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(2S)-1,1-Dichloro-2-(2-chlorophenyl)-2-(4-chlorophenyl)ethane

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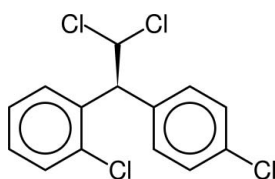
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 Key indicators: single-crystal X-ray study; $T = 100$ K; mean $\sigma(\text{C}-\text{C}) = 0.002$ Å; R factor = 0.026; wR factor = 0.060; data-to-parameter ratio = 26.0.

The title compound, $\text{C}_{14}\text{H}_{10}\text{Cl}_4$, is easily crystallized while the other enantiomorph only forms an oil upon crystallization attempts. The title compound has a considerably higher density, $\rho \simeq 1.562$ Mg m⁻³ compared to the racemic substance, $\rho \simeq 1.514$ Mg m⁻³. This is supported by the fact there are two intermolecular halogen-halogen contacts in the title compound compared with only one the racemic compound. The dihedral angle between the two phenyl rings is 76.83 (5)°

Related literature

For related literature regarding the structure of the racemic compound, see: Arora & Bates (1976). For related literature on the toxicological effects, see: Allolio & Fassnacht (2006), Benecke *et al.* (1991), Bergenstal *et al.* (1960); Cantillana *et al.* (2009).



Experimental

Crystal data

 $\text{C}_{14}\text{H}_{10}\text{Cl}_4$
 $M_r = 320.02$
 Monoclinic, $P2_1$
 $a = 6.13530$ (10) Å

 $b = 12.0715$ (2) Å
 $c = 9.4525$ (2) Å
 $\beta = 103.5490$ (18)°
 $V = 680.59$ (2) Å³
 $Z = 2$
 Mo $K\alpha$ radiation
 $\mu = 0.85$ mm⁻¹
 $T = 100$ (2) K
 $0.34 \times 0.24 \times 0.04$ mm

Data collection

 Oxford Diffraction Xcalibur-3 κ -diffractometer with Sapphire-III CCD
 Absorption correction: gaussian (*CrysAlis RED*; Oxford)

 Diffraction, 2008)
 $T_{\min} = 0.814$, $T_{\max} = 0.968$
 18569 measured reflections
 4258 independent reflections
 3935 reflections with $I > 2\sigma(I)$
 $R_{\text{int}} = 0.032$

Refinement

 $R[F^2 > 2\sigma(F^2)] = 0.026$
 $wR(F^2) = 0.060$
 $S = 1.01$
 4258 reflections
 164 parameters
 1 restraint

 H-atom parameters constrained
 $\Delta\rho_{\text{max}} = 0.40$ e Å⁻³
 $\Delta\rho_{\text{min}} = -0.31$ e Å⁻³
 Absolute structure: Flack (1983),
 1755 Friedel pairs
 Flack parameter: 0.00 (4)

Table 1

Selected interatomic distances (Å).

$\text{Cl1} \cdots \text{Cl4}^{\text{i}}$	3.4370 (5)	$\text{Cl2} \cdots \text{Cl3}^{\text{ii}}$	3.4888 (5)
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 Symmetry codes: (i) $-x + 2, y - \frac{1}{2}, -z + 1$; (ii) $-x + 1, y - \frac{1}{2}, -z$.

Data collection: *CrysAlis CCD* (Oxford Diffraction, 2008); cell refinement: *CrysAlis RED* (Oxford Diffraction, 2008); data reduction: *CrysAlis RED*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *DIAMOND* (Bergerhoff, 1996); software used to prepare material for publication: *PLATON* (Spek, 2003) and *SHELXL97*.

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Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: BQ2116).

