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Monoclinic and orthorhombic polymorphs of 4,4′,6,6′-tetrachloro-2,2′-(piperazine-1,4-diyldimethylene)-diphenol

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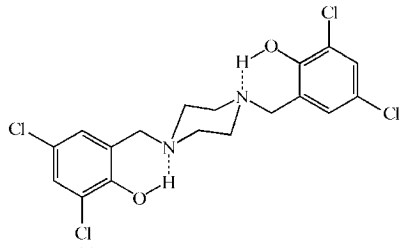
The title compound, $C_{18}H_{18}Cl_4N_2O_2$, crystallizes as monoclinic and orthorhombic polymorphs from $CHCl_3$–CH_3OH solution. In both polymorphic forms, the molecule lies on a crystallographic centre of inversion (at the piperazine ring centroid) and exhibits an intramolecular O—H···N hydrogen bond. In the monoclinic polymorph (space group $P2_1/c$), the molecules are linked by intermolecular C—H···Cl hydrogen bonds into a ribbon sheet built from $R_8^8(34)$ rings. In the orthorhombic polymorph (space group *Pbcn*), the molecules are linked by intermolecular C—H···O hydrogen bonds into a ribbon sheet of $R_6^6(34)$ rings. The sheets in the orthorhombic polymorph are crosslinked into a three-dimensional framework by π–π stacking interactions.

Comment

The design and synthesis of piperidine and piperazine derivatives are of interest in pharmacology (Geng *et al.*, 2002; Favor *et al.*, 2007). In addition, derivatives with phenol or pyridine arms can act as complexing reagents with metal ions (Chi *et al.*, 2002; Okamatsu *et al.*, 2007). Recently, we reported the crystal structure of the piperidine compound 2,4-dichloro-6-(piperidin-1-ylmethyl)phenol (HClbpipe) (Kubono *et al.*, 2005). In the supramolecular structure, intermolecular C···C and Cl···Cl contacts are observed (Kubono *et al.*, 2005); however, in the crystal structure of the Cu^{II} complex of HClbpipe, *viz*. $Cu(Clbpipe)_2$, there are no significant intermolecular interactions (Kubono *et al.*, 2006). Therefore, we designed and synthesized the new supramolecular tetradentate ligand 4,4′,6,6′-tetrachloro-2,2′-(piperazine-1,4-diyldimethylene)diphenol (H_2Cl_2bpi), consisting of two dichlorophenol arms and a piperazine ring. H_2Cl_2bpi crystallizes in monoclinic, (I), and orthorhombic, (II), polymorphic forms from $CHCl_3$–CH_3OH solution. There are numerous recent studies on polymorphism in drugs (Gelbrich *et al.*, 2007; Drebushchak *et al.*, 2007) and supramolecular compounds (Wardell *et al.*, 2007; Li *et al.*, 2006). We report here the molecular and supramolecular structures of polymorphs (I) and (II)



(I) monoclinic polymorph
(II) orthorhombic polymorph

The molecular structures of polymorphs (I) and (II) are shown in Figs. 1 and 2, respectively. In both polymorphic forms, the molecule lies on a centre of inversion at the piperazine ring centroid. The bond lengths and angles in (I) and (II) are similar, and agree with the values in both the *p*-cresol derivative (Kuppayee *et al.*, 1999) and the 5-bromosalicylaldehyde system (Thirumurugan *et al.*, 1998). In both (I) and (II), the piperazine rings adopt a chair conformation. The molecular structures of (I) and (II) are very similar, and thus only small differences are observed. The largest differences in bond distances and angles between the two polymorphs are less than 0.02 Å [O1—C11 = 1.343 (2) Å in (I) and 1.358 (3) Å in (II)] and less than 2° [O1—C1—C6 = 122.56 (19)° in (I) and 121.4 (2)° in (II)], respectively. The greatest differences are for the torsion angles involving atoms C6 and C7, *viz*. C5—C6—C7—N1 [−143.7 (2)° in (I) and −146.7 (2)° in (II)] (Tables 1 and 3). The differences are reflected in the orientation of the

