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4,6-Diamino-2-morpholino-5-nitrosopyrimidine: a polarized molecular structure within hydrogen-bonded sheets

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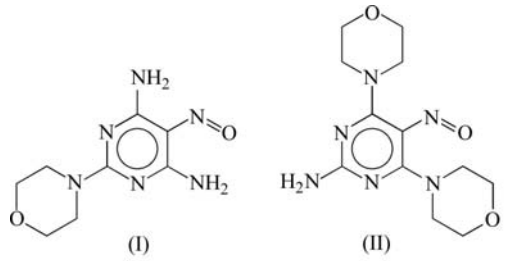
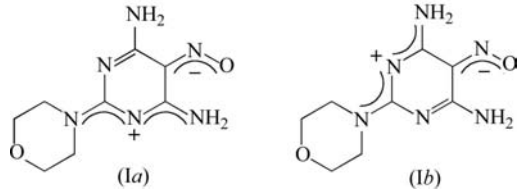
In the title compound, $C_8H_{12}N_6O_2$, the molecular dimensions provide evidence for significant polarization of the electronic structure. There is an intramolecular N—H···N hydrogen bond, and the molecules are linked into complex sheets by a combination of two-centre hydrogen bonds, one each of the N—H···N and N—H···O types, and a three-centre N—H···(N,O) hydrogen bond.

Comment

As part of a study of synthetic routes to 2-substituted 6-amino-5-nitrosopyrimidines for use as intermediates for the introduction of a wide variety of substituents at the 2-position in fused pyrimidine derivatives, we have recently reported the use of the methoxy group (Melguizo *et al.*, 2002) and the methylsulfanyl group (Orozco *et al.*, 2008) as leaving groups at position 2 in order to introduce a variety of amino groups into pyrimidin-4(3*H*)-one systems. We have already incorporated a morpholino moiety at C2 by reaction of 6-amino-2-methylsulfanyl-5-nitrosopyrimidine with morpholine (Orozco *et al.*, 2008), and accordingly we have used similar conditions in order to prepare 4,6-diamino-2-morpholino-5-nitrosopyrimidine from 4,6-diamino-2-methylsulfanyl-5-nitrosopyrimidine. Thus, we compare here the molecular and supramolecular structure of symmetrically substituted 4,6-diamino-2-morpholino-5-nitrosopyrimidine, (I) (Fig. 1), with symmetrically substituted 2-amino-4,6-dimorpholino-5-nitrosopyrimidine, (II) (see scheme), whose structural properties were reported several years ago as part of a wider study of 4,6-disubstituted 2-aminopyrimidines and 2-amino-5-nitrosopyrimidines (Quesada *et al.*, 2002, 2004).

The morpholino ring in compound (I) adopts a chair conformation with the N21—C2 bond (Fig. 1) occupying an equatorial site. Despite the presence of four substituents on the pyrimidine ring, three of them at adjacent sites, the pyrimidine ring is effectively planar; the maximum deviation of any ring atom from the mean plane of the ring atoms is 0.012 (3) Å for atom N3. This planarity may be contrasted with the boat conformation adopted by the pyrimidine ring in compound (II), where ring atoms C2 and C5 represent the stem and stern of the boat, such that the amino and nitroso substituents are markedly displaced to one side of the ring, while the two morpholino substituents are displaced to the opposite side (Quesada *et al.*, 2004).





Within the molecule of (I), the bond distances (Table 1) provide evidence for considerable polarization of the electronic structure, which resembles that in (II) despite the different substituents on the pyrimidine rings in (I) and (II). Thus, for example, the C—N distances in (I) for the atom sequence N21—C2—N1—C6—N6 all lie within a fairly narrow range; however, the shortest distance in this sequence is found for the formal single bond C6—N6, while the longest distance corresponds to the formally aromatic bond C2—N1. In addition, the similarity between the C4—N3 (formally an aromatic bond) and C4—N4 (formally a single bond) distances

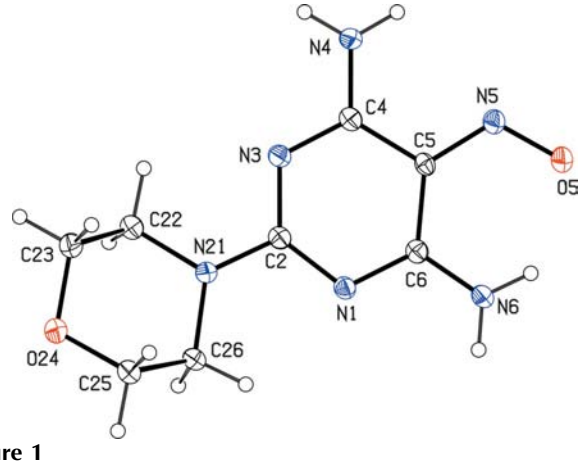


Figure 1
The molecular structure of compound (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level.

