

3-Hydroxy-2-(4-methylphenyl)-4*H*-chromen-4-one

Clifford W. Padgett,* Will E. Lynch, Kirkland Sheriff, Raven Dean and Sarah Zingales

Georgia Southern University, 11935 Abercorn St., Department of Chemistry and Biochemistry, Savannah GA 31419, USA. *Correspondence e-mail: cpadgett@georgiasouthern.edu

Received 27 June 2018
Accepted 9 August 2018

Edited by S. Bernès, Benemérita Universidad Autónoma de Puebla, México

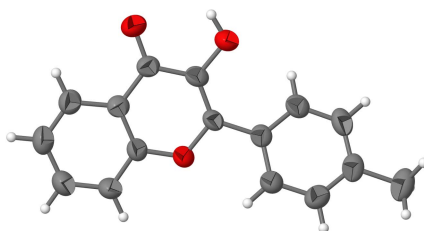
Keywords: crystal structure; benzopyran; flavone; hydrogen bond.

CCDC reference: 1861212

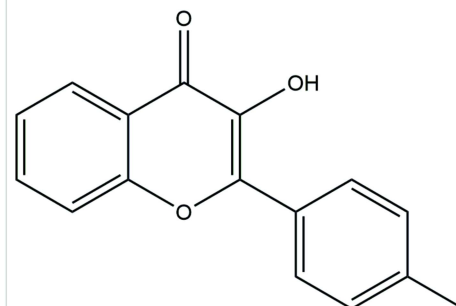
Structural data: full structural data are available from iucrdata.iucr.org

Our work in the area of carbon-monoxide-releasing molecules led to the synthesis and crystallization of new flavone derivatives as intermediates. Herein we report the first crystal structure of the title compound, C₁₆H₁₂O₃, a hydroxy-substituted flavone where the 2-phenyl group has been replaced by a *p*-tolyl group. The introduction of the 3-hydroxy group allows the formation of intermolecular O—H···O=C hydrogen bonds, used to build centrosymmetric R₂²(10) ring motifs in the crystal.

3D view



Chemical scheme



Structure description

Flavones contain the 2-phenylbenzopyran pharmacophore and are secondary metabolites of plants. They possess many biological activities, including antibiotic, anticancer, and antioxidant behavior. Recently, there has been interest in flavones as carbon-monoxide-releasing molecules (CORMs; Anderson *et al.*, 2015). Our work in this area led to the synthesis and crystallization of flavones as intermediates. Herein we report the first crystal structure of a new 3-hydroxyflavone (Fig. 1), which forms a hydrogen-bonded dimer. The hydrogen bonding occurs between O atoms of the benzopyranone ring with an R(10) synthon. The hydrogen bond between O2 and O3ⁱ is characterized by an O···O separation of 2.721 (2) Å [symmetry code: (i) $-x + 2, -y + 2, -z + 1$; Table 1], and the ring motifs R₂²(10) are placed on inversion centers in the space group *P*2₁/*n* (Fig. 2). A secondary intramolecular C—H···O hydrogen bond (Table 1, entry 2) also involves the hydroxy O2 atom as an acceptor group, forming an S(6) motif. The centroid Cg1 of the tolyl ring (C10–C15) and the centroid Cg2 of a symmetry-related pyranone ring (C1–C4/C9/O1; symmetry code: $x, y - 1, z$) are separated by 3.7525 (15) Å, with both rings almost parallel. This is the only significant π – π interaction observed in the crystal. The molecule is nearly planar, with the tolyl and benzopyranone rings forming a dihedral angle of 18.27 (8)°. This is consistent with several other similar flavonoids, for example, 2-(4-

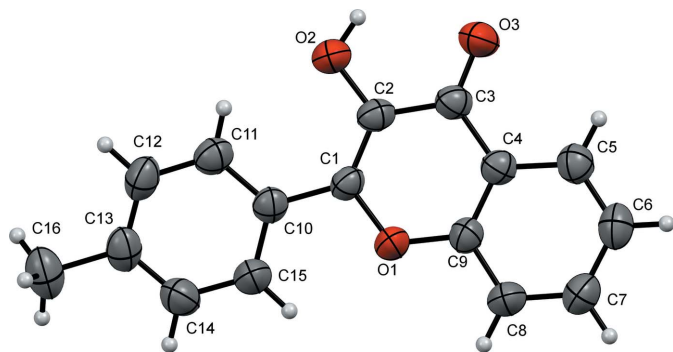


Figure 1
A view of the molecular structure of the title compound, showing the atom labeling. Displacement ellipsoids are drawn at the 50% probability level.

