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2,3-Dichloro-3′,4′-dihydroxybiphenyl

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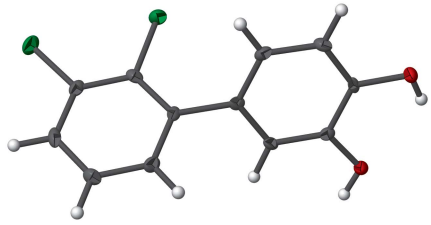
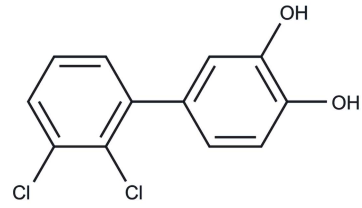
The title compound [systematic name: 4-(2,3-Dichlorophenyl)benzene-1,2-diol], $C_{12}H_8Cl_2O_2$, is a putative dihydroxylated metabolite of 2,3-dichlorobiphenyl (PCB 5). The title structure displays intramolecular O—H···O hydrogen bonding, and the π–π stacking distance between inversion-related chlorinated benzene rings of the title compound is 3.371 (3) Å. The dihedral angle between two benzene rings is 59.39 (8)°.

3D view



Chemical scheme



Structure description

Polychlorinated biphenyls (PCBs) are a class of environmental pollutants banned under the Stockholm Convention on Persistent Organic Pollutants (Stockholm Convention, 2008). Exposure to PCBs is associated with a range of adverse health effects, for example cancer and adverse neurotoxic outcomes (ATSDR, 2000; IARC, 2017). Cytochrome P450 enzymes oxidize PCB congeners in two steps to dihydroxylated metabolites (Lu *et al.*, 2013; McLean *et al.*, 1996). PCB metabolites with *ortho*- or *para*-substituted hydroxyl groups can be further oxidized to reactive and highly toxic PCB quinones (Dhakal *et al.*, 2018; Grimm *et al.*, 2015). Only a few solid-state structures of dihydroxylated PCBs have been reported to date (Lehmler *et al.*, 2001*a*; McKinney & Singh, 1988). 2,3-Dichloro-3′,4′-dihydroxybiphenyl is a putative metabolite of PCB 5, a minor constituent of technical PCB mixtures, such as Aroclor 1221 (Frame, 1997). The present study reports the solid-state structure of this dihydroxylated PCB metabolite, thus adding to the number of available crystal structures of this important class of PCB metabolites.

2,3-Dichloro-3′,4′-dihydroxybiphenyl crystallizes in the monoclinic $P2_1/n$ space group. The dihedral angle between the least-squares planes of the two benzene rings, an important determinant of the three-dimensional structure of PCB derivatives, is 59.39 (8)°. Similarly, the solid-state dihedral angle of other mono *ortho*-chlorine-substituted PCB derivatives ranges from 47.34 (5) to 59.92 (9)° (Boyarskiy *et al.*, 2010; Kania-

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

D—H···A	D—H	H···A	D···A	D—H···A
O1—H1O···O2^{i}	0.79	1.98	2.763 (2)	168
O2—H2O···O1	0.79	2.24	2.677 (2)	116

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

Korwel *et al.* 2004; Lehmler *et al.* 2001*b*; Li *et al.* 2010; Luthe *et al.* 2007; van der Sluis *et al.*, 1990; Sutherland & Ali-Adib, 1987; Vyas *et al.*, 2006). In the crystal, the title compound displays intra and intermolecular O—H···O hydrogen bonds involving both of the two hydroxy groups (Figs. 1 and 2). The intramolecular bond distance for O1—H1···O2 is 2.763 (2) Å, while that for O2—H2···O1 is 2.677 (2) Å, Table 1. The π–π stacking distance between inversion-related C1–C6 rings of the title compound is 3.371 (3) Å.

Synthesis and crystallization

The title compound was synthesized *via* a Suzuki cross-coupling reaction of 4-bromo-1,2-dimethoxybenzene with 2,3-dichlorophenylboronic acid in the presence of $Pd(PPh_3)_4$, and a 2 *M* aqueous solution of Na_2CO_3 followed by demethylation with BBr_3 (Bauer *et al.*, 1995; Lehmler & Robertson, 2001). Crystals suitable for crystal-structure analysis were obtained by recrystallization of the title compound from diethyl ether: hexanes (approximately 1:3, *v*/*v*) as previously described (Bauer *et al.*, 1995; Lehmler & Robertson, 2001).

Refinement

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

Acknowledgements

The KappaCCD diffractometer was funded by the University of Kentucky.

