

## The Crystal and Molecular Structure of Flourensadiol, a Natural Product Sesquiterpene Isolated from a West Texas Shrub

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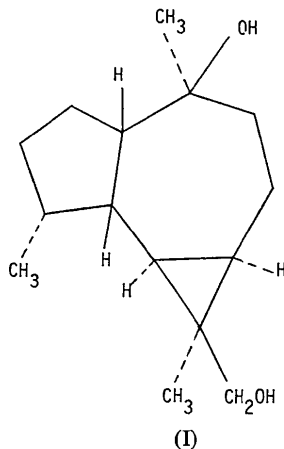
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Flourensadiol,  $C_{15}H_{26}O_2$ , is a newly discovered aromadendrane sesquiterpene isolated from the common western shrub *Flourensia cernua*. The compound crystallizes in space group  $P2_12_12_1$  with  $a = 8.401$  (4),  $b = 16.318$  (3),  $c = 20.251$  (4) Å and  $Z = 8$ . The structure was solved by direct-phasing methods and refined by block-diagonal least-squares calculations to a weighted  $R$  value of 0.077 and an unweighted  $R$  value of 0.078. The basic skeletal structure of flourensadiol was found to be tricyclic, consisting of a cyclopropane ring fused to a hydroazulene moiety. The two independent molecules in the asymmetric unit are virtually identical except for the orientation of a hydroxymethyl group. A network of hydrogen bonding is observed in the molecular packing arrangement.

### Introduction

Flourensadiol (I) is a member of the rare class of aromadendrane sesquiterpenes (Devon & Scott, 1972).



It was isolated from the plant *Flourensia cernua*, a sample of which was collected near Alpine, Texas, in March, 1968. Elemental analysis gave results consistent with the composition  $C_{15}H_{26}O_2$ . Spectroscopic and chemical derivative analyses were not conclusive in establishing the molecular structure. For this purpose an X-ray analysis was undertaken. Chemical details of flourensadiol have been presented elsewhere (Kingston, Rao, Spittler, Petersen & Cullen, 1975).

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### Experimental

Cell data are summarized in Table 1. The cell dimensions were determined by least-squares calculations, minimizing the differences between observed and calculated  $2\theta$  values of 18 reflections measured on a Daxex-Syntex automated diffractometer. For these measurements and the subsequent intensity measurements, Mo  $K\alpha$  radiation ( $\lambda = 0.71069$  Å) monochromatized by pyrolytic graphite was employed. The ambient temperature was 18°C. The density was measured by the flotation method in an aqueous zinc nitrate solution. Comparison with the calculated density indicated eight molecules per unit cell, or two crystallographically independent molecules in the asymmetric unit.

Table 1. Crystal data

$C_{15}H_{26}O_2$	F.W. 238.4
Space group $P2_12_12_1$	Systematic absences:
$a = 8.401$ (4) Å	$h00: h = 2n + 1$
$b = 16.318$ (3)	$0k0: k = 2n + 1$
$c = 20.251$ (4)	$00l: l = 2n + 1$
$V = 2776$ Å <sup>3</sup>	$Z = 8$
$\mu = 0.79$ cm <sup>-1</sup> (Mo $K\alpha$ radiation)	$D_c = 1.139$ g cm <sup>-3</sup>
Crystal shape: hexagonal plates	$D_m = 1.14$ g cm <sup>-3</sup>
Crystal size: $0.73 \times 0.62 \times 0.31$ mm	

The intensity data were collected by the  $\theta$ - $2\theta$  scan method, monitoring the intensity scale by remeasuring a group of five standard reflections periodically. The intensities of all reflections were corrected by a factor calculated from the weighted mean of the intensities of the check reflections. The maximum correction was 4%.

The intensities were also corrected for coincidence using the method of Sletten, Sletten & Jensen (1969) ( $\tau = 1.35 \times 10^{-6}$  counts $^{-1}$ ). The small linear absorption coefficient indicated absorption effects could be neglected. A total of 2768 independent reflections was measured out to a  $\sin \theta/\lambda$  of 0.595 or  $25^\circ$  in  $\theta$ . The scan rate was  $4^\circ \text{ min}^{-1}$ , while the scan range was  $2.5^\circ$  for those reflections with  $2\theta \leq 40^\circ$ , and  $2.75^\circ$  for those with  $2\theta > 40^\circ$ . Backgrounds were measured for half the scan time at each end of the scan range. The standard deviation of the intensities,  $\sigma_I$ , was defined in terms of the statistical variances of the counts as  $\sigma_I^2 = \sigma_I^2(\text{count}) + K^2[S + B1 + B2]^2$  where  $S$ ,  $B1$  and  $B2$  are the observed counts for the scan and two backgrounds respectively.  $\sigma_I(\text{count})$  is the standard deviation derived purely from counting statistics. A value of 0.015, which was determined empirically, was used for  $K$ . A total of 1516 reflections had  $I \geq 3\sigma_I$  and were used in the analysis. Structure factors were calculated in the usual way assuming an ideally imperfect monochromator for the polarization correction.

