

Photosantonin

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Abstract. C₁₇H₂₄O₄, $M_r = 292.37$, orthorhombic, $P2_12_12_1$, $Z = 4$, $\lambda(\text{Mo } K\alpha) = 0.71069 \text{ \AA}$; at 242 K: $a = 8.767 (2)$, $b = 8.773 (3)$, $c = 21.101 (6) \text{ \AA}$, $D_c = 1.197 \text{ Mg m}^{-3}$, $\mu(\text{Mo } K\alpha) = 0.09 \text{ mm}^{-1}$; at 298 K: $D_m = 1.145 \text{ Mg m}^{-3}$. $R = 0.056$ for 1986 observed reflections. The molecule contains a five-membered lactone fused *trans* to a six-membered carbocyclic ring bearing a bis-exocyclic conjugated diene with a torsional angle of $64.3 (4)^\circ$.

Introduction. The title compound, which crystallized from acetone–hexane as colourless platelets, was prepared by irradiation of commercial α -santonin (Sigma Chemical Co., USA) in ethanol solution with a medium-pressure mercury-vapour lamp through Pyrex essentially as described by Barton, de Mayo & Shafiq (1958).

Precession photography showed that the crystals were orthorhombic and belonged to the space group $P2_12_12_1$ ($h00$ reflections absent when h odd, $0k0$ absent when k odd and $00l$ absent when l odd). The cell dimensions and reflection intensities were measured on a Syntex $P\bar{1}$ automatic diffractometer under the conditions specified in Table 1. Lorentz and polarization corrections were applied, but no absorption or extinction corrections were made.

The structure was solved with the program *MULTAN* (Germain, Main & Woolfson, 1971). The E map contained all the non-hydrogen atoms except for C(14) and O(1). The positions of these two non-

hydrogen atoms were easily located by Fourier synthesis from 1986 observed reflections with $I > 3\sigma(I)$ and phases calculated from the partial structure. After the positional and anisotropic thermal parameters of all non-hydrogen atoms were refined, 22 H atoms could be located on a difference electron density map. The positions of the remaining two H atoms on methyl carbon C(14) were calculated assuming a C–H distance of 0.95 \AA (Churchill, 1973). The final discrepancy factors for 1986 observed reflections, after refinement of positional and anisotropic thermal parameters for non-hydrogen atoms and positional parameters for 19 H atoms with fixed isotropic temperature factors, are $R = \sum ||F_o| - |F_c|| / \sum |F_o| = 0.056$ and $R' = [\sum w(|F_o| - |F_c|)^2 / \sum wF_o^2]^{1/2} = 0.063$. The ethyl, C(13)–C(14), H atoms were included in the structure factor calculation with fixed isotropic temperature factors but their positions were not refined. The R value for all 2723 independent reflections is 0.086 . The final difference map showed features reaching $\pm 2 e \text{ \AA}^{-3}$ near the side-chain atoms O(2), C(13) and C(14).

The depicted absolute configuration of the title compound is established by the X-ray structure (Asher & Sim, 1965) and the configuration determined by chemical methods (Cocker & McMurry, 1960; Nakazaki & Arakawa, 1962) of the starting material, α -santonin. Moreover, the absolute configuration of β -santonin, which differs from that of α -santonin only in the configuration of the methyl group in the lactone ring, has been determined through X-ray diffraction by anomalous-dispersion effects (Coggon & Sim, 1969).

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Table 1. *Experimental conditions*

| |
|--|
| Crystal dimensions: $0.30 \times 0.40 \times 0.45 \text{ mm}$ |
| Diffractometer: Syntex $P\bar{1}$ |
| Source: Mo $K\alpha$, $\lambda = 0.71069 \text{ \AA}$ |
| Scan mode: $\theta-2\theta$ |
| 2θ scan rate: variable ($0.49-2.0^\circ \text{ min}^{-1}$) depending on intensity |
| 2θ scan range: 2° plus the spectral width of Mo $K\alpha_1$ and Mo $K\alpha_2$; $0^\circ < 2\theta < 60^\circ$ |
| Zr filter |
| Total number of independent reflections: 2723 |
| Number of observed [$I > 3\sigma(I)$] reflections: 1986 |
| Temperature of crystal during data collection: 242 K |

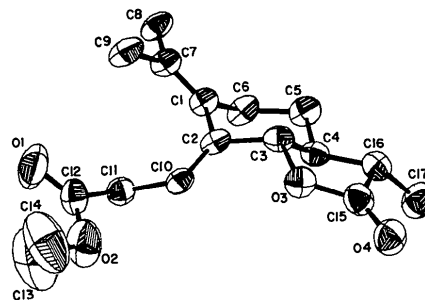


Fig. 1. ORTEP (Johnson, 1965) view of photosantonin. Thermal ellipsoids enclose 50% probability.