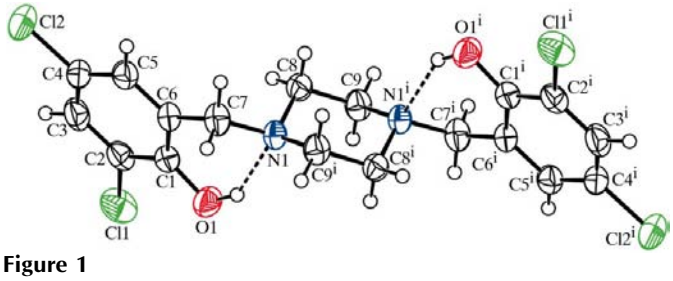


Figure 1
A view of polymorph (I), showing the atom-labelling scheme and displacement ellipsoids drawn at the 50% probability level. H atoms are represented by circles of arbitrary size. [Symmetry code: (i) $1-x, -y, 1-z$.]

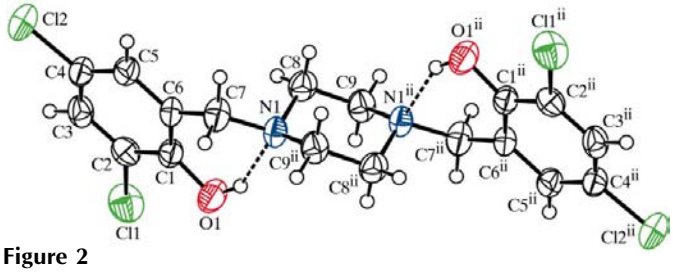


Figure 2
A view of polymorph (II), showing the atom-labelling scheme and displacement ellipsoids drawn at the 50% probability level. H atoms are represented by circles of arbitrary size. [Symmetry code: (ii) $2-x, -y, 1-z$.]

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aryl rings with respect to the central piperazine rings. The dihedral angles between the mean planes of the piperazine ring and the aryl rings are slightly different in the two polymorphs, *viz*. 101.28 (10)° in (I) and 104.00 (9)° in (II). The intramolecular O1—H1···N1 hydrogen-bond distances in (I) and (II) are 2.700 (2) and 2.660 (2) Å, respectively (Tables 2 and 4).

In the crystal structure of polymorph (I), there is an intermolecular C—H···Cl hydrogen bond (Table 1). Atom C7 in the molecule at (x, y, z) acts as a hydrogen-bond donor to atom Cl2 in the molecule at (x, $\frac{1}{2}-y$, $\frac{1}{2}+z$), forming a $C(6)$ (Bernstein *et al.*, 1995) chain running parallel to the [$\bar{1}$01] direction and generated by the *c*-glide plane at y = 0.25. A weak intermolecular C···C contact [C2···C4^{v} = 3.581 (5) Å; symmetry code: (v) x, $\frac{1}{2}-y$, $-\frac{1}{2}+z$] is also observed. The molecules are linked by the $C(6)$ chains and C···C contacts into a (100) ribbon sheet of $R_8^8(34)$ rings (Fig. 3). In addition, there is a weak intermolecular C—H···Cl contact [H9···Cl1^{vi} = 2.962 Å; symmetry code: (vi) 1 + x, y, z] between adjacent sheets.

