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4-(Allylamino)-2-amino-6-benzyloxy-5-nitrosopyrimidine from synchrotron data at 150 K: double chains built from N—H···N, N—H···O, N—H···π(arene) and aromatic π–π-stacking interactions

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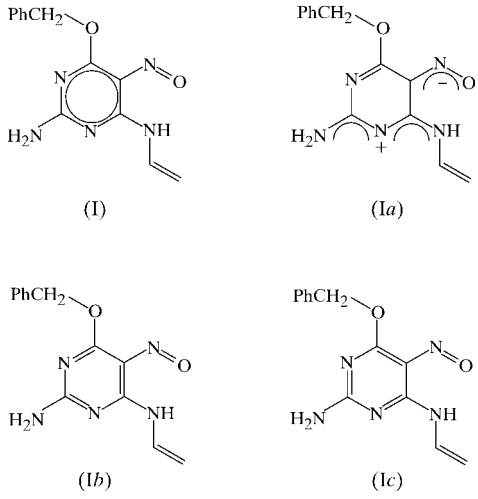
In the title compound, $C_{14}H_{15}N_5O_2$, the intramolecular dimensions are consistent with a highly polarized electronic structure. The molecules are linked into chains by a combination of N—H···N, N—H···O and N—H···π(arene) hydrogen bonds, and the chains are linked in pairs by aromatic π–π-stacking interactions

Comment

Alkoxy- and amino-substituted O^6-benzyloxy-5-nitrosopyrimidines (Marchal *et al.*, 2000, 2002) are important as potential, or proven, *in vitro* inhibitors of the human DNA repair protein O^6-alkylguanine–DNA-transferase (Chae *et al.*, 1995; Quesada, Marchal *et al.*, 2002). We report here the molecular and supramolecular structure of an analogue, namely 4-(allylamino)-2-amino-6-benzyloxy-5-nitrosopyrimidine, (I), containing an *N*-allyl substituent.

The intramolecular dimensions of (I) (Table 1) show a number of features typical of substituted 5-nitrosopyrimidines (Low *et al.*, 2000; Quesada, Marchal *et al.*, 2002). In particular, the sequence of four C—N bonds between N2 and N4 (Fig. 1) spans only a very small range of distances, 1.329 (2)–1.339 (2) Å, while the C6—N1 bond is significantly shorter and C2—N1 is significantly longer; the C4—C5 and C5—C6 distances are rather similar; and, in addition, the C—N and N—O distances in each C-nitroso fragment differ by only *ca* 0.11 Å, whereas in simple neutral compounds, where there is no possibility of significant electronic delocalization, these distances normally differ by at least 0.20 Å (Talberg, 1977; Schlemper *et al.*, 1986) and the NO distance rarely exceeds 1.25 Å (Davis *et al.*, 1965; Bauer & Andreassen, 1972; Talberg, 1977; Schlemper *et al.*, 1986). These observations all point to the charge-separated form (I*a*) as an important contributor to the overall electronic structure, at the expense of classically bond-fixed forms, such as (I*b*) and (I*c*).



The nitrosyl O atom is almost coplanar with the pyrimidine ring (Table 2). This is associated both with the electronic delocalization and with intramolecular hydrogen bonding (see below). Similarly, the torsion angles indicate that atom C7 of the allylamino substituent, and both C67 and C61 of the benzyloxy substituent, are also nearly coplanar with the pyrimidine ring; however, there are substantial twists away from planarity about the N4—C7 and C61—C67 bonds.

There is an intramolecular N—H···O hydrogen bond (Table 2) generating an *S*(6) motif (Bernstein *et al.*, 1995); the N—H···O angle is small, constrained both by the ring size and shape, and by the near coplanarity of the nitroso group and the pyrimidine ring, but both the donor and acceptor in this interaction carry partial charges [*cf.* structure (I*a*)], and hence this interaction is an example of a resonance-assisted hydrogen bond (Gilli *et al.*, 1994). The molecules are linked by further hydrogen bonds into chains running parallel to the [001] direction. Amino atom N2 acts as hydrogen-bond donor,

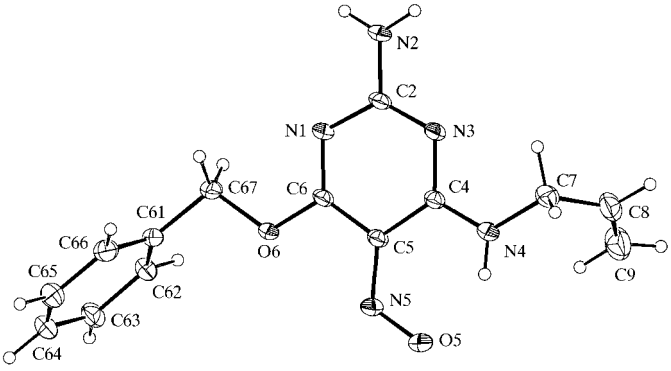


Figure 1
View of the molecule of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level.

