



Crystal structure of 1-(2,4-dihydroxy-6-methylphenyl)ethanone

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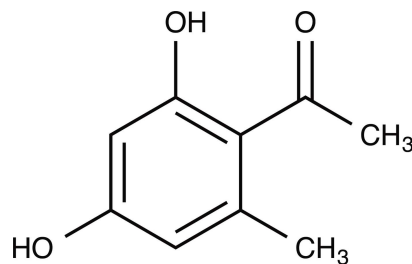
The title compound, $C_9H_{10}O_3$, is a bioactive secondary metabolite, isolated from the endophytic fungus *Nodulisporium* sp. The compound exhibits an intramolecular O—H...O hydrogen bond between the phenolic H atom and the carbonyl O atom of the adjacent acetyl group. In the crystal, molecules are linked by hydrogen bonds involving the 4-phenolic H atom and a symmetry-related carbonyl O atom of a neighboring molecule, resulting in extended supramolecular chains along the *a*-axis direction. Aromatic π – π stacking interactions between the nearly parallel benzene rings of adjacent chains [centroid–centroid distance = 3.7478 (8) Å] further stabilize the three-dimensional supramolecular framework.

Keywords: crystal structure; 1-(2,4-dihydroxy-6-methylphenyl)ethanone; bioactive secondary metabolite; hydrogen bonding; π – π stacking.

CCDC reference: 1412605

1. Related literature

For biological activities of acetophenone derivatives, see: Das & Khosla (2009); Suzuki *et al.* (2006); Tabuchi *et al.* (2014). For related structures, see: Azeezaa *et al.* (2009); Chakkaravarthi *et al.* (2007); Hill *et al.* (2012).



2. Experimental

2.1. Crystal data

$C_9H_{10}O_3$	$V = 807.50 (8) \text{ \AA}^3$
$M_r = 166.17$	$Z = 4$
Monoclinic, $P2_1/c$	Mo $K\alpha$ radiation
$a = 7.3570 (3) \text{ \AA}$	$\mu = 0.10 \text{ mm}^{-1}$
$b = 15.001 (1) \text{ \AA}$	$T = 298 \text{ K}$
$c = 7.3180 (5) \text{ \AA}$	$0.25 \times 0.25 \times 0.25 \text{ mm}$
$\beta = 91.017 (4)^\circ$	

2.2. Data collection

Nonius KappaCCD diffractometer	1319 reflections with $I > 2\sigma(I)$
3260 measured reflections	$R_{\text{int}} = 0.028$
1828 independent reflections	

2.3. Refinement

$R[F^2 > 2\sigma(F^2)] = 0.053$	114 parameters
$wR(F^2) = 0.150$	H-atom parameters constrained
$S = 1.03$	$\Delta\rho_{\text{max}} = 0.22 \text{ e \AA}^{-3}$
1828 reflections	$\Delta\rho_{\text{min}} = -0.17 \text{ e \AA}^{-3}$

Table 1

Hydrogen-bond geometry (Å, °).

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
O10—H10 \cdots O9	0.82	1.77	2.4991 (16)	147
O11—H11 \cdots O9 ⁱ	0.82	1.97	2.7843 (16)	173

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

Data collection: *COLLECT* (Nonius, 2000); cell refinement: *SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO* (Otwinowski & Minor, 1997) and *SCALEPACK*; program(s) used to solve structure: *SIR97* (Altomare *et al.*, 1999); program(s) used to refine structure: *SHELXL2013* (Sheldrick, 2015); molecular graphics: *OLEX2* (Dolomanov *et al.*, 2009) and *Mercury* (Macrae *et al.*, 2008); software used to prepare material for publication: *pubCIF* (Westrip, 2010).

Acknowledgements

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Supporting information for this paper is available from the IUCr electronic archives (Reference: XU5859).