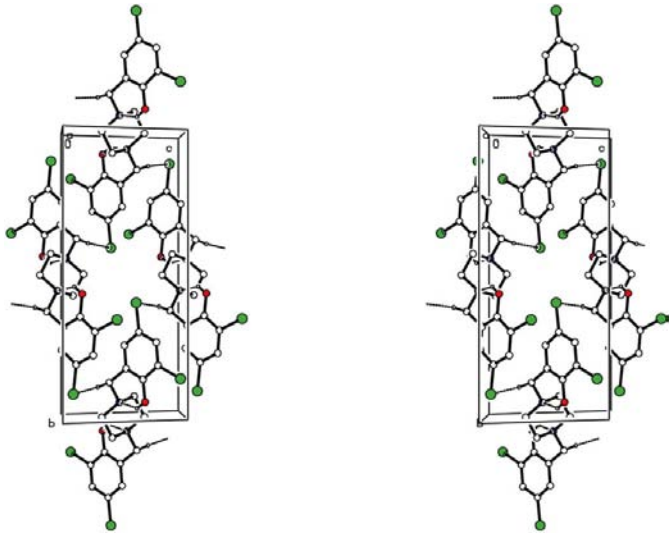

Figure 3
A stereoview of part of the crystal structure of polymorph (I), showing the formation of a centrosymmetric $R_8^8(34)$ ring. The O—H···N and C—H···Cl hydrogen bonds are shown as dashed lines. For the sake of clarity, H atoms not involved in the hydrogen bonds have been omitted.

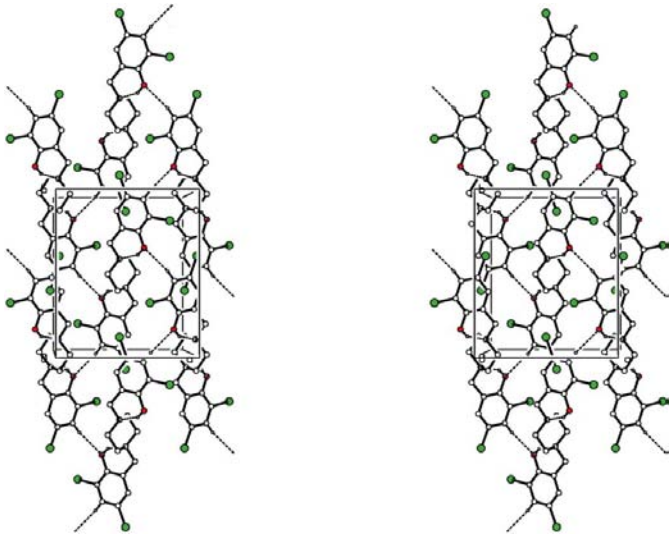

Figure 4
A stereoview of part of the crystal structure of polymorph (II), showing the formation of $R_6^6(34)$ rings. The O—H···N and C—H···O hydrogen bonds are shown as dashed lines. For the sake of clarity, H atoms not involved in the hydrogen bonds have been omitted.

In the crystal structure of polymorph (II), there is an intermolecular C—H···O hydrogen bond (Table 2). Atom C3 in the molecule at (x, y, z) acts as a hydrogen-bond donor to atom O1 in the molecule at ($\frac{3}{2}-x$, $\frac{1}{2}+y$, z), forming a $C(5)$ chain running parallel to the [010] direction and generated by the *b*-glide plane at x = 0.75. The molecules are linked by the $C(5)$ chains into a (001) ribbon sheet of $R_6^6(34)$ rings (Fig. 4). The sheets are crosslinked into a three-dimensional framework by $\pi\cdots\pi$ interactions [C1···C1^{vii} = 3.528 (3) Å, C2···C5^{vii} = 3.564 (3) Å and C3···C4^{vii} = 3.427 (3) Å; symmetry code: (vii) 1 + x, y, $\frac{3}{2}-z$].

Each polymorph is characterized by the supramolecular interactions: for (I), C—H···Cl hydrogen bonds and weak C···C contacts, and for (II), C—H···O hydrogen bonds and $\pi\cdots\pi$ interactions. There are no short Cl···Cl interactions in either polymorph.

