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Isogentisin (1,3-dihydroxy-7-methoxyxanthone)

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Key indicators

Single-crystal X-ray study
T = 120 K
Mean σ(C–C) = 0.005 Å
R factor = 0.034
wR factor = 0.117
Data-to-parameter ratio = 10.8

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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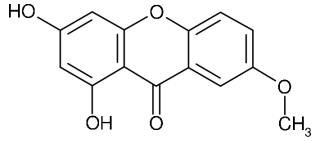
The crystal structure of isogentisin, $C_{14}H_{10}O_5$, a natural product isolated from *Gentiana lutea*, has been determined. The phenolic ring system is essentially planar and the displacement of the methoxy substituent from the mean molecular plane is very small. The structure is stabilized by a one-dimensional chain of intermolecular hydrogen bonds.

Comment

Xanthone compounds commonly occur in several higher plant families, such as *Gentianaceae*, *Guttiferae*, *Moraceae* and *Polygalaceae*. The study of xanthones is interesting both from the chemosystematic and pharmacological point of view. Inhibition of Type A and Type B monoamine oxidases (MAO) by a number of xanthones has been observed (Suzuki *et al.*, 1980, 1981). Among the xanthones that have been tested, isogentisin revealed potent MAO inhibition (Suzuki *et al.*, 1978). Four ethanolic extracts prepared from leaves, flowers and roots of *Gentiana lutea* were tested for antitubercular activity against *Mycobacterium bovis* (BCG-strain). The extract obtained from flowers showed strong inhibition at a concentration of 1000 μg ml^{-1} and slight inhibition at 500 μg ml^{-1}. This activity increased during the various purification steps, which finally led to the isolation of the active compound isogentisin (Menković *et al.*, 1999). Mutagenicity in the Ames test in *Salmonella typhimurium* was also shown for isogentisin (Morimoto *et al.*, 1983, Matsushima *et al.*, 1985). Isogentisin was first isolated by Cannonica & Pelizzoni (1955). The present paper presents the first single-crystal X-ray analysis of isogentisin and confirms that the crystal structure correpsonds to 1,3-dihydroxy-7-methoxyxanthone, (I) (Fig. 1). The 1,3-dihydroxy-7-methoxyxanthone fragment is essentially planar, with the largest displacement within the phenolic ring system of 0.062 (3) Å for C1. The methyl group of the methoxy substituent lies close to the mean plane of the molecule, as shown by the torsion angle of C10—C9—O15—C19 of 5.2 (5)°.



(I)

The packing diagram for isogentisin is shown in Figs. 2 and 3. The crystal structure can be described in terms of parallel molecules stacked along the direction of the *a* crystallographic axis, with the normal to the plane forming an angle of about 20° relative to it, and an intermolecular separation of about 3.5 Å. Within a xanthone unit, an intramolecular hydrogen bond with a length of 1.91 Å exists between the hydroxyl H

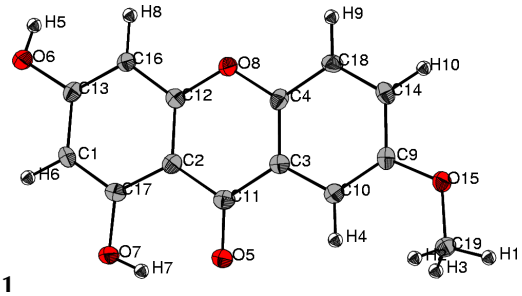


Figure 1
The molecular structure of isogentisin and the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

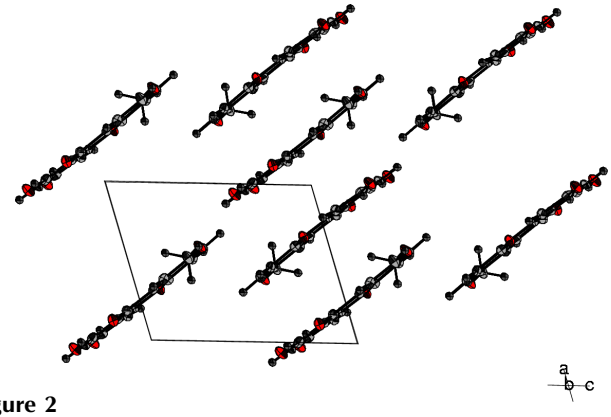


Figure 2
One view of the packing diagram for isogentisin.

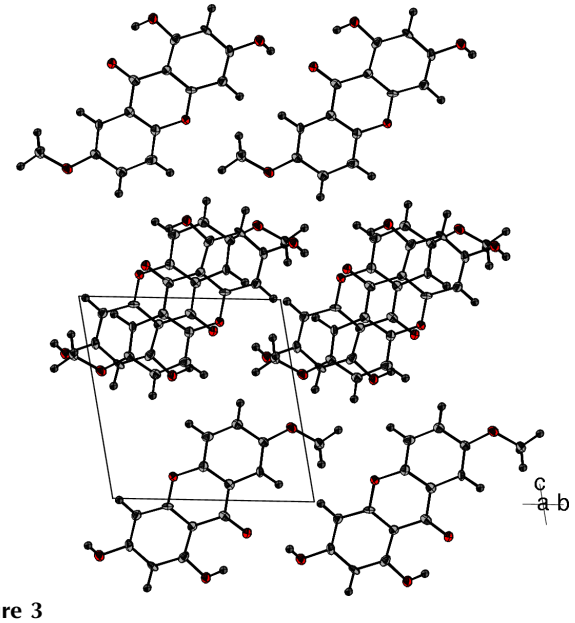


Figure 3
A second view of the packing diagram for isogentisin.