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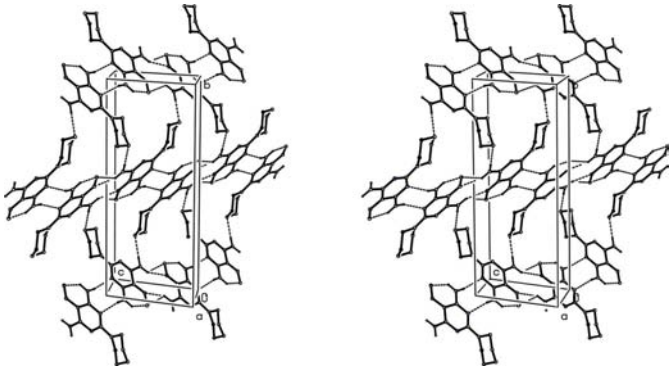

Figure 2
A stereoview of part of the crystal structure of compound (I), showing the formation of a hydrogen-bonded sheet parallel to $(10\bar{2})$ built from four types of hydrogen bond and containing five types of ring. For the sake of clarity, H atoms bonded to C atoms have been omitted.

is striking. The C5—N5 and N5—O5 distances in the nitroso group are rather similar, differing by less than 0.06 Å, whereas in simple unperturbed *C*-nitroso compounds, where no polarization of the structure can occur, the N—O distance is generally less than 1.25 Å (Davis *et al.*, 1965; Bauer & Andreassen, 1972; Talberg, 1977; Schlemper *et al.*, 1986), while the difference between the C—N and N—O distances is usually greater than 0.20 Å (Talberg, 1977; Schlemper *et al.*, 1986). In sum, these observations point to the occurrence of significant contributions to the overall electronic structure from polarized forms (I*a*) and (I*b*), as well as from classical aromatic form (I) (see scheme).

The molecules of compound (I) contain an intramolecular N—H···O hydrogen bond (Table 2), forming an *S*(6) motif (Bernstein *et al.*, 1995), and this feature in substituted 5-nitroso-6-aminopyrimidines lends the molecules an overall shape similar to that in substituted purines (Quesada *et al.*, 2002; Melguizo *et al.*, 2003), which, in turn, may underlie the biological activity of this type of substituted pyrimidine (Chae *et al.*, 1995). The molecules are linked into sheets of considerable complexity by a combination of two independent two-centre hydrogen bonds and one three-centre N—H···(N,O) hydrogen bond which is asymmetric but planar (Table 2). Because of the polarization of the electronic structure in (I), it is likely that all of the hydrogen bonds apart from the one having a morpholino O atom as the acceptor can be regarded as charge-assisted hydrogen bonds (Gilli *et al.*, 1994); it is thus surprising that the shorter component of the three-centre hydrogen bond involves the N atom of the nitroso substituent as the acceptor rather than the O atom. The asymmetry of this three-centre system may, in fact, be largely a consequence of the overall intermolecular packing rather than of any local intermolecular energies.

The formation of the hydrogen-bonded sheet in compound (I) is readily analysed in terms of the centrosymmetric $R_2^2(8)$ dimer unit generated by the N—H···N hydrogen bond, with the reference dimer unit centred at $(0, \frac{1}{2}, \frac{1}{2})$ (Fig. 2). The action of the two-centre N—H···O hydrogen bond is to link this reference dimer directly to four further such dimer units, those centred at (−1, 0, 0), (−1, 1, 0), (1, 0, 1) and (1, 1, 1), while the action of the three-centre hydrogen bond links the reference dimer centred at $(0, \frac{1}{2}, \frac{1}{2})$ directly to the dimer units centred at $(2, \frac{1}{2}, \frac{3}{2})$ and $(-2, \frac{1}{2}, -\frac{1}{2})$ (Fig. 2).

