

# The Structure and Absolute Configuration of Tauremisin

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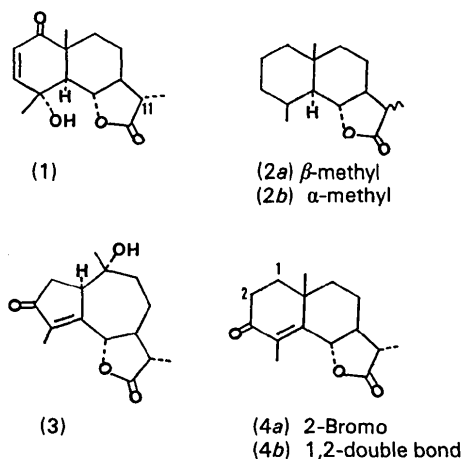
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**Abstract.**  $C_{15}H_{20}O_4$ ,  $M_r = 264.32$ , orthorhombic,  $P2_12_12_1$ ,  $a = 7.649$  (2),  $b = 9.045$  (2),  $c = 19.682$  (2) Å,  $V = 1361.5$  (3) Å<sup>3</sup>,  $Z = 4$ ,  $D_m = 1.276$ ,  $D_x = 1.289$  g cm<sup>-3</sup>,  $\lambda(\text{Cu K}\alpha) = 1.54178$  Å,  $\mu = 7.19$  cm<sup>-1</sup>,  $F(000) = 568$ ,  $T = 295$  K,  $R = 0.44$  for 1081 unique reflections with  $I > 3\sigma(I)$ . (4*S*,5*S*,6*S*,7*S*,10*R*,11*S*)-4-Hydroxyeudesman-1-one-6,12-olide has been isolated from a number of plants and has been named tauremisin, vulgarin and judaicin. The absolute configuration at C(11) has been in question, and both configurations are reported in the literature. This work shows the configuration at C(11) to be *S* and the attached methyl group is designated as  $\alpha$ . The cyclohexenone ring adopts a distorted 1,2-diplanar conformation, the cyclohexane ring a chair conformation and the five-membered lactone ring a half-chair conformation.

**Introduction.** The 11,13-dihydro sesquiterpene lactone tauremisin (1) was first isolated in 1960 (Rybalko, Bankovskij & Perelzon, 1960; Rybalko & Dolejs, 1961). The configuration of the C(11) methyl group was assigned as  $\beta$  on the basis of chemical transformations and correlation with the assigned configuration of santanolide C (2*a*) (Kovacs, Herout, Horak & Sorm, 1956). Geissman & Ellestad (1962) and Saber, Abushady & El-Antably (1964) independently isolated and reported the same compound with identical stereochemistry and named it vulgarin and judaicin, respectively. (We refer to the compound as tauremisin since this name has precedence in the literature.) The absolute configurations of a derivative of a phototransformation product of santonin, (3) (Asher & Sim, 1965), and of 2-bromo- $\alpha$ -santonin, (4) (Asher & Sim, 1962), were established by heavy-atom X-ray diffraction techniques and the C(11) methyl group was found to be  $\alpha$ . Barton, Miki, Pinhey & Wells (1962) showed that the configuration at C(11) did not change upon transformation of  $\alpha$ -santonin (4*b*) to isophotosantonin lactone (3) and also the configuration

of santolide C is that of (2*b*). <sup>13</sup>C NMR studies of eudesmanolides (Pregosin, Randall & McMurray, 1972; Moss, Pregosin & Randall, 1974) show small but consistent chemical-shift differences for the methyl group attached to C(11). When the methyl group is a  $\beta$  configuration shown for compound (1)], the chemical shifts are 12–16 p.p.m. and when  $\alpha$  the shifts are 9–10 p.p.m. Ohno, Gershenzon, Roane & Mabry (1980) report a 12.4 p.p.m. C(11) methyl chemical shift in tauremisin; however, they continued to use the  $\beta$  assignment of earlier workers. Although recent workers (Villar, Zarfa-Polo, Nicoletti & Galeffi, 1983; Gonzalez, Bermejo & Zaragoza, 1983) used the  $\alpha$  configuration for tauremisin, the latest reviews of sesquiterpene lactones (Fischer, Oliver & Fischer, 1979; Seaman, 1982) report the configuration as  $\beta$ . In order to firmly establish the stereochemistry, we report the structure of tauremisin. Since only the absolute configuration at C(11) is in question, the relative configuration is adequate to assign the absolute configuration.



