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3,5-Dichloro-3′,4′-dimethoxybiphenyl

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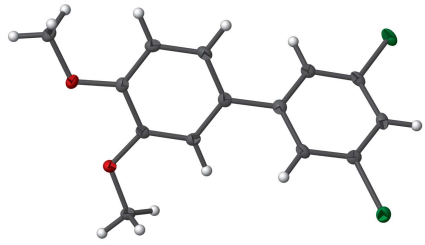
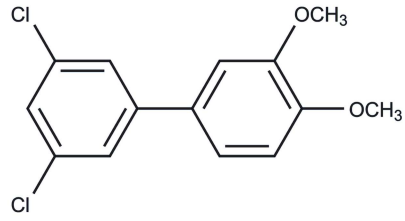
The title compound, $C_{14}H_{12}Cl_2O_2$, is a dimethoxylated derivative of 3,4-dichlorobiphenyl (PCB 14). The dihedral angle between the benzene rings is 42.49 (6)°. The methoxy groups on the non-chlorinated ring lie essentially in the plane of the benzene ring, with C—C—O—C torsion angles of 4.0 (2) and −2.07 (19)°. In the crystal, the compound displays π–π stacking interactions between inversion-related chlorinated benzene rings, with an interplanar stacking distance of 3.3695 (17) Å.

3D view



Chemical scheme



Structure description

Polychlorinated biphenyls (PCBs) are persistent organic pollutants that can be metabolized to mono- and di-hydroxylated PCB metabolites (Grimm *et al.*, 2015; Kania-Korwel & Lehmler, 2016). The interaction of PCB metabolites with biological macromolecules, such as proteins, depends on their three-dimensional structure. For example, non-*ortho*-substituted PCB congeners bind to the aryl hydrocarbon receptor (AhR) (Bandiera *et al.*, 1982), whereas PCB congeners with multiple *ortho*-chlorine substituents are potent sensitizers of ryanodine receptors (RyR) (Holland *et al.*, 2017; Pessah *et al.*, 2006). The three-dimensional structure of PCB derivatives depends on their substitution pattern and the dihedral angle between the two benzene rings of the biphenyl moiety. However, only limited information about the structure of PCBs and their metabolites is currently available. Here we report the crystal structure of the title compound, 3,5-dichloro-3′,4′-dimethoxybiphenyl, a precursor for the synthesis of 3,5-dichloro-3′,4′-dihydroxybiphenyl, a putative dihydroxylated PCB metabolite of PCB 12.

The title compound (Fig. 1) crystallizes in the monoclinic space group $P2_1/c$ and shows π–π stacking interactions between inversion-related C1–C6 rings, with an interplanar stacking distance of 3.3695 (17) Å. The dihedral angle between the least-squares mean planes of the two benzene rings is 42.49 (6)°. Similarly, the solid-state dihedral angles of

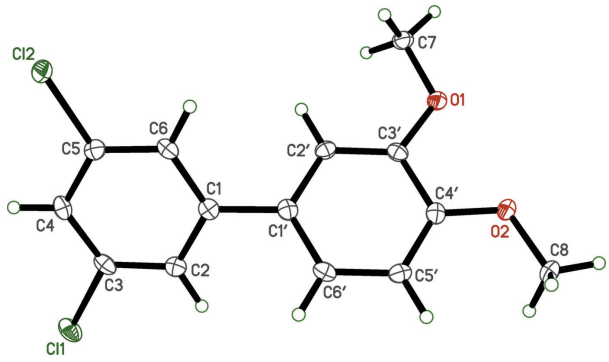


Figure 1
View of the title compound showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level.

other non-*ortho*-chlorine-substituted PCB derivatives range from 4.9 to 43.94° (*e.g.*, see: Li *et al.*, 2010; Shaikh *et al.*, 2008). Larger dihedral angles are typically reported for PCB derivatives with one or more *ortho*-chlorine substituents (*e.g.*, see: Lehmler *et al.*, 2001; Vyas *et al.*, 2006). Both methoxy groups are almost coplanar with the benzene ring, with torsion angles of 4.0 (2)° and −2.09 (19)° for the methoxy groups at C3′ and C4′, respectively. This orientation of the methoxy groups relative to the plane of the benzene ring is typical for methoxylated benzene derivatives that do not have substituents *ortho* to the respective methoxy group (Lehmler *et al.*, 2013).