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supporting information

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(2S)-1,1-Dichloro-2-(2-chlorophenyl)-2-(4-chlorophenyl)ethane

Tatiana Cantillana and Lars Eriksson

S1. Comment

The title compound is commercially available as a racemate which has been structurally characterized earlier (Arora & Bates, 1976). When purifying and separating the two enantiomers of the racemate, one of the enantiomers, the title compound easily formed crystals while the other enantiomer only formed an oil upon crystallization attempts. A salient feature of the racemic compound *o,p'*-DDD (Mitotane) is its selective toxicity to the adrenal cortex. It has been used for 40 years for treatment of adrenocortical carcinoma (ACC) (Bergental *et al.*, 1960) and Cushing's syndrome (Benecke *et al.*, 1991). The efficacy and potency is however low, and *o,p'*-DDD treatment is frequently associated with severe side effects (Allolio & Fassnacht, 2006). The differences in toxicity of the two enantiomers of *o,p'*-DDD and the pharmacokinetics connected with these two compounds has recently been examined in Göttingen mini pigs and will be reported elsewhere (Cantillana *et al.*, 2009).

The crystal structure of (I) shown in Fig. 1 show normal bond distances and angles. The dihedral angle between the two phenyl rings is 76.83 (5)°. Both phenyl rings are planar within 0.01 Å with the C13 deviating 0.103 (2) Å from the least square plane calculated from C3→C8 and the C14 deviating 0.048 (2) from the least square plane of C9→C14. All four chlorines are involved in the intermolecular Cl...Cl contacts between the different molecules building up a corrugated layer extending in the [010] and [101] directions. The title compound has a considerably higher density, $\rho \approx 1.562 \text{ g/cm}^3$ compared to the racemate, $\rho \approx 1.514 \text{ g/cm}^3$ (Arora & Bates, 1976). A tentative model for the higher density of the pure enantiomer is that it may be a result of the more numerous intermolecular short halogen-halogen contacts.

S2. Experimental

The title compound was purified from a racemic mixture present in the commercially available product, 1,1-Dichloro-2-(2-chlorophenyl)-2-(4-chlorophenyl)ethane (*o,p'*-DDD) using high performance liquid chromatography (HPLC), Shimadzu LC-9 A (Kyoto, Japan) equipped with an UV detector, UV100 from Spectra-Physics (Fremont, USA) and a permethylated γ -cyclodextrin column, Nucleodex gamma-PM (250 x 10 mm, 5 μm , Macherey-Nagel GmbH & Co, Düren, Germany). The detection wavelength was 240 nm and the flow rate was 4 ml/min and injection volume of 200 μl . The mobile phase was methanol:water (80:20) and 1% triethylamine:acetic acid (1:2 *v/v*). Thin plate-like crystals suitable for X-ray analysis were obtained upon recrystallization from methanol.

S3. Refinement

The hydrogen atoms were geometrically positioned at C—H distances of 0.95 and 1.00 Å for the aromatic and methine hydrogen's. Both types of hydrogen's were given $U(\text{iso}) = 1.2U_{\text{eq}}(\text{C})$. The completeness of the data increases to 0.994 if one cuts the reflection data at $2\theta = 50^\circ$.

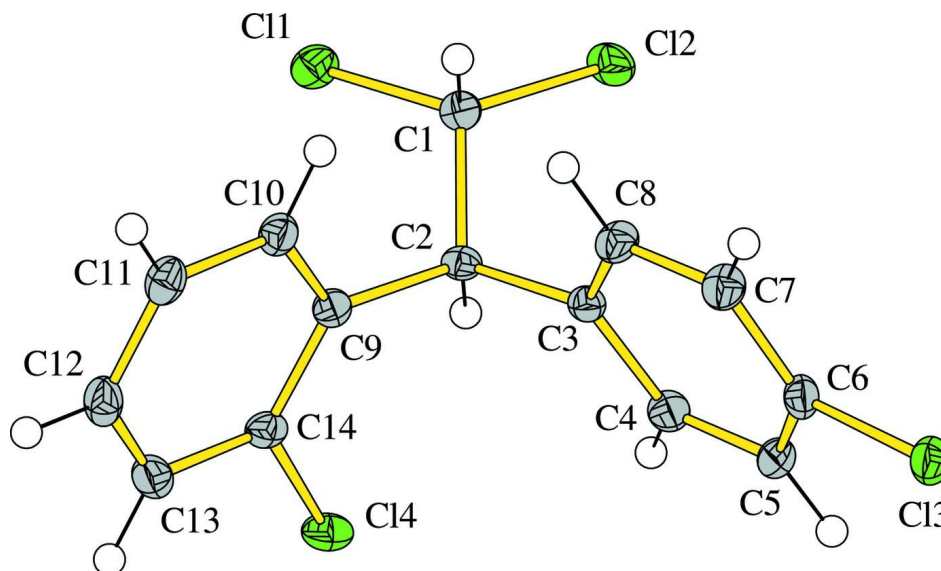


Figure 1

The title compound (I) with displacement ellipsoids at 50% probability with the unique atoms labeled.