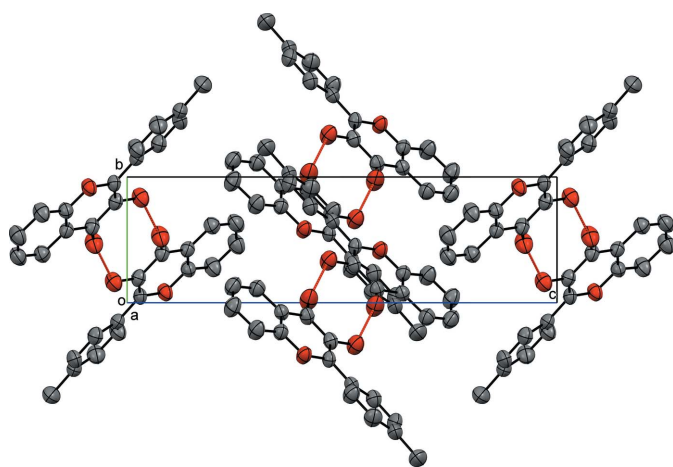


Figure 2
Crystal packing diagram of the title compound, viewed along the *a* axis. H atoms have been omitted for clarity and O...O bonds represent hydrogen-bonded O-atom sites.

chlorophenyl)-3-hydroxy-4*H*-chromen-4-one is nearly planar, with the phenyl ring tilted by 15.92 (8)° with respect to the benzopyranone ring (Zingales & Padgett, 2017), 3-hydroxy-2-(4-hydroxyphenyl)-4*H*-chromen-4-one, where the angle is 18.9 (4)° (Wera *et al.*, 2011*a*), and 3-hydroxy-2-(4-methoxyphenyl)-4*H*-chromen-4-one, where the corresponding angle is 12.3 (1)° (Wera *et al.*, 2011*b*). The crystal structure exhibits a classic herringbone pattern (Fig. 2) with the blocks consisting of the hydrogen-bonded dimers.

Synthesis and crystallization

The title compound was synthesized (Fig. 3) by the aldol condensation of 2-hydroxyacetophenone and 4-methyl-

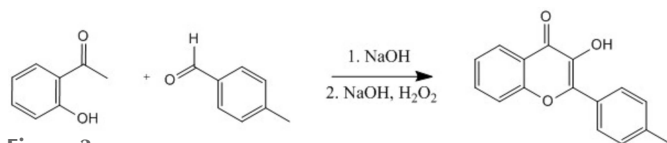


Figure 3
Synthesis of the title compound.

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

<i>D</i> —H... <i>A</i>	<i>D</i> —H	H... <i>A</i>	<i>D</i> ... <i>A</i>	<i>D</i> —H... <i>A</i>
O2—H2...O3 ⁱ	0.88 (2)	1.92 (2)	2.721 (2)	151 (3)
C11—H11...O2	0.93	2.24	2.838 (3)	122

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

benzaldehyde to yield the chalcone (*E*)-1-(2-hydroxyphenyl)-3-(*p*-tolyl)prop-2-en-1-one, followed by its oxidative cyclization to the flavone, as reported in the literature (Kurzwehnart *et al.*, 2012). 2-Hydroxyacetophenone (4.8 g, 36 mmol) and 4-methylbenzaldehyde (4.3 g, 36 mmol) were dissolved in ethanol (90 ml). An NaOH solution (5 *M*, 30 ml) was added and the reaction was stirred until a precipitate formed. The reaction mixture was acidified to pH 6 with dilute acetic acid. The solids were filtered off and taken directly to the next step. (*E*)-1-(2-Hydroxyphenyl)-3-(*p*-tolyl)prop-2-en-1-one (3.5 g, 14 mmol) was then suspended in EtOH (30 ml) and cooled in an ice water bath. An NaOH solution (5 *M*, 5 ml) and H₂O₂ (30%, 2.2 equiv., 3 ml) were added and the reaction stirred overnight, warming to room temperature. The reaction mixture was acidified to pH 1 with HCl (6 *M*) and poured into cold water (400 ml). The white solid was collected by filtration and recrystallization of an MeOH solution afforded yellow

Table 2
Experimental details.

