



# Crystal structure of 5-hydroxymethyl-2-methoxyphenol

Mubashir Hassan,<sup>a</sup> Zaman Ashraf,<sup>a,b</sup> Sung-Yum Seo,<sup>a</sup>  
Daeyoung Kim<sup>c</sup> and Sung Kwon Kang<sup>c\*</sup>

<sup>a</sup>Department of Biology, College of Natural Sciences, Kongju National University, Gongju 314-701, Republic of Korea, <sup>b</sup>Department of Chemistry, Allama Iqbal Open University, Islamabad 44000, Pakistan, and <sup>c</sup>Department of Chemistry, Chungnam National University, Daejeon 305-764, Republic of Korea. \*Correspondence e-mail: skkang@cnu.ac.kr

Received 25 June 2015; accepted 26 June 2015

Edited by E. R. T. Tiekink, University of Malaya, Malaysia

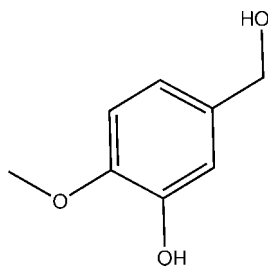
In the title compound, C<sub>8</sub>H<sub>10</sub>O<sub>3</sub>, the hydroxymethyl group is twisted by 74.51 (13)° from the plane of the benzene ring to which it is connected. By contrast, the benzene and methoxy groups are almost coplanar, making a dihedral angle of 4.0 (2)°. In the crystal, O—H...O hydrogen bonds link the molecules into a three-dimensional network.

**Keywords:** crystal structure; alcoholic hydroxy compounds; O—H...O hydrogen bonding.

**CCDC reference:** 1409010

## 1. Related literature

For the background to alcoholic hydroxy compounds and their applications, see: Patrick (2001); Yasohara *et al.* (2001); Rodríguez-Barrios & Gago (2004); Wu *et al.* (2008); Matteelli *et al.* (2010); Coimbra *et al.* (2010); Hans *et al.* (2010); Cordova *et al.* (2006). For the synthesis of derivatives of the title compound, see: Ashraf *et al.* (2014, 2015).



## 2. Experimental

### 2.1. Crystal data

C <sub>8</sub> H <sub>10</sub> O <sub>3</sub>	$V = 1523.6 (7) \text{ \AA}^3$
$M_r = 154.16$	$Z = 8$
Orthorhombic, <i>Pbca</i>	Mo $K\alpha$ radiation
$a = 15.011 (4) \text{ \AA}$	$\mu = 0.10 \text{ mm}^{-1}$
$b = 6.1354 (18) \text{ \AA}$	$T = 296 \text{ K}$
$c = 16.543 (5) \text{ \AA}$	$0.28 \times 0.25 \times 0.23 \text{ mm}$

### 2.2. Data collection

Bruker SMART CCD area-detector diffractometer	1900 independent reflections
28952 measured reflections	1530 reflections with $I > 2\sigma(I)$
	$R_{\text{int}} = 0.025$

### 2.3. Refinement

$R[F^2 > 2\sigma(F^2)] = 0.051$	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.149$	$\Delta\rho_{\text{max}} = 0.38 \text{ e \AA}^{-3}$
$S = 1.07$	$\Delta\rho_{\text{min}} = -0.42 \text{ e \AA}^{-3}$
1900 reflections	
108 parameters	

**Table 1**

Hydrogen-bond geometry (Å, °).

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
O1—H1...O9 <sup>i</sup>	0.74 (4)	2.11 (4)	2.773 (2)	150 (4)
O1—H1...O10 <sup>i</sup>	0.74 (4)	2.54 (4)	3.152 (2)	142 (4)
O9—H9...O1 <sup>ii</sup>	0.88 (4)	1.78 (4)	2.641 (2)	163 (3)

Symmetry codes: (i)  $x, -y + \frac{1}{2}, z + \frac{1}{2}$ ; (ii)  $-x + 1, y - \frac{1}{2}, -z + \frac{3}{2}$ .

Data collection: *SMART* (Bruker, 2002); cell refinement: *SAINT* (Bruker, 2002); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS2013* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL2013* (Sheldrick, 2015); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 2012); software used to prepare material for publication: *WinGX* (Farrugia, 2012).

Supporting information for this paper is available from the IUCr electronic archives (Reference: TK5370).