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S1. Comment

The title compound $C_9H_{10}O_3$ (Fig. 1), 2,4-dihydroxy-6-methylacetophenone [systematic name: 1-(2,4-dihydroxy-6-methylphenyl) ethanone], was a pentaketide secondary metabolite isolated from the culture media of the endophytic fungus *Nodulisporium* sp. Derivatives of this acetophenone have been demonstrated to possess interesting pharmacological activities, such as inhibition of lettuce seeds (Tabuchi *et al.*, 2014), bacterial plasmid transfer inhibition (Das and Khosla, 2009) and anticancer activity (Suzuki *et al.*, 2006). It is an important biosynthesis precursor for a large varieties of bioactive polyketides.

The geometric parameters of this compound (Fig. 2) are comparable with previously reported values of similar acetophenone compounds (Azeezaa *et al.*, 2009; Chakkaravarthi *et al.*, 2007a; Hill *et al.*, 2012). The bond lengths of C7—C8 and C6—C12 (1.4970 (2) and 1.5050 (2) Å), longer than that of C1—C7 (1.4580 (2) Å), may be a result of a resonant effect between C7—O9 (1.2485 (18) Å) carbonyl group and the aromatic ring. The bond length of C2—O10 (1.3466 (18) Å) is shorter than C4—O11 (1.3573 (19) Å). This may be a result of O10 being involved in an intramolecular hydrogen bond. The acetyl group is coplanar with the aromatic ring C2—C1—C7—O9 (dihedral angle of 7.2 (2) °). The torsion angles C7—C1—C6—C12 and C7—C1—C6—C5 [1.9 (2)° and -179.75 (13)°, respectively] indicate a planar conformation of the respective moieties. An intramolecular hydrogen bond was observed between the 2-phenolic hydrogen to the carbonyl group, O10—H10...O9 (D—H...A = 2.4983 (16) Å and O—H...O = 145°) to hold a carbonyl functionality in the coplanar plane of the aromatic ring. Intermolecular hydrogen bonds between the 4-hydroxyl group to the carbonyl oxygen O11—H11...O9 (D—H...A = 2.7862 (18) Å and O—H...O = 171°) link the molecules in to an extended polymeric structure (Fig. 1). The π ... π stacking intermolecular interactions between two aromatic rings (centroid C1—C6) with a distance of (3.7478 (8) Å) (Fig. 2), further stabilize the three-dimensional network.

S2. Experimental

The culture media of the endophytic fungus *Nodulisporium* sp. (10 L) were extracted with EtOAc (6 x 500 mL). After removal of the solvent under reduced pressure, the EtOAc extract (2.25 g) was subjected to column chromatography over silica gel eluting with EtOAc:hexane (30-100%), followed by MeOH:EtOAc (0-100%) to yield fractions 1-19. After combination and removal of the solvents, fraction 4 (162.9 mg) was further purified by Sephadex LH-20 (20% H₂O-MeOH) to yield 2,4-dihydroxy-6-methylacetophenone (133 mg). Single crystals were obtained by slow evaporation from EtOAc solution.

S3. Refinement

The methyl H atoms were constrained to an ideal geometry with C—H distances of 0.98 Å and each group was allowed to rotate freely about its C—C bond. All other hydrogen atoms were placed in idealized locations (C—H = 0.96–0.98 Å, O—H = 0.82 Å) and refined as riding with $U_{iso}(H) = 1.2U_{eq}(C)$ or $1.5U_{eq}(O, \text{methyl } C)$.