**Experimental.** Tauremisin was isolated from *Artemisia ludoviciana* var. *ludoviciana* (Ohno, Gershenzon, Roane & Mabry, 1980), rectangular prism of dimensions 0.35 × 0.40 × 0.60 mm, density by flotation

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in aqueous CsCl solution, Nicolet *R3m/μ* update of a *P2<sub>1</sub>* diffractometer, data collected in the  $\omega$ -scan mode ( $4 \leq 2\theta \leq 110^\circ$ ); graphite-monochromated Cu *Kα* radiation; lattice parameters from least-squares refinement of 25 reflections ( $41.70 \leq 2\theta \leq 77.36^\circ$ ); systematic absences (*h*00; 0*k*0; 00*l*; *h*, *k*, or *l* = 2*n* + 1) and Laue symmetry *mmm* consistent with space group *P2<sub>1</sub>2<sub>1</sub>2<sub>1</sub>*; two monitored reflections ( $\bar{1}0\bar{2}$  and  $\bar{1}02$ ) showed no changes in intensities; 1112 independent intensities measured ( $0 \leq h \leq 8$ ,  $0 \leq k \leq 9$ ,  $0 \leq l \leq 21$ ),

Table 1. Atomic coordinates ( $\times 10^4$ ) and equivalent isotropic thermal parameters ( $\text{\AA}^2 \times 10^3$ )

	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> <sub>eq</sub>
C(1)	2548 (4)	8881 (4)	4049 (1)	37 (1)
O(1)	1298 (3)	9352 (3)	4370 (1)	51 (1)
C(2)	2302 (4)	7632 (4)	3586 (2)	50 (1)
C(3)	3610 (4)	7060 (4)	3227 (2)	44 (1)
C(4)	5464 (4)	7642 (3)	3207 (1)	34 (1)
O(4)	5863 (3)	7743 (3)	2496 (1)	44 (1)
C(5)	5497 (4)	9225 (3)	3500 (1)	29 (1)
C(6)	7269 (4)	9875 (3)	3639 (1)	29 (1)
O(6)	8528 (3)	9765 (2)	3087 (1)	35 (1)
C(7)	7194 (4)	11531 (3)	3775 (1)	34 (1)
C(8)	6142 (4)	11822 (3)	4408 (2)	43 (1)
C(9)	4330 (4)	11133 (3)	4320 (2)	40 (1)
C(10)	4394 (4)	9457 (3)	4154 (1)	32 (1)
C(11)	9117 (4)	11925 (3)	3720 (1)	34 (1)
C(12)	9688 (4)	10890 (3)	3158 (1)	36 (1)
O(12)	10948 (3)	10988 (3)	2796 (1)	54 (1)
C(13)	9618 (5)	13519 (3)	3576 (2)	52 (1)
C(14)	5030 (5)	8599 (4)	4786 (1)	45 (1)
C(15)	6678 (5)	6533 (3)	3544 (2)	44 (1)

Equivalent isotropic *U* defined as one third of the trace of the orthogonalized *U*<sub>*ij*</sub> tensor.

Table 2. Bond lengths ( $\text{\AA}$ ) and angles ( $^\circ$ )

C(1)—O(1)	1.222 (4)	C(1)—C(2)	1.464 (5)
C(1)—C(10)	1.519 (4)	C(2)—C(3)	1.330 (5)
C(3)—C(4)	1.513 (4)	C(4)—O(4)	1.434 (3)
C(4)—C(5)	1.544 (4)	C(4)—C(15)	1.519 (4)
C(5)—C(6)	1.503 (4)	C(5)—C(10)	1.554 (4)
C(6)—O(6)	1.456 (3)	C(6)—C(7)	1.522 (4)
O(6)—C(12)	1.356 (4)	C(7)—C(8)	1.507 (4)
C(7)—C(11)	1.517 (4)	C(8)—C(9)	1.529 (5)
C(9)—C(10)	1.552 (4)	C(10)—C(14)	1.545 (4)
C(11)—C(12)	1.514 (4)	C(11)—C(13)	1.519 (4)
C(12)—O(12)	1.202 (4)		

