32	3·36	5·68
Plane (*C*):	C(8), C(9), C(11)—(14)	9·34	−9·28	3·58	5·22
Plane (*CD*):	C(8), C(9), C(11)—(17)	9·27	−9·26	3·61	5·20
Plane (*D*1):	C(13)—(17)	9·22	−9·23	3·64	5·19
Plane (*D*2):	C(13)—(17), O(26)	9·20	−9·29	3·62	5·19
Plane (*D*3):	C(13), C(14), C(17), O(26)	9·20	−9·36	3·60	5·20
Plane (*E*):	C(4)—(6), C(23), O(24)	11·53	−3·63	4·09	6·20

(*b*) Deviations (Å) of relevant atoms from the planes

Plane (*A*1): C(1) −0·571, C(2) −0·005, C(3) 0·005, C(4) 0·110, C(5) −0·005, C(6) −0·183, C(9) −0·780, C(10) 0·005, C(18) 1·146, O(19) −0·434, O(22) −0·075, C(23) 0·054, O(24) −0·104

Plane (*A*2): C(2) 0·000, C(3) 0·002, C(4) 0·000, O(22) −0·001

Plane (*A*3): C(1) −0·540, C(2) 0·008, C(3) −0·031, C(4) 0·050, C(5) −0·043, C(10) 0·016

Plane (*B*1): C(1) −0·535, C(4) −0·358, C(5) 0·007, C(6) −0·008, C(7) 0·108, C(8) 0·007, C(9) −0·007, C(10) 0·304, C(11) −0·185, C(14) −0·153, C(18) 1·182, C(23) −0·509, O(24) −0·283, O(25) 0·233

Plane (*B*2): C(6) −0·003, C(7) 0·011, C(8) −0·003, O(25) −0·004

Plane (*C*): C(1) −0·708, C(5) 0·336, C(6) 0·363, C(7) 0·091, C(8) −0·004, C(9) 0·000, C(10) −0·136, C(11) 0·004, C(12) −0·004, C(13) 0·000, C(14) 0·004, C(15) 0·048, C(16) 0·006, C(17) 0·017, O(25) 0·013, O(26) −0·017

Plane (*CD*): C(7) −0·075, C(8) 0·004, C(9) 0·000, C(10) 0·132, C(11) −0·003, C(12) −0·007, C(13) 0·006, C(14) 0·017, C(15) −0·026, C(16) 0·015, C(17) −0·006, O(26) −0·009

Plane (*D*1): C(8) −0·001, C(12) 0·023, C(13) 0·002, C(14) −0·015, C(15) 0·020, C(16) −0·019, C(17) 0·011, O(26) 0·018

Plane (*D*2): C(13) 0·000, C(14) −0·012, C(15) 0·023, (C16) −0·022, C(17) 0·005, O(26) 0·006

Plane (*D*3): C(13) 0·001, C(14) −0·002, C(15) 0·037, C(16) −0·016, C(17) 0·003, O(26) −0·002

Plane (*E*): C(1) −0·712, C(2) −0·303, C(3) −0·284, C(4) −0·011, C(5) 0·019, C(6) −0·020, C(7) −0·207, C(8) −0·594, C(9) −0·589, C(10) 0·034, O(22) −0·489, C(23) −0·001, O(24) 0·013, O(25) −0·094 planarity (Table 7 and Figure 3). However, substituents C(7) and C(10) are bent well out of the ring plane, the former in the α and the latter in the β direction. This is doubtless a consequence of the strain induced by the ABE ring fusions.

Ring D is of some interest; from its bond lengths and angles, it is formally almost a cyclopentanone. The sp^2 hybrid orbitals at C(13) and C(14) cause the angles C(14)–C(13)–C(17) (109·2°) and C(13)–C(14)–C(15) (111·7°) to deviate markedly from the corresponding angles of 99 and 104° for the normal steroidal cyclopentane ring D, in androsterone.[12] Ring D is almost, but not quite, planar. Planes (*CD*) and (*D*3) in Table 7 show that is slightly envelope in conformation, with C(15) displaced 0·037 Å ($>3\sigma$) from the plane of the four-atom conjugated system C(14)–C(13)–C(17)–O(26) for plane (*D*3). The only other ring-C benzenoid steroids whose crystal structures have been determined,[5b,13] have sp^3 hybridisation at C(17); ring D is then in effect a cyclopentene and the predicted envelope conformation with C(16) as flap was indeed found. One might have expected ring D in viridin to be flat, as is the situation in the alkaloid actumine,[14] with a planar cyclopentenone ring. Bromogeigerin acetate,[15] on the other hand, has the carbon which is analogous to C(16) here, displaced more than 0·3 Å from the plane of the ring. But the cyclopentenone is there fused to a cycloheptane chair at the equivalents of C(14) and C(15), *i.e.* it is not fused across a double bond, and thus does not have the rather severe steric constraints imposed on it that are important in the viridin situation. So, it might reasonably be expected that ring D (and indeed the C–D ring system) would be essentially flat. The slight perturbation of C(15) is perhaps due to its proximity to O(25); their distance apart is 2·836 Å, which is less than their van der Waals contact distance of 3·0 Å.[16]