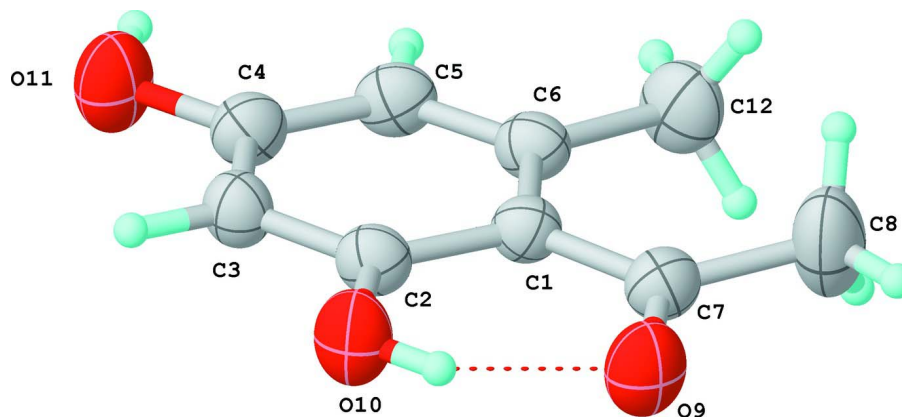


Figure 1

The molecular structure of the title compound with displacement ellipsoids drawn at the 50% probability level.

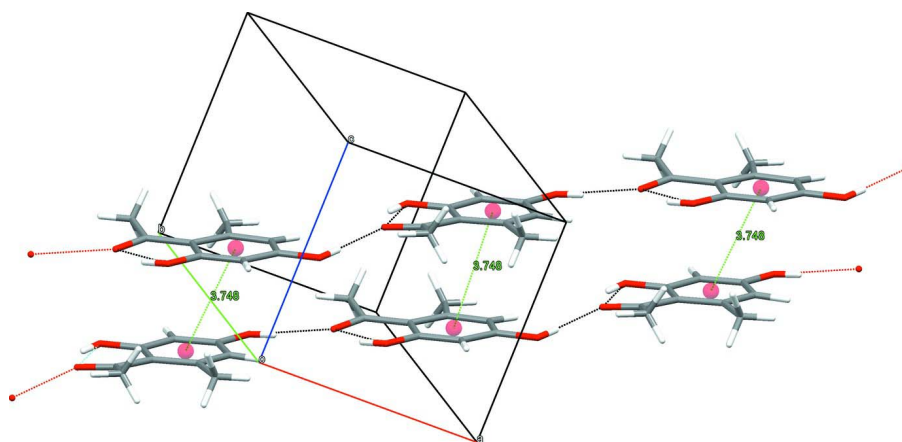


Figure 2

The partial packing diagram shows layers of molecules built up by bifurcated O—H...O hydrogen bonds and π – π intermolecular interactions between phenyl rings.

1-(2,4-Dihydroxy-6-methylphenyl)ethanone

Crystal data

$\text{C}_9\text{H}_{10}\text{O}_3$

$M_r = 166.17$

Monoclinic, $P2_1/c$

$a = 7.3570$ (3) Å

$b = 15.001$ (1) Å

$c = 7.3180$ (5) Å

$\beta = 91.017$ (4)°

$V = 807.50$ (8) Å³

$Z = 4$

$F(000) = 352$

$D_x = 1.367$ Mg m⁻³

Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å

Cell parameters from 1754 reflections

$\theta = 1.0$ – 27.5°

$\mu = 0.10$ mm⁻¹

$T = 298$ K

Block, yellow

$0.25 \times 0.25 \times 0.25$ mm

Data collection

Nonius KappaCCD
diffractometer

Radiation source: fine-focus sealed tube

Detector resolution: 9 pixels mm⁻¹

CCD scans

3260 measured reflections

1828 independent reflections

1319 reflections with $I > 2\sigma(I)$

$R_{\text{int}} = 0.028$
 $\theta_{\text{max}} = 27.5^\circ$, $\theta_{\text{min}} = 3.1^\circ$
 $h = -9 \rightarrow 9$

$k = -17 \rightarrow 19$
 $l = -9 \rightarrow 9$

Refinement

Refinement on F^2
 Least-squares matrix: full
 $R[F^2 > 2\sigma(F^2)] = 0.053$
 $wR(F^2) = 0.150$
 $S = 1.03$
 1828 reflections
 114 parameters
 0 restraints
 Primary atom site location: structure-invariant
 direct methods
 Secondary atom site location: difference Fourier
 map

Hydrogen site location: inferred from
 neighbouring sites
 H-atom parameters constrained
 $w = 1/[\sigma^2(F_o^2) + (0.0739P)^2 + 0.1187P]$
 where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{\text{max}} < 0.001$
 $\Delta\rho_{\text{max}} = 0.22 \text{ e } \text{\AA}^{-3}$
 $\Delta\rho_{\text{min}} = -0.17 \text{ e } \text{\AA}^{-3}$
 Extinction correction: *SHELXL2013* (Sheldrick,
 2015), $F_c^* = kF_c[1 + 0.001x F_c^2 \lambda^3 / \sin(2\theta)]^{-1/4}$
 Extinction coefficient: 0.06 (2)

Special details

Geometry. All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes.

