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Methyl 5-hydroxy-2-(2-hydroxy-6-methoxy-4-methylbenzoyl)-3-methoxybenzoate

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Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.003 Å
R factor = 0.063
wR factor = 0.150
Data-to-parameter ratio = 15.1

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

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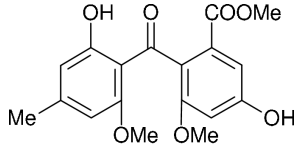
The title compound, $C_{18}H_{18}O_7$, is an anti-*Helicobacter pylori* compound. It was characterized from the chloroform–methanol (1:1) extract of *Fusarium sp.* IFB-121, an endophytic fungus in *Quercus variabilis*. The two benzene rings form a dihedral angle of 79.0 (2)° and intramolecular hydrogen bonds keep the phenolic hydroxy and carbonyl groups coplanar with one of the aromatic rings. The strong intermolecular hydrogen-bond contacts are consistent with the high melting point of the compound.

Comment

The human pathogenic bacterium *Helicobacter pylori* has been ascertained to be an antiological agent for chronic active gastritis and a significant determinant in peptic and duodenal ulcer diseases (Gebert *et al.*, 2003). Sustained infection with this bacterium can lead to development of gastric cancer (Moran & Upton, 1986). Endophytic metabolites are being recognized as a versatile arsenal of antimicrobial agents, since some endophytes have been shown to possess superior biosynthetic capabilities owing to their presumed gene recombination with the host, while residing and reproducing inside the healthy plant tissues (Tan & Zou, 2001). In continuation of our characterization of chemically new and/or bioactive constituents from various endophytic fungi (Liu *et al.*, 2002; Lu *et al.*, 2000; Shu *et al.*, 2004; Zou *et al.*, 2000), our particular attention was extended to anti-*Helicobacter pylori* constituents. A detailed bioassay-guided fractionation of the culture extract of *Fusarium sp.*, an endophytic fungus in *Quercus variabilis Bl.*, was performed to afford a strong anti-*H. pylori* secondary metabolite. This isolated compound was identified through a combination of single-crystal X-ray diffraction and nuclear magnetic resonance methods to be monomethylsulochrin (Turner, 1965). In this paper, we report the structural information for the title compound, (I).



(I)

In (I), the two aromatic rings are nearly perpendicular to each other, and the dihedral angle is 79.0 (2)° (as shown in Fig. 1), which greatly minimizes the steric effects among the substituent groups attached to the benzene rings. The strong intramolecular hydrogen bond [O7—H7···O5 = 2.529 (2) Å] between the phenolic OH group and the neighbouring

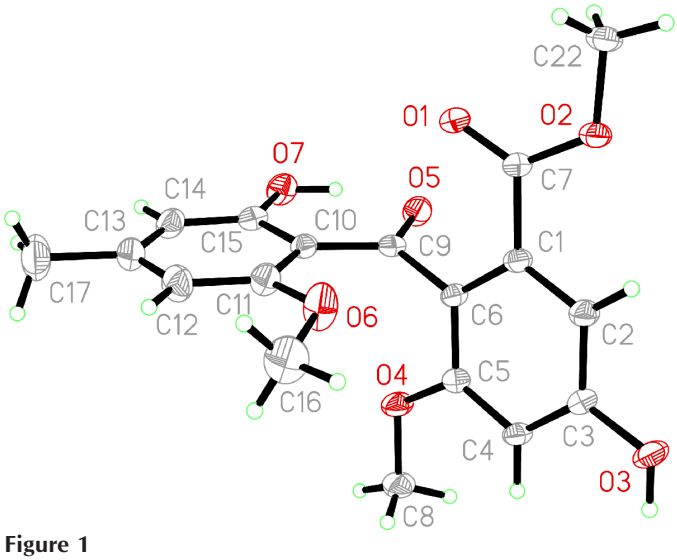


Figure 1
The molecular structure of the title compound, showing 30% probability displacement ellipsoids and the atom-numbering scheme.

carboxyl O atom keeps the ketone coplanar with the benzene ring C10–C15. This is consistent with most reported structures containing flavone and/or isoflavone. Strong intermolecular hydrogen bonds (Table 1) link the molecules to form a one-dimensional structure, consistent with the high melting point (m.p. 470–471 K) of the compound.

