Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

Two tautomeric polymorphs of 2,6-dichloropurine

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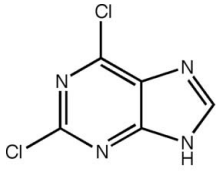
Received 19 September 2011
Accepted 20 October 2011
Online 5 November 2011

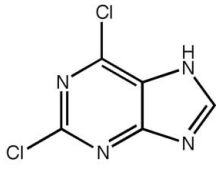
Two polymorphs of 2,6-dichloropurine, $C_5H_2Cl_2N_4$, have been crystallized and identified as the 9*H*- and 7*H*-tautomers. Despite differences in the space group and number of symmetry-independent molecules, they exhibit similar hydrogen-bonding motifs. Both crystal structures are stabilized by intermolecular N—H···N interactions that link adjacent molecules into linear chains, and by some nonbonding contacts of the C—Cl···π type and by π–π stacking interactions, giving rise to a crossed two-dimensional herringbone packing motif. The main structural difference between the two polymorphs is the different role of the molecules in the π–π stacking interactions.

Comment

2,6-Dichloropurine is an important pharmaceutical intermediate (Schaefer *et al.*, 1978) used in the preparation of purine nucleosides and nucleotides, and other purine derivatives of great importance owing to their biological properties (Nair & Pal, 1998; Rao Kode & Phadtare, 2011).



(I)



(II)

Polymorphism, the ability of a given molecule to crystallize in different crystal structures, is a phenomenon often observed for organics (Bernstein, 2011; Brittain, 2011). The term 'tautomeric polymorphs' refers to those tautomers of a given compound that crystallize in different crystal structures and they are very rarely observed (Cruz Cabeza *et al.*, 2011). We present here the crystal structure of the 9*H*-, (I), and 7*H*-, (II), tautomers of 2,6-dichloropurine.

The molecular geometric parameters in the two presented polymorphs are similar, but the structures differ in the finer details of their crystal packing. As shown in Fig. 1, polymorph (I) crystallizes with two independent molecules in the asymmetric unit (*A* and *B*, top and middle) as the 9*H*-tautomer, while polymorph (II) crystallizes with one symmetry-independent molecule (bottom) as the 7*H*-tautomer.

The effect of the different –N(H) position in the tautomeric forms (N9 or N7) gives rise to subtle differences between the relevant bond lengths and angles in both structures in the imidazole ring. In (I), the N=Csp^2 bond corresponds to N7—C8 [1.310 (5) Å] and N17—C18 [1.307 (5) Å] for molecules *A* and *B*, respectively, while in (II) it is N9—C8 [1.327 (3) Å]. These N=Csp^2 bond lengths are comparable with those in related structures with 9*H*- (Mahapatra *et al.*, 2008; Trávníček & Rosenker, 2006; Soriano-Garcia & Parthasarathy, 1977) and 7*H*-tautomers (Bo *et al.*, 2006; Ikonen *et al.*, 2009; Watson *et al.*, 1965). The –N(H) tautomeric position is also evident from the greater ring angle at the site where the H atom is attached, namely N9 [C4—N9—C8 = 105.9 (3)°] and N19 [C14—N19—C18 = 105.6 (3)°] for (I), and N7 [C5—N7—C8 = 105.9 (2)°] for (II), compared with the ring angle involving the –N=C– bond [for (I), C5—N7—C8 = 103.6 (3)° and C15—N17—C18 = 103.8 (3)°; for (II), C4—N9—C8 = 103.6 (2)°]. In both polymorphs, the 2,6-dichloropurine molecules form linear chains along the *b* axis through

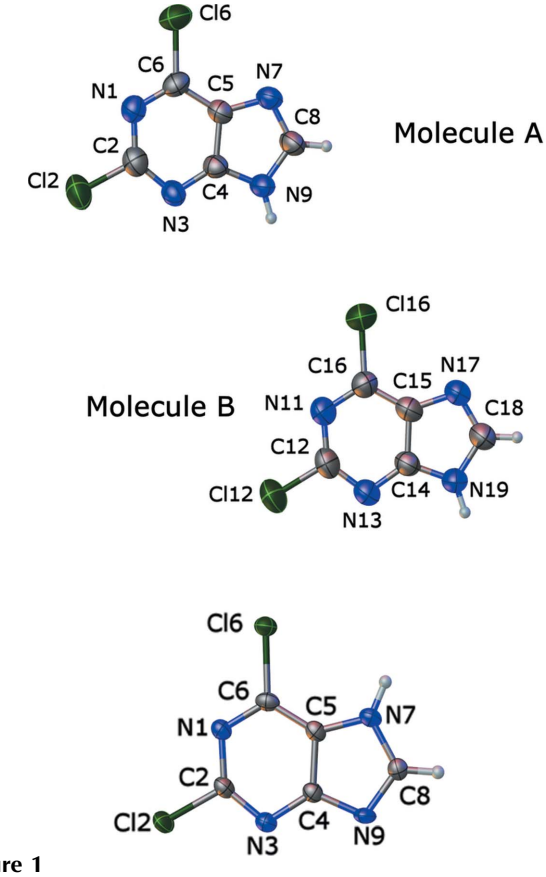


Figure 1
The contents of the asymmetric units of polymorph (I) (top and middle) and polymorph (II) (bottom), showing the atom-numbering schemes. Displacement ellipsoids are drawn at the 50% probability level.

