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2-Amino-4,6-bis(benzyloxy)-5-nitrosopyrimidine: chains built from three-centre N—H···(N,O) and N—H···π(arene) hydrogen bonds

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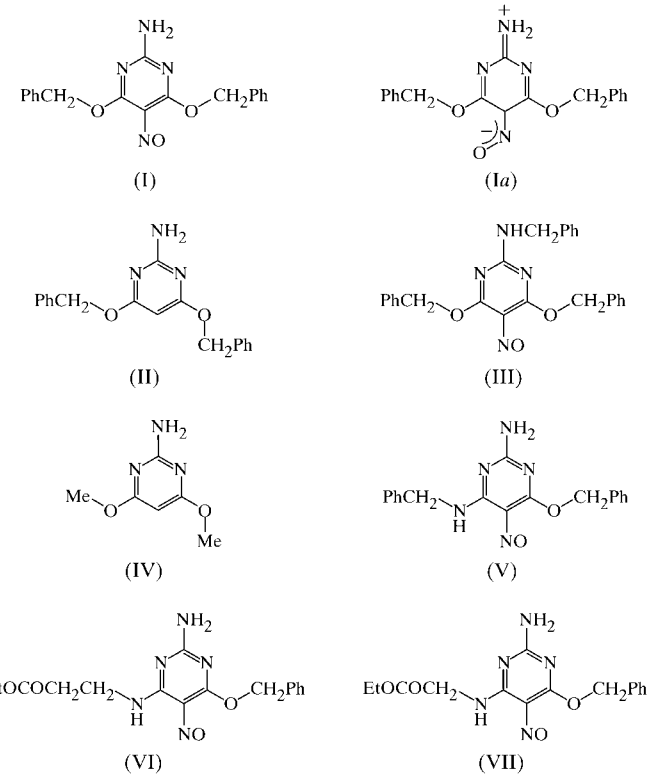
The molecules of the title compound, $C_{18}H_{16}N_4O_3$, exhibit a very polarized molecular–electronic structure. The molecules are linked into chains by a combination of an asymmetric three-centre N—H···(N,O) hydrogen bond [H···N 2.19, H···O 2.54, N···N 3.041 (4) and N···O 2.977 (4) Å, and N—H···N 168, N—H···O 112 and N···H···O 67°] and an N—H···π(arene) interaction [H···*Cg* 2.67 Å, N···*Cg* 3.496 (4) Å and N—H···*Cg* 163°; *Cg* is a benzyl ring centroid].

Comment

We recently reported the molecular and supramolecular structures of a number of benzyloxy-substituted 2-amino-5-nitrosopyrimidines (Quesada *et al.*, 2002). The majority of the compounds in that study contained a 4-amino substituent, derived either from a simple primary amine or from an amino acid ester. Here, we report the structure of the title compound, (I), an example containing an unsubstituted 2-amino group and a 4-benzyloxy substituent, and we compare the conformation, molecular dimensions and supramolecular aggregation of (I) with those of the related compounds (II) and (III) (Quesada *et al.*, 2002).

In (I) (Fig. 1), the N—C—O—C and C—O—C—C torsion angles (Table 1) defining the orientation of the benzyloxy groups are very similar for the two independent substituents, and indicate that atoms C41, C47, C61 and C67 all lie close to the plane defined by the pyrimidine ring, with both benzyl groups oriented remote from the nitrosyl substituent. The torsion angles around the C41—C47 and C61—C67 bonds are, however, entirely different. In (II), for comparison, the two independent N—C—O—C torsion angles indicate a different conformation, which does not even approximately manifest the potential twofold rotation symmetry available to molecules of (II), although atoms C41, C47, C61 and C67 are again close to the plane of the pyrimidine ring. In (III), the N—C—O—C angles resemble those in (I), but the C6—O6—C67—C61 torsion angle is unlike any of the other analogous angles in this series. In connection with this, it is interesting to note that in (IV) (Low *et al.*, 2002), the conformation of the alkoxy substituents is similar to that in (II).



