X-RAY CRYSTALLOGRAPHY OF THE SESQUITERPENE LACTONE ERIVANIN*

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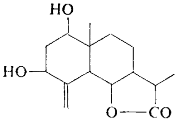
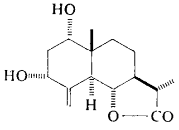
X-Ray structure analysis of the sesquiterpene lactone erivanin proved the correctness of the structure *II* proposed for this native compound earlier.

Sesquiterpene lactone erivanin (*I*) was isolated from the species *Artemisia fragrans* WILLD. var. *erivanica* BESS. (family *Compositae*, tribus *Anthemideae*) by Soviet authors who proposed[1] the structure represented by the formula *I*. Later we isolated erivanin from the species *Tanacetum balsamita* L. (family *Compositae*, tribus *Anthemideae*)[2]. On the basis of spectral evidences, especially on the basis of a detailed analysis of ^{1}H-NMR spectra of the native compound and some of its derivatives, we proposed its relative and absolute configuration represented by the formula *II*.



I



II

Now we have studied the structure of erivanin by means of the X-ray structural analysis. Its results are listed in Tables I–IV. A perspective view of the molecule and the numbering of its atoms are shown in Fig. 1.

According to our present results the molecule of erivanin contains two *trans*-fused six-membered rings, two α-oriented hydroxyl groups, one at C(1) and the second

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TABLE I

Fractional coordinates for non-hydrogen atoms (. 10^4) and for H atoms (. 10^3)

Atom	x	y	z
C(1)	6 138(6)	3 511(9)	5 998(4)
C(2)	7 441(6)	3 700(9)	5 165(4)
C(3)	8 955(6)	4 402(10)	5 786(4)
C(4)	9 360(5)	3 252(9)	6 891(4)
C(5)	8 070(5)	3 134(9)	7 738(4)
C(6)	8 379(5)	2 028(9)	8 859(3)
C(7)	7 092(5)	2 230(9)	9 688(4)
C(8)	5 608(6)	1 343(10)	9 145(5)
C(9)	5 236(5)	2 287(11)	7 938(4)
C(10)	6 576(5)	2 285(9)	7 097(4)
C(11)	7 856(5)	1 522(9)	10 866(4)
C(12)	9 495(5)	2 243(9)	10 743(4)
C(13)	7 167(6)	2 173(10)	12 002(4)
C(14)	6 870(7)	283(10)	6 642(5)
C(15)	10 727(5)	2 422(11)	7 032(4)
O(1)	5 618(4)	5 333(7)	6 339(3)
O(3)	8 684(4)	6 334(8)	6 089(3)
O(6)	9 751(3)	2 649(7)	9 611(2)
O(12)	10 485(4)	2 500[a]	11 521(3)
H(1)	510	282	558
H(2a)	694	460	444
H(2b)	754	241	481
H(3)	992	436	505
H(5)	785	455	799
H(6)	865	46	875
H(7)	663	358	982
H(8a)	584	−5	903
H(8b)	477	122	978
H(9a)	490	369	810
H(9b)	426	161	752
H(11)	794	1	1 074
H(13a)	600	204	1 210
H(13b)	792	167	1 271
H(13c)	697	371	1 203
H(14a)	631	−3	592
H(14b)	661	−68	728
H(14c)	806	15	646
H(15a)	1 107	162	776
H(15b)	1 158	263	636
H[O(1)]	667	583	667
H[O(3)]	928	663	678

[a] Fixed value.

one at C(3), one exomethylene group at C(4), one β-oriented angular methyl group at C(10) and a *trans*-annelated γ-lactone ring at C(6) and C(7) with an α-situated methyl group at C(11) in a quasi-equatorial position. It has been established that this methyl group is a subject of a smaller strain than in the quasi-axial orientation[3-6]. The present observations are in accordance with these findings.

The conformation of the molecule may be described in terms of torsion angles listed in Table IV and of asymmetry parameters given in Table V. The values of the asymmetry parameters for the ring A are low and indicate that the ring shows a good approximation to the chair conformation. Similarly the ring B has a symmetrical chair conformation but the mirror symmetry through C(6) and C(9) prevails in this case indicating a slight distortion towards a sofa conformation. Presumably this is an effect caused by the fusion with the γ-lactone ring. The γ-lactone ring adopts a conformation intermediate between the envelope type with C(7) constituting the