### Structure determination and refinement

Normalized structure factors were computed using the program *FAME*, a modified version of Dewar & Stone's (1969) program for Wilson statistics and calculation of  $E$ 's. The 293 normalized structure amplitudes with  $|E| \geq 1.55$  were used in the phasing program *MULTAN* (Germain, Main & Woolfson, 1971). The three origin-determining reflections and that defining the enantiomorph were chosen manually on the basis of criteria suggested by Karle & Hauptman (1956) for space group  $P2_12_12_1$ . Three other reflections were also chosen manually on the basis of their high  $|E|$  values and numerous triplet interactions. Of these three, the two general reflections (682 and 593) were allowed to take on values of  $\pm\pi/4$  and  $\pm 3\pi/4$ , while the 081 reflection was assigned phases of 0 and  $\pi$ . This generated 32 possible starting sets for the tangent refinement. The phases for the starting set which gave the highest absolute figure of merit (1.18), as defined by Germain, Main & Woolfson (1971), were as follows:

$h$	$k$	$l$	$ E $	$\phi$	
0	3	12	3.20	$\pi/2$	} (origin-defining)
1	6	0	2.92	$\pi/2$	
6	0	3	2.46	$\pi/2$	
5	7	0	3.07	$\pi/2$	(enantiomorph-defining)
6	8	2	3.30	$-3\pi/4$	
5	9	3	3.24	$-3\pi/4$	
0	8	1	2.06	0	

This starting set proved to be the correct solution. 28 of the 34 nonhydrogen atoms in the asymmetric unit were located on the corresponding  $E$  map. The remaining six atoms were located from a subsequent  $F_o$  Fourier synthesis.

The structure was refined by block-diagonal least-squares calculations. The function minimized was

$\sum w(F_o - F_c)^2$ . Isotropic temperature factors were used throughout. The limited number of data precluded anisotropic refinement. Initially all reflections were assigned equal weights, but in the later stages of refinement a weighting factor,  $w$ , of  $1/\sigma_F^2$  was introduced. The scattering contribution from hydrogen was included in the final cycles of refinement by introducing calculated positions and isotropic  $B$ 's of 4.5 for each of the 52 hydrogen atoms. The C-H and O-H distances were fixed at 1.00 Å and the C-C-H and C-O-H angles fixed at 109.57 and 105.0° respectively. Terminal methyl group hydrogen atoms were calculated to be in a staggered configuration. Three staggered positions are possible for the hydrogen atom of the tertiary hydroxyl group [O(1) and O(101)]. For each molecule in this case, one of the three calculated hydroxyl hydrogen positions was observed to correspond to a region of positive electron density in a difference Fourier map and this calculated position was selected as the correct hydrogen atom position. None of the hydrogen atom parameters were allowed to vary in the refinement.

The final  $R$  value defined as  $\sum |F_o - |F_c|| / \sum F_o$  was 0.078, while the weighted  $R$  value, defined as  $[\sum w|F_o - |F_c||^2 / \sum wF_o^2]^{1/2}$  was 0.077.\* In the final cycles of refinement, all parameter shifts were less than one standard deviation, most being of the order of 0.1 $\sigma$ . The error in an observation of unit weight, defined as  $[\sum w|F_o - |F_c||^2 / (M - S)]^{1/2}$  was 3.32.  $M$  is the number of observations (1516) and  $S$  is the number of variables (197). A final difference map showed a maximum electron density of 0.5 e Å $^{-3}$ .