The C2—N2, N3—C4 and C6—N1 bond distances (Table 2) in (I) are all short for their types (Allen *et al.*, 1987). These distances and those in the C–nitroso fragment point to the charge-separated form, (I*a*), as an important contributor to the overall molecular–electronic structure, as generally found for substituted 2-amino-5-nitrosopyrimidines (Low *et al.*, 2000; Quesada *et al.*, 2002). By contrast, when the 5-nitroso group is absent, as in (II) and (IV), there is no geometric evidence for any significant polarization of the electronic structure.

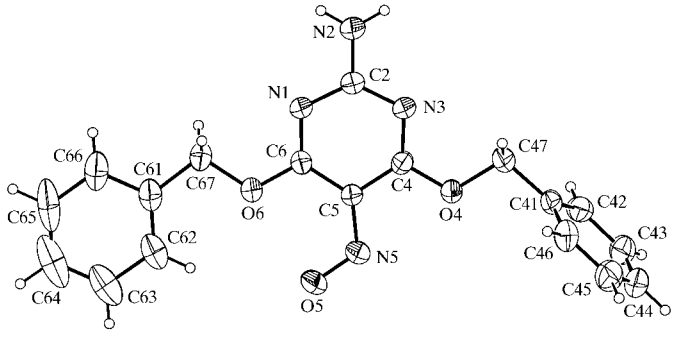


Figure 1
A view of the molecule of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

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The supramolecular aggregation in (I) (Table 3) involves both conventional hydrogen bonds and an N—H···π(arene) hydrogen bond, now a well recognized intermolecular interaction (Malone *et al.*, 1997; Braga *et al.*, 1998). The amino atom N2 in the molecule at (x, y, z) acts as a hydrogen-bond donor, *via* atom H2*A*, to nitrosyl atom N5 in the molecule at (x, $y-1$, z), so generating by translation a $C(7)$ chain parallel to [010] (Fig. 2). Both the donor atom, N2, and the acceptor atom, N5, in this hydrogen bond carry significant partial charges, and hence this interaction is an example of a resonance-assisted hydrogen bond (Gilli *et al.*, 1994). The same atom H2*A* at (x, y, z) also makes a rather long contact with atom O4 in the molecule at (x, $y-1$, z), so forming a very asymmetric three-centre N—H···(N,O) hydrogen bond, but the H···O contact may well be more adventitious than significant. The other H atom of the amino group, H2*B*, does not form a conventional hard hydrogen bond (Braga *et al.*, 1995), but instead forms a nearly linear N—H···π(arene) contact with the centroid, *Cg*2, of the C41–C46 phenyl ring in the molecule at (x, $y-1$, z) (Fig. 2), so that all three contacts may be mutually co-operative.

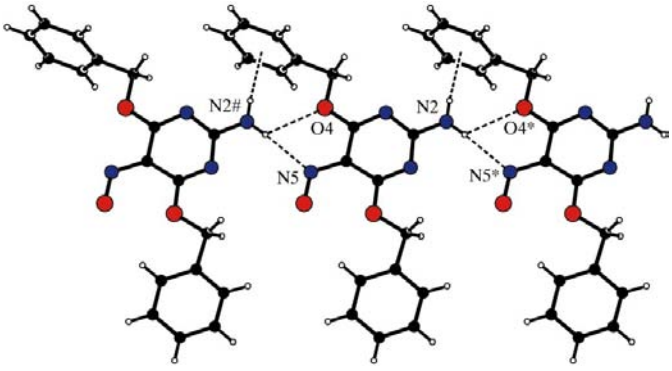

Figure 2
Part of the crystal structure of (I), showing the formation of a chain along [010]. For the sake of clarity, the unit-cell box has been omitted. Atoms marked with an asterisk (*) or hash sign (#) are at the symmetry positions (x, $y-1$, z) and (x, $1+y$, z), respectively.