Synthesis and crystallization

The title compound was prepared *via* a Suzuki cross-coupling reaction of 3-bromo-1,2-dimethoxybenzene with 3,5-dichlorophenylboronic acid in the presence of $Pd(PPh_3)_4$ and a 2*M* aqueous solution of Na_2CO_3 (Bauer *et al.*, 1995). Crystals suitable for structure analysis were obtained by recrystallization of the title compound from diethyl ether:hexanes (approximately 1:3, *v*/*v*) as described by Bauer *et al.* (1995).

Refinement

Crystal data, data collection and structure refinement details are summarized in Table 1. Refinement progress was checked using *PLATON* (Spek, 2009) and by an *R*-tensor (Parkin, 2000).

Acknowledgements

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Funding information

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Table 1
Experimental details.

Crystal data	
Chemical formula	$C_{14}H_{12}Cl_2O_2$
M_r	283.14
Crystal system, space group	Monoclinic, $P2_1/c$
Temperature (K)	90
a, b, c (Å)	10.8596 (10), 15.1262 (10), 7.9040 (3)
β (°)	103.749 (10)
V (Å^3)	1261.14 (16)
Z	4
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.50
Crystal size (mm)	0.35 × 0.35 × 0.30
Data collection	
Diffractometer	Nonius KappaCCD diffractometer
Absorption correction	Multi-scan (*SCALEPACK*; Otwinowski & Minor, 2006)
T_{min}, T_{max}	0.843, 0.863
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	11657, 2899, 2521
R_{int}	0.036
(sin $\theta/\lambda)_{max}$ (Å^{-1})	0.649
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.030, 0.072, 1.09
No. of reflections	2899
No. of parameters	166
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.29, −0.24

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

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full crystallographic data

IUCrData (2019). **4**, x190518 [https://doi.org/10.1107/S2414314619005182]

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Crystal data

$C_{14}H_{12}Cl_2O_2$
M_r = 283.14
Monoclinic, $P2_1/c$
a = 10.8596 (10) Å
b = 15.1262 (10) Å
c = 7.9040 (3) Å
β = 103.749 (10)°
V = 1261.14 (16) Å^3
Z = 4
$F(000)$ = 584
D_x = 1.491 Mg m^{-3}
Mo $K\alpha$ radiation, λ = 0.71073 Å
Cell parameters from 6723 reflections
θ = 1.0–27.5°
μ = 0.50 mm^{-1}
T = 90 K
Block, colourless
0.35 × 0.35 × 0.30 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} = 0.843, T_{max} = 0.863
11657 measured reflections
2899 independent reflections
2521 reflections with $I > 2\sigma(I)$
R_{int} = 0.036
θ_{max} = 27.5°, θ_{min} = 1.9°
h = −14→13
k = −19→19
l = −10→10

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.030
$wR(F^2)$ = 0.072
S = 1.09
2899 reflections
166 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-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0274P)^2 + 0.5814P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.29 e Å^{-3}
$\Delta\rho_{min}$ = −0.24 e Å^{-3}
Extinction correction: SHELXL2018 (Sheldrick, 2015), $Fc^* = kFc[1+0.001xFc^2\lambda^3/\sin(2\theta)]^{-1/4}$
Extinction coefficient: 0.0036 (10)

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.
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.

Refinement. Refinement progress was checked using *PLATON* (Spek, 2009) and by an *R*-tensor (Parkin, 2000). The final model was further checked with the IUCr utility *checkCIF*.