TABLE II

Bond lengths (Å) with estimated standard deviations in parentheses

Bond	Length	Bond	Length
C(1)—C(2)	1·513(7)	C(1)—H(1)	1·11
C(1)—C(10)	1·547(8)	O(1)—H	1·02
C(1)—O(1)	1·440(8)	C(2)—H(2a)	1·11
C(2)—C(3)	1·532(8)	C(2)—H(2b)	1·02
C(3)—C(4)	1·517(7)	C(3)—H(3)	1·21
C(3)—O(3)	1·499(9)	O(3)—H	0·93
C(4)—C(5)	1·511(6)	C(5)—H(5)	1·08
C(4)—C(15)	1·323(7)	C(6)—H(6)	1·16
C(5)—C(6)	1·502(7)	C(7)—H(7)	1·06
C(5)—C(10)	1·566(7)	C(8)—H(8a)	1·02
C(6)—C(7)	1·499(6)	C(8)—H(8b)	1·05
C(6)—O(6)	1·486(5)	C(9)—H(9a)	1·07
C(7)—C(8)	1·527(7)	C(9)—H(9b)	1·06
C(7)—C(11)	1·535(6)	C(11)—H(11)	1·10
C(8)—C(9)	1·536(8)	C(13)—H(13a)	1·02
C(9)—C(10)	1·537(6)	C(13)—H(13b)	1·06
C(10)—C(14)	1·549(9)	C(13)—H(13c)	1·11
C(11)—C(12)	1·520(7)	C(14)—H(14a)	0·95
C(11)—C(13)	1·515(7)	C(14)—H(14b)	1·03
C(12)—O(12)	1·203(5)	C(14)—H(14c)	1·07
C(12)—O(6)	1·340(5)	C(15)—H(15a)	1·03
		C(15)—H(15b)	1·10

TABLE III

Valency angles (°) with estimated standard deviations in parentheses

Segment	Angle	Segment	Angle
C(10)—C(1)—C(2)	113·0(5)	C(5)—C(6)—O(6)	114·8(4)
C(10)—C(1)—O(1)	111·6(4)	C(5)—C(10)—C(14)	111·5(4)
O(1)—C(1)—C(2)	109·8(4)	C(6)—C(7)—C(8)	110·2(4)
C(1)—C(2)—C(3)	113·1(5)	C(6)—C(7)—C(11)	102·1(4)
C(1)—C(10)—C(14)	107·4(4)	C(6)—O(6)—C(12)	107·9(4)
C(2)—C(3)—C(4)	110·3(5)	C(7)—C(8)—C(9)	107·5(5)
C(2)—C(3)—O(3)	106·0(4)	C(7)—C(11)—C(13)	117·3(4)
O(3)—C(3)—C(4)	111·0(4)	C(7)—C(11)—C(12)	99·5(4)
C(3)—C(4)—C(5)	113·9(4)	C(11)—C(12)—O(6)	111·5(4)
C(3)—C(4)—C(15)	120·3(5)	C(11)—C(12)—O(12)	127·8(5)
C(15)—C(4)—C(5)	125·8(5)	C(8)—C(9)—C(10)	114·7(5)
C(4)—C(5)—C(6)	117·3(4)	C(9)—C(10)—C(5)	110·2(4)
C(4)—C(5)—C(10)	110·4(4)	C(9)—C(10)—C(14)	110·4(4)
C(5)—C(6)—C(7)	111·7(4)	C(9)—C(10)—C(1)	109·5(4)

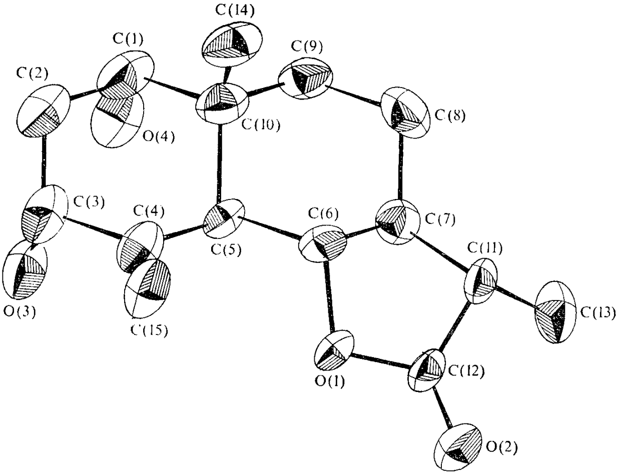

FIG. 1

Perspective view of the erivanin molecule out-of-plane atom, and the half-chair form with C(6), C(7) out of plane of the remaining atoms.