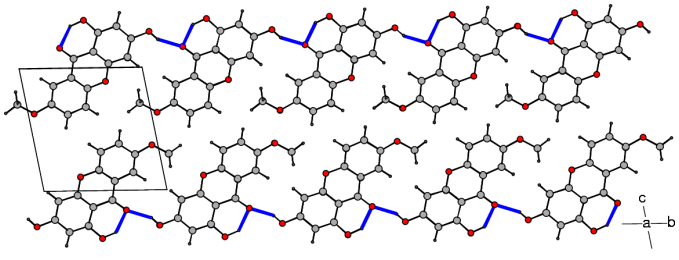


Figure 4
Hydrogen bonding in isogentisin.

atom H7 and the O5 acceptor of an adjacent carbonyl group. In addition, the same carbonyl O atom participates in a one-dimensional intermolecular hydrogen bond with the hydroxyl group on a neighbouring molecule (O5—H5 = 1.997 Å). The hydrogen-bonding patterns are shown in Fig. 4.

Experimental

Isolation of isogentisin from *Gentiana lutea* was carried out following a procedure described previously (Menković, 1997; Menković *et al.*, 1990).

Crystal data

$C_{14}H_{10}O_5$
M_r = 258.23
Triclinic, $P\overline{1}$
a = 7.2287 (14) Å
b = 8.6286 (15) Å
c = 9.0370 (16) Å
α = 97.896 (5)°
β = 105.962 (6)°
γ = 97.698 (5)°
V = 528.00 (17) Å^3
Z = 2
D_x = 1.611 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 826 reflections
θ = 6.0–49.1°
μ = 0.12 mm^{-1}
T = 120 K
Needle, yellow
0.08 × 0.04 × 0.02 mm

Data collection

Bruker SMART 6000 diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.956, T_{max} = 1.000
4830 measured reflections
1866 independent reflections
783 reflections with $I > 2\sigma(I)$
R_{int} = 0.01
θ_{max} = 25.0°
$h = -8 \rightarrow 8$
$k = -10 \rightarrow 10$
$l = -10 \rightarrow 10$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.034
$wR(F^2)$ = 0.117
S = 0.96
1858 reflections
172 parameters
H-atom parameters constrained
Weighting scheme: see text
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.69 e Å^{-3}
$\Delta\rho_{min}$ = −0.59 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

C1—C13	1.392 (4)	O6—C13	1.352 (4)
C1—C17	1.369 (4)	O7—C17	1.349 (4)
C2—C11	1.441 (4)	O8—C12	1.364 (3)
C2—C12	1.401 (4)	C9—C10	1.376 (4)
C2—C17	1.425 (4)	C9—C14	1.400 (5)
C3—C4	1.387 (4)	C9—O15	1.362 (4)
C3—C10	1.404 (4)	C12—C16	1.376 (4)
C3—C11	1.454 (4)	C13—C16	1.390 (4)
C4—O8	1.373 (4)	C14—C18	1.372 (4)
C4—C18	1.401 (4)	O15—C19	1.422 (4)
O5—C11	1.256 (4)		
C13—C1—C17	119.9 (3)	C3—C11—O5	122.0 (3)
C11—C2—C12	120.8 (3)	C2—C11—O5	122.2 (3)
C11—C2—C17	122.4 (3)	C2—C12—O8	121.5 (3)
C12—C2—C17	116.8 (3)	C2—C12—C16	122.8 (3)
C4—C3—C10	118.7 (3)	O8—C12—C16	115.7 (3)
C4—C3—C11	119.7 (3)	C1—C13—O6	116.8 (3)
C10—C3—C11	121.6 (3)	C1—C13—C16	121.1 (3)
C3—C4—O8	122.8 (3)	O6—C13—C16	122.0 (3)
C3—C4—C18	121.4 (3)	C9—C14—C18	120.2 (3)
O8—C4—C18	115.8 (3)	C9—O15—C19	117.9 (2)
C4—O8—C12	119.4 (2)	C13—C16—C12	118.4 (3)
C10—C9—C14	120.6 (3)	C2—C17—C1	121.0 (3)
C10—C9—O15	125.2 (3)	C2—C17—O7	120.8 (3)
C14—C9—O15	114.2 (3)	C1—C17—O7	118.2 (3)
C3—C10—C9	120.0 (3)	C4—C18—C14	119.1 (3)
C3—C11—C2	115.8 (3)		

Table 2
Hydrogen-bonding geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O6—H5···O5^{i}	0.82	2.00	2.738 (3)	150
O7—H7···O5	0.82	1.91	2.634 (3)	147

Symmetry code: (i) $x, y-1, z$.

A Chebychev polynomial (Carruthers & Watkin, 1979; Prince, 1982) was used for the weighting scheme, with $w = 1.0/[A_0T_0(x) + A_1T_1(x)\ldots + A_{n-1}]T_{n-1}(x)]$ where A_i are the Chebychev coefficients listed below and $x = F_{calc}/F_{max}$; robust weighting (Prince, 1982): $W = w[1 - (\delta F/6\sigma F)^2]^2$, A_i are 1.96, 2.45 and 0.676. H atoms were positioned geometrically (C—H = 1.0 Å and O—H = 0.82 Å) and refined using a riding model, with $U_{iso}(H) = 1.2U_{eq}(C)$ and $1.1U_{eq}(O)$.

Data collection: *SMART* (Bruker, 1999); cell refinement: *SAINT* (Bruker, 1999); data reduction: *SAINT* (Bruker, 1999); program(s) used to solve structure: *SIR*92 (Altomare *et al.*, 1994); program(s) used to refine structure: *CRYSTALS* (Betteridge *et al.*, 2003); molecular graphics: *ATOMS* (Shape Software, 2000); software used to prepare material for publication: *CRYSTALS*.

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