Crystal data	
Chemical formula	C ₁₆ H ₁₂ O ₃
<i>M_r</i>	252.26
Crystal system, space group	Monoclinic, <i>P</i> 2 ₁ / <i>n</i>
Temperature (K)	293
<i>a</i> , <i>b</i> , <i>c</i> (Å)	13.2958 (13), 5.1981 (4), 18.8162 (15)
β (°)	109.212 (9)
<i>V</i> (Å ³)	1228.02 (19)
<i>Z</i>	4
Radiation type	Mo <i>K</i> α
μ (mm ⁻¹)	0.09
Crystal size (mm)	0.50 × 0.20 × 0.05
Data collection	
Diffractometer	Rigaku XtaLAB mini
Absorption correction	Multi-scan (<i>CrysAlis PRO</i> ; Rigaku OD, 2018)
<i>T</i> _{min} , <i>T</i> _{max}	0.838, 1.000
No. of measured, independent and observed [<i>I</i> > 2σ(<i>I</i>)] reflections	12529, 2252, 1394
<i>R</i> _{int}	0.056
(sin θ / λ) _{max} (Å ⁻¹)	0.602
Refinement	
<i>R</i> [<i>F</i> ² > 2σ(<i>F</i> ²)], <i>wR</i> (<i>F</i> ²), <i>S</i>	0.054, 0.170, 1.04
No. of reflections	2252
No. of parameters	176
No. of restraints	1
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å ⁻³)	0.21, -0.20

Computer programs: *CrysAlis PRO* (Rigaku OD, 2018), *SHELXT2018* (Sheldrick, 2015*a*), *SHELXL2018/3* (Sheldrick, 2015*b*) and *OLEX2* (Dolomanov *et al.*, 2009).

crystals (1.7 g, 19% yield over two steps). The structure was confirmed to match the literature (Kurzwehnart *et al.*, 2012). ^1H NMR (300 MHz, CDCl_3 , p.p.m.): δ 8.26 (*dd*, $J = 1.2, 8.1$ Hz, 1H, Ar–H), 8.17 (*d*, $J = 8.2$ Hz, 2H, Ar–H), 7.72 (*td*, $J = 1.7, 8.6$ Hz, 1H, Ar–H), 7.6 (*d*, $J = 8.2$ Hz, 1H, Ar–H), 7.42 (*t*, $J = 7.6$ Hz, 1H, Ar–H), 7.36 (*d*, $J = 8.2$ Hz, 2H, Ar–H), 7.01 (*bs*, 1H, OH), 2.45 (*s*, 3H, CH_3).

Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2.

Acknowledgements

The authors would like to thank Georgia Southern University for support of this work.

References

- Anderson, S. N., Richards, J. M., Esquer, H. J., Benninghoff, A. D., Arif, A. M. & Berreau, L. M. (2015). *ChemistryOpen*, **4**, 590–594.
- Dolomanov, O. V., Bourhis, L. J., Gildea, R. J., Howard, J. A. K. & Puschmann, H. (2009). *J. Appl. Cryst.* **42**, 339–341.
- Kurzwehnart, A., Kandioller, W., Bächler, S., Bartel, C., Martic, S., Buczkowska, M., Mühlgassner, G., Jakupec, M. A., Kraatz, H.-B., Bednarski, P. J., Arion, V. B., Marko, D., Keppler, B. K. & Hartinger, C. G. (2012). *J. Med. Chem.* **55**, 10512–10522.
- Rigaku OD (2018). *CrysAlis PRO*. Oxford Diffraction/Agilent Technologies UK Ltd, Yarnton, Oxfordshire, England.
- Sheldrick, G. M. (2015a). *Acta Cryst.* **A71**, 3–8.
- Sheldrick, G. M. (2015b). *Acta Cryst.* **C71**, 3–8.
- Wera, M., Pivovarenko, V. G. & Błażejowski, J. (2011a). *Acta Cryst.* **E67**, o264–o265.
- Wera, M., Serdiuk, I. E., Roshal, A. D. & Błażejowski, J. (2011b). *Acta Cryst.* **E67**, o440.
- Zingales, S. & Padgett, C. (2017). *IUCrData*, **2**, x170996.

