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3-Hydroxy-1-(2-hydroxy-3,4-dimethoxyphenyl)-2-methylpropanone

Abul Azim,[a] William Errington[b]* and Virinder S. Parmar[a]

[a]Department of Chemistry, University of Delhi, Delhi 110 007, India, and [b]Department of Chemistry, University of Warwick, Coventry CV4 7AL, England

Correspondence e-mail:
w.errington@warwick.ac.uk

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Key indicators

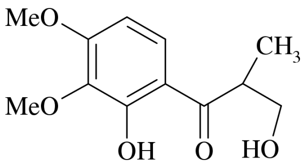
Single-crystal X-ray study
T = 200 K
Mean σ(C–C) = 0.002 Å
R factor = 0.037
wR factor = 0.110
Data-to-parameter ratio = 15.4

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

The title compound, $C_{12}H_{16}O_5$, is an important precursor in the synthesis of polyphenolics. The orientation of the 3-hydroxy-2-methylpropanone group is largely controlled by intramolecular hydrogen bonding, whilst intermolecular hydrogen bonding links the molecules together in pairs.

Comment

Polyphenolics occur widely in nature and many of their analogues possess a variety of biological activities *viz*.. antitumor, antiviral, antibiotic and antifungal. Aryl alkyl ketones with a phenolic hydroxy group in the *ortho* position are starting materials for the synthesis of different classes of biopolyphenolics. The title compound, (I), in addition to being used as a precursor for complex polyphenolics, may also be a suitable substrate for enantioselective acylation studies using lipases. In the present investigation, several aryl alkyl ketones were hydroxymethylated using formaldehyde in aqueous sodium hydroxide (Barlocco *et al.*, 1985) and then subjected to acylation in organic solvents with vinyl acetate and porcine pancreatic lipase (PPL) and Candida rugosa lipase (CRL). The title compound, (I), was reported to be obtained as an oil by Jain *et al.* (1989), and due to its importance in synthetic chemistry and in biotransformation studies, we have repeated their procedure only to obtain unsatisfactory results; however, compound (I) was obtained in good yields by the hydroxymethylation of 2-hydroxy-3,4-dimethoxypropiophenone (Ahluwalia *et al.*, 1979). This paper reports its X-ray structure in order to ascertain the constitution unambiguously.



(I)

The molecular structure of (I) is illustrated in Fig. 1. The bond lengths and angles are largely unexceptional. Of the two methoxy groups, one (at C4′) is coplanar with the phenyl ring, whilst the other (at C3′) has a C5—O4—C3′—C2′ torsion angle of 97.6 (1)°. The orientation of the 3-hydroxy-2-methylpropanone group is largely controlled by intramolecular hydrogen bonding linking the O3 hydroxyl H atom with O1 (see Fig. 2); this results in C2 and O1 being almost coplanar with the phenyl group [*e.g.* O1—C1—C1′—C2′ = −1.9 (2)°].

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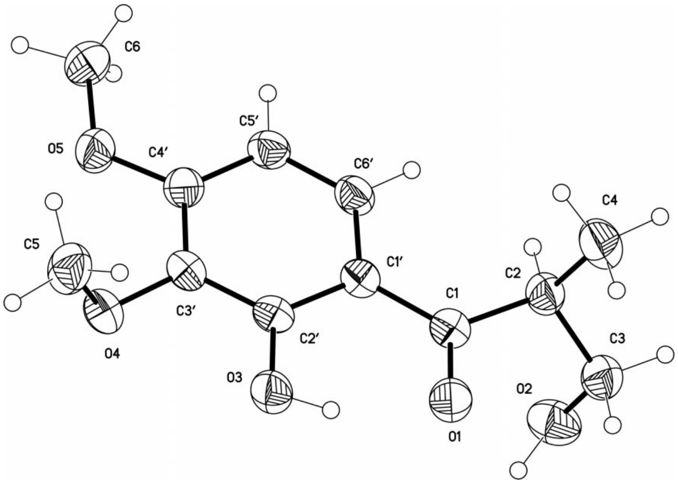

Figure 1
View of the title molecule showing the atomic numbering. Displacement ellipsoids are drawn at the 50% probability level for non-H atoms. H atoms are shown as spheres of arbitrary radii.

