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4-Amino-2,6-dichloro-5-nitropyrimidine

Declan McKeveney, Ronald J. Quinn, Christian O. Janssen and Peter C. Healy*

School of Science, Griffith University, Nathan, Brisbane 4111, Australia

Correspondence e-mail: p.healy@griffith.edu.au

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Key indicators

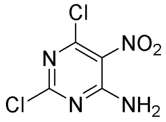
Single-crystal X-ray study
T = 295 K
Mean σ(C–C) = 0.004 Å
R factor = 0.047
wR factor = 0.144
Data-to-parameter ratio = 16.1

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

The title compound, $C_4H_2Cl_2N_4O_2$, is a key intermediate in the synthesis of a purine scaffold, as nucleophilic substitution of the chlorides allows access to a diverse array of potentially biologically active compounds. The molecules exhibit an intramolecular N—H···O hydrogen bond between the *ortho* amino and nitro substituents. Pairs of molecules associate across a crystallographic centre of symmetry through N—H···N intermolecular hydrogen bonding between the *ortho* amino group and the ring N atom.

Comment

The title compound, (I), is a key intermediate in the synthesis of a purine scaffold, as nucleophilic substitution of the chlorides allows convenient access to a diverse array of potentially biologically active compounds (Dille & Christensen, 1953). We synthesized (I) as part of a project involving combinatorial library production on solid phase resins, as it can be attached to the resin *via* a carbamate linkage. This allows three points of combinatorial variation, as a nitro reduction followed by a one-pot cyclization cleavage step gives the substituted purine product.



(I)

The crystal structure of (I) contains one independent molecule in the asymmetric unit, the structure of which is shown in Fig. 1. The molecules exhibit a characteristic intramolecular N—H···O hydrogen bond between the *ortho* amino and nitro groups [H41···O51 = 2.08, N4···O51 = 2.670 (5) Å and N4—H41···O51 = 126°] (*cf.* Glidewell *et al.*, 2003; Linden *et al.*, 1994; Larson *et al.*, 1988). Pairs of molecules associate across a

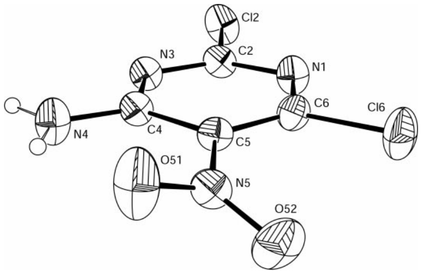


Figure 1
ORTEP-3 (Farrugia, 1997) plot, showing the atomic numbering scheme for (I). Displacement ellipsoids for non-H atoms are drawn at the 30% probability level.

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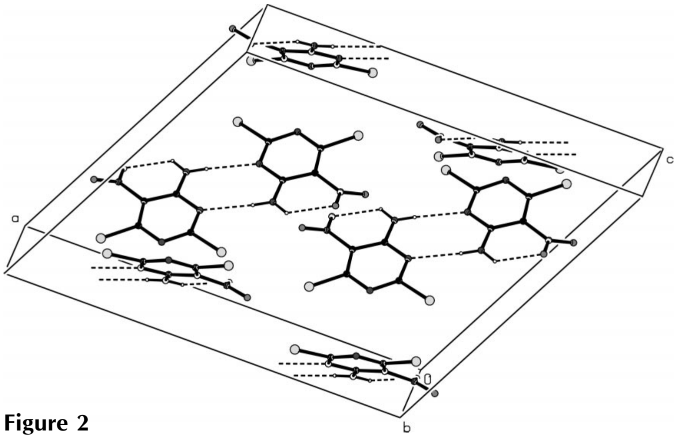

Figure 2
Perspective view of the packing in the unit cell, viewed approximately down the *b* axis, showing the hydrogen-bonding associations as dashed lines.

centre of symmetry through classical $R_2^2(8)$ (Bernstein *et al.*, 1995) N—H···N hydrogen bonding interactions between the *ortho* amino group and the ring N atom [H42···N3^{i} = 2.23, N4···N3^{i} = 3.084 (4) Å and N4—H42···N3^{i} = 172°; symmetry code: (i) $\frac{1}{2}-x$, $\frac{1}{2}-y$, $1-z$] (Fig. 2). A similar dimeric hydrogen-bonding pattern has been reported for the structure of the related compound 4-amino-2,6-dimethoxy-5-nitropyrimidine, (II) (Glidewell *et al.*, 2003). In this latter structure, the two molecules of the dimer are crystallographically independent and disposed about a pseudo-centre of symmetry. The nitro group in (II) was found to be coplanar with the pyrimidine ring. In (I), however, the nitro group is significantly twisted out of the plane of the pyrimidine ring, with an O51—N5—C5—C4 torsion angle of −25.1 (4)°. This conformational change is most likely a consequence of steric repulsion effects between O52 and the *ortho* chloride, Cl6. It is interesting to note that the difference of *ca* 0.03 Å observed between the two N—O bond lengths in both molecules of (II), with the longer bonds involved in the intramolecular N—H···O hydrogen bonding, is not observed in the structure of (I) with bond lengths of 1.208 (4) and 1.206 (4) Å.