Table 2. Fractional atomic coordinates ($\times 10^4$) and equivalent isotropic temperature factors, with e.s.d.'s in parentheses

| | <i>x</i> | <i>y</i> | <i>z</i> | B_{eq} (Å ²)* |
|-------|-----------|------------|----------|-----------------------------|
| C(1) | 4255 (3) | -795 (4) | 4304 (1) | 3.36 (7) |
| C(2) | 2547 (3) | -748 (4) | 4232 (1) | 2.93 (6) |
| C(3) | 1900 (3) | 419 (4) | 4671 (1) | 3.21 (7) |
| C(4) | 2288 (3) | 32 (4) | 5352 (1) | 3.21 (7) |
| C(5) | 3993 (4) | 107 (5) | 5454 (1) | 4.09 (8) |
| C(6) | 4750 (4) | -1021 (5) | 4994 (1) | 4.06 (8) |
| C(7) | 5218 (3) | -589 (4) | 3828 (1) | 3.71 (7) |
| C(8) | 6936 (3) | -625 (6) | 3897 (2) | 4.58 (10) |
| C(9) | 4703 (4) | -305 (6) | 3153 (2) | 4.70 (10) |
| C(10) | 1681 (3) | -1687 (3) | 3901 (1) | 3.01 (6) |
| C(11) | 2225 (4) | -3024 (4) | 3523 (2) | 3.69 (8) |
| C(12) | 1584 (4) | -3108 (4) | 2870 (2) | 4.44 (9) |
| C(13) | -685 (7) | -3483 (10) | 2280 (3) | 10.74 (26) |
| C(14) | -1394 (9) | -2203 (6) | 2051 (3) | 9.35 (21) |
| C(15) | -214 (4) | 868 (4) | 5279 (2) | 3.84 (8) |
| C(16) | 1167 (4) | 1048 (4) | 5711 (2) | 4.04 (8) |
| C(17) | 847 (6) | 613 (7) | 6392 (2) | 5.72 (12) |
| O(1) | 2307 (4) | -3090 (4) | 2396 (1) | 7.46 (10) |
| O(2) | 68 (3) | -3254 (4) | 2890 (1) | 7.31 (10) |
| O(3) | 245 (2) | 510 (2) | 4679 (1) | 3.58 (5) |
| O(4) | -1540 (3) | 1015 (3) | 5408 (1) | 4.78 (6) |

$$* B_{eq} = \frac{1}{3} \sum_i \sum_j \beta_{ij} a_i \cdot a_j$$

Table 3. Bond lengths (Å)

| | | | |
|-------------|-----------|-------------|------------|
| C(1)–C(2) | 1.505 (2) | C(7)–C(1) | 1.324 (3) |
| C(2)–C(3) | 1.492 (4) | C(7)–C(8) | 1.514 (3) |
| C(3)–C(4) | 1.514 (4) | C(7)–C(9) | 1.514 (3) |
| C(4)–C(5) | 1.512 (3) | | |
| C(5)–C(6) | 1.537 (4) | C(10)–C(2) | 1.321 (4) |
| C(6)–C(1) | 1.532 (3) | C(10)–C(11) | 1.497 (4) |
| | | C(11)–C(12) | 1.490 (5) |
| C(3)–O(3) | 1.453 (3) | C(12)–O(1) | 1.185 (4) |
| O(3)–C(15) | 1.367 (4) | C(12)–O(2) | 1.335 (3) |
| C(15)–C(16) | 1.523 (4) | O(2)–C(13) | 1.461 (4) |
| C(15)–O(4) | 1.201 (4) | C(13)–C(14) | 1.372 (6)* |
| C(16)–C(17) | 1.512 (4) | | |
| C(16)–C(4) | 1.528 (4) | | |

* The temperature factors for C(13) and C(14) are large, 10.74 and 9.35 Å² respectively. This bond length becomes 1.375 (7) Å when averaged over thermal motion assuming the second atom rides on the first and 1.570 (6) Å when averaged assuming the motions are independent.

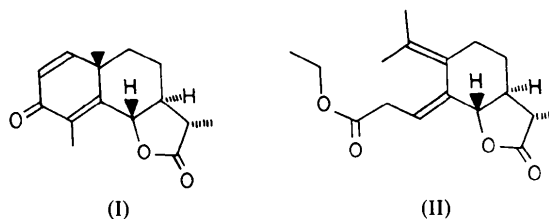
The structure and atom numbering (arbitrary) for the molecule are shown in Fig. 1. Table 2 contains the atomic coordinates; Tables 3 and 4 contain bond lengths and angles.*

* Lists of structure factors and thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 36325 (11 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 4. Bond angles (°)