full crystallographic data

IUCrData (2018). 3, x181138 [https://doi.org/10.1107/S2414314618011380]

3-Hydroxy-2-(4-methylphenyl)-4*H*-chromen-4-one

Clifford W. Padgett, Will E. Lynch, Kirkland Sheriff, Raven Dean and Sarah Zingales

3-Hydroxy-2-(4-methylphenyl)-4*H*-chromen-4-one*Crystal data*

$C_{16}H_{12}O_3$	$F(000) = 528$
$M_r = 252.26$	$D_x = 1.364 \text{ Mg m}^{-3}$
Monoclinic, $P2_1/n$	Mo $K\alpha$ radiation, $\lambda = 0.71073 \text{ \AA}$
$a = 13.2958 (13) \text{ \AA}$	Cell parameters from 1203 reflections
$b = 5.1981 (4) \text{ \AA}$	$\theta = 2.3\text{--}21.8^\circ$
$c = 18.8162 (15) \text{ \AA}$	$\mu = 0.09 \text{ mm}^{-1}$
$\beta = 109.212 (9)^\circ$	$T = 293 \text{ K}$
$V = 1228.02 (19) \text{ \AA}^3$	Needle, yellow
$Z = 4$	$0.50 \times 0.20 \times 0.05 \text{ mm}$

Data collection

Rigaku XtaLAB mini diffractometer	$T_{\min} = 0.838, T_{\max} = 1.000$
Radiation source: Sealed Tube, Rigaku (Mo) X-ray Source	12529 measured reflections
Graphite Monochromator monochromator	2252 independent reflections
Detector resolution: 13.6612 pixels mm^{-1}	1394 reflections with $I > 2\sigma(I)$
profile data from ω -scans	$R_{\text{int}} = 0.056$
Absorption correction: multi-scan	$\theta_{\max} = 25.3^\circ, \theta_{\min} = 2.3^\circ$
CrysAlisPro (Rigaku OD, 2018)	$h = -15 \rightarrow 16$
	$k = -5 \rightarrow 6$
	$l = -22 \rightarrow 22$

Refinement

Refinement on F^2	Secondary atom site location: difference Fourier map
Least-squares matrix: full	Hydrogen site location: mixed
$R[F^2 > 2\sigma(F^2)] = 0.054$	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.170$	$w = 1/[\sigma^2(F_o^2) + (0.0872P)^2 + 0.0826P]$
$S = 1.04$	where $P = (F_o^2 + 2F_c^2)/3$
2252 reflections	$(\Delta/\sigma)_{\max} < 0.001$
176 parameters	$\Delta\rho_{\max} = 0.21 \text{ e \AA}^{-3}$
1 restraint	$\Delta\rho_{\min} = -0.19 \text{ e \AA}^{-3}$
Primary atom site location: dual	

Special details

Refinement. All C-bound H atoms were positioned geometrically and refined as riding, with C—H = 0.93 or 0.96 Å and $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$ or $U_{\text{iso}}(\text{H}) = 1.5U_{\text{eq}}(\text{C})$ for C(H) and CH₃ groups, respectively. H atoms involved in O—H⋯O hydrogen bonds were located on a difference Fourier map and refined isotropically with $U_{\text{iso}}(\text{H}) = 1.5U_{\text{eq}}(\text{O})$. The H2—O2 distance was restrained to a target value of 0.84 (2) Å, using a DFIX command in *SHELXL* (Sheldrick, 2015b).