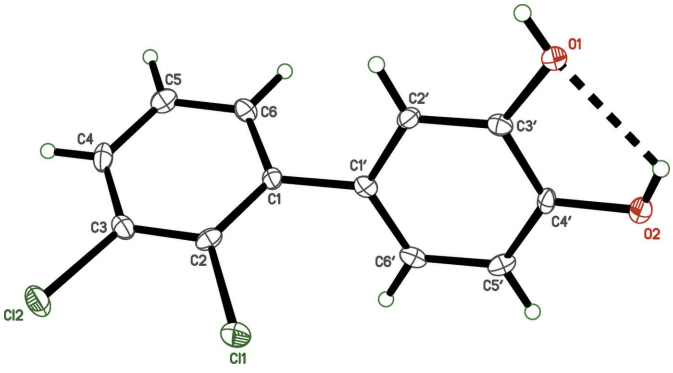


Figure 1
View of the title compound showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level. The intramolecular hydrogen bond (Table 1) is shown as a dashed line.

Table 2
Experimental details.

Crystal data	
Chemical formula	$C_{12}H_8Cl_2O_2$
M_r	255.08
Crystal system, space group	Monoclinic, $P2_1/n$
Temperature (K)	90
a, b, c (Å)	6.8542 (4), 19.9526 (11), 7.6704 (4)
β (°)	95.762 (3)
V (Å^3)	1043.7 (1)
Z	4
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.60
Crystal size (mm)	0.25 × 0.15 × 0.10
Data collection	
Diffractometer	Nonius KappaCCD
Absorption correction	Multi-scan (*SCALEPACK*; Otwinowski & Minor, 2006)
T_{min}, T_{max}	0.865, 0.942
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	6305, 1834, 1333
R_{int}	0.078
(sin $\theta/\lambda)_{max}$ (Å^{-1})	0.595
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.046, 0.074, 1.05
No. of reflections	1834
No. of parameters	149
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.37, −0.35

Computer programs: *COLLECT* (Nonius, 1998), *SCALEPACK* and *DENZO-SMN* (Otwinowski & Minor, 2006), *SHELXS*, *XP in SHELXTL* and *SHELX* (Sheldrick, 2008), *SHELXL2018/1* (Sheldrick, 2015) and *CIFFIX* (Parkin, 2013).

Funding information

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References

ATSDR (2000). *Toxicological profile for polychlorinated biphenyls (PCBs)*. https://www. atsdr. cdc. gov/toxprofiles/tp. asp?id=142&tid=26.

Bauer, U., Amaro, A. R. & Robertson, L. W. (1995). *Chem. Res. Toxicol.* **8**, 92–95.

Boyarskiy, V. P., Boyarskaya, I. A., Savicheva, E. A., Gdaniec, M., Fonari, M. S. & Simonov, Y. A. (2010). *J. Mol. Struct.* **975**, 180–185.

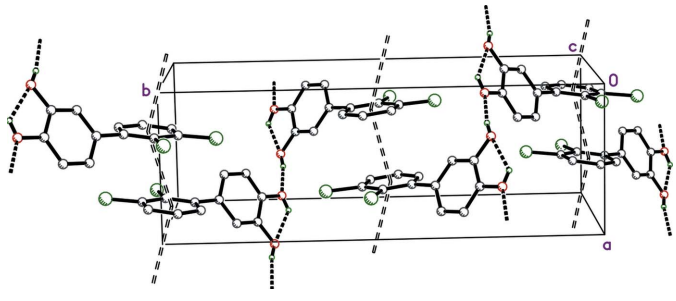

Figure 2
A packing plot viewed approximately along the *c* axis. Hydrogen bonds (Table 1) are drawn as solid dashed lines, and the π–π interactions are depicted as dashed open lines between the centroids of stacked rings.