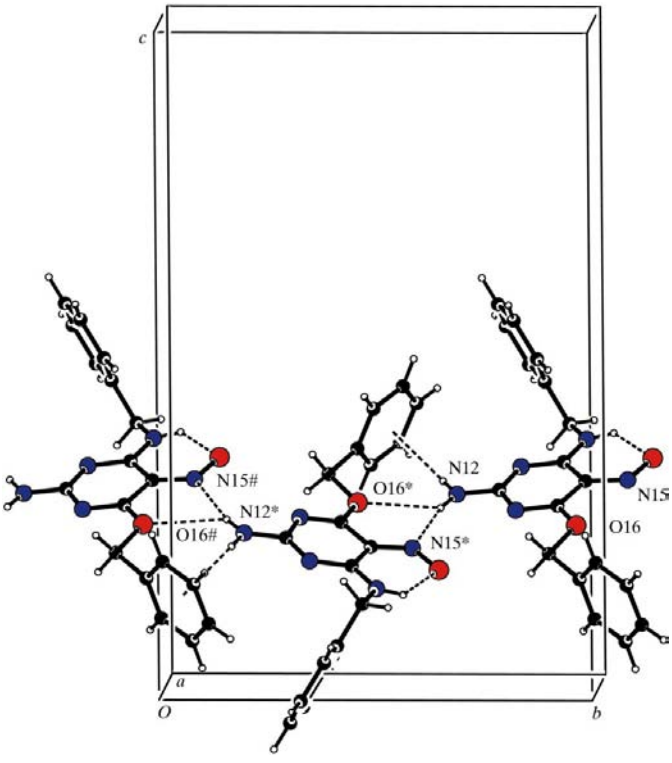

Figure 3
Part of the crystal structure of (V), showing the hard hydrogen bonds and the N—H···π(arene) interaction formed by type 1 molecules. Atoms marked with an asterisk (*) or hash sign (#) are at the symmetry positions ($\frac{3}{2}-x$, $y-\frac{1}{2}$, $\frac{1}{2}-z$) and (x, $y-1$, z), respectively.

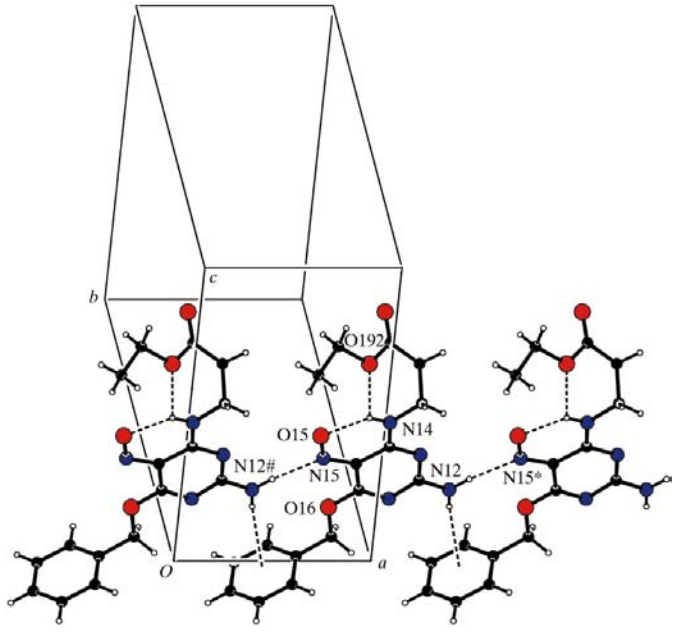

Figure 4
Part of the crystal structure of (VI), showing the N—H···N hydrogen bond and the N—H···π(arene) interaction formed by type 1 molecules. Atoms marked with an asterisk (*) or hash sign (#) are at the symmetry positions ($1+x$, y, z) and ($x-1$, y, z), respectively.