## References

- Ashraf, Z., Rafiq, M., Seo, S. Y., Babar, M. M. & Zaidi, N. S. S. (2014). *J. Enzyme Inhib. Med. Chem.* pp. 1–10.
- Ashraf, Z., Rafiq, M., Seo, S. Y., Kwon, K. S., Babar, M. M. & Zaidi, N. U. S. (2015). *Eur. J. Med. Chem.* **98**, 203–211.
- Bruker (2002). *SAINT* and *SMART*. Bruker AXS Inc., Madison, Wisconsin, USA.
- Coimbra, E. S., de Almeida, M. V., JÁ<sup>o</sup>nior, C. O. R., Taveira, A. F., da Costa, C. F., de Almeida, A. C., Reis, E. F. C. & da Silva, A. D. (2010). *Chem. Biol. Drug Des.* **75**, 233–235.
- Córdova, I., León, L. G., León, F., San Andrés, L., Luis, J. G. & Padrón, J. M. (2006). *Eur. J. Med. Chem.* **41**, 1327–1332.
- Farrugia, L. J. (2012). *J. Appl. Cryst.* **45**, 849–854.
- Hans, R. H., Gut, J., Rosenthal, P. J. & Chibale, K. (2010). *Bioorg. Med. Chem. Lett.* **20**, 2234–2237.
- Matteelli, A., Carvalho, A. C., Dooley, K. E. & Kritski, A. (2010). *Future Microbiol.* **5**, 849–858.
- Patrick, G. L. (2001). In *An Introduction to Medicinal Chemistry*. Oxford: University Press.
- Rodríguez-Barrios, F. & Gago, F. (2004). *Curr. Top. Med. Chem.* **4**, 991–1007.

Sheldrick, G. M. (2008). *Acta Cryst.* **A64**, 112–122.

Sheldrick, G. M. (2015). *Acta Cryst.* **C71**, 3–8.

Wu, X., Öhrngren, P., Ekegren, J. K., Unge, J., Unge, T., Wallberg, H., Samuelsson, B., Hallberg, A. & Larhed, M. (2008). *J. Med. Chem.* **51**, 1053–1057.

Yasohara, Y., Miyamoto, K., Kizaki, N. & Hasegawa, J. (2001). *Tetrahedron Lett.* **42**, 3331–3333.

---

# supporting information

*Acta Cryst.* (2015). E71, o540–o541 [https://doi.org/10.1107/S205698901501230X]

## Crystal structure of 5-hydroxymethyl-2-methoxyphenol

Mubashir Hassan, Zaman Ashraf, Sung-Yum Seo, Daeyoung Kim and Sung Kwon Kang

### S1. Chemical context

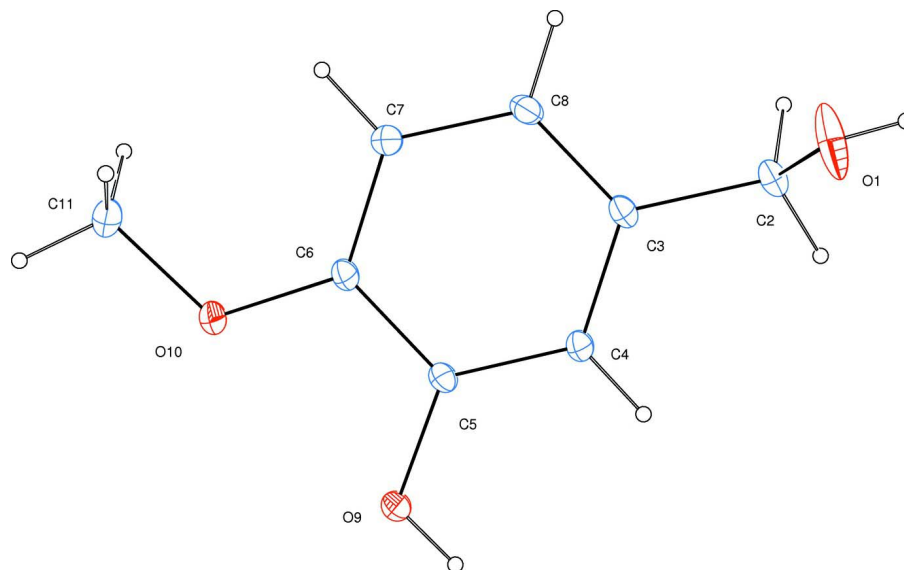
It has been identified that the presence of alcoholic, phenolic hydroxyl and amino groups are particularly important functionalities in biologically active compounds (Patrick, 2001). These important functionalities displayed biological activities because they can facilitate interactions with appropriate receptor molecules (Yasohara *et al.*, 2001). A new class of compounds having an alcoholic hydroxyl group showed high enzyme inhibitory potential and excellent permeation through a Caco-2 cell membrane (Rodríguez-Barrios & Gag, 2004). Some tertiary alcohol derivatives showed significant HIV-1 protease inhibitory activity (Wu *et al.*, 2008). Heterocyclic compounds such as diarylquinolines having a quinolinic central nucleus and alcoholic –OH group at the side-chains exhibited anti-mycobacterial activity (Matteelli *et al.*, 2010).  $\beta$ -Amino alcohols are a class of compounds with a wide range of bioactivities, such as anti-plasmodial (Hans *et al.*, 2010), anti-leishmanial (Coimbra *et al.*, 2010) and anti-proliferative (Cordova *et al.*, 2006). The hydroxy substituted benzoic acids and cinnamic acid analogues have been reported as mushroom tyrosinase inhibitors (Ashraf *et al.*, 2014; Ashraf *et al.*, 2015). Keeping in view the wide range of biological activities of hydroxylated compounds, here we report the synthesis and crystal structure of the title compound, isolated as an intermediate. The title alcohol is a valuable starting material for the synthesis of hydroxy substituted scaffolds.