Dhakal, K., Gadupudi, G. S., Lehmler, H. J., Ludewig, G., Duffel, M. W. & Robertson, L. W. (2018). *Environ. Sci. Pollut. Res. Int.* **25**, 16277–16290.
Frame, G. M. (1997). *Fresenius J. Anal. Chem.* **357**, 714–722.
Grimm, F. A., Hu, D., Kania-Korwel, I., Lehmler, H. J., Ludewig, G., Hornbuckle, K. C., Duffel, M. W., Bergman, A. & Robertson, L. W. (2015). *Crit. Rev. Toxicol.* **45**, 245–272.
IARC (2017). *Polychlorinated biphenyls and polybrominated biphenyls.* https://monographs. iarc. fr/wp-content/uploads/2018/08/mono107.pdf.
Kania-Korwel, I., Parkin, S., Robertson, L. W. & Lehmler, H.-J. (2004). *Acta Cryst.* E**60**, o1652–o1653.
Lehmler, H.-J., Parkin, S. & Robertson, L. W. (2001*b*). *Acta Cryst.* E**57**, o111–o112.
Lehmler, H.-J. & Robertson, L. W. (2001). *Chemosphere*, **45**, 1119–1127.
Lehmler, H.-J., Robertson, L. W. & Parkin, S. (2001*a*). *Acta Cryst.* E**57**, o590–o591.
Li, X., Parkin, S., Duffel, M. W., Robertson, L. W. & Lehmler, H.-J. (2010). *Environ. Int.* **36**, 843–848.
Lu, Z., Kania-Korwel, I., Lehmler, H. J. & Wong, C. S. (2013). *Environ. Sci. Technol.* **47**, 12184–12192.
Luthe, G., Swenson, D. C. & Robertson, L. W. (2007). *Acta Cryst.* B**63**, 319–327.
McKinney, J. D. & Singh, P. (1988). *Acta Cryst.* C**44**, 558–562.
McLean, M. R., Bauer, U., Amaro, A. R. & Robertson, L. W. (1996). *Chem. Res. Toxicol.* **9**, 158–164.
Nonius (1998). *Collect* Nonius BV, Delft, The Netherlands.
Otwinowski, Z. & Minor, W. (2006). *International Tables for Crystallography*, Vol. F, *Crystallography of biological macromolecules*, edited by M. G. Rossmann & E. Arnold, ch. 11.4, pp. 226–235. Chester, England: International Union of Crystallography.
Parkin, S. (2013). *CIFFIX*. http://xray.uky.edu/people/parkin/programs/ciffix.
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.
Sheldrick, G. M. (2015). *Acta Cryst.* C**71**, 3–8.
Sluis, P. van der, Moes, G. W. H., Behm, H., Smykalla, C., Beurskens, P. T. & Lenstra, A. T. H. (1990). *Acta Cryst.* C**46**, 2169–2171.
Stockholm Convention (2008). http://www.pops.int/
Sutherland, H. H. & Ali-Adib, Z. (1987). *Acta Cryst.* C**43**, 1406–1407.
Vyas, S. M., Parkin, S., Robertson, L. W. & Lehmler, H.-J. (2006). *Acta Cryst.* E**62**, o4162–o4163.

full crystallographic data

IUCrData (2019). **4**, x190662 [https://doi.org/10.1107/S2414314619006620X]

2,3-Dichloro-3′,4′-dihydroxybiphenyl

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4-(2,3-Dichlorophenyl)benzene-1,2-diol

Crystal data

$C_{12}H_8Cl_2O_2$
M_r = 255.08
Monoclinic, $P2_1/n$
a = 6.8542 (4) Å
b = 19.9526 (11) Å
c = 7.6704 (4) Å
β = 95.762 (3)°
V = 1043.7 (1) Å^3
Z = 4
$F(000)$ = 520
D_x = 1.623 Mg m^{-3}
Mo $K\alpha$ radiation, λ = 0.71073 Å
Cell parameters from 7512 reflections
θ = 1.0–25.3°
μ = 0.60 mm^{-1}
T = 90 K
Block, colourless
0.25 × 0.15 × 0.10 mm

Data collection

Nonius KappaCCD diffractometer
Radiation source: fine-focus sealed-tube
Detector resolution: 9.1 pixels mm^{-1}
φ and ω scans at fixed χ = 55°
Absorption correction: multi-scan (*SCALEPACK*; Otwinowski & Minor, 2006)
T_{min} = 0.865, T_{max} = 0.942
6305 measured reflections
1834 independent reflections
1333 reflections with $I > 2\sigma(I)$
R_{int} = 0.078
θ_{max} = 25.0°, θ_{min} = 2.0°
h = −8→8
k = −23→23
l = −9→9

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.046
$wR(F^2)$ = 0.074
S = 1.05
1834 reflections
149 parameters
0 restraints
Primary atom site location: structure-invariant direct methods
Secondary atom site location: difference Fourier map
Hydrogen site location: difference Fourier map
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0177P)^2 + 0.1242P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.37 e Å^{-3}
$\Delta\rho_{min}$ = −0.35 e Å^{-3}

Special details

Experimental. The crystal was mounted using polyisobutene oil on the tip of a fine glass fibre, which was fastened in a copper mounting pin with electrical solder. It was placed directly into the cold gas stream of a liquid-nitrogen based cryostat (Hope, 1994; Parkin & Hope, 1998).
Diffraction data were collected with the crystal at 90K, which is standard practice in this laboratory for the majority of flash-cooled crystals.