| | | | |
|-------------------|-----------|-------------------|-----------|
| C(6)–C(1)–C(2) | 112.4 (2) | C(1)–C(7)–C(8) | 123.9 (3) |
| C(1)–C(2)–C(3) | 109.5 (2) | C(1)–C(7)–C(9) | 123.1 (3) |
| C(2)–C(3)–C(4) | 110.5 (2) | C(8)–C(7)–C(9) | 113.0 (3) |
| C(3)–C(4)–C(5) | 110.3 (2) | C(6)–C(1)–C(7) | 123.9 (2) |
| C(4)–C(5)–C(6) | 108.0 (2) | C(2)–C(1)–C(7) | 123.6 (2) |
| C(5)–C(6)–C(1) | 113.3 (2) | | |
| | | O(3)–C(3)–C(2) | 115.1 (2) |
| C(2)–C(10)–C(11) | 126.0 (3) | O(3)–C(3)–C(4) | 103.1 (2) |
| C(10)–C(11)–C(12) | 114.3 (3) | C(3)–O(3)–C(15) | 108.5 (2) |
| C(11)–C(12)–O(1) | 125.4 (2) | O(3)–C(15)–O(4) | 121.3 (3) |
| C(11)–C(12)–O(2) | 110.5 (3) | O(4)–C(15)–C(16) | 128.6 (3) |
| O(1)–C(12)–O(2) | 124.1 (3) | O(3)–C(15)–C(16) | 110.1 (2) |
| C(12)–O(2)–C(13) | 115.8 (4) | C(15)–C(16)–C(17) | 113.2 (2) |
| O(2)–C(13)–C(14) | 113.7 (3) | C(15)–C(16)–C(4) | 98.9 (2) |
| C(1)–C(2)–C(10) | 127.4 (2) | C(17)–C(16)–C(4) | 116.4 (3) |
| C(3)–C(2)–C(10) | 122.5 (2) | C(16)–C(4)–C(3) | 101.3 (2) |
| | | C(16)–C(4)–C(5) | 122.7 (2) |

Discussion. Irradiation of α -santonin (I) with sunlight or ultraviolet light in ethanol produces a series of rearrangements, resulting in the formation of photosantonin (II) (Chapman & Englert, 1963; Fisch & Richards, 1963).



The structure of photosantonin had been the subject of much investigation and dispute (Barton, de Mayo & Shafiq, 1958) until finally settled by van Tamelen, Levin, Brenner, Wolinsky & Aldrich (1958, 1959), who suggested that the conjugated diene moiety of the molecule must deviate significantly from planarity, as indicated by the absence of an ultraviolet absorption maximum above 200 nm. It was of interest to determine the sign and magnitude of the diene torsional angle in this molecule in order to correlate chiroptical properties with the geometry of dienes in general. The crystallographic study reported herein supplies these data. The circular dichroism of photosantonin is reported separately (Burgstahler, 1981).

Initial attempts at structure solution and refinement at room temperature were complicated by disorder of four atoms, O(1), O(2), C(13) and C(14), in the side chain. The cell dimensions and calculated density at 298 K are $a = 8.791$ (2), $b = 8.965$ (2), $c = 21.168$ (4) Å and $D_c = 1.164$ Mg m⁻³. The present study utilized the diffraction data re-collected at 242 K.

The dihedral angle C(7)–C(1)–C(2)–C(10) of the diene is 64.3 (4)°. This value is significantly larger than

those previously reported for other highly skewed bis-exocyclic dienes, -49 and 46° for the two ring-*A* chair conformers of vitamin D₂ (Hull, Leban, Main, White & Woolfson, 1976), -53.6 and 55.2° in the corresponding α and β forms of vitamin D₃ (Trinh-Toan, DeLuca & Dahl, 1976), and 52.3° for a chiral 1,2-bis(alkylidene)diazacyclopentane derivative (Pasto & Scheidt, 1975). Steric repulsion between the C(9) methyl and C(11) methylene groups probably makes a significant contribution to the large twist of the diene system in photosantonin. The observed C(9)–C(11) contact distance is $3.320(4)$ Å. The central bond, C(1)–C(2), of the diene is somewhat longer [$1.505(2)$ Å] than that in the two conformers of vitamin D₂ (1.44 and 1.47 Å) and vitamin D₃ [$1.45(1)$ and $1.45(1)$ Å] perhaps indicating some lengthening of this bond in photosantonin due to ring strain as well as loss of conjugation.

The six-membered ring, which contains two trigonally hybridized C atoms, has a highly puckered chair conformation. In fact, the average endocyclic torsional bond angle is 56.7° , slightly greater than that (55.9°) in cyclohexane (Geise, Buys & Mijlhoff, 1971). The conformation of this ring is of particular interest since the diene chirality is reversed in the alternative boat or twist conformation. Although possibly present to some extent in solution, the boat conformation is probably destabilized by strong eclipsing between the H atoms of the C(5) and C(6) methylene groups.

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Diethylammonium 2,5-Dihydroxy-1,4-benzenedisulphonate

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Abstract. $2[\text{NH}_2(\text{C}_2\text{H}_5)_2]^+ \cdot \text{C}_6\text{H}_4\text{O}_8\text{S}_2^{2-}$, $M_r = 416.5$, monoclinic, $P2_1/a$, $a = 11.533(3)$, $b = 10.544(2)$, $c = 8.888(2)$ Å, $\beta = 114.67(2)^\circ$, $V = 982.2(7)$ Å³, $Z = 2$, $D_c = 1.41$ Mg m⁻³. The structure was solved with the *MULTAN* system and refined by the full-matrix least-squares method. The final *R* value is 0.043 for 1122 observed reflections. The 2,5-dihydroxy-1,4-benzenedisulphonate ion is located on an inversion

centre. The hydrogen bonds determine the packing of the ions.

Introduction. The title compound is a commercial pharmacological compound. In order to determine the geometry of the ions, the X-ray analysis was carried out.