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via H2*A*, to both N5^{i} and O6^{i} [symmetry code: (i) $x, y, 1 + z$], so generating by translation a $C(6)C(7)[R_1^2(5)]$ chain of rings (Fig. 2). This three-centre N—H···(N,O) hydrogen bond has an angle sum at H2*A* of 355°, but the H···O distance is long and the N—H···O angle is small (Table 2); hence, it may be that the H···O contact is more adventitious than significant. The conventional chain-forming hydrogen bonds are augmented by an N—H···π(arene) interaction; amino atom N2 also acts as donor, *via* H2*B*, which is not involved in any conventional hydrogen bonds, to the centroid ($Cg2^{i}$) of arene ring C61–C66 (Table 2 and Fig. 2).

Four [001] chains run through each unit cell, two in the domain $0.29 < y < 0.71$ and two in the domain $0.79 < y < 1.21$. Within each domain, the [001] chains are pairwise linked by π–π-stacking interactions; the parallel pyrimidine rings in the molecules at (x, y, z) and $(-x, 1 - y, 1 - z)$ have an interplanar spacing of 3.310 (2) Å and a centroid separation of 3.779 (2) Å (Fig. 3). While the ring-centroid offset, *ca* 1.82 Å, is quite large, the offset direction is such that the cationic and anionic regions of adjacent molecules [*cf.* structure (I*a*)] are reasonably close (Fig. 3), thus enhancing this attractive interaction.

All three independent N—H bonds in (I) are thus involved in the overall hydrogen bonding, with each forming a different type of interaction. Although the hard (Braga *et al.*, 1995) hydrogen-bond donors are all utilized, unusually (Low *et al.*, 2000; Quesada, Marchal *et al.* 2002) there are neither hard intermolecular hydrogen bonds involving the nitrosyl atom O5 nor any soft hydrogen bonds involving atom O5.

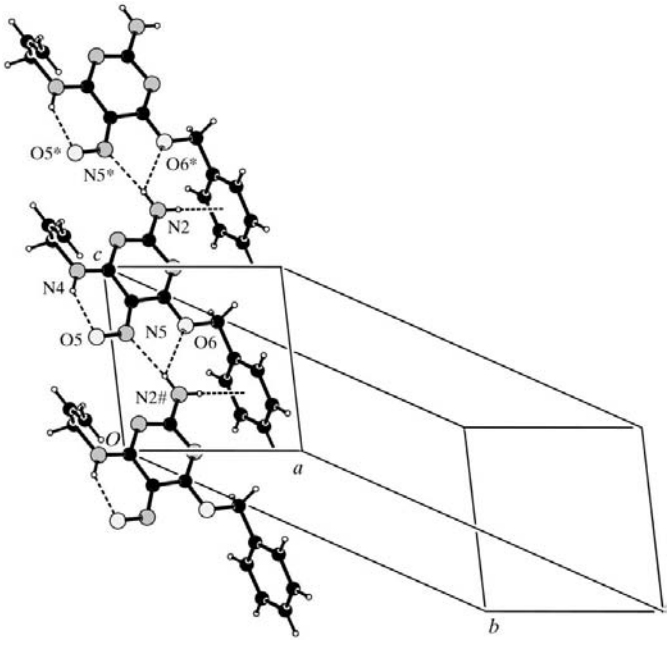

Figure 2
Part of the crystal structure of (I), showing the formation of a chain along [001]. Atoms marked with an asterisk (*) or hash (#) are at the symmetry positions $(x, y, 1 + z)$ and $(x, y, -1 + z)$, respectively.

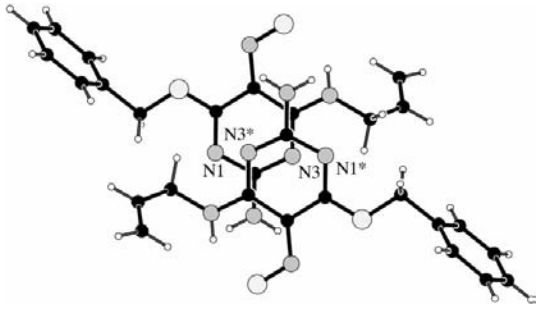

Figure 3
Part of the crystal structure of (I), showing the π–π-stacking interaction which links the [001] chains. Atoms marked with an asterisk (*) are at the symmetry position $(-x, 1 - y, 1 - z)$.

Experimental

A sample of (I) was prepared by reaction of 2-amino-4,6-bis-(benzyloxy)-5-nitrosopyrimidine (Quesada, Low *et al.*, 2002) with allylamine in ethanol at ambient temperature. Crystals suitable for single-crystal X-ray diffraction analysis were grown from a water–ethanol mixture (1:1 *v*/*v*).