  doi:10.1107/S0108270111043575

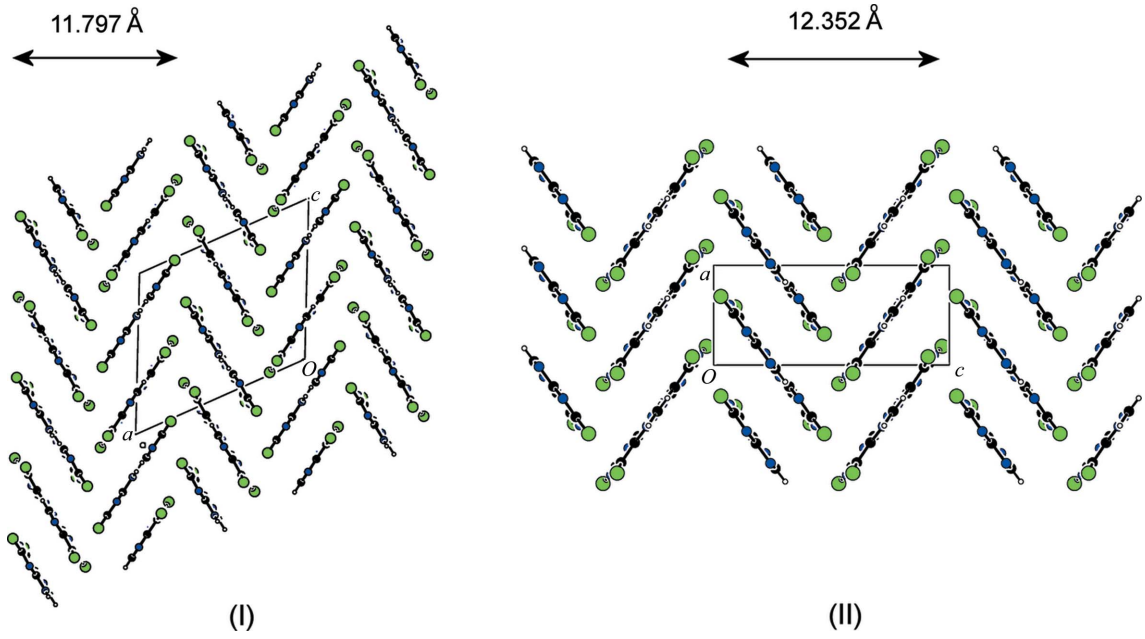


Figure 2
A view of the crystal packing, showing the herringbone arrangement of 2,6-dichloropurine molecules in polymorph (I) (left) and polymorph (II) (right).

intermolecular N—H···N interactions forming $C(4)$ motifs (Bernstein *et al.*, 1995).

In polymorph (I), chains built by molecules of type *A* are linked by intermolecular face-to-face π–π stacking interactions involving the N1/C2/N3/C4–C6 ring and a symmetry-related counterpart at $(-x+1, -y+1, -z+1)$, with a centroid–centroid distance of 3.493 (3) Å. Molecules of type *B* are not involved in π–π stacking interactions. There are also C—Cl···π interactions involving atom Cl16 and ring N1/C2/N3/C4–C6 ($Cg1_I$), with a Cl···centroid distance of 3.468 (2) Å and a C16—Cl16···$Cg1_I^{i}$ angle of 113.46 (17)° [symmetry code: (i) $x, -y+\frac{1}{2}, z+\frac{1}{2}$], and atom Cl6 and ring N11/C12/N13/C14–C16 ($Cg2_I$), with a Cl···centroid distance of 3.664 (2) Å and a C6—Cl6···$Cg2_I$ angle of 94.54 (13)°, resulting in a structure containing a two-dimensional herringbone-like motif of constituent molecules.