(2S)-1,1-Dichloro-2-(2-chlorophenyl)-2-(4-chlorophenyl)ethane

Crystal data

$C_{14}H_{10}Cl_4$

$M_r = 320.02$

Monoclinic, $P2_1$

Hall symbol: P 2yb

$a = 6.1353$ (1) Å

$b = 12.0715$ (2) Å

$c = 9.4525$ (2) Å

$\beta = 103.5490$ (18)°

$V = 680.59$ (2) Å³

$Z = 2$

$F(000) = 324$

$D_x = 1.562$ Mg m⁻³

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

Cell parameters from 11963 reflections

$\theta = 3.8$ – 32.1 °

$\mu = 0.85$ mm⁻¹

$T = 100$ K

Plate, colourless

$0.34 \times 0.24 \times 0.04$ mm

Data collection

Oxford Diffraction Xcalibur-3 κ -
diffractometer with Sapphire-III CCD

Radiation source: Enhance (Mo) X-ray Source

Graphite monochromator

Detector resolution: 16.54 pixels mm⁻¹

ω scans at different φ

Absorption correction: gaussian

(*CrysAlis RED*; Oxford Diffraction, 2008)

$T_{\min} = 0.814$, $T_{\max} = 0.968$

18569 measured reflections

4258 independent reflections

3935 reflections with $I > 2\sigma(I)$

$R_{\text{int}} = 0.032$

$\theta_{\max} = 32.2$ °, $\theta_{\min} = 3.8$ °

$h = -9 \rightarrow 9$

$k = -17 \rightarrow 15$

$l = -13 \rightarrow 14$

Refinement

Refinement on F^2

Least-squares matrix: full

$R[F^2 > 2\sigma(F^2)] = 0.026$

$wR(F^2) = 0.060$

$S = 1.01$

4258 reflections

164 parameters

1 restraint

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

$$w = 1/[\sigma^2(F_o^2) + (0.0358P)^2]$$

$$\text{where } P = (F_o^2 + 2F_c^2)/3$$

$$(\Delta/\sigma)_{\max} = 0.001$$

$$\Delta\rho_{\max} = 0.40 \text{ e } \text{\AA}^{-3}$$

$$\Delta\rho_{\min} = -0.31 \text{ e } \text{\AA}^{-3}$$

Extinction correction: *SHELXL97* (Sheldrick, 2008), $F_c^* = kFc[1 + 0.001x \text{Fc}^2 \lambda^3 / \sin(2\theta)]^{-1/4}$

Extinction coefficient: 0.009 (2)

Absolute structure: Flack (1983), 1755 Friedel pairs

Absolute structure parameter: 0.00 (4)

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	0.5723 (2)	0.58327 (13)	0.35281 (15)	0.0153 (3)
H1	0.4179	0.5513	0.3360	0.018*
C2	0.5682 (2)	0.70231 (12)	0.40708 (16)	0.0136 (3)
H2	0.7233	0.7330	0.4219	0.016*
C11	0.75951 (6)	0.50047 (3)	0.48348 (4)	0.02031 (8)
C12	0.66068 (6)	0.58092 (3)	0.18581 (4)	0.02172 (9)
C3	0.4118 (2)	0.77539 (12)	0.29597 (15)	0.0143 (3)
C4	0.4896 (3)	0.87540 (13)	0.25332 (16)	0.0178 (3)
H4	0.6434	0.8943	0.2871	0.021*
C5	0.3459 (3)	0.94815 (14)	0.16209 (16)	0.0196 (3)
H5	0.4006	1.0162	0.1335	0.024*
C6	0.1222 (3)	0.92006 (14)	0.11361 (15)	0.0174 (3)
C7	0.0412 (3)	0.81928 (14)	0.15077 (17)	0.0197 (3)
H7	-0.1116	0.7996	0.1141	0.024*
C8	0.1859 (2)	0.74824 (14)	0.24185 (17)	0.0185 (3)
H8	0.1310	0.6796	0.2683	0.022*
C13	-0.06289 (6)	1.01373 (3)	0.00690 (4)	0.02230 (9)
C9	0.5012 (2)	0.70772 (12)	0.55256 (16)	0.0149 (3)
C10	0.3199 (3)	0.64714 (13)	0.57858 (16)	0.0177 (3)
H10	0.2424	0.5974	0.5062	0.021*
C11	0.2503 (3)	0.65801 (14)	0.70765 (17)	0.0192 (3)
H11	0.1263	0.6162	0.7223	0.023*
C12	0.3609 (3)	0.72933 (15)	0.81459 (17)	0.0212 (3)
H12	0.3129	0.7366	0.9026	0.025*
C13	0.5417 (3)	0.79019 (14)	0.79373 (17)	0.0207 (3)
H13	0.6192	0.8389	0.8674	0.025*
C14	0.6088 (2)	0.77922 (13)	0.66334 (16)	0.0157 (3)
C14	0.83309 (6)	0.86142 (3)	0.64058 (4)	0.02012 (8)