O(1)—C(1)—C(2)	119.4 (3)	O(1)—C(1)—C(10)	122.5 (3)
C(2)—C(1)—C(10)	117.9 (3)	C(1)—C(2)—C(3)	122.3 (3)
C(2)—C(3)—C(4)	125.7 (3)	C(3)—C(4)—O(4)	104.3 (2)
C(3)—C(4)—C(5)	109.2 (2)	O(4)—C(4)—C(5)	107.6 (2)
C(3)—C(4)—C(15)	109.4 (3)	O(4)—C(4)—C(15)	109.7 (2)
C(5)—C(4)—C(15)	116.0 (2)	C(4)—C(5)—C(6)	116.5 (2)
C(4)—C(5)—C(10)	115.2 (2)	C(6)—C(5)—C(10)	106.6 (2)
C(5)—C(6)—O(6)	115.7 (2)	C(5)—C(6)—C(7)	112.5 (2)
O(6)—C(6)—C(7)	102.9 (2)	C(6)—O(6)—C(12)	107.7 (2)
C(6)—C(7)—C(8)	109.7 (2)	C(6)—C(7)—C(11)	100.5 (2)
C(8)—C(7)—C(11)	122.4 (2)	C(7)—C(8)—C(9)	108.6 (2)
C(8)—C(9)—C(10)	113.1 (3)	C(1)—C(10)—C(5)	110.2 (2)
C(1)—C(10)—C(9)	109.5 (2)	C(5)—C(10)—C(9)	108.9 (2)
C(1)—C(10)—C(14)	103.3 (2)	C(5)—C(10)—C(14)	115.4 (2)
C(9)—C(10)—C(14)	109.3 (2)	C(7)—C(11)—C(12)	100.7 (2)
C(7)—C(11)—C(13)	118.8 (3)	C(12)—C(11)—C(13)	112.2 (3)
O(6)—C(12)—C(11)	110.5 (2)	O(6)—C(12)—O(12)	121.2 (3)
C(11)—C(12)—O(12)	128.2 (3)		

1081 greater than  $3\sigma(I)$ ; Friedel pairs collected over the same range,  $\psi$ -scan empirical absorption correction (transmission factors 0.212–0.314); Lorentz and polarization corrections applied; direct methods revealed the positions of all non-hydrogen atoms, block-cascade least-squares refinement with riding model for H atoms, hydroxyl hydrogen refined, absolute configuration could not be determined by use of Friedel pairs (Rogers, 1981), final *R* = 0.044, *wR* = 0.050, 178 parameters, 1081 reflections, *S* = 1.50, ( $\Delta/\sigma$ )<sub>max</sub> = 0.11, ( $\Delta/\sigma$ )<sub>ave</sub> = 0.031, largest peaks in the final difference Fourier map of 0.20 and  $-0.18 \text{ e \AA}^{-3}$ ;  $\sum w(|F_o| - |F_c|)^2$  minimized,  $w = [\sigma^2(F_o) + 0.0015F_o^2]^{-1}$ , all computer programs supplied by Nicolet for Desktop 30 Microeclipse and Nova 4/C configuration; atomic scattering factors and anomalous-dispersion corrections contained in the program package. Table 1 lists atomic positional parameters while Table 2 contains distances and valence angles.\*

\* Lists of structure factors, H-atom parameters and anisotropic thermal parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 43794 (11 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

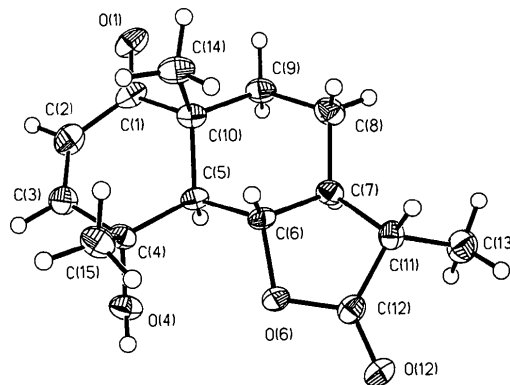


Fig. 1. Thermal-ellipsoid plot of tauremisin. Thermal ellipsoids are drawn at the 35% probability level. H atoms are represented by spheres of arbitrary size.