Experimental

A mixture of 2,4-dichlorophenol (13.04 g, 80 mmol), piperazine (3.45 g, 40 mmol) and paraformaldehyde (2.40 g, 80 mmol) in methanol (60 ml) was refluxed for 6 h. The mixture was cooled to room temperature and the solvent evaporated under vacuum. The product was recrystallized from $CHCl_3$–CH_3OH to give colourless crystals suitable for X-ray analysis. Visual examination of the crystals under a microscope showed that most of them consisted of (I), with a small amount of (II). By crystallizing H_2Cl_2bpi under various conditions, we attempted to obtain extra amounts of (II); however, no remarkable improvement was observed. Samples of the two polymorphs were isolated manually [yield 10.40 g (59.6%); m.p. 510.0–512.1 K for (I) and 510.4–512.8 K for (II)]. Phase transitions of one polymorph into another were not observed by differential scanning calorimetry (DSC). Analysis calculated for $C_{18}H_{18}Cl_4N_2O_2$: C 49.57, H 4.16, N 6.42%; found: C 49.54, H 4.20, N 6.46%. ^{1}H NMR ($CDCl_3$, p.p.m., 400 MHz): δ 2.66 (*brs*, 8H, CH_2), 3.72 (*s*, 4H, CH_2), 6.90 (*d*, J = 2.4 Hz, 2H, ArH), 7.28 (*d*, J = 2.4 Hz, 2H, ArH), 11.2 (*brs*, 2H, OH).

Polymorph (I)

Crystal data

$C_{18}H_{18}Cl_4N_2O_2$
M_r = 436.14
Monoclinic, $P2_1/c$
a = 7.4861 (13) Å
b = 17.2008 (13) Å
c = 8.0283 (19) Å
β = 111.972 (13)°
V = 958.7 (3) Å^3
Z = 2
Mo $K\alpha$ radiation
μ = 0.63 mm^{-1}
T = 298 K
0.25 × 0.15 × 0.15 mm

Data collection

Rigaku AFC-7*R* diffractometer
2364 measured reflections
2215 independent reflections
1526 reflections with $F^2 > 2\sigma(F^2)$
R_{int} = 0.017
3 standard reflections
every 150 reflections
intensity decay: 0.1%

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.040$	127 parameters
$wR(F^2) = 0.125$	H-atom parameters constrained
$S = 1.01$	$\Delta\rho_{max} = 0.68$ e Å^{-3}
1528 reflections	$\Delta\rho_{min} = -0.35$ e Å^{-3}

Table 1
Selected torsion angles (°) for polymorph (I).

C2—C1—C6—C7	177.8 (2)	C5—C6—C7—N1	−143.7 (2)
C1—C6—C7—N1	39.8 (3)	C4—C5—C6—C7	−176.1 (3)

Table 2
Hydrogen-bond geometry (Å, °) for polymorph (I).

D—H···A	D—H	H···A	D···A	D—H···A
O1—H1···N1	0.85	1.97	2.700 (2)	145
C7—H4···Cl2^{iii}	0.95	2.78	3.688 (3)	159

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

Polymorph (II)

Crystal data

$C_{18}H_{18}Cl_4N_2O_2$	$V = 1936.4$ (9) Å^3
$M_r = 436.14$	$Z = 4$
Orthorhombic, *Pbcn*	Mo $K\alpha$ radiation
$a = 10.360$ (3) Å	$\mu = 0.63$ mm^{-1}
$b = 12.1910$ (17) Å	$T = 298$ K
$c = 15.332$ (5) Å	0.20 × 0.15 × 0.12 mm

Data collection

Rigaku AFC-7*R* diffractometer	$R_{int} = 0.024$
3228 measured reflections	3 standard reflections
2222 independent reflections	every 150 reflections
1922 reflections with $F^2 > 2\sigma(F^2)$	intensity decay: 0.3%

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.037$	127 parameters
$wR(F^2) = 0.106$	H-atom parameters constrained
$S = 1.00$	$\Delta\rho_{max} = 0.46$ e Å^{-3}
1925 reflections	$\Delta\rho_{min} = -0.68$ e Å^{-3}

Table 3
Selected torsion angles (°) for polymorph (II).