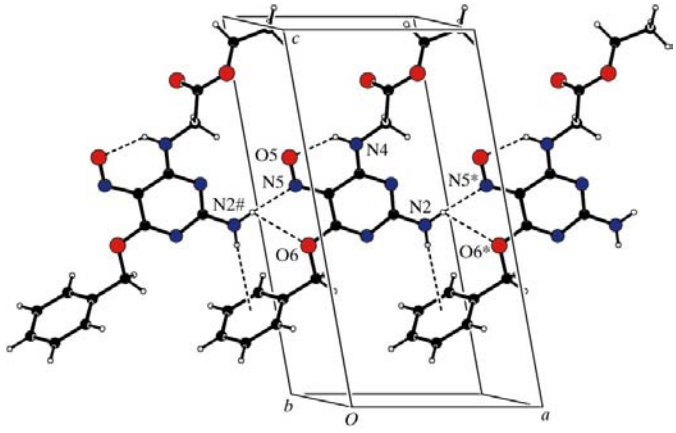

Figure 5
Part of the crystal structure of (VII), showing the hard hydrogen bonds and the long N—H···π(arene) contact. Atoms marked with an asterisk (*) or hash sign (#) are at the symmetry positions ($1+x$, y, z) and ($x-1$, y, z), respectively.

In view of the N—H···π(arene) interaction found in (I), we have reviewed the supramolecular structures of other substituted 2-amino-6-benzyloxy-5-nitrosopyrimidines (Quesada *et al.*, 2002), and we have now, indeed, identified N—H···π(arene) interactions in three such compounds, (V)–(VII) (Figs. 3–5). In compound (V) (Fig. 3), the amino groups in both independent molecules participate in exactly the same type of asymmetric three-centre N—H···(N,O) hydrogen bond as found in (I), together with an N—H···π(arene) interaction with the centroids *Cg*1 and *Cg*2 of the adjacent benzyl rings on O6 [for type 1 molecules, H···*Cg*1^{ii} 2.61 Å, N···*Cg*1^{ii} 3.418 (2) Å and N—H···*Cg*1^{ii} 153°; for type 2 molecules, H···*Cg*2^{iii} 2.50 Å, N···*Cg*2^{iii} 3.318 (2) Å and N—H···*Cg*2^{iii} 156°; symmetry codes: (ii) $\frac{3}{2}-x, y-\frac{1}{2}, \frac{1}{2}-z$; (iii) $\frac{5}{2}-x, \frac{1}{2}+y, \frac{1}{2}-z$].

In the $P2_1$ polymorph (Quesada *et al.*, 2002) of compound (VI) (Fig. 4), while the hard intermolecular hydrogen bonds formed by each of the two independent molecules are of the two-centre N—H···N type, there are again N—H···π(arene) interactions with the ring centroids, *Cg*3 and *Cg*4, of the adjacent benzyl groups [for type 1 molecules, H···*Cg*3^{iv} 2.79 Å, N···*Cg*3^{iv} 3.621 (4) Å and N—H···*Cg*3^{iv} 158°; for type 2 molecules, H···*Cg*4^{v} 2.68 Å, N···*Cg*4^{v} 3.546 (4) Å and N—H···*Cg*4^{v} 170°; symmetry codes: (iv) $1+x, y, z$; (v) $x-1, y, z$].

Compound (VII), where $Z' = 1$, exhibits the same type of asymmetric three-centre N—H···(N,O) hydrogen bonds as found in both (I) and (V), but here the corresponding N—H···*Cg*5 contact (Fig. 5) is long, although still close to linear [H···*Cg*5^{iv} 2.91 Å, N···*Cg*5^{iv} 3.748 (3) Å and N—H···*Cg*5^{iv} 161°; symmetry code: (iv) $1+x, y, z$].

In all of these examples, the multiple intermolecular contacts appear to be mutually co-operative. However, it is clear that the distinction between genuine attractive interactions and adventitious contacts, or near contacts, is not easy to judge. Nonetheless, the conformation of the benzyloxy group involved in each such putative interaction, which effectively prevents access of any other acceptor to the NH bond in question, is suggestive.

Experimental

A sample of (I) was synthesized following the published methods of Quesada *et al.* (2000) and Marchal *et al.* (2002). Compound (IV) (purchased from Aldrich) was converted to (II) by reaction with sodium benzylate in toluene, and (II) was then nitrosated with isoamyl nitrite in dimethyl sulfoxide solution at room temperature. Crystals of (I) for single-crystal X-ray diffraction were grown by slow evaporation of a solution in acetone.