Atomic displacement parameters (\AA^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0144 (6)	0.0158 (7)	0.0172 (6)	0.0000 (5)	0.0071 (5)	-0.0006 (6)
C2	0.0121 (6)	0.0131 (7)	0.0159 (6)	-0.0025 (5)	0.0041 (5)	-0.0019 (5)
C11	0.01984 (16)	0.01761 (17)	0.02400 (17)	0.00417 (14)	0.00622 (12)	0.00057 (14)
C12	0.02671 (18)	0.02192 (19)	0.02051 (16)	-0.00424 (15)	0.01356 (14)	-0.00507 (14)
C3	0.0158 (6)	0.0140 (7)	0.0139 (6)	-0.0016 (5)	0.0054 (5)	-0.0012 (5)
C4	0.0171 (6)	0.0189 (8)	0.0175 (6)	-0.0054 (6)	0.0042 (5)	-0.0007 (6)
C5	0.0261 (8)	0.0167 (7)	0.0162 (7)	-0.0061 (6)	0.0054 (6)	0.0018 (5)
C6	0.0210 (7)	0.0189 (7)	0.0129 (6)	0.0025 (6)	0.0052 (5)	0.0020 (5)
C7	0.0173 (7)	0.0212 (8)	0.0202 (7)	-0.0024 (6)	0.0039 (6)	0.0019 (6)
C8	0.0171 (7)	0.0174 (7)	0.0206 (7)	-0.0043 (6)	0.0037 (5)	0.0021 (6)
C13	0.02784 (18)	0.02156 (19)	0.01717 (15)	0.00582 (15)	0.00459 (13)	0.00309 (14)
C9	0.0156 (6)	0.0138 (7)	0.0154 (6)	0.0041 (5)	0.0034 (5)	0.0005 (5)
C10	0.0205 (7)	0.0166 (7)	0.0172 (6)	0.0015 (6)	0.0070 (5)	0.0021 (6)
C11	0.0186 (7)	0.0203 (8)	0.0205 (7)	0.0034 (6)	0.0081 (6)	0.0048 (6)
C12	0.0263 (8)	0.0224 (8)	0.0163 (7)	0.0089 (7)	0.0077 (6)	0.0029 (6)
C13	0.0258 (8)	0.0189 (8)	0.0158 (7)	0.0070 (6)	0.0020 (6)	-0.0012 (6)
C14	0.0146 (6)	0.0126 (7)	0.0185 (6)	0.0029 (5)	0.0013 (5)	-0.0002 (5)
C14	0.01702 (16)	0.01679 (17)	0.02510 (18)	-0.00235 (13)	0.00201 (13)	-0.00440 (14)