Most of the bond lengths and angles are within normal ranges. The C(sp^3) – C(sp^3) lengths range from 1·502 to 1·556 Å. The longest bonds are associated with the fully substituted C(10) atom, while the two shortest bonds involve the C(6) atom. Two C(sp^3)-O distances associated with two hydroxyl groups at C(1) and C(3) differ in length by about 0·06 Å. The significant difference in the C(sp^3)-O bond length might be connected with the different involvement of the two hydroxyl groups in hydrogen bonding (Fig. 2). The hydroxyl group at C(3) acts as a donor and as an acceptor of proton, and takes place in the formation of an intra- and intermolecular hydrogen bond. The hydroxyl group at C(1) acts only in the formation

TABLE IV

Torsion angles (°) with estimated standard deviations in parentheses

Segment	Angle	Segment	Angle
C(10)—C(1)—C(2)—C(3)	− 54·2(6)	C(11)—C(12)—O(6)—C(6)	− 6·6(5)
O(1)—C(1)—C(2)—C(3)	71·1(6)	O(12)—C(12)—O(6)—C(6)	175·1(6)
C(1)—C(2)—C(3)—C(4)	50·4(7)	C(12)—O(6)—C(6)—C(7)	29·8(5)
C(1)—C(2)—C(3)—O(3)	− 69·8(6)	C(12)—O(6)—C(6)—C(5)	151·0(5)
C(2)—C(3)—C(4)—C(5)	− 53·4(6)	C(13)—C(11)—C(7)—C(8)	− 80·0(6)
C(2)—C(3)—C(4)—C(15)	125·0(7)	O(6)—C(6)—C(7)—C(8)	−170·5(5)
C(3)—C(4)—C(5)—C(10)	58·0(5)	C(6)—C(7)—C(8)—C(9)	− 57·0(6)
C(3)—C(4)—C(5)—C(6)	−179·7(6)	C(11)—C(7)—C(8)—C(9)	−176·0(6)
C(15)—C(4)—C(5)—C(10)	−120·3(6)	C(7)—C(8)—C(9)—C(10)	52·9(6)
C(15)—C(4)—C(5)—C(6)	2·0(8)	C(8)—C(9)—C(10)—C(5)	− 53·5(6)
C(4)—C(5)—C(6)—C(7)	172·6(5)	C(8)—C(9)—C(10)—C(1)	−171·9(6)
C(4)—C(5)—C(6)—O(6)	56·8(6)	C(8)—C(9)—C(10)—C(14)	70·1(6)
C(10—C(5)—C(6)—C(7)	− 63·2(5)	C(9)—C(10)—C(5)—C(6)	55·3(6)
C(10)—C(5)—C(6)—O(6)	−179·0(5)	C(9)—C(10)—C(5)—C(4)	−176·3(6)
C(5)—C(6)—C(7)—C(8)	66·3(5)	C(1)—C(10)—C(5)—C(6)	174·8(5)
C(5)—C(6)—C(7)—C(11)	−163·5(5)	C(1)—C(10)—C(5)—C(4)	− 56·8(5)
O(6)—C(6)—C(7)—C(11)	− 40·3(5)	C(14)—C(10)—C(5)—C(6)	− 67·6(6)
C(6)—C(7)—C(11)—C(12)	35·4(5)	C(14)—C(10)—C(5)—C(4)	60·8(5)
C(6)—C(7)—C(11)—C(13)	157·1(6)	C(9)—C(10)—C(1)—O(1)	51·5(5)
C(8)—C(7)—C(11)—C(12)	158·3(5)	C(9)—C(10)—C(1)—C(2)	175·8(6)
C(8)—C(7)—C(11)—C(13)	− 80·0(6)	C(14)—C(10)—C(1)—O(1)	171·4(4)
C(7)—C(11)—C(12)—O(6)	− 18·6(6)	C(14)—C(10)—C(1)—C(2)	− 64·3(6)
C(13)—C(11)—C(12)—O(6)	−143·6(7)	C(5)—C(10)—C(1)—O(1)	− 68·4(6)
C(7)—C(11)—C(12)—O(12)	159·6(6)	C(5)—C(10)—C(1)—C(2)	55·9(6)
C(13)—C(11)—C(12)—O(12)	34·6(7)		

of an intramolecular hydrogen bond (between O(1) and O(3)). The bond distances and angles in the hydrogen bonds are listed in Table VI.

The projection of the structure along the x axis showing the hydrogen bonds is demonstrated in Fig. 2. The molecules are connected together *via* an intermolecular hydrogen bond (from the hydroxyl group O(3)H to the O(12)) of the carbonyl groups of an adjacent molecule to form the infinite chains running along the y axis.

Our present results confirm that the molecule of erivanin has the constitution and relative configuration represented by the formula *II*. The basic structural feature of crivanin, *i.e.*, the chair conformation of both *trans*-annelated six-membered homocycles and the *trans*-annelation of the γ-lactone ring closed to C(6) is relatively common in the series of eudesmanolide. The structure of erivanin including the relative configuration derived from the described X-ray analysis is in full accordance with the structure of erivanin proposed by us earlier[2].