Experimental

N,N-Dimethylaniline (DMA; 15.4 ml, 0.120 mol) was added dropwise to a boiling suspension of 4-amino-2,6-dihydroxy-5-nitropyrimidine (10.0 g, 0.058 mol) in $POCl_3$ (64.2 ml). A pale blue mixture was formed initially and this changed to an intense deep blue on further addition. The mixture was then refluxed for 2.5 h and allowed to cool to room temperature. The reaction mixture was carefully poured on to 600 g of ice with vigorous stirring, resulting in the formation of a black precipitate. The precipitate was filtered off and extracted with ether (200 ml × 3). The filtrate was also extracted with ether (300 ml × 4). The extracts were combined and reduced under vacuum to allow easier treatment with activated carbon. The resultant golden yellow solution was then washed with $NaHCO_3$ (300 ml × 5) and dried with $MgSO_4$. The remaining ether was then removed and the resultant precipitate taken up in a minimum amount of hot toluene and left at 268 K overnight to give yellow crystals of the complex suitable for X-ray diffraction studies (m.p. 422–426 K). Analysis found: C 22.98, H 0.97, N 27.06%; calculated for $C_4H_2Cl_2N_4O_2$: C 22.99, H 0.96, N 26.81%.

Crystal data

$C_4H_2Cl_2N_4O_2$
M_r = 209.00
Monoclinic, $C2/c$
a = 17.667 (3) Å
b = 6.708 (2) Å
c = 14.425 (3) Å
β = 116.608 (15)°
V = 1528.5 (6) Å^3
Z = 8

D_x = 1.816 Mg m^{-3}
Mo Kα radiation
Cell parameters from 25 reflections
θ = 12.6–17.0°
μ = 0.81 mm^{-1}
T = 295 K
Prism, yellow
0.30 × 0.30 × 0.25 mm

Data collection

Rigaku AFC-7*R* diffractometer
ω–2θ scans
Absorption correction: none
2123 measured reflections
1766 independent reflections
1290 reflections with $I > 2\sigma(I)$
$R_{\rm int}$ = 0.046

$\theta_{\rm max}$ = 27.5°
$h = -10 \rightarrow 22$
$k = -8 \rightarrow 4$
$l = -18 \rightarrow 16$
3 standard reflections
every 150 reflections
intensity decay: 0.7%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.047
$wR(F^2)$ = 0.144
S = 1.04
1766 reflections
110 parameters
H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.0646P)^2 + 2.5264P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\rm max} < 0.001$
$\Delta\rho_{\rm max}$ = 0.57 e Å^{-3}
$\Delta\rho_{\rm min}$ = −0.40 e Å^{-3}
Extinction correction: *SHELXL*97
Extinction coefficient: 0.0046 (10)

Table 1
Selected geometric parameters (Å, °).

Cl2—C2	1.729 (3)	N3—C2	1.305 (4)
Cl6—C6	1.712 (3)	N3—C4	1.356 (4)
O51—N5	1.208 (4)	N4—C4	1.318 (4)
O52—N5	1.206 (4)	N5—C5	1.449 (4)
N1—C2	1.323 (4)	C4—C5	1.423 (4)
N1—C6	1.325 (5)	C5—C6	1.388 (4)
C2—N1—C6	114.1 (3)	N3—C4—N4	115.4 (3)
C2—N3—C4	116.5 (3)	N3—C4—C5	118.5 (2)
O51—N5—O52	122.6 (3)	N4—C4—C5	126.1 (3)
O51—N5—C5	118.2 (3)	N5—C5—C4	119.9 (2)
O52—N5—C5	119.1 (3)	N5—C5—C6	122.4 (3)
Cl2—C2—N3	114.5 (2)	Cl6—C6—N1	114.1 (2)
Cl2—C2—N1	115.2 (2)	Cl6—C6—C5	123.0 (3)
N1—C2—N3	130.3 (3)	N1—C6—C5	122.8 (3)

H atoms were constrained in the riding-model approximation, fixed to their parent N atoms, with N—H set to 0.86 Å. $U_{\rm iso}$ values for the H atoms were set at 1.2$U_{\rm eq}$ of the parent atom.

Data collection: *MSC/AFC-*7 *Diffractometer Control Software* (Molecular Structure Corporation, 1999); cell refinement: *MSC/AFC-*7 *Diffractometer Control Software*; data reduction: *TEXSAN for Windows* (Molecular Structure Corporation, 1997–2001); program(s) used to solve structure: *TEXSAN for Windows*; program(s) used to refine structure: *TEXSAN for Windows* and *SHELXL*97 (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 1980–2001) and *ORTEP*-3 (Farrugia, 1997); software used to prepare material for publication: *TEXSAN for Windows* and *PLATON*.

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