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

C1—C2	1.528 (2)	C7—C8	1.381 (2)
C1—C11	1.7831 (15)	C7—H7	0.9500
C1—C12	1.7855 (14)	C8—H8	0.9500
C1—H1	1.0000	C9—C14	1.398 (2)
C2—C9	1.526 (2)	C9—C10	1.400 (2)
C2—C3	1.526 (2)	C10—C11	1.390 (2)
C2—H2	1.0000	C10—H10	0.9500
C3—C4	1.392 (2)	C11—C12	1.379 (2)
C3—C8	1.399 (2)	C11—H11	0.9500
C4—C5	1.391 (2)	C12—C13	1.382 (2)
C4—H4	0.9500	C12—H12	0.9500
C5—C6	1.383 (2)	C13—C14	1.394 (2)
C5—H5	0.9500	C13—H13	0.9500
C6—C7	1.390 (2)	C14—C14	1.7503 (16)
C6—C13	1.7462 (16)		
C11...C14 ⁱ	3.4370 (5)	C12...C13 ⁱⁱ	3.4888 (5)
C2—C1—C11	110.68 (10)	C8—C7—C6	119.01 (14)
C2—C1—C12	110.12 (10)	C8—C7—H7	120.5
C11—C1—C12	108.88 (8)	C6—C7—H7	120.5
C2—C1—H1	109.0	C7—C8—C3	121.31 (14)
C11—C1—H1	109.0	C7—C8—H8	119.3
C12—C1—H1	109.0	C3—C8—H8	119.3

C9—C2—C3	109.67 (11)	C14—C9—C10	116.49 (13)
C9—C2—C1	111.82 (12)	C14—C9—C2	121.46 (13)
C3—C2—C1	111.69 (12)	C10—C9—C2	121.92 (13)
C9—C2—H2	107.8	C11—C10—C9	121.65 (15)
C3—C2—H2	107.8	C11—C10—H10	119.2
C1—C2—H2	107.8	C9—C10—H10	119.2
C4—C3—C8	118.35 (14)	C12—C11—C10	120.19 (15)
C4—C3—C2	119.83 (13)	C12—C11—H11	119.9
C8—C3—C2	121.69 (13)	C10—C11—H11	119.9
C5—C4—C3	121.07 (14)	C11—C12—C13	120.04 (14)
C5—C4—H4	119.5	C11—C12—H12	120.0
C3—C4—H4	119.5	C13—C12—H12	120.0
C6—C5—C4	119.09 (15)	C12—C13—C14	119.25 (15)
C6—C5—H5	120.5	C12—C13—H13	120.4
C4—C5—H5	120.5	C14—C13—H13	120.4
C5—C6—C7	121.11 (15)	C13—C14—C9	122.37 (15)
C5—C6—C13	119.54 (13)	C13—C14—C14	117.29 (12)
C7—C6—C13	119.33 (12)	C9—C14—C14	120.33 (12)
C11—C1—C2—C9	-57.58 (13)	C2—C3—C8—C7	174.53 (14)
C12—C1—C2—C9	-178.02 (9)	C3—C2—C9—C14	-96.67 (15)
C11—C1—C2—C3	179.08 (9)	C1—C2—C9—C14	138.85 (14)
C12—C1—C2—C3	58.64 (13)	C3—C2—C9—C10	78.99 (17)
C9—C2—C3—C4	107.05 (15)	C1—C2—C9—C10	-45.48 (18)
C1—C2—C3—C4	-128.40 (14)	C14—C9—C10—C11	0.2 (2)
C9—C2—C3—C8	-68.77 (17)	C2—C9—C10—C11	-175.63 (14)
C1—C2—C3—C8	55.78 (18)	C9—C10—C11—C12	-0.3 (2)
C8—C3—C4—C5	1.6 (2)	C10—C11—C12—C13	-0.1 (2)
C2—C3—C4—C5	-174.36 (14)	C11—C12—C13—C14	0.6 (2)
C3—C4—C5—C6	0.1 (2)	C12—C13—C14—C9	-0.7 (2)
C4—C5—C6—C7	-2.1 (2)	C12—C13—C14—C14	178.08 (12)
C4—C5—C6—C13	176.66 (12)	C10—C9—C14—C13	0.3 (2)
C5—C6—C7—C8	2.3 (2)	C2—C9—C14—C13	176.15 (14)
C13—C6—C7—C8	-176.42 (12)	C10—C9—C14—C14	-178.44 (11)
C6—C7—C8—C3	-0.6 (2)	C2—C9—C14—C14	-2.55 (19)
C4—C3—C8—C7	-1.3 (2)		

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