EXPERIMENTAL

Crystal data: $C_{15}H_{22}O_4$, monoclinic. space group $P2_1$, $a = 8{\cdot}638(1)$, $b = 7{\cdot}1678(8)$, $c = 11{\cdot}267(2)$ Å, $\beta = 93{\cdot}27(1)°$, $V = 696{\cdot}5(2)$ Å^3, $D_m = 1{\cdot}24$ flotation, $D_c = 1{\cdot}27$ Mg m^{-3}, $z = 2$.

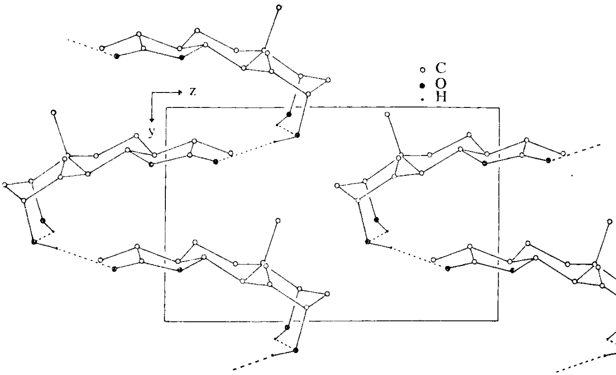

FIG. 2

Hydrogen bonds of the erivanin molecule in crystal

Suitable crystals were grown from butanol. A crystal *c.* 0·3 × 0·3 × 0·4 mm was chosen for the X-ray analysis. Preliminary cell data were obtained from oscillation and Weissenberg photographs; accurate unit-cell dimensions were obtained from a least-squares refinement of diffractometer setting angles of 15 strong reflections. Intensity data were collected to $2\Theta < 115°$ on a Syntex $P2_1$ diffractometer using graphite monochromatized CuKα radiation. 952 independent reflections were measured by $\Theta-2\Theta$ scan technique with a variable scan rate of 1·95 ÷ 29·3° $\min^{-1}$. The background and integrated intensity for each reflection were obtained by Lehmann and Larsen profile analysis method[7] (program PRAN (ref.[8]). 936 reflections were judged to be observed having $I \geqq 1{\cdot}96\sigma\ (I)$. The intensities were corrected for Lorentz and polarization effects, but the rather low absorption effects (μ(Cukα) = 0·75 mm^{-1}) were neglected. Corrections for the real and imaginary terms of the anomalous dispersion were included.

The structure was solved with MULTAN[9]. *E*-map showed the positions of all 19 non-hydrogen atoms. The structure was refined with isotropic and then anisotropic thermal parameters to an *R* value of 0·09, using a full-matrix least-squares method. Fifteen of the H atoms were located in a difference map by means of nineteen-point electron-density interpolation and calculated positions were used for the remaining seven hydrogen atoms. The H atoms were included in the refinement with fixed isotropic temperature parameter (5·0 Å^2) and fixed positional coordinatest Full-matrix least squares refinement was carried out initially with statistical weights. In the last

TABLE V

Asymmetry parameters

Ring A		Ring B		Ring C	
parametre	value	parametre	value	parametre	value
$C_2^{2.3}$	1·6	C_s^6	2·1	C_s^7	8·6
C_s^2	2·7	$C_2^{6.7}$	4·7	$C_2^{6.7}$	9·4
C_s^1	4·7	$C_2^{7.8}$	11·7	C_s^6	21·7

TABLE VI

Distances (Å) and angles (°) in the hydrogen-bonding system

D—H ... A acceptor position	D—H	H ... A	D ... A	Angle D—H ... A
O(1)—H ... O(3) $x,\quad y,\quad z$	1·02	1·93	2·774(5)	138
O(3)—H ... O(12) $2-x,\ 1/2+y,\ 2-z$	0·93	2·01	2·871(4)	152

cycles of the refinement the following weighing scheme was applied: $w = F_0^2/a^2$ if $F_0 < a$; $w = 1$ if $a \leqq F_0 \leqq b$; $w = b^2/F_0^2$ if $F_0 > b$ where $a = 2{\cdot}2$ and $b = 15{\cdot}0$. The quantity minimized in the least-squares calculations was $\sum w(F_0 - F_c)^2$. Nine of the most intense reflections were judged to suffer from extinction and were excluded from the final stages of refinement. The final R value was 0·043 for 927 reflections. All calculations were performed on a Nova minicomputer using original and locally modified Syntex XTL programs.

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