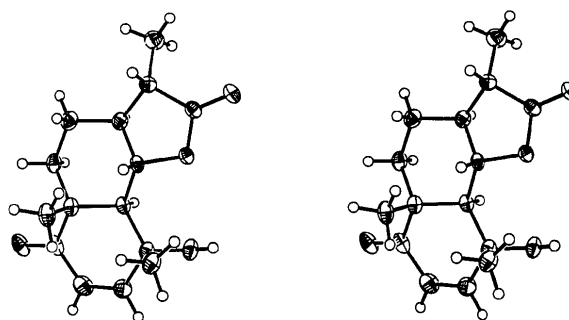


Fig. 2. Stereo drawing of tauremisin.

**Discussion.** Fig. 1 is a thermal-ellipsoid plot of the title compound while Fig. 2 is a stereo drawing. The two six-membered rings are *trans*-fused with the cyclohexenone ring in a 1,2-diplanar conformation slightly distorted towards a half-chair and the cyclohexane ring in a chair conformation. The *trans*-fused lactone is in a half-chair conformation. With the stereochemistry at C(4), C(5), C(6), C(7) and C(10) established by chemical transformations and correlations with santolide C (Rybalko & Dolejs, 1961), the C(11) methyl group can be assigned the  $\alpha$  configuration. The bond lengths and angles all fall within the expected range. The only short intramolecular contact is between H(6) and H(14*b*), 1.99 (4) Å. An intermolecular hydrogen bond is formed between O(12) and O(4) ( $2.0-x$ ,  $0.5+y$ ,  $0.5-z$ );  $O(12)\cdots O(4) = 2.967$  (3),  $O(12)\cdots HO(4) = 2.08$  (4) Å,  $O(12)\cdots H-O(4) = 165.7$  (6)°.

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## 3-(*p*-Cyanophenoxy)quadricyclane and a Redetermination of the Structure of a Hexachloroquadricyclane Dicarboxylate

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**Abstract.** Dimethyl 2,3,3,4,6,7-hexachlorotetracyclo-[3.2.0.0<sup>2,7</sup>.0<sup>4,6</sup>]heptane-1,5-dicarboxylate (1),  $C_{11}H_6Cl_6O_4$ ,  $M_r = 414.88$ , monoclinic,  $P2_1/c$ ,  $a = 10.558$  (3),  $b = 12.594$  (4),  $c = 11.732$  (3) Å,  $\beta = 96.33$  (2)°,  $V = 1550$  (1) Å<sup>3</sup>,  $Z = 4$ ,  $D_x = 1.778$  g cm<sup>-3</sup>,  $\lambda(Mo K\alpha) = 0.71073$  Å,  $\mu = 11.23$  cm<sup>-1</sup>,  $F(000) = 824$ ,  $T = 300$  K,  $R = 0.052$  for 1909 unique reflections. 3-(Tetracyclo[3.2.0.0<sup>2,7</sup>.0<sup>4,6</sup>]heptyl)oxybenzonitrile (2),  $C_{14}H_{11}NO$ ,  $M_r = 209.25$ , triclinic,  $P\bar{1}$ ,  $a = 6.034$  (2),  $b = 9.322$  (3),  $c =$

$9.458$  (3) Å,  $\alpha = 92.89$  (2),  $\beta = 93.67$  (2),  $\gamma = 101.83$  (2)°,  $V = 518.5$  (2) Å<sup>3</sup>,  $Z = 2$ ,  $D_x = 1.340$  g cm<sup>-3</sup>,  $\lambda(Cu K\alpha) = 1.54178$  Å,  $\mu = 6.34$  cm<sup>-1</sup>,  $F(000) = 220$ ,  $T = 300$  K,  $R = 0.052$  for 1312 unique reflections. The two three-membered rings of the quadricyclane (2) form statistically equivalent equilateral triangles with sides and angles averaging 1.495 (3), 1.486 (4) Å, 60.0 (2) and 60.0 (3)°. The four-membered ring forming the base of the quadricyclane is a rectangle with sides of 1.492 (3) and 1.543 (3) Å. Owing to the chloro substitution in (1), the distances around the three-membered rings are

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