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

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
O1	0.64822 (13)	0.5830 (3)	0.41165 (9)	0.0524 (5)
O2	0.92078 (14)	0.6646 (4)	0.53130 (10)	0.0596 (5)
H2	0.965 (2)	0.788 (5)	0.5307 (17)	0.089*
O3	0.90470 (15)	1.0256 (4)	0.42282 (10)	0.0690 (6)
C1	0.74245 (18)	0.5511 (4)	0.46966 (12)	0.0432 (6)
C2	0.82869 (18)	0.6966 (5)	0.47341 (13)	0.0454 (6)
C3	0.82503 (19)	0.8942 (5)	0.41869 (13)	0.0475 (6)
C4	0.72316 (19)	0.9250 (4)	0.35938 (13)	0.0444 (6)
C5	0.7068 (2)	1.1130 (5)	0.30258 (14)	0.0542 (7)
H5	0.761741	1.224393	0.303120	0.065*
C6	0.6103 (2)	1.1322 (5)	0.24672 (15)	0.0633 (8)
H6	0.599902	1.256239	0.209369	0.076*
C7	0.5278 (2)	0.9665 (6)	0.24576 (16)	0.0652 (8)
H7	0.462708	0.979595	0.207336	0.078*
C8	0.5412 (2)	0.7834 (5)	0.30083 (14)	0.0609 (8)
H8	0.485876	0.672806	0.300054	0.073*
C9	0.6391 (2)	0.7672 (5)	0.35765 (13)	0.0474 (6)
C10	0.73289 (19)	0.3510 (4)	0.52236 (12)	0.0448 (6)
C11	0.8214 (2)	0.2358 (5)	0.57398 (13)	0.0537 (7)
H11	0.889464	0.284054	0.575491	0.064*
C12	0.8091 (2)	0.0512 (5)	0.62279 (15)	0.0601 (7)
H12	0.869413	-0.024043	0.656593	0.072*
C13	0.7094 (2)	-0.0264 (5)	0.62317 (14)	0.0569 (7)
C14	0.6227 (2)	0.0887 (5)	0.57241 (15)	0.0641 (8)
H14	0.555015	0.041315	0.571865	0.077*
C15	0.6321 (2)	0.2730 (5)	0.52190 (15)	0.0599 (7)
H15	0.571313	0.344940	0.487657	0.072*
C16	0.6976 (3)	-0.2350 (6)	0.67638 (15)	0.0745 (9)
H16A	0.709676	-0.400200	0.657852	0.112*
H16B	0.626982	-0.229299	0.679462	0.112*
H16C	0.748656	-0.207334	0.725449	0.112*

Atomic displacement parameters (\AA^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0470 (10)	0.0573 (11)	0.0434 (10)	-0.0100 (8)	0.0021 (8)	0.0074 (8)
O2	0.0438 (11)	0.0700 (13)	0.0563 (11)	-0.0092 (9)	0.0045 (9)	0.0091 (10)
O3	0.0565 (12)	0.0855 (14)	0.0582 (12)	-0.0253 (11)	0.0099 (9)	0.0103 (10)
C1	0.0399 (14)	0.0497 (14)	0.0345 (12)	-0.0004 (11)	0.0048 (10)	-0.0002 (10)
C2	0.0389 (14)	0.0545 (15)	0.0399 (13)	-0.0022 (11)	0.0089 (11)	-0.0050 (11)
C3	0.0456 (15)	0.0565 (16)	0.0393 (13)	-0.0089 (12)	0.0123 (12)	-0.0036 (11)
C4	0.0466 (14)	0.0485 (14)	0.0374 (13)	-0.0045 (11)	0.0130 (11)	-0.0046 (10)
C5	0.0595 (17)	0.0555 (16)	0.0478 (15)	-0.0037 (13)	0.0179 (14)	0.0028 (12)
C6	0.074 (2)	0.0633 (18)	0.0525 (17)	0.0055 (15)	0.0211 (16)	0.0145 (13)
C7	0.0559 (18)	0.077 (2)	0.0538 (16)	0.0015 (15)	0.0057 (14)	0.0140 (14)