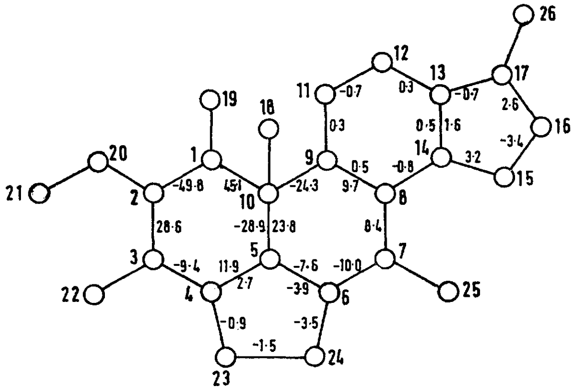

FIGURE 3 Dihedral angles (deg.) in the viridin molecule. The angle quoted is that required to rotate the projection of bond 1 → 2 to coincide with that of bond 3 → 4, when looking down the 2 → 3 bond. A positive sign denotes clockwise rotation

Ring B shows considerable deviations from the usual geometry of a cyclohexadienone. Thus C(5), C(6), C(8), and C(9) are closely coplanar [plane (*B*1) of Table 7], whilst C(7) and C(10) are displaced 0·108 Å and 0·304 Å respectively from this plane. The ring can best be described as a slightly flattened boat with both prow and stern β oriented. As expected, the C(10) and C(18) displacements are considerably larger since C(7) and O(25) are conjugated with both rings C and E. This contrasts with the cyclohexadiene system in, for example, 2-bromo-β-santonin,[17] which has all six ring atoms reasonably coplanar. Steric considerations probably play a major role in the case of viridin, with angular strain at the ABE ring junctions producing a situation in which ring B is forced to pucker and adopt a boat shape, as attempts at constructing a model of the molecule have shown.

The furan system (ring E) shows no significant deviations from the expected geometry. It is planar within experimental error [plane (*E*), Table 7] and its bond lengths and angles accord well with the values found for furan itself by microwave methods [18] and for several natural products incorporating a furan ring,[19] as well as furan-αα′-dicarboxylic acid.[20] There is, however, substantial non-planarity of the ring substituents, especially C(3) and C(7).

The crystal structures of a number of steroids with a cyclohex-2-en-1-one type ring A have recently been determined. Both in 6β-bromoprogesterone [21] and 17β-acetoxy-6β,7β-methyleneandrost-4-en-3-one [22] a five-atom coplanar arrangement is found, with C(1) out of the plane. The general trend seems to be planarity, or near-planarity for at least the conjugated system in the ring.[23-25] Braun *et al.*[22] term this ring shape the ' sofa ' conformation. Plane (*A*3) in Table 7 shows clearly that this conformation is only roughly approximated to in viridin. Table 8 compares the ring A dihedral angles here with those in several steroids. There is obviously not much in common between the conformations in these rings. Perhaps the most significant differences between viridin and the others are in the values for the bonds around atom C(4). This is not surprising since it re-

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TABLE 8

The dihedral angles (in degrees) about the bonds (in ring A), subtended in each case by the two adjacent ring bonds. For sign convention, see Figure 3

	C(1)–C(2)	C(2)–C(3)	C(3)–C(4)	C(4)–C(5)	C(5)–C(10)	C(10)–C(1)
Viridin	−49·8	28·6	−9·4	11·9	−28·9	45·1
6β-Bromoprogesterone [a]	−50·7	21·9	3·7	0·7	−28·7	52·6
Testosterone [b]	−58	31	2	−12	−13	49
12α-Bromo-11β-hydroxyprogesterone [c]	−53·9	39·4	−15·2	2·0	−12·1	39·6
4-Chlorocortisone [d]	−53·2	25·4	−0·3	4·0	−31·0	54·8

[a] Ref. 21. [b] Ref. 23. [c] Ref. 24. [d] Ref. 25.