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

	x	*y*	*z*	U_{iso}*/U_{eq}
Cl1	0.60753 (3)	0.14404 (3)	0.24758 (5)	0.02195 (11)
Cl2	0.68140 (3)	0.00465 (2)	0.89050 (4)	0.01849 (11)
C1	0.38939 (13)	0.13567 (9)	0.59009 (18)	0.0143 (3)
C2	0.43570 (13)	0.15454 (9)	0.44322 (18)	0.0158 (3)
H2	0.384740	0.185934	0.347780	0.019*
C3	0.55644 (14)	0.12705 (10)	0.43819 (18)	0.0161 (3)
C4	0.63554 (13)	0.08233 (9)	0.57460 (18)	0.0162 (3)
H4	0.718627	0.064728	0.569857	0.019*
C5	0.58725 (13)	0.06454 (9)	0.71870 (18)	0.0147 (3)
C6	0.46684 (13)	0.09022 (9)	0.72952 (18)	0.0153 (3)
H6	0.437275	0.077075	0.830574	0.018*
C1′	0.25668 (13)	0.15968 (9)	0.59000 (17)	0.0144 (3)
C2′	0.17925 (13)	0.09856 (9)	0.65066 (17)	0.0141 (3)
H2′	0.213997	0.044236	0.700603	0.017*
C3′	0.05248 (13)	0.11749 (9)	0.63765 (17)	0.0138 (3)
C4′	0.00084 (13)	0.19851 (9)	0.56645 (17)	0.0142 (3)
C5′	0.07794 (14)	0.25948 (9)	0.51099 (18)	0.0155 (3)
H5′	0.044267	0.314924	0.465840	0.019*
C6′	0.20519 (14)	0.23956 (10)	0.52135 (18)	0.0166 (3)
H6′	0.257030	0.281250	0.480869	0.020*
O1	−0.03319 (9)	0.06153 (6)	0.68480 (13)	0.0172 (2)
C7	0.01422 (14)	−0.02040 (9)	0.76311 (19)	0.0174 (3)
H7A	0.057591	−0.052147	0.685996	0.026*
H7B	−0.056387	−0.056294	0.782171	0.026*
H7C	0.074053	−0.009068	0.874989	0.026*
O2	−0.12548 (9)	0.20904 (6)	0.55654 (13)	0.0171 (2)
C8	−0.18099 (14)	0.29114 (9)	0.4881 (2)	0.0177 (3)
H8A	−0.140273	0.339681	0.562957	0.027*
H8B	−0.271851	0.290436	0.484248	0.027*
H8C	−0.168898	0.299578	0.370183	0.027*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
Cl1	0.0224 (2)	0.0305 (2)	0.01586 (18)	−0.00474 (15)	0.01035 (14)	−0.00050 (15)
Cl2	0.01430 (18)	0.0238 (2)	0.01618 (18)	0.00001 (13)	0.00128 (13)	0.00173 (14)
C1	0.0154 (7)	0.0134 (7)	0.0142 (6)	−0.0019 (5)	0.0035 (5)	−0.0031 (5)
C2	0.0172 (7)	0.0156 (7)	0.0146 (7)	−0.0014 (5)	0.0036 (5)	−0.0002 (5)
C3	0.0185 (7)	0.0180 (7)	0.0136 (7)	−0.0060 (6)	0.0072 (6)	−0.0027 (5)
C4	0.0128 (7)	0.0177 (7)	0.0188 (7)	−0.0034 (5)	0.0051 (5)	−0.0042 (6)
C5	0.0153 (7)	0.0144 (7)	0.0131 (6)	−0.0020 (5)	0.0006 (5)	−0.0013 (5)
C6	0.0160 (7)	0.0169 (7)	0.0141 (6)	−0.0038 (5)	0.0059 (5)	−0.0009 (6)
C1′	0.0154 (7)	0.0170 (7)	0.0109 (6)	−0.0005 (5)	0.0033 (5)	−0.0023 (5)
C2′	0.0166 (7)	0.0136 (6)	0.0113 (6)	0.0008 (5)	0.0019 (5)	0.0002 (5)
C3′	0.0155 (7)	0.0150 (7)	0.0111 (6)	−0.0027 (5)	0.0034 (5)	−0.0007 (5)
C4′	0.0140 (7)	0.0169 (7)	0.0114 (6)	0.0006 (5)	0.0025 (5)	−0.0026 (5)
C5′	0.0203 (7)	0.0129 (7)	0.0133 (6)	0.0014 (5)	0.0040 (6)	0.0006 (5)
C6′	0.0193 (7)	0.0172 (7)	0.0150 (7)	−0.0022 (6)	0.0071 (6)	0.0012 (6)
O1	0.0141 (5)	0.0150 (5)	0.0228 (5)	0.0000 (4)	0.0049 (4)	0.0057 (4)
C7	0.0175 (7)	0.0158 (7)	0.0183 (7)	−0.0001 (5)	0.0029 (6)	0.0040 (6)
O2	0.0137 (5)	0.0164 (5)	0.0213 (5)	0.0033 (4)	0.0042 (4)	0.0033 (4)
C8	0.0176 (7)	0.0144 (7)	0.0212 (7)	0.0047 (5)	0.0049 (6)	0.0007 (6)

Geometric parameters (Å, º)