### S2. Synthesis and crystallization

The title compound was synthesized by the reduction of isovanillin in the presence of sodium borohydride and methanol. The sodium borohydride reduction of aldehydes and ketones to the corresponding alcohols is a commonly used method in organic synthesis. Isovanillin was dissolved in methanol and then sodium borohydride was added at a slow rate to keep the reaction temperature below 25 °C. The excess of sodium borohydride was used to assure the completion of the reaction. After the completion of the reaction the product was obtained by acidic workup (86%, m.p. 135–137 °C). The title compound was crystallized as cubic crystals from a solution of ethyl acetate by slow evaporation.

### S3. Refinement

H atoms on OH groups were located in a difference Fourier map and refined freely [refined O—H distances = 0.74 (4) – 0.88 (4) Å]. The C-bound H atoms were positioned geometrically and refined using riding model, with  $d(\text{C—H}) = 0.93 - 0.97$  Å, and with  $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$  for phenyl-H and methylene-H and  $1.5U_{\text{eq}}(\text{C})$  for methyl-H atoms.



**Figure 1**

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

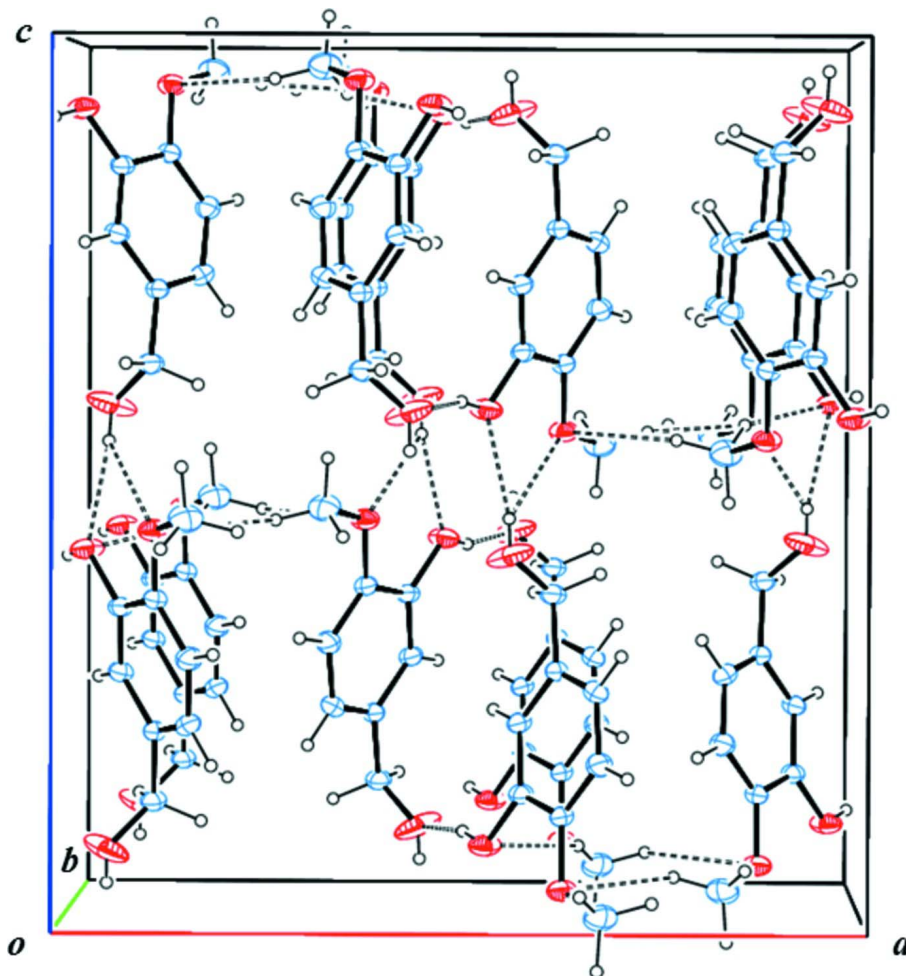


Figure 2

Part of the crystal structure of the title compound, showing the 3-D network of molecules linked by intermolecular O—H...O hydrogen bonds (dashed lines).