C2—C1—C6—C7	176.0 (2)	C5—C6—C7—N1	−146.7 (2)
C1—C6—C7—N1	38.0 (3)	C4—C5—C6—C7	−173.7 (2)

For both polymorphs, the H atoms of the hydroxyl groups were found from a difference Fourier map. The other H atoms were placed at idealized positions, with C—H = 0.95 Å. All the H atoms were refined as riding, with $U_{iso}(H) = 1.2U_{eq}(C)$.

Table 4
Hydrogen-bond geometry (Å, °) for polymorph (II).

D—H···A	D—H	H···A	D···A	D—H···A
O1—H1···N1	0.84	1.89	2.660 (2)	151
C3—H2···O1^{iv}	0.95	2.48	3.347 (3)	152

Symmetry code: (iv) $-x+\frac{3}{2}, y+\frac{1}{2}, z$.

For both polymorphs, data collection: *WinAFC* (Rigaku/MSC, 2006); cell refinement: *WinAFC*; data reduction: *CrystalStructure* (Rigaku/MSC, 2006); program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1993); program(s) used to refine structure: *CRYSTALS* (Betteridge *et al.*, 2003); molecular graphics: *PLATON* (Spek, 2003); software used to prepare material for publication: *CrystalStructure*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GG3104). Services for accessing these data are described at the back of the journal.

References

Altomare, A., Cascarano, G., Giacovazzo, C. & Guagliardi, A. (1993). *J. Appl. Cryst.* **26**, 343–350.
Bernstein, J., Davis, R. E., Shimoni, L. & Chang, N.-L. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 1555–1573.
Betteridge, P. W., Carruthers, J. R., Cooper, R. I., Prout, K. & Watkin, D. J. (2003). *J. Appl. Cryst.* **36**, 1487.
Chi, K.-L., Ahn, Y. S., Shim, K. T., Huh, H. & Ahn, J. S. (2002). *Bull. Korean Chem. Soc.* **23**, 688–692.
Drebushchak, T. N., Chukanov, N. V. & Boldyreva, E. V. (2007). *Acta Cryst.* C**63**, o355–o357.
Favor, D. A., Johnson, D. S., Powers, J. J., Li, T. & Madabattula, R. (2007). *Tetrahedron Lett.* **48**, 3039–3041.
Gelbrich, T., Threlfall, T. L., Bingham, A. L. & Hursthouse, M. B. (2007). *Acta Cryst.* C**63**, o323–o326.
Geng, B., Fleming, P. R., Umlauf, S., Lin, A. & Pallai, P. V. (2002). *Bioorg. Med. Chem. Lett.* **12**, 775–778.
Kubono, K., Oshima, S., Hirayama, N. & Yokoi, K. (2005). *Acta Cryst.* E**61**, o3706–o3708.
Kubono, K., Oshima, S., Hirayama, N. & Yokoi, K. (2006). *Acta Cryst.* E**62**, m2858–m2859.
Kuppayee, M., Kumaran, D., Ponnuswamy, M. N., Kandaswamy, M., Violet, M. J., Chinnakali, K. & Fun, H.-K. (1999). *Acta Cryst.* C**55**, 2147–2149.
Li, C.-Q., Zhu, L.-N., Li, X.-Z. & Li, R. (2006). *Acta Cryst.* E**62**, m870–m872.
Okamatsu, T., Irie, R. & Katsuki, T. (2007). *J. Organomet. Chem.* **692**, 645–653.
Rigaku/MSC (2006). *WinAFC* (Version 1.0.5) and *CrystalStructure* (Version 3.8.1). Rigaku/MSC, The Woodlands, Texas, USA.
Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.
Thirumurugan, R., Shanmuga Sundara Raj, S., Shanmugam, G., Fun, H.-K., Chinnakali, K., Chantrapromma, S., Marappan, M. & Kandaswamy, M. (1998). *Acta Cryst.* C**54**, 780–781.
Wardell, S. M. S. V., de Souza, M. V. N., Wardell, J. L., Low, J. N. & Glidewell, C. (2007). *Acta Cryst.* B**63**, 101–110.