The combination of all these hydrogen bonds, when propagated by the space-group symmetry operations, generates a hydrogen-bonded sheet parallel to $(10\bar{2})$ in which rings of *S*(6), $R_1^2(3)$, $R_2^2(8)$, $R_2^2(10)$ and $R_5^4(22)$ types can be identified (Fig. 2). The only direction-specific interaction between adjacent sheets is a C—H···N contact involving a C—H bond of low acidity, arising from the morpholino substituent, which is expected to be only very weakly attractive and thus probably of only marginal structural significance.

By contrast with the sheet formation in compound (I), where both N and O atoms are utilized as hydrogen-bond acceptors, in compound (II) there are only two intermolecular hydrogen bonds, both of the N—H···O type with each involving an O atom from a different morpholino substituent as the hydrogen-bond acceptor. These two hydrogen bonds generate a very simple and elegant sheet in the form of a (4,4) net (Batten & Robson, 1998) built from a single type of $R_4^4(32)$ ring (Quesada *et al.*, 2004).

Experimental

Morpholine (100 mmol) was added dropwise with magnetic stirring to a hot suspension of 4,6-diamino-2-methylsulfanyl-5-nitrosopyrimidine (10 mmol) in methanol (40 ml) over a period of 9 h. The reaction proceeded with a change of colour from blue to violet and liberation of methanethiol. The reaction mixture was cooled to ambient temperature and the solvent was then removed under reduced pressure; the resulting solid product was washed with water and crystallized by slow evaporation, at ambient temperature in air, of a solution in dimethyl sulfoxide to give red–violet crystals suitable for single-crystal X-ray diffraction [yield 98%; m.p. 512–513 K (decomposition)]. MS (EI) *m*/*z*: 224 [M^+], 207, 139, 137.

Crystal data

$C_8H_{12}N_6O_2$
M_r = 224.24
Monoclinic, $P2_1/c$
a = 6.3340 (7) Å
b = 19.247 (3) Å
c = 8.4472 (12) Å
β = 110.562 (13)°
V = 964.2 (2) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.12 mm^{-1}
T = 120 K
0.47 × 0.26 × 0.24 mm

Data collection

Bruker–Nonius KappaCCD diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
T_{min} = 0.955, T_{max} = 0.973
13807 measured reflections
1902 independent reflections
1151 reflections with $I > 2\sigma(I)$
R_{int} = 0.077

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.059
$wR(F^2)$ = 0.174
S = 1.12
1902 reflections
145 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.44 e Å^{-3}
$\Delta\rho_{min}$ = −0.34 e Å^{-3}

All H atoms were located in difference maps, and then treated as riding atoms in geometrically idealized positions, with C—H = 0.99 Å and N—H = 0.88 Å, and with U_{iso}(H) = 1.2U_{eq}(carrier).

Table 1
Selected bond lengths (Å).

N1—C2	1.350 (4)	C2—N21	1.342 (4)
C2—N3	1.345 (3)	C4—N4	1.319 (4)
N3—C4	1.318 (4)	C5—N5	1.336 (4)
C4—C5	1.430 (4)	N5—O5	1.278 (3)
C5—C6	1.439 (4)	C6—N6	1.308 (4)
C6—N1	1.333 (4)		

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

D—H$\cdots A$	D—H	H$\cdots A$	$D\cdots A$	D—H$\cdots A$
N4—H4$A\cdots$O24^{i}	0.88	2.18	3.040 (3)	166
N4—H4$B\cdots$O5^{ii}	0.88	2.50	3.023 (3)	119
N4—H4$B\cdots$N5^{ii}	0.88	2.16	2.954 (4)	149
N6—H6$A\cdots$N1^{iii}	0.88	2.25	3.102 (4)	163
N6—H6$B\cdots$O5	0.88	1.94	2.603 (3)	131
C23—H23$B\cdots$N3^{iv}	0.99	2.58	3.547 (4)	167

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

Data collection: *COLLECT* (Hooft, 1999); cell refinement: *DIRAX*/*LSQ* (Duisenberg *et al.*, 2000); data reduction: *EVALCCD* (Duisenberg *et al.*, 2003); program(s) used to solve structure: *SIR2004* (Burla *et al.*, 2005); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *PLATON* (Spek, 2009); software used to prepare material for publication: *SHELXL97* and *PLATON*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: EG3030). Services for accessing these data are described at the back of the journal.

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