The crystal structure of polymorph (II) is similar to that of polymorph (I). Despite the fact that π–π stacking interactions are not observed in (II), the supramolecular structure features a similar herringbone motif to that in (I), due to the presence of C—Cl···π interactions between atom Cl6 and ring N1/C2/N3/C4–C6 ($Cg1_{II}$), with a Cl···centroid distance of 3.3471 (15) Å and a C6—Cl6···$Cg1_{II}^{ii}$ angle of 108.45 (10)° [symmetry code: (ii) $x-\frac{1}{2}, -y+\frac{3}{2}, -z+1$]. As a consequence of the absence of stacking interactions in (II), the width of the herringbone motif (12.352 Å) is greater than that of (I) (11.797 Å) (Fig. 2) [the width of the motifs was calculated as the distance between the two planes containing the furthermost atoms in the herringbone motif, corresponding to the Cl atoms of 2,6-dichloropurine; *Mercury* (Macrae *et al.*, 2008)].

Experimental

Polymorph (I) (m.p. 466.05–466.75 K) was obtained unintentionally in an attempted synthesis of (*RS*)-2,6-dichloro-9-(2,3-dihydro-1,4-benzoxathiin-3-ylmethyl)-9*H*-purine (Díaz-Gavilán *et al.*, 2008). Unreacted 2,6-dichloropurine was recovered using ethyl acetate as eluent. After concentrating the solvent under reduced pressure, suitable crystals of 2,6-dichloropurine were obtained after dissolving the compound in CH_2Cl_2. A vial with a screw top allowed slow evaporation of the solvent at room temperature to produce colourless crystals. Crystals of polymorph (II) (m.p. 467.95–468.85 K) were obtained by solvent evaporation with commercially available 2,6-dichloropurine using ethanol as solvent. The remarkable similarity of the crystal structures of the reported polymorphs yields minimal differences in the shape and position of the peaks in the FT–IR spectra (polycrystalline samples in KBr disks). Hence, the stretching mode ν(N—H) (a weak peak at 3210 cm^{-1}) and the in-plane deformation mode δ(N—H) (1513 cm^{-1}) appear at the same site in (I) and (II).

Polymorph (I)

Crystal data

$C_5H_2Cl_2N_4$
M_r = 189.01
Monoclinic, $P2_1/c$
a = 14.0867 (12) Å
b = 9.4898 (7) Å
c = 12.2656 (9) Å
β = 115.381 (4)°
V = 1481.4 (2) Å^3
Z = 8
Cu $K\alpha$ radiation
μ = 7.36 mm^{-1}
T = 296 K
0.12 × 0.10 × 0.06 mm

Data collection

Bruker X8 Proteum diffractometer
Absorption correction: multi-scan (*SADABS*; Bruker, 2001)
T_{min} = 0.377, T_{max} = 0.753
18199 measured reflections
2547 independent reflections
1713 reflections with $I > 2\sigma(I)$
R_{int} = 0.085

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.051
$wR(F^2)$ = 0.154
S = 1.10
2547 reflections
199 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.27 e Å^{-3}
$\Delta\rho_{min}$ = −0.29 e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
N9—H9···N7^{i}	0.86	1.96	2.785 (4)	161
N19—H19···N17^{ii}	0.86	1.94	2.768 (5)	160

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

Polymorph (II)

Crystal data

$C_5H_2Cl_2N_4$
M_r = 189.01
Orthorhombic, $P2_12_12_1$
a = 5.5716 (9) Å
b = 9.5820 (16) Å
c = 13.159 (2) Å
V = 702.5 (2) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.85 mm^{-1}
T = 120 K
0.12 × 0.10 × 0.08 mm

Data collection

Bruker SMART APEX diffractometer
Absorption correction: multi-scan (*SADABS*; Bruker, 2001)
T_{min} = 0.905, T_{max} = 0.935
6847 measured reflections
1243 independent reflections
1156 reflections with $I > 2\sigma(I)$
R_{int} = 0.041

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.033
$wR(F^2)$ = 0.071
S = 1.38
1243 reflections
100 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.33 e Å^{-3}
$\Delta\rho_{min}$ = −0.22 e Å^{-3}
Absolute structure: Flack (1983), with 489 Friedel pairs
Flack parameter: 0.03 (10)

H atoms on N atoms were located in difference maps and refined as riding, with N—H = 0.86 [in (I)] and 0.94 Å [in (II)], and U_{iso}(H) = 1.2U_{eq}(N). Other H atoms were positioned geometrically and treated as riding, with C—H = 0.93–0.95 Å and U_{iso}(H) = 1.2U_{eq}(C).

For both compounds, data collection: *APEX2* (Bruker, 2010); cell refinement: *SAINT* (Bruker, 2010); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *PLATON* (Spek, 2009); software used to prepare material for publication: *publCIF* (Westrip, 2010).

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

D—H···A	D—H	H···A	D···A	D—H···A
N7—H7···N9^{i}	0.94	1.88	2.774 (3)	158

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

The project 'Factoría de Cristalización, CONSOLIDER INGENIO-2010' provided X-ray structural facilities for this work.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GG3264). Services for accessing these data are described at the back of the journal.

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