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

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²)

	x	*y*	*z*	U_{iso}*/U_{eq}
O1	0.3278 (3)	0.25608 (9)	−0.0075 (2)	0.0178 (5)
H1O	0.257 (3)	0.2624 (10)	0.067 (3)	0.027*
O2	0.6024 (3)	0.23958 (9)	−0.2285 (2)	0.0175 (5)
H2O	0.497 (4)	0.2241 (11)	−0.228 (2)	0.026*
Cl1	0.74285 (10)	0.52729 (3)	0.06782 (8)	0.0204 (2)
Cl2	0.77595 (10)	0.63119 (3)	0.37417 (9)	0.0218 (2)
C1	0.7234 (3)	0.43053 (13)	0.3178 (3)	0.0113 (6)
C2	0.7451 (3)	0.49894 (13)	0.2822 (3)	0.0131 (7)
C3	0.7609 (3)	0.54586 (12)	0.4169 (3)	0.0143 (7)
C4	0.7593 (3)	0.52551 (13)	0.5897 (3)	0.0166 (7)
H4	0.773622	0.557486	0.681882	0.020*
C5	0.7366 (3)	0.45841 (13)	0.6266 (3)	0.0159 (7)
H5	0.733444	0.444169	0.744443	0.019*
C6	0.7184 (3)	0.41181 (13)	0.4922 (3)	0.0154 (7)
H6	0.702020	0.365856	0.519651	0.018*
C1′	0.6972 (4)	0.37913 (12)	0.1762 (3)	0.0113 (6)
C2′	0.5271 (4)	0.33991 (12)	0.1597 (3)	0.0136 (7)
H2′	0.433327	0.344812	0.241955	0.016*
C3′	0.4945 (4)	0.29424 (13)	0.0252 (3)	0.0124 (7)
C4′	0.6346 (4)	0.28487 (13)	−0.0917 (3)	0.0116 (7)
C5′	0.8067 (4)	0.32105 (13)	−0.0734 (3)	0.0146 (7)
H5′	0.904134	0.313550	−0.151069	0.018*
C6′	0.8374 (4)	0.36868 (12)	0.0594 (3)	0.0145 (7)
H6′	0.954896	0.394255	0.070420	0.017*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0186 (12)	0.0175 (11)	0.0187 (12)	−0.0056 (10)	0.0087 (9)	−0.0050 (9)
O2	0.0185 (13)	0.0189 (12)	0.0158 (11)	−0.0048 (9)	0.0055 (10)	−0.0055 (9)
Cl1	0.0275 (5)	0.0166 (4)	0.0177 (4)	−0.0023 (3)	0.0051 (3)	0.0032 (3)
Cl2	0.0258 (5)	0.0112 (4)	0.0286 (5)	−0.0007 (3)	0.0040 (4)	−0.0003 (3)
C1	0.0078 (15)	0.0107 (16)	0.0158 (17)	0.0006 (12)	0.0029 (12)	−0.0023 (13)
C2	0.0096 (16)	0.0192 (17)	0.0107 (16)	0.0020 (13)	0.0018 (13)	0.0009 (13)
C3	0.0112 (17)	0.0107 (16)	0.0210 (18)	0.0000 (13)	0.0019 (13)	−0.0001 (14)
C4	0.0128 (17)	0.0161 (17)	0.0207 (18)	0.0000 (13)	0.0012 (13)	−0.0086 (15)
C5	0.0154 (17)	0.0208 (18)	0.0112 (16)	0.0019 (14)	−0.0001 (13)	0.0015 (14)
C6	0.0181 (17)	0.0107 (16)	0.0176 (17)	0.0000 (13)	0.0026 (13)	0.0020 (14)
C1′	0.0141 (16)	0.0083 (15)	0.0112 (16)	0.0031 (13)	−0.0001 (13)	0.0052 (12)
C2′	0.0174 (17)	0.0115 (16)	0.0130 (16)	0.0019 (13)	0.0067 (13)	0.0007 (13)

C3′	0.0117 (16)	0.0113 (16)	0.0141 (16)	0.0000 (13)	0.0017 (13)	0.0024 (13)
C4′	0.0190 (17)	0.0070 (15)	0.0084 (15)	0.0038 (13)	0.0001 (13)	0.0000 (13)
C5′	0.0120 (17)	0.0199 (17)	0.0124 (16)	0.0015 (14)	0.0034 (13)	0.0022 (14)
C6′	0.0142 (16)	0.0131 (17)	0.0161 (17)	−0.0027 (13)	0.0006 (13)	0.0044 (13)