Cl1—C3	1.7439 (14)	C3′—O1	1.3732 (16)
Cl2—C5	1.7464 (14)	C3′—C4′	1.4082 (19)
C1—C6	1.398 (2)	C4′—O2	1.3646 (16)
C1—C2	1.3998 (19)	C4′—C5′	1.385 (2)
C1—C1′	1.4861 (19)	C5′—C6′	1.398 (2)
C2—C3	1.385 (2)	C5′—H5′	0.9500
C2—H2	0.9500	C6′—H6′	0.9500
C3—C4	1.385 (2)	O1—C7	1.4256 (17)
C4—C5	1.389 (2)	C7—H7A	0.9800
C4—H4	0.9500	C7—H7B	0.9800
C5—C6	1.386 (2)	C7—H7C	0.9800
C6—H6	0.9500	O2—C8	1.4293 (16)
C1′—C6′	1.387 (2)	C8—H8A	0.9800
C1′—C2′	1.408 (2)	C8—H8B	0.9800
C2′—C3′	1.3858 (19)	C8—H8C	0.9800
C2′—H2′	0.9500		
C6—C1—C2	119.12 (13)	O1—C3′—C4′	114.44 (12)
C6—C1—C1′	121.49 (12)	C2′—C3′—C4′	120.25 (13)
C2—C1—C1′	119.29 (12)	O2—C4′—C5′	125.39 (13)
C3—C2—C1	119.46 (13)	O2—C4′—C3′	115.09 (12)
C3—C2—H2	120.3	C5′—C4′—C3′	119.52 (13)
C1—C2—H2	120.3	C4′—C5′—C6′	120.11 (13)
C4—C3—C2	122.72 (13)	C4′—C5′—H5′	119.9

C4—C3—Cl1	118.61 (11)	C6′—C5′—H5′	119.9
C2—C3—Cl1	118.57 (11)	C1′—C6′—C5′	120.78 (13)
C3—C4—C5	116.61 (13)	C1′—C6′—H6′	119.6
C3—C4—H4	121.7	C5′—C6′—H6′	119.6
C5—C4—H4	121.7	C3′—O1—C7	117.10 (11)
C6—C5—C4	122.82 (13)	O1—C7—H7A	109.5
C6—C5—Cl2	118.94 (11)	O1—C7—H7B	109.5
C4—C5—Cl2	118.22 (11)	H7A—C7—H7B	109.5
C5—C6—C1	119.27 (13)	O1—C7—H7C	109.5
C5—C6—H6	120.4	H7A—C7—H7C	109.5
C1—C6—H6	120.4	H7B—C7—H7C	109.5
C6′—C1′—C2′	119.18 (13)	C4′—O2—C8	116.80 (11)
C6′—C1′—C1	120.93 (13)	O2—C8—H8A	109.5
C2′—C1′—C1	119.79 (12)	O2—C8—H8B	109.5
C3′—C2′—C1′	120.13 (13)	H8A—C8—H8B	109.5
C3′—C2′—H2′	119.9	O2—C8—H8C	109.5
C1′—C2′—H2′	119.9	H8A—C8—H8C	109.5
O1—C3′—C2′	125.28 (13)	H8B—C8—H8C	109.5

C6—C1—C2—C3	0.7 (2)	C1—C1′—C2′—C3′	−174.65 (12)
C1′—C1—C2—C3	−175.75 (13)	C1′—C2′—C3′—O1	176.85 (12)
C1—C2—C3—C4	−1.1 (2)	C1′—C2′—C3′—C4′	−1.1 (2)
C1—C2—C3—Cl1	175.29 (11)	O1—C3′—C4′—O2	0.44 (17)
C2—C3—C4—C5	1.0 (2)	C2′—C3′—C4′—O2	178.57 (12)
Cl1—C3—C4—C5	−175.35 (11)	O1—C3′—C4′—C5′	−178.72 (12)
C3—C4—C5—C6	−0.6 (2)	C2′—C3′—C4′—C5′	−0.6 (2)
C3—C4—C5—Cl2	177.65 (10)	O2—C4′—C5′—C6′	−177.32 (13)
C4—C5—C6—C1	0.3 (2)	C3′—C4′—C5′—C6′	1.8 (2)
Cl2—C5—C6—C1	−177.94 (10)	C2′—C1′—C6′—C5′	−0.4 (2)
C2—C1—C6—C5	−0.3 (2)	C1—C1′—C6′—C5′	175.76 (13)
C1′—C1—C6—C5	176.03 (13)	C4′—C5′—C6′—C1′	−1.3 (2)
C6—C1—C1′—C6′	142.42 (14)	C2′—C3′—O1—C7	4.0 (2)
C2—C1—C1′—C6′	−41.23 (19)	C4′—C3′—O1—C7	−177.97 (12)
C6—C1—C1′—C2′	−41.44 (19)	C5′—C4′—O2—C8	−2.07 (19)
C2—C1—C1′—C2′	134.91 (14)	C3′—C4′—O2—C8	178.82 (12)
C6′—C1′—C2′—C3′	1.6 (2)		