Experimental

The cultivation of *Fusarium sp.* IFB-121, an endophytic fungus in *Quercus variabilis*, extraction and isolation were described in a previous communication (Shu *et al.*, 2004). A residue (130 g) from the dark-brown tarry mass was obtained after depositing lipids, and was then subjected to column chromatography (CC) on silica gel (1300 g, 200–300 mesh), eluting with chloroform /methanol (1:0–0:1) to give seven fractions (fraction 1: 28.3 g; fraction 2: 12.2 g; fraction 3: 12.5 g; fraction 4: 14.0 g; fraction 5: 13.7 g; fraction 6: 12.3 g; fraction 7: 27.4 g). F-2, showing pronounced anti-*Helicobacter pylori* activity, was rechromatographed on a silica-gel column, eluting with chloroform/acetone (50:1–4:1) to afford four subfractions (F-2–1: 4.5 g; F-2–2: 1.4 g; F-2–3: 2.3 g; F-2–4: 2.0 g). F-2–2 was subjected to gel filtration over Sephadex LH-20 with chloroform/methanol (1:1), followed by repeated recrystallization to give monomethylsulochrin, a yellow crystalline solid (260 mg) [also known as methyl 5-hydroxy-2-(2-hydroxy-6-methoxy-4-methylbenzoyl)-3-methoxybenzoate; m.p. 470–471 K; ^{1}H NMR (500 MHz, $CDCl_3$): 6.99 (1H, *d*, *J* = 2.0 Hz, H-6), 6.58 (1H, *d*, *J* = 2.0 Hz, H-4), 6.45 (1H, *br s*, H-3′), 6.06 (1H, *br s* H-5′), 3.67 (3H, *s*, $COOCH_3$), 3.66 (3H, *s*, H-8), 3.36 (3H, *s*, H-9′), 2.28 (3H, *s*, H-7′); ^{13}C NMR (125 MHz, $CDCl_3$): 199.8 (C-8′), 166.3 (C-7), 164.2 (C-2′), 160.9 (C-6′), 157.0 (C-5), 156.5 (C-3), 148.1(C-4′), 128.3(C-1), 127.6 (C-2), 110.9 (C-1′), 110.4 (C-3′), 107.9 (C-6), 103.2 (C-5′), 102.9(C-4), 56.1 (C-8), 55.6 (C-9′), 52.2 ($COOCH_3$), 22.5 (C-7′)]. The *in vitro* growth inhibition assay against *H. pylori* was carried out according to the Agar dilution method (Bae *et al.*, 1999). A reference strain (ATCC 43504) and five randomly selected clinical strains from antral biopsies from children and adults were used in this study. The results indicated that monomethylsulochrin displayed significant growth inhibition against all the six strains of *H. pylori* with the minimum inhibitory concentrations (MICs) of 10.0 μg ml^{-1}. The MIC of ampicillin used as the positive control against these strains was 2.0 μg ml^{-1}.

Crystal data

$C_{18}H_{18}O_7$
M_r = 346.32
Triclinic, $P\overline{1}$
a = 8.5896 (14) Å
b = 9.3966 (15) Å
c = 10.9312 (18) Å
α = 96.489 (2)°
β = 99.109 (2)°
γ = 103.805 (2)°
V = 835.5 (2) Å^3
Z = 2
D_x = 1.377 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 1035 reflections
θ = 2.7–27.8°
μ = 0.11 mm^{-1}
T = 293 (2) K
Prism, colourless
0.25 × 0.12 × 0.10 mm

Data collection

Bruker SMART CCD area-detector diffractometer
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.974, T_{max} = 0.989
9287 measured reflections
3602 independent reflections
3035 reflections with $I > 2\sigma(I)$
R_{int} = 0.050
θ_{max} = 27.0°
$h = -10 \rightarrow 10$
$k = -11 \rightarrow 11$
$l = -13 \rightarrow 13$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.063
$wR(F^2)$ = 0.151
S = 1.16
3602 reflections
238 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0444P)^2 + 0.4501P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.010
$\Delta\rho_{max}$ = 0.23 e Å^{-3}
$\Delta\rho_{min}$ = −0.22 e Å^{-3}

Table 1
Hydrogen-bonding geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O3—H3···O1^{i}	0.920 (18)	1.98 (2)	2.853 (2)	159 (3)
O7—H7···O5	0.934 (18)	1.68 (2)	2.529 (2)	149 (3)

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

All H atoms attached to C atoms were positioned geometrically and constrained to ride on their parent atoms, with C—H distances of 0.96 Å and U_{iso}(H) = 1.2U_{eq}(C). H atoms attached to O atoms were refined isotropically.

Data collection: *SMART* (Siemens, 1996); cell refinement: *SAINT* (Siemens, 1996); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997*a*); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997*a*); molecular graphics: *SHELXTL* (Sheldrick, 1997*b*); software used to prepare material for publication: *SHELXTL*.

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