Geometric parameters (Å, º)

O1—C3′	1.375 (3)	C5—C6	1.385 (3)
O1—H1O	0.79 (2)	C5—H5	0.9500
O2—C4′	1.386 (3)	C6—H6	0.9500
O2—H2O	0.79 (2)	C1′—C6′	1.394 (3)
Cl1—C2	1.737 (3)	C1′—C2′	1.399 (3)
Cl2—C3	1.739 (3)	C2′—C3′	1.378 (3)
C1—C6	1.393 (3)	C2′—H2′	0.9500
C1—C2	1.403 (3)	C3′—C4′	1.391 (3)
C1—C1′	1.492 (3)	C4′—C5′	1.378 (3)
C2—C3	1.391 (3)	C5′—C6′	1.394 (3)
C3—C4	1.387 (3)	C5′—H5′	0.9500
C4—C5	1.380 (3)	C6′—H6′	0.9500
C4—H4	0.9500		
C3′—O1—H1O	109.5	C1—C6—H6	119.1
C4′—O2—H2O	109.5	C6′—C1′—C2′	118.7 (2)
C6—C1—C2	117.5 (2)	C6′—C1′—C1	122.0 (2)
C6—C1—C1′	120.2 (2)	C2′—C1′—C1	119.3 (2)
C2—C1—C1′	122.3 (2)	C3′—C2′—C1′	120.6 (2)
C3—C2—C1	120.8 (2)	C3′—C2′—H2′	119.7
C3—C2—Cl1	118.5 (2)	C1′—C2′—H2′	119.7
C1—C2—Cl1	120.7 (2)	O1—C3′—C2′	124.9 (2)
C4—C3—C2	120.4 (2)	O1—C3′—C4′	115.0 (2)
C4—C3—Cl2	118.2 (2)	C2′—C3′—C4′	120.1 (2)
C2—C3—Cl2	121.4 (2)	C5′—C4′—O2	119.2 (2)
C5—C4—C3	119.4 (2)	C5′—C4′—C3′	120.2 (2)
C5—C4—H4	120.3	O2—C4′—C3′	120.5 (2)
C3—C4—H4	120.3	C4′—C5′—C6′	119.8 (2)
C4—C5—C6	120.2 (2)	C4′—C5′—H5′	120.1
C4—C5—H5	119.9	C6′—C5′—H5′	120.1
C6—C5—H5	119.9	C5′—C6′—C1′	120.6 (2)
C5—C6—C1	121.7 (2)	C5′—C6′—H6′	119.7
C5—C6—H6	119.1	C1′—C6′—H6′	119.7
C6—C1—C2—C3	0.1 (4)	C6—C1—C1′—C2′	57.1 (3)
C1′—C1—C2—C3	177.2 (2)	C2—C1—C1′—C2′	−120.0 (3)
C6—C1—C2—Cl1	−177.37 (18)	C6′—C1′—C2′—C3′	−3.2 (4)
C1′—C1—C2—Cl1	−0.2 (4)	C1—C1′—C2′—C3′	176.9 (2)
C1—C2—C3—C4	1.2 (4)	C1′—C2′—C3′—O1	−176.3 (2)
Cl1—C2—C3—C4	178.69 (19)	C1′—C2′—C3′—C4′	2.5 (4)
C1—C2—C3—Cl2	−176.86 (19)	O1—C3′—C4′—C5′	179.1 (2)

Cl1—C2—C3—Cl2	0.6 (3)	C2′—C3′—C4′—C5′	0.2 (4)
C2—C3—C4—C5	−1.7 (4)	O1—C3′—C4′—O2	−0.3 (3)
Cl2—C3—C4—C5	176.45 (19)	C2′—C3′—C4′—O2	−179.3 (2)
C3—C4—C5—C6	0.9 (4)	O2—C4′—C5′—C6′	177.4 (2)
C4—C5—C6—C1	0.4 (4)	C3′—C4′—C5′—C6′	−2.1 (4)
C2—C1—C6—C5	−0.9 (4)	C4′—C5′—C6′—C1′	1.3 (4)
C1′—C1—C6—C5	−178.1 (2)	C2′—C1′—C6′—C5′	1.3 (4)
C6—C1—C1′—C6′	−122.7 (3)	C1—C1′—C6′—C5′	−178.9 (2)
C2—C1—C1′—C6′	60.2 (3)		

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O1—H1*O*···O2^{i}	0.79	1.98	2.763 (2)	168
O2—H2*O*···O1	0.79	2.24	2.677 (2)	116

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