No evidence of secondary extinction was found. No correction for anomalous dispersion was applied. Scattering factors for neutral atoms were from *International Tables for X-ray Crystallography* (1974). The final positional and thermal parameters are given in Table 2. A list of the observed and calculated structure factors and a list of the coordinates of the calculated hydrogen-atom positions are available.†

### Results and discussion

The structural solution shows the molecule to be tricyclic, consisting of three- and five-membered rings fused to a seven-membered ring. A perspective *ORTEP* drawing (Johnson, 1965) of the two independent molecules is shown in Fig. 1. The two molecules are seen to be identical except for the orientation of the hydroxyl group O(2) and O(102). This orientation difference can be attributed to the hydrogen-bonding scheme

\* At the suggestion of a referee, the  $R$  value was computed for all reflections, including those with  $I < 3\sigma_I$ . This value for  $R$  unweighted is 0.134, and for  $R$  weighted, 0.081.

† These tables have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 30836 (21 pp., 1 microfiche). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England. The structure-factor table includes all of the reflections (2768).

Table 2. Fractional coordinates ( $\times 10^4$ ) and thermal parameters for flourensadiol

Estimated standard deviations are given in parentheses.

	<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i>
C(1)	4549 (10)	4453 (4)	1527 (4)	3.2 (1)
C(2)	6144 (10)	4849 (4)	1346 (3)	3.0 (1)
C(3)	6750 (10)	4769 (4)	636 (4)	3.6 (2)
C(4)	8218 (11)	5332 (5)	593 (4)	4.2 (2)
C(5)	8184 (10)	5847 (4)	1243 (4)	3.6 (2)
C(6)	6457 (9)	5773 (4)	1476 (3)	2.5 (1)
C(7)	5434 (10)	6342 (4)	1065 (3)	2.5 (1)
C(8)	4658 (10)	7122 (4)	1330 (3)	3.0 (1)
C(9)	3648 (10)	6389 (4)	1137 (4)	3.1 (1)
C(10)	2899 (10)	5785 (4)	1617 (4)	3.4 (2)
C(11)	3041 (10)	4912 (5)	1331 (4)	4.0 (2)
C(12)	4477 (12)	3597 (5)	1243 (4)	5.0 (2)
C(13)	8839 (12)	6720 (5)	1151 (4)	4.8 (2)
C(14)	4629 (12)	7835 (5)	842 (4)	4.6 (2)
C(15)	4865 (10)	7374 (5)	2039 (4)	4.0 (2)
O(1)	4447 (7)	4392 (3)	2249 (2)	3.9 (1)
O(2)	3684 (7)	7966 (3)	2231 (2)	4.1 (1)
C(101)	411 (11)	7279 (4)	3408 (4)	3.2 (1)
C(102)	1893 (10)	6825 (4)	3660 (4)	3.3 (2)
C(103)	2356 (11)	6906 (5)	4388 (4)	4.1 (2)
C(104)	3786 (11)	6300 (5)	4477 (4)	4.4 (2)
C(105)	3892 (10)	5802 (5)	3829 (4)	3.7 (2)
C(106)	2219 (10)	5900 (4)	3522 (4)	2.8 (1)
C(107)	1039 (10)	5336 (4)	3880 (3)	3.0 (1)
C(108)	197 (10)	4602 (4)	3581 (4)	3.1 (1)
C(109)	-737 (10)	5369 (4)	3745 (3)	3.2 (1)
C(110)	-1346 (11)	5980 (4)	3249 (4)	3.5 (2)
C(111)	-1185 (11)	6866 (4)	3532 (4)	3.7 (2)
C(112)	361 (12)	8141 (5)	3693 (4)	4.7 (2)
C(113)	4488 (12)	4933 (5)	3926 (4)	4.6 (2)
C(114)	-23 (11)	3856 (5)	4021 (4)	4.3 (2)
C(115)	371 (11)	4386 (5)	2849 (4)	3.3 (1)
O(101)	663 (7)	7353 (3)	2693 (2)	3.8 (1)
O(102)	1543 (7)	3748 (3)	2763 (2)	4.0 (1)

which is referred to below. The structure as determined was unpredicted. The structural details are not unusual. Bond lengths and angles with standard deviations are listed in Table 3. Pertinent torsion angles are given in Table 4. To conserve space in both of these tables, the atom labels are listed only for molecule 1 (Fig. 1). The corresponding labels for molecule 2 can be obtained by adding 100 to each of them.