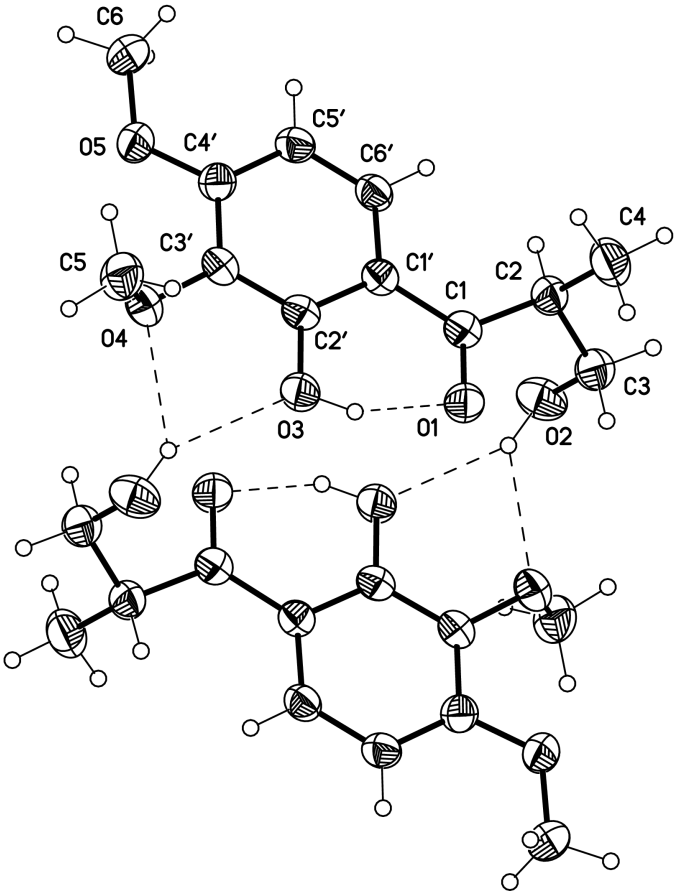

Figure 2
Representation of the intra- and intermolecular hydrogen bonding.

Bifurcated hydrogen bonding involving the O2 hydroxyl H atom (the sum of the three angles about this atom is 360°, within the precision of the experiment) links the molecules together in pairs.

Experimental

A solution of 2-hydroxy-3,4-dimethoxypropiophenone (1.05 g, 0.005 mol) in sodium hydroxide (0.5 *M*, 10 ml, 0.005 mol) and formaldehyde (37%, 0.40 ml, 0.005 mol) was stirred at 303 K for 16 h. The mixture was cooled and acidified to pH 4–5 with concentrated hydrochloric acid and the product was extracted with diethyl ether (2 × 25 ml). The organic layer was dried over sodium sulfate and the solvent evaporated. The residue was chromatographed on silica gel to yield 3-hydroxy-1-(2-hydroxy-3,4-dimethoxyphenyl)-2-methylpropanone as white needles (0.72 g, 60% yield, m.p. 343 K).

Crystal data

$C_{12}H_{16}O_5$
$M_r = 240.25$
Monoclinic, *C*2/*c*
$a = 20.9568\ (12)$ Å
$b = 10.6129\ (6)$ Å
$c = 14.7853\ (9)$ Å
$\beta = 134.586\ (3)^\circ$
$V = 2342.0\ (2)$ Å^3
$Z = 8$

$D_x = 1.363$ Mg m^{-3}
Mo *K*α radiation
Cell parameters from 4598 reflections
$\theta = 2.4$–27.0°
$\mu = 0.11$ mm^{-1}
$T = 200\ (2)$ K
Block, colourless
0.5 × 0.4 × 0.4 mm

Data collection

Siemens SMART CCD area-detector diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
$T_{\min} = 0.949$, $T_{\max} = 0.959$
6539 measured reflections

2534 independent reflections
2008 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.018$
$\theta_{\max} = 27.0^\circ$
$h = -21 \rightarrow 26$
$k = -12 \rightarrow 13$
$l = -18 \rightarrow 11$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.037$
$wR(F^2) = 0.110$
$S = 1.06$
2534 reflections
165 parameters
H atoms treated by a mixture of independent and constrained refinement

$w = 1/[\sigma^2(F_o^2) + (0.0603P)^2 + 0.4432P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\max} < 0.001$
$\Delta\rho_{\max} = 0.20$ e Å^{-3}
$\Delta\rho_{\min} = -0.18$ e Å^{-3}

Table 1
Selected torsion angles (°).

O1—C1—C1′—C6′	178.20 (11)	C5—O4—C3′—C2′	97.59 (14)
C2—C1—C1′—C6′	−0.43 (19)	C5—O4—C3′—C4′	−83.85 (15)
O1—C1—C1′—C2′	−1.92 (18)	C6—O5—C4′—C3′	177.60 (11)
C2—C1—C1′—C2′	179.46 (11)	C6—O5—C4′—C5′	−3.00 (19)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O3—H3···O1	0.87 (2)	1.73 (2)	2.5252 (13)	150.8 (18)
O2—H2···O3$^{\rm i}$	0.91 (2)	2.19 (3)	3.0004 (15)	149 (2)
O2—H2···O4$^{\rm i}$	0.91 (2)	2.28 (2)	3.0025 (14)	137 (2)

Symmetry code: (i) $\frac{1}{2} - x, \frac{1}{2} - y, 1 - z$.

The temperature of the crystal was controlled using an Oxford Cryosystems Cryostream Cooler (Cosier & Glazer, 1986). Data were collected over a hemisphere of reciprocal space, by a combination of three sets of exposures. Each set had a different φ angle for the crystal and each exposure of 10 s covered 0.3° in ω. The crystal to detector distance was 5.01 cm. Coverage of the unique set was over 97% complete to at least 28° in θ. Crystal decay was monitored by repeating the initial frames at the end of the data collection and analyzing the duplicate reflections.

The hydroxyl H atoms were located from an electron-density map and freely refined. Other H atoms were added at calculated positions and refined using a riding model. Anisotropic displacement parameters were used for all non-H atoms; H atoms were given isotropic displacement parameters equal to 1.2 (or 1.5 for methyl H atoms) times the equivalent isotropic displacement parameter of their parent atoms.

Data collection: *SMART* (Siemens, 1994*a*); cell refinement: *SAINT* (Siemens, 1995); data reduction: *SAINT*; program(s) used to solve structure: *SHELXTL*/*PC* (Siemens, 1994*b*); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *SHELXTL*/*PC*; software used to prepare material for publication: *SHELXTL*/*PC*.

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