Crystal data

$C_{18}H_{16}N_4O_3$
$M_r = 336.35$
Monoclinic, $P2_1/c$
$a = 11.0731$ (5) Å
$b = 7.3642$ (3) Å
$c = 22.9129$ (11) Å
$\beta = 111.456$ (2)°
$V = 1738.94$ (13) Å^3
$Z = 4$
$D_x = 1.285$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 3895 reflections
$\theta = 2.9$–27.6°
$\mu = 0.09$ mm^{-1}
$T = 298$ (2) K
Needle, blue
0.25 × 0.10 × 0.08 mm

Table 1
Selected torsion angles (°) for compounds (I), (II) and (III).

	(I)	(II)	(III)
N1—C6—O6—C67	−3.0 (4)	−178.4 (2)	1.7 (2)
C6—O6—C67—C61	177.1 (3)	179.2 (2)	−81.6 (2)
O6—C67—C61—C62	179.9 (3)	−6.9 (2)	−62.1 (2)
N3—C4—O4—C47	4.9 (4)	−2.4 (2)	−1.9 (2)
C4—O4—C47—C41	176.4 (3)	−176.0 (2)	−179.6 (2)
O4—C47—C41—C42	92.6 (4)	23.7 (2)	−11.8 (2)

Table 2
Selected bond lengths (Å) for (I).

C6—N1	1.306 (4)	C2—N2	1.316 (4)
N1—C2	1.347 (4)	C4—O4	1.342 (3)
C2—N3	1.353 (4)	C6—O6	1.334 (4)
N3—C4	1.310 (4)	C5—N5	1.374 (4)
C4—C5	1.408 (4)	N5—O5	1.245 (3)
C5—C6	1.419 (4)		

Table 3
Hydrogen-bonding geometry (Å, °) for (I).

*Cg*2 is the centroid of the C41–C46 ring.

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N2—H2*A*···O4^{i}	0.86	2.54	2.977 (4)	112
N2—H2*A*···N5^{i}	0.86	2.19	3.041 (4)	168
N2—H2*B*···*Cg*2^{i}	0.86	2.67	3.496 (4)	163

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

Data collection

Nonius KappaCCD area-detector diffractometer
φ scans, and ω scans with κ offsets
Absorption correction: multi-scan (*DENZO-SMN*; Otwinowski & Minor, 1997)
$T_{min} = 0.975$, $T_{max} = 0.993$
13 067 measured reflections
3895 independent reflections
1203 reflections with $I > 2\sigma(I)$
$R_{int} = 0.014$
$\theta_{max} = 27.6°$
$h = -14 \rightarrow 12$
$k = -8 \rightarrow 9$
$l = -25 \rightarrow 29$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.063$
$wR(F^2) = 0.169$
$S = 0.90$
3895 reflections
226 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0536P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.14$ e Å^{-3}
$\Delta\rho_{min} = -0.19$ e Å^{-3}

Compound (I) crystallized in the monoclinic system; space group $P2_1/c$ was uniquely assigned from the systematic absences. H atoms were treated as riding atoms, with C—H = 0.93–0.97 Å and N—H = 0.86 Å. The data were collected at 298 (2) K, where the proportion of data labelled observed is only 0.31, because all attempts to cool the crystals caused irreversible damage; this may underlie the high R_{int} value and the comparatively low precision in the refined structure.

Data collection: *KappaCCD Server Software* (Nonius, 1997); cell refinement: *DENZO–SMN* (Otwinowski & Minor, 1997); data reduction: *DENZO–SMN*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2002); software used to prepare material for publication: *SHELXL*97 and *PRPKAPPA* (Ferguson, 1999).

The X-ray data were collected at the EPSRC X-ray Crystallographic Service, University of Southampton, England. The authors thank the staff for all their help and advice. JNL thanks NCR Self-Service, Dundee, for grants which have provided computing facilities for this work.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1553). Services for accessing these data are described at the back of the journal.

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