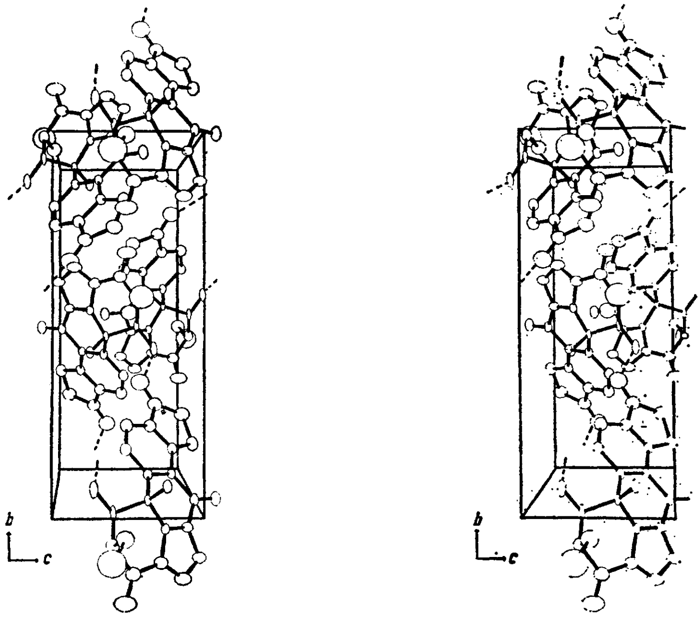

FIGURE 4 A stereodiagram of the unit-cell contents viewed along the *a* axis. Dashed lines represent hydrogen bonds

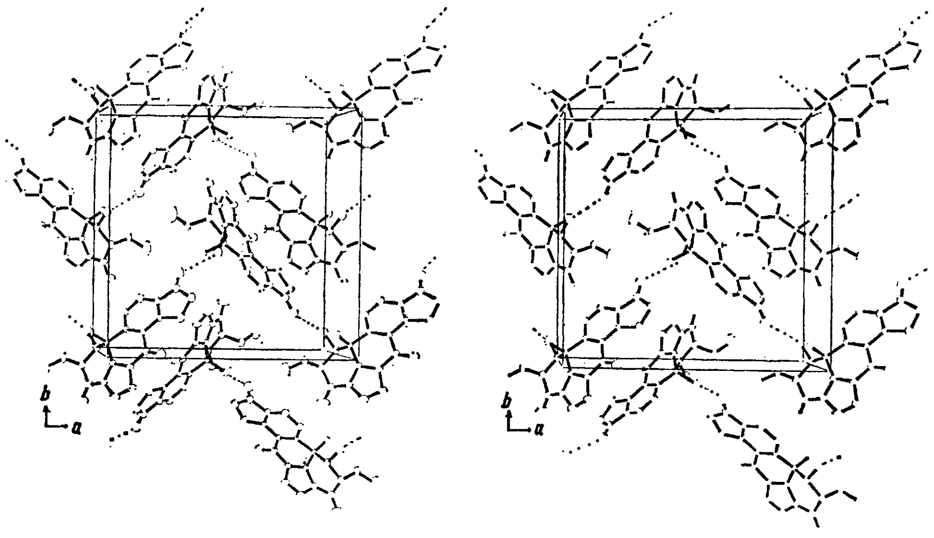

FIGURE 5 A stereodiagram of the unit-cell contents viewed along the *c* axis. Dashed lines represent hydrogen bonds

flects the increased strain caused by the fusion to ring E. As mentioned before, this strain has given rise to several non-planar sp^2-hybrids. Perhaps the best representation of ring A is to consider it as a distorted chair cyclohexenone [plane (*A*1)], with C(1) and C(4) respectively α and β to the plane.

Intermolecular Distances and Packing.—The (100) and (001) projections of the crystal structure are shown in Figures 4 and 5. The intermolecular contact O(19) ··· O(26) of 2·86 Å corresponds to a hydrogen bond of the O–H ··· O type.[16] The other intermolecular distances are all unexceptional; they are all greater than the sum of the van der Waals radii for the atoms involved. The structure may be considered to consist of infinite chains of molecules linked by the single hydrogen bond, spiralling round two of the *a* axis screws. The chains are packed together in a zig-zag arrangement.

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