### 5-Hydroxymethyl-2-methoxyphenol

#### Crystal data

$C_8H_{10}O_3$

$M_r = 154.16$

Orthorhombic,  $Pbca$

Hall symbol:  $-P\ 2ac\ 2ab$

$a = 15.011\ (4)\ \text{\AA}$

$b = 6.1354\ (18)\ \text{\AA}$

$c = 16.543\ (5)\ \text{\AA}$

$V = 1523.6\ (7)\ \text{\AA}^3$

$Z = 8$

$F(000) = 656$

$D_x = 1.344\ \text{Mg m}^{-3}$

Mo  $K\alpha$  radiation,  $\lambda = 0.71073\ \text{\AA}$

Cell parameters from 7746 reflections

$\theta = 2.5\text{--}28.2^\circ$

$\mu = 0.10\ \text{mm}^{-1}$

$T = 296\ \text{K}$

Block, brown

$0.28 \times 0.25 \times 0.23\ \text{mm}$

#### Data collection

Bruker SMART CCD area-detector  
diffractometer

Radiation source: fine-focus sealed tube  
 $\varphi$  and  $\omega$  scans

28952 measured reflections

1900 independent reflections

1530 reflections with  $I > 2\sigma(I)$

$R_{\text{int}} = 0.025$

$\theta_{\max} = 28.4^\circ$ ,  $\theta_{\min} = 2.5^\circ$   
 $h = -20 \rightarrow 19$

$k = -8 \rightarrow 8$   
 $l = -22 \rightarrow 20$

*Refinement*

Refinement on  $F^2$   
 Least-squares matrix: full  
 $R[F^2 > 2\sigma(F^2)] = 0.051$   
 $wR(F^2) = 0.149$   
 $S = 1.07$   
 1900 reflections  
 108 parameters  
 0 restraints

Hydrogen site location: mixed  
 H atoms treated by a mixture of independent  
 and constrained refinement  
 $w = 1/[\sigma^2(F_o^2) + (0.0668P)^2 + 0.6464P]$   
 where  $P = (F_o^2 + 2F_c^2)/3$   
 $(\Delta/\sigma)_{\max} < 0.001$   
 $\Delta\rho_{\max} = 0.38 \text{ e } \text{\AA}^{-3}$   
 $\Delta\rho_{\min} = -0.42 \text{ e } \text{\AA}^{-3}$

*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.

*Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters ( $\text{\AA}^2$ )*

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
O1	0.56019 (17)	0.3078 (3)	0.91644 (10)	0.1025 (9)
H1	0.559 (2)	0.268 (6)	0.959 (2)	0.129 (13)*
C2	0.61335 (11)	0.1812 (3)	0.86876 (9)	0.0462 (4)
H2A	0.5895	0.0345	0.8663	0.055*
H2B	0.6727	0.1737	0.8919	0.055*
C3	0.61828 (10)	0.2752 (3)	0.78509 (9)	0.0383 (4)
C4	0.57178 (10)	0.1775 (3)	0.72196 (8)	0.0388 (4)
H4	0.5385	0.0524	0.7316	0.047*
C5	0.57476 (10)	0.2651 (3)	0.64505 (8)	0.0375 (3)
C6	0.62554 (10)	0.4516 (3)	0.62970 (9)	0.0368 (3)
C7	0.67100 (11)	0.5504 (3)	0.69227 (10)	0.0452 (4)
H7	0.7042	0.6757	0.6828	0.054*
C8	0.66682 (11)	0.4616 (3)	0.76955 (9)	0.0454 (4)
H8	0.6973	0.5292	0.8116	0.054*
O9	0.52924 (10)	0.1784 (2)	0.58164 (7)	0.0554 (4)
H9	0.498 (2)	0.060 (6)	0.5924 (18)	0.124 (12)*
O10	0.62581 (8)	0.5189 (2)	0.55089 (7)	0.0472 (3)
C11	0.67256 (15)	0.7139 (3)	0.53259 (12)	0.0588 (5)
H11A	0.6682	0.7433	0.4757	0.088*
H11B	0.7341	0.6976	0.5473	0.088*
H11C	0.647	0.8328	0.5624	0.088*