Crystal data

$C_{14}H_{15}N_5O_2$
$M_r = 285.31$
Monoclinic, $P2_1/c$
$a = 8.0338$ (6) Å
$b = 24.627$ (2) Å
$c = 7.4087$ (5) Å
$\beta = 106.872$ (2)°
$V = 1402.7$ (2) Å^3
$Z = 4$
$D_x = 1.351$ Mg m^{-3}
Synchrotron radiation
$\lambda = 0.6867$ Å
Cell parameters from 2791 reflections
$\theta = 2.6$–$25.4°$
$\mu = 0.10$ mm^{-1}
$T = 150$ (2) K
Plate, purple
0.08 × 0.04 × 0.01 mm

Data collection

Bruker SMART 1K CCD diffractometer
ω rotation scans with narrow frames
Absorption correction: multi-scan (*SADABS*; Bruker, 2000)
$T_{min} = 0.992$, $T_{max} = 0.999$
7631 measured reflections
2791 independent reflections
1931 reflections with $I > 2\sigma(I)$
$R_{int} = 0.038$
$\theta_{max} = 25.4°$
$h = -10 \rightarrow 9$
$k = -28 \rightarrow 30$
$l = -9 \rightarrow 9$
Intensity decay: 15%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.047$
$wR(F^2) = 0.125$
$S = 1.03$
2791 reflections
190 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0633P)^2 + 0.1705P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.17$ e Å^{-3}
$\Delta\rho_{min} = -0.27$ e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

N1—C2	1.378 (2)	N4—C7	1.462 (2)
C2—N3	1.335 (2)	C7—C8	1.485 (3)
N3—C4	1.339 (2)	C8—C9	1.298 (3)
C4—C5	1.448 (2)	C5—N5	1.358 (2)
C5—C6	1.429 (3)	N5—O5	1.278 (2)
C6—N1	1.305 (2)	O6—C6	1.343 (2)
C2—N2	1.329 (2)	O6—C67	1.457 (2)
C4—N4	1.329 (2)		
C4—C5—N5—O5	−1.7 (3)	N1—C6—O6—C67	3.3 (2)
N3—C4—N4—C7	−0.9 (3)	C6—O6—C67—C61	170.4 (2)
C4—N4—C7—C8	113.9 (2)	O6—C67—C61—C62	85.5 (2)
N4—C7—C8—C9	0.9 (4)		

Table 2
Hydrogen-bonding geometry (Å, °).

Cg2 is the centroid of arene ring C61–C66.

D—H···A	D—H	H···A	D···A	D—H···A
N4—H4···O5	0.84	1.95	2.636 (2)	138
N2—H2A···N5^{i}	0.88	2.16	3.035 (2)	174
N2—H2A···O6^{i}	0.88	2.54	2.997 (2)	113
N2—H2B···$Cg2^{i}$	0.88	2.81	3.655 (2)	161

Symmetry code: (i) $x, y, 1+z$.

H atoms were treated as riding atoms, with C—H distances of 0.95 (aromatic) or 0.99 Å (CH_2) and N—H distances of 0.84 (for N4—H4) or 0.88 Å (NH_2). An initial data set was collected at 120 (2) K on a KappaCCD diffractometer using Mo $K\alpha$ radiation. While it was possible to achieve a satisfactory description of the molecular and supramolecular structures from these data, from a refinement to R = 0.059 (wR = 0.153), the proportion of data labelled observed, even at 120 K, was only 0.48, and the average value of σ(C—C) was 0.012 Å. We therefore collected a second data set, at 150 (2) K, at the Daresbury synchrotron radiation source, Station 9.8 (Cernik *et al.*, 1997; Clegg *et al.*, 1998), and the proportion of data labelled observed rose to 0.69 and the refinement gave a mean σ(C—C) of only 0.003 Å. The greatly enhanced quality of the synchrotron data set may be significant for compounds of this type; as noted earlier (Quesada, Marchal *et al.*, 2002), it is not always a straightforward matter to obtain crystals of substituted 5-nitrosopyrimidines suitable for single-crystal X-ray diffraction analysis and, indeed, some compounds of this type cannot be obtained in crystalline form at all. It seems clear that, for some compounds of this series, conventional diffractometry at ambient temperature would be fruitless, and even CCD data at 120 K can lead to structural refinements of, at best, questionable acceptability.

Data collection: *SMART* (Bruker, 1998); cell refinement: *SAINT* (Bruker, 2000); data reduction: *SAINT*; program(s) used to solve structure: *SHELXTL* (Sheldrick, 1998); program(s) used to refine structure: *SHELXTL* and *SHELXL*97 (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2002); software used to prepare material for publication: *SHELXL*97 and *PRPKAPPA* (Ferguson, 1999).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: NA1579). Services for accessing these data are described at the back of the journal.

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