The molecules are connected in the crystalline lattice by a network of hydrogen bonds as illustrated in Fig. 2. There are no other intermolecular contact distances less than 3.50 Å. By inspection of the coordinates in Table 2, it can be seen that the two independent molecules are related by pseudosymmetry. The operations

required roughly to superimpose the first molecule onto the second (with the exception of the secondary hydroxyl group) are mirror planes at approximately  $z = 0.25$  and  $y = 0.585$  and a translation along  $x$  of 0.435

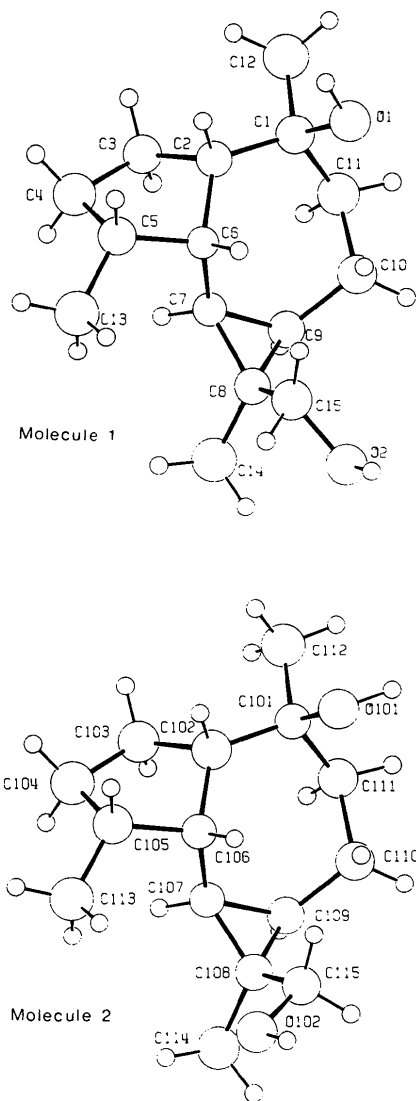


Fig. 1. A perspective view of the two crystallographically independent molecules of flourensadiol.

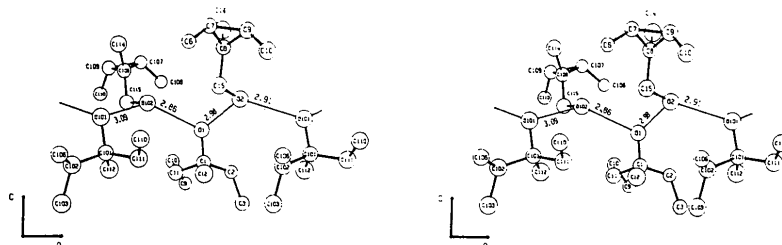


Fig. 2. A stereographic view of the hydrogen-bonding scheme for flourensadiol.

Table 3. Bond lengths (Å) and valency angles (°) with estimated standard errors in parentheses

To conserve space, the atom labels are listed only for molecule 1 (see Fig. 1). To obtain the corresponding atom labels for molecule 2, add 100 to the number index of each label.