Refinement. Refinement of F^2 against ALL reflections. The weighted R -factor wR and goodness of fit S are based on F^2 , conventional R -factors R are based on F , with F set to zero for negative F^2 . The threshold expression of $F^2 > \sigma(F^2)$ is used only for calculating R -factors(gt) etc. and is not relevant to the choice of reflections for refinement. R -factors based on F^2 are statistically about twice as large as those based on F , and R -factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (\AA^2)

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
C1	0.70787 (19)	0.22482 (9)	0.77437 (17)	0.0385 (4)
C2	0.70538 (18)	0.32006 (10)	0.77086 (18)	0.0407 (4)
C3	0.8510 (2)	0.37042 (10)	0.83381 (19)	0.0436 (4)
H3	0.8441	0.4381	0.8326	0.052*
C4	1.00510 (19)	0.32826 (10)	0.89794 (19)	0.0447 (4)
C5	1.0142 (2)	0.23520 (10)	0.9001 (2)	0.0446 (4)
H5	1.1320	0.2021	0.9410	0.053*
C6	0.87053 (19)	0.18331 (10)	0.84171 (17)	0.0416 (4)
C7	0.5457 (2)	0.17763 (10)	0.70990 (19)	0.0456 (4)
C8	0.5184 (3)	0.07921 (13)	0.7285 (3)	0.0776 (6)
H8A	0.6044	0.0483	0.6544	0.116*
H8B	0.3972	0.0640	0.6891	0.116*
H8C	0.5360	0.0622	0.8541	0.116*
O9	0.41657 (15)	0.21912 (7)	0.63688 (18)	0.0588 (4)
O10	0.55972 (15)	0.36627 (7)	0.70969 (17)	0.0552 (4)
H10	0.4830	0.3316	0.6688	0.083*
O11	1.14661 (16)	0.37918 (8)	0.95736 (18)	0.0631 (4)
H11	1.2256	0.3471	1.0026	0.095*
C12	0.9014 (3)	0.08414 (11)	0.8510 (2)	0.0607 (5)
H12A	0.8165	0.0580	0.9335	0.073*

H12B	1.0231	0.0725	0.8940	0.073*
H12C	0.8842	0.0588	0.7315	0.073*

Atomic displacement parameters (\AA^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0408 (8)	0.0373 (8)	0.0373 (7)	0.0021 (6)	−0.0033 (6)	0.0009 (5)
C2	0.0384 (7)	0.0409 (8)	0.0426 (7)	0.0061 (6)	−0.0036 (5)	0.0034 (6)
C3	0.0438 (8)	0.0373 (8)	0.0496 (8)	0.0011 (6)	−0.0048 (6)	0.0029 (6)
C4	0.0404 (8)	0.0485 (9)	0.0449 (8)	−0.0015 (6)	−0.0053 (6)	0.0013 (6)
C5	0.0402 (8)	0.0481 (9)	0.0452 (8)	0.0092 (6)	−0.0059 (6)	0.0017 (6)
C6	0.0464 (8)	0.0393 (8)	0.0390 (7)	0.0068 (6)	−0.0027 (6)	0.0024 (5)
C7	0.0462 (8)	0.0469 (9)	0.0436 (8)	−0.0020 (7)	−0.0047 (6)	0.0001 (6)
C8	0.0771 (13)	0.0495 (11)	0.1050 (15)	−0.0156 (9)	−0.0344 (11)	0.0089 (10)
O9	0.0443 (7)	0.0558 (7)	0.0756 (8)	−0.0015 (5)	−0.0172 (5)	0.0004 (5)
O10	0.0447 (7)	0.0420 (6)	0.0782 (8)	0.0077 (5)	−0.0177 (5)	0.0043 (5)
O11	0.0475 (7)	0.0556 (7)	0.0853 (9)	−0.0071 (5)	−0.0213 (6)	0.0027 (6)
C12	0.0671 (11)	0.0429 (9)	0.0717 (11)	0.0126 (8)	−0.0123 (8)	0.0029 (8)