*Atomic displacement parameters ( $\text{\AA}^2$ )*

	$U^{11}$	$U^{22}$	$U^{33}$	$U^{12}$	$U^{13}$	$U^{23}$
O1	0.1593 (19)	0.1051 (14)	0.0432 (8)	0.0824 (14)	0.0458 (10)	0.0312 (9)
C2	0.0512 (9)	0.0580 (10)	0.0293 (7)	0.0082 (7)	-0.0009 (6)	0.0039 (7)
C3	0.0371 (7)	0.0506 (9)	0.0272 (7)	0.0057 (6)	0.0004 (5)	0.0000 (6)

C4	0.0443 (8)	0.0425 (8)	0.0296 (7)	-0.0036 (6)	0.0043 (6)	-0.0003 (6)
C5	0.0429 (7)	0.0434 (8)	0.0263 (7)	-0.0021 (6)	0.0013 (5)	-0.0039 (6)
C6	0.0395 (7)	0.0431 (8)	0.0277 (7)	0.0011 (6)	0.0025 (5)	0.0014 (6)
C7	0.0469 (8)	0.0503 (9)	0.0384 (8)	-0.0110 (7)	-0.0005 (6)	-0.0007 (7)
C8	0.0443 (8)	0.0590 (10)	0.0327 (8)	-0.0063 (7)	-0.0063 (6)	-0.0050 (7)
O9	0.0752 (9)	0.0631 (8)	0.0279 (6)	-0.0280 (7)	-0.0037 (5)	-0.0024 (5)
O10	0.0610 (7)	0.0505 (7)	0.0302 (6)	-0.0110 (5)	0.0009 (5)	0.0060 (5)
C11	0.0761 (13)	0.0528 (11)	0.0476 (10)	-0.0137 (9)	0.0028 (9)	0.0127 (8)

*Geometric parameters (Å, °)*

O1—C2	1.365 (2)	C6—O10	1.3677 (18)
O1—H1	0.74 (4)	C6—C7	1.380 (2)
C2—C3	1.501 (2)	C7—C8	1.391 (2)
C2—H2A	0.97	C7—H7	0.93
C2—H2B	0.97	C8—H8	0.93
C3—C8	1.380 (2)	O9—H9	0.88 (4)
C3—C4	1.392 (2)	O10—C11	1.420 (2)
C4—C5	1.382 (2)	C11—H11A	0.96
C4—H4	0.93	C11—H11B	0.96
C5—O9	1.3601 (18)	C11—H11C	0.96
C5—C6	1.398 (2)		
C2—O1—H1	112 (3)	O10—C6—C5	114.96 (13)
O1—C2—C3	110.07 (15)	C7—C6—C5	119.54 (14)
O1—C2—H2A	109.6	C6—C7—C8	119.66 (16)
C3—C2—H2A	109.6	C6—C7—H7	120.2
O1—C2—H2B	109.6	C8—C7—H7	120.2
C3—C2—H2B	109.6	C3—C8—C7	121.29 (14)
H2A—C2—H2B	108.2	C3—C8—H8	119.4
C8—C3—C4	118.80 (14)	C7—C8—H8	119.4
C8—C3—C2	121.06 (14)	C5—O9—H9	116 (2)
C4—C3—C2	120.12 (15)	C6—O10—C11	117.34 (13)
C5—C4—C3	120.48 (15)	O10—C11—H11A	109.5
C5—C4—H4	119.8	O10—C11—H11B	109.5
C3—C4—H4	119.8	H11A—C11—H11B	109.5
O9—C5—C4	122.81 (14)	O10—C11—H11C	109.5
O9—C5—C6	116.99 (13)	H11A—C11—H11C	109.5
C4—C5—C6	120.20 (13)	H11B—C11—H11C	109.5
O10—C6—C7	125.50 (15)		

*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>
O1—H1 $\cdots$ O9 <sup>i</sup>	0.74 (4)	2.11 (4)	2.773 (2)	150 (4)

---

O1—H1...O10 <sup>i</sup>	0.74 (4)	2.54 (4)	3.152 (2)	142 (4)
O9—H9...O1 <sup>ii</sup>	0.88 (4)	1.78 (4)	2.641 (2)	163 (3)

---

Symmetry codes: (i)  $x, -y+1/2, z+1/2$ ; (ii)  $-x+1, y-1/2, -z+3/2$ .