	Molecule 1	Molecule 2
C(1)—C(2)	1.53 (1)	1.54 (1)
C(1)—C(11)	1.52 (1)	1.52 (1)
C(1)—C(12)	1.51 (1)	1.52 (1)
C(1)—O(1)	1.47 (1)	1.47 (1)
C(2)—C(3)	1.53 (1)	1.53 (1)
C(2)—C(6)	1.55 (1)	1.56 (1)
C(3)—C(4)	1.54 (1)	1.57 (1)
C(4)—C(5)	1.56 (1)	1.55 (1)
C(5)—C(6)	1.54 (1)	1.55 (1)
C(5)—C(13)	1.56 (1)	1.52 (1)
C(6)—C(7)	1.51 (1)	1.53 (1)
C(7)—C(8)	1.53 (1)	1.52 (1)
C(7)—C(9)	1.51 (1)	1.52 (1)
C(8)—C(9)	1.52 (1)	1.51 (1)
C(8)—C(14)	1.53 (1)	1.52 (1)
C(8)—C(15)	1.50 (1)	1.53 (1)
C(9)—C(10)	1.52 (1)	1.50 (1)
C(10)—C(11)	1.54 (1)	1.56 (1)
C(15)—O(2)	1.44 (1)	1.44 (1)
C(2)—C(1)—C(11)	117.2 (7)	116.5 (7)
C(2)—C(1)—C(12)	109.5 (7)	110.0 (7)
C(2)—C(1)—O(1)	108.5 (7)	104.5 (7)
C(11)—C(1)—C(12)	108.7 (7)	108.8 (7)
C(11)—C(1)—O(1)	104.2 (7)	109.0 (7)
C(12)—C(1)—O(1)	108.3 (6)	107.6 (6)
C(1)—C(2)—C(3)	118.7 (7)	118.7 (7)
C(1)—C(2)—C(6)	121.1 (7)	123.3 (7)
C(3)—C(2)—C(6)	100.7 (6)	102.2 (6)
C(2)—C(3)—C(4)	105.5 (7)	104.5 (7)
C(3)—C(4)—C(5)	105.1 (7)	106.2 (7)
C(4)—C(5)—C(6)	103.6 (7)	103.5 (7)
C(4)—C(5)—C(13)	113.0 (7)	113.6 (7)
C(6)—C(5)—C(13)	116.7 (7)	116.7 (7)
C(2)—C(6)—C(5)	100.6 (6)	100.8 (6)
C(2)—C(6)—C(7)	113.9 (6)	112.5 (7)
C(5)—C(6)—C(7)	108.6 (6)	109.6 (7)
C(6)—C(7)—C(8)	124.0 (7)	125.9 (7)
C(6)—C(7)—C(9)	122.8 (7)	121.9 (7)
C(8)—C(7)—C(9)	59.9 (5)	59.9 (5)
C(7)—C(8)—C(9)	59.4 (5)	60.1 (5)
C(7)—C(8)—C(14)	114.4 (7)	117.1 (7)
C(7)—C(8)—C(15)	120.9 (7)	121.5 (7)
C(9)—C(8)—C(14)	115.2 (7)	118.1 (7)
C(9)—C(8)—C(15)	121.7 (7)	116.8 (7)
C(14)—C(8)—C(15)	114.3 (7)	113.3 (7)
C(7)—C(9)—C(8)	60.7 (5)	60.0 (5)
C(7)—C(9)—C(10)	116.1 (7)	118.6 (7)
C(8)—C(9)—C(10)	125.3 (7)	125.3 (7)
C(9)—C(10)—C(11)	109.1 (7)	109.9 (7)
C(1)—C(11)—C(10)	114.9 (7)	115.2 (7)
C(8)—C(15)—O(2)	111.2 (7)	110.3 (7)

of a unit cell. No significance is attached to this fact. Note that the molecules retain the same relative configuration throughout the lattice.

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Table 4. Pertinent torsion angles for flourensadiol (°)

The torsion angle  $W(IJKL)$  is defined as the angle between the vector  $\vec{JI}$  and the vector  $\vec{KL}$  when viewed along  $\vec{JK}$ . The sign of  $W$  is positive if  $\vec{JI}$  is to be rotated clockwise into  $\vec{KL}$  and negative if anticlockwise. To conserve space, the atom labels are listed only for molecule 1 (see Fig. 1). To obtain the corresponding atom labels for molecule 2, add 100 to the number index of each label.

	Molecule 1	Molecule 2
Seven-membered ring		
C(11)—C(1)—C(2)—C(6)	46	49
C(1)—C(2)—C(6)—C(7)	-66	-68
C(2)—C(6)—C(7)—C(9)	65	61
C(6)—C(7)—C(9)—C(10)	-4	-1
C(7)—C(9)—C(10)—C(11)	-69	-70
C(9)—C(10)—C(11)—C(1)	90	87
C(10)—C(11)—C(1)—C(2)	-58	-57
Five-membered ring		
C(6)—C(2)—C(3)—C(4)	37	35
C(2)—C(3)—C(4)—C(5)	-11	-9
C(3)—C(4)—C(5)—C(6)	-20	-20
C(4)—C(5)—C(6)—C(2)	42	42
C(5)—C(6)—C(2)—C(3)	-49	-47
Three-membered ring		
C(6)—C(7)—C(8)—C(9)	-111	-109
C(6)—C(7)—C(9)—C(8)	113	116
C(10)—C(9)—C(7)—C(8)	-118	-117
Substituents		
C(12)—C(1)—C(2)—C(3)	45	43
O(1)—C(1)—C(2)—C(3)	163	158
C(12)—C(1)—C(11)—C(10)	177	178
O(1)—C(1)—C(11)—C(10)	62	61
C(3)—C(4)—C(5)—C(13)	-147	-148
C(7)—C(6)—C(5)—C(13)	47	48
C(7)—C(8)—C(15)—O(2)	-163	99
C(9)—C(8)—C(15)—O(2)	-92	168
C(14)—C(8)—C(15)—O(2)	54	-49

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