Geometric parameters (\AA , $^\circ$)

C1—C6	1.4288 (18)	C6—C12	1.506 (2)
C1—C2	1.429 (2)	C7—O9	1.2481 (18)
C1—C7	1.4585 (19)	C7—C8	1.497 (2)
C2—O10	1.3462 (16)	C8—H8A	0.9600
C2—C3	1.3831 (19)	C8—H8B	0.9600
C3—C4	1.374 (2)	C8—H8C	0.9600
C3—H3	1.0170	O10—H10	0.8200
C4—O11	1.3566 (18)	O11—H11	0.8200
C4—C5	1.398 (2)	C12—H12A	0.9600
C5—C6	1.375 (2)	C12—H12B	0.9600
C5—H5	1.0380	C12—H12C	0.9600
C6—C1—C2	116.89 (13)	O9—C7—C1	120.57 (14)
C6—C1—C7	125.12 (13)	O9—C7—C8	115.38 (14)
C2—C1—C7	117.99 (12)	C1—C7—C8	124.04 (14)
O10—C2—C3	115.89 (13)	C7—C8—H8A	109.5
O10—C2—C1	122.05 (13)	C7—C8—H8B	109.5
C3—C2—C1	122.04 (12)	H8A—C8—H8B	109.5
C4—C3—C2	119.47 (14)	C7—C8—H8C	109.5
C4—C3—H3	120.3	H8A—C8—H8C	109.5
C2—C3—H3	120.3	H8B—C8—H8C	109.5
O11—C4—C3	118.31 (14)	C2—O10—H10	109.5
O11—C4—C5	121.49 (13)	C4—O11—H11	109.5
C3—C4—C5	120.19 (13)	C6—C12—H12A	109.5
C6—C5—C4	121.71 (13)	C6—C12—H12B	109.5
C6—C5—H5	116.9	H12A—C12—H12B	109.5
C4—C5—H5	121.4	C6—C12—H12C	109.5

C5—C6—C1	119.68 (13)	H12A—C12—H12C	109.5
C5—C6—C12	115.52 (13)	H12B—C12—H12C	109.5
C1—C6—C12	124.79 (14)		
C6—C1—C2—O10	179.79 (12)	C4—C5—C6—C1	0.9 (2)
C7—C1—C2—O10	−0.3 (2)	C4—C5—C6—C12	179.57 (14)
C6—C1—C2—C3	−1.66 (19)	C2—C1—C6—C5	0.41 (19)
C7—C1—C2—C3	178.24 (13)	C7—C1—C6—C5	−179.48 (13)
O10—C2—C3—C4	−179.77 (13)	C2—C1—C6—C12	−178.14 (14)
C1—C2—C3—C4	1.6 (2)	C7—C1—C6—C12	2.0 (2)
C2—C3—C4—O11	179.41 (13)	C6—C1—C7—O9	−172.96 (13)
C2—C3—C4—C5	−0.2 (2)	C2—C1—C7—O9	7.2 (2)
O11—C4—C5—C6	179.36 (14)	C6—C1—C7—C8	8.5 (2)
C3—C4—C5—C6	−1.0 (2)	C2—C1—C7—C8	−171.41 (16)

Hydrogen-bond geometry (Å, °)

<i>D</i> —H \cdots <i>A</i>	<i>D</i> —H	H \cdots <i>A</i>	<i>D</i> \cdots <i>A</i>	<i>D</i> —H \cdots <i>A</i>
O10—H10 \cdots O9	0.82	1.77	2.4991 (16)	147
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