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

The title compound, C₆H₂Cl₂N₄O₂, 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.

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.
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 $[H42] = 172^\circ$; 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-dihydroxy-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 $-25.1^\circ$. 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 $\text{POCl}_3$ (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 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 $\text{NaHCO}_3$ (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 $\text{C}_4\text{H}_2\text{Cl}_2\text{N}_4\text{O}_2$: C 22.99, H 0.96, N 26.81%.

**Crystal data**

$\text{C}_4\text{H}_2\text{Cl}_2\text{N}_4\text{O}_2$

$m = 209.00$

Monoclinic, $\text{C}2/c$

$a = 17.667 (3)$ Å

$b = 6.708 (2)$ Å

$c = 14.425 (3)$ Å

$\beta = 116.608 (15)^\circ$

$V = 1528.5 (6)$ Å$^3$

$Z = 8$

$D_\text{m} = 1.816 \text{ Mg m}^{-3}$

Mo Kα radiation

Cell parameters from 25 reflections

$\theta = 12.6–17.0^\circ$

$\mu = 0.81 \text{ mm}^{-1}$

$T = 295$ K

Prism, yellow

0.30 × 0.30 × 0.25 mm

**Data collection**

Rigaku AFC-7R diffractometer

$\omega$–$2\theta$ scans

Absorption correction: none

2123 measured reflections

1766 independent reflections

1290 reflections with $I > 2\sigma(I)$

$R_{int} = 0.046$

**Refinement**

Refinement on $F^2$

$R^2 (F^2) = 0.047$

$S = 1.04$

1766 reflections

110 parameters

H-atom parameters constrained

$w = 1/[\sigma^2(F^2) + (0.0646P)^2 + 2.5264P]$

where $P = (F^2 + 2F_C^2)/3$

$\Delta P_{\text{max}} = 0.40 \text{ e Å}^{-3}$

Extinction correction: SHELXL97

Extinction coefficient: 0.0046 (10)

**Table 1**

<table>
<thead>
<tr>
<th>Selected geometric parameters (Å, °)</th>
</tr>
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<tbody>
<tr>
<td>C2–C2</td>
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<tr>
<td>C6–C6</td>
</tr>
<tr>
<td>O51–N5</td>
</tr>
<tr>
<td>O52–N5</td>
</tr>
<tr>
<td>N1–C2</td>
</tr>
<tr>
<td>N1–C6</td>
</tr>
<tr>
<td>C2–N1–C6</td>
</tr>
<tr>
<td>C2–N3–C4</td>
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<tr>
<td>O52–N5–C5</td>
</tr>
<tr>
<td>C2–C2–N3</td>
</tr>
<tr>
<td>C2–C2–N1</td>
</tr>
<tr>
<td>N1–C2–N3</td>
</tr>
</tbody>
</table>

**Experimental**

H atoms were constrained in the riding-model approximation, fixed to their parent N atoms, with N–H set to 0.86 Å. $U_{eq}$ values for the H atoms were set to 1.2$U_{eq}$ 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 SHELXL97 (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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References