C8	0.0465 (16)	0.0712 (18)	0.0551 (16)	-0.0122 (13)	0.0032 (13)	0.0087 (14)
C9	0.0491 (15)	0.0487 (14)	0.0401 (13)	-0.0023 (12)	0.0089 (11)	0.0040 (11)
C10	0.0508 (15)	0.0422 (13)	0.0368 (13)	-0.0047 (11)	0.0082 (11)	-0.0039 (10)
C11	0.0517 (16)	0.0588 (16)	0.0445 (14)	-0.0024 (13)	0.0077 (12)	-0.0025 (12)
C12	0.0697 (19)	0.0577 (17)	0.0427 (14)	0.0055 (14)	0.0047 (13)	0.0064 (12)
C13	0.081 (2)	0.0459 (15)	0.0391 (14)	-0.0079 (14)	0.0129 (14)	-0.0024 (11)
C14	0.0619 (19)	0.0672 (18)	0.0596 (17)	-0.0179 (14)	0.0153 (15)	0.0034 (14)
C15	0.0508 (16)	0.0649 (18)	0.0542 (15)	-0.0108 (14)	0.0042 (12)	0.0100 (13)
C16	0.110 (3)	0.0560 (18)	0.0596 (18)	-0.0103 (17)	0.0310 (18)	0.0045 (14)

Geometric parameters (Å, °)

O1—C9	1.372 (3)	C8—C9	1.389 (3)
O1—C1	1.374 (3)	C8—H8	0.9300
O2—C2	1.355 (3)	C10—C11	1.391 (3)
O2—H2	0.878 (18)	C10—C15	1.398 (4)
O3—C3	1.241 (3)	C11—C12	1.375 (4)
C1—C2	1.356 (3)	C11—H11	0.9300
C1—C10	1.471 (3)	C12—C13	1.387 (4)
C2—C3	1.444 (3)	C12—H12	0.9300
C3—C4	1.453 (3)	C13—C14	1.369 (4)
C4—C9	1.378 (3)	C13—C16	1.518 (4)
C4—C5	1.411 (3)	C14—C15	1.384 (4)
C5—C6	1.368 (4)	C14—H14	0.9300
C5—H5	0.9300	C15—H15	0.9300
C6—C7	1.390 (4)	C16—H16A	0.9600
C6—H6	0.9300	C16—H16B	0.9600
C7—C8	1.375 (4)	C16—H16C	0.9600
C7—H7	0.9300		
C9—O1—C1	120.49 (18)	O1—C9—C8	116.4 (2)
C2—O2—H2	110 (2)	C4—C9—C8	122.0 (2)
C2—C1—O1	120.6 (2)	C11—C10—C15	118.0 (2)
C2—C1—C10	128.2 (2)	C11—C10—C1	122.3 (2)
O1—C1—C10	111.23 (19)	C15—C10—C1	119.8 (2)
O2—C2—C1	119.9 (2)	C12—C11—C10	120.5 (3)
O2—C2—C3	118.0 (2)	C12—C11—H11	119.8
C1—C2—C3	122.0 (2)	C10—C11—H11	119.8
O3—C3—C2	121.3 (2)	C11—C12—C13	122.0 (3)
O3—C3—C4	123.3 (2)	C11—C12—H12	119.0
C2—C3—C4	115.5 (2)	C13—C12—H12	119.0
C9—C4—C5	118.2 (2)	C14—C13—C12	117.1 (2)
C9—C4—C3	119.8 (2)	C14—C13—C16	121.7 (3)
C5—C4—C3	122.0 (2)	C12—C13—C16	121.1 (3)
C6—C5—C4	120.3 (2)	C13—C14—C15	122.4 (3)
C6—C5—H5	119.9	C13—C14—H14	118.8
C4—C5—H5	119.9	C15—C14—H14	118.8
C5—C6—C7	120.1 (2)	C14—C15—C10	120.0 (3)

C5—C6—H6	120.0	C14—C15—H15	120.0
C7—C6—H6	120.0	C10—C15—H15	120.0
C8—C7—C6	120.9 (3)	C13—C16—H16A	109.5
C8—C7—H7	119.6	C13—C16—H16B	109.5
C6—C7—H7	119.6	H16A—C16—H16B	109.5
C7—C8—C9	118.6 (2)	C13—C16—H16C	109.5
C7—C8—H8	120.7	H16A—C16—H16C	109.5
C9—C8—H8	120.7	H16B—C16—H16C	109.5
O1—C9—C4	121.6 (2)		

Hydrogen-bond geometry (Å, °)

<i>D—H...A</i>	<i>D—H</i>	<i>H...A</i>	<i>D...A</i>	<i>D—H...A</i>
O2—H2...O3 ⁱ	0.88 (2)	1.92 (2)	2.721 (2)	151 (3)
C11—H11...O2	0.93	2.24	2.838 (3)	122

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