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Different hydrogen-bonded structures in the isomeric solvates 2-amino-6-anilino-4-methoxy-5-[(*E*)-4-nitrobenzylideneamino]pyrimidine dimethyl sulfoxide solvate and 2-amino-6-[methyl(phenyl)amino]-5-[(*E*)-4-nitrobenzylideneamino]pyrimidin-4(3*H*)-one dimethyl sulfoxide solvate

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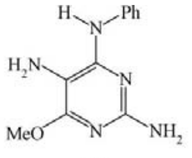
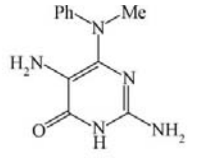
The title solvates, (I) and (II), both $C_{18}H_{16}N_6O_3{\cdot}C_2H_6OS$, are isomeric. The conformations adopted by the 6-substituent are significantly different, with the 6-aminophenyl unit remote from the nitrophenyl ring in methoxypyrimidine (I) but adjacent to it in pyrimidinone (II). Pairs of pyrimidine molecules in (I) are linked by N—H···N hydrogen bonds to form cyclic centrosymmetric dimers from which the dimethyl sulfoxide molecules are pendent, while in (II) a combination of three independent N—H···O hydrogen bonds links the components into a chain containing both $R_2^2(8)$ and $R_4^2(8)$ rings, in which the dimethyl sulfoxide component acts as a double acceptor of hydrogen bonds. The significance of this study lies in its observation of different conformations for the pyrimidine components in (I) and (II), and different hydrogen-bonded structures, apparently dominated by the different roles adopted by the dimethyl sulfoxide components.

Comment

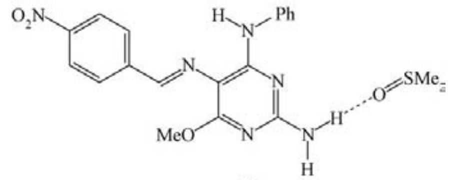
Pyrimidodiazepines belong to the so-called bicyclic privileged structures, which may be useful in the field of medicinal chemistry (Horton *et al.*, 2003). We have already reported the preparations (Cobo *et al.*, 2008) and structures (Rodríguez *et al.*, 2008) of some 2-amino-6-aryl-4-methoxy-11*H*-pyrimido[4,5-*b*][1,4]benzodiazepines using as the final key step a Bischler–Napieralski cyclocondensation involving the reaction of 2,5-diamino-4-anilino-6-methoxypyrimidine with acid derivatives. We have now modified this procedure, replacing the aromatic acid used previously (Cobo *et al.*, 2008) with an aromatic aldehyde, in the expectation of producing the corresponding dihydropyrimidobenzo[4,5-*b*][1,4]diazepine analogue. By the use of 4-nitrobenzaldehyde in the absence of phosphoryl choride, so preventing the cyclization step, we have isolated the intermediate Schiff bases 2-amino-6-anilino-4-methoxy-5-[(*E*)-4-nitrobenzylideneamino]pyrimidine dimethyl sulfoxide solvate, (I), and 2-amino-6-[methyl(phenyl)-amino]-5-[(*E*)-4-nitrobenzylideneamino]pyrimidin-4(3*H*)-one dimethyl sulfoxide solvate, (II), whose molecular and supramolecular structures we report here, both of them as stoichiometric monosolvates with dimethyl sulfoxide. The Schiff base components of the title solvates are isomeric, and they were prepared by the acid-promoted condensation of 4-nitrobenzaldehyde with the isomeric heterocycles (*A*) for the formation of (I) and (*B*) for the formation of (II).



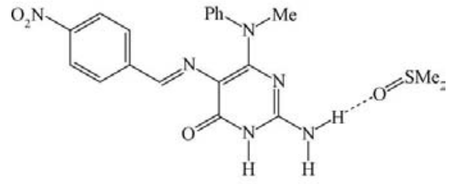
(*A*)



(*B*)



(I)



(II)

The molecular conformations can be defined in terms of a rather small number of torsion angles (Table 1). These show that the Schiff base backbone, running from amine atom N2 to nitro atom N51, has the *E* configuration, and that it does not deviate markedly from planarity. Similarly, the nitro group in each compound deviates only a little from the plane of the adjacent aryl ring, as does methoxy atom C41 in (I). On the other hand, the substituent at N6 shows some differences between (I) and (II), particularly in the location and orientation of the C61–C66 aryl ring. The location of this ring in (II) may be influenced both by the intramolecular C—H···π(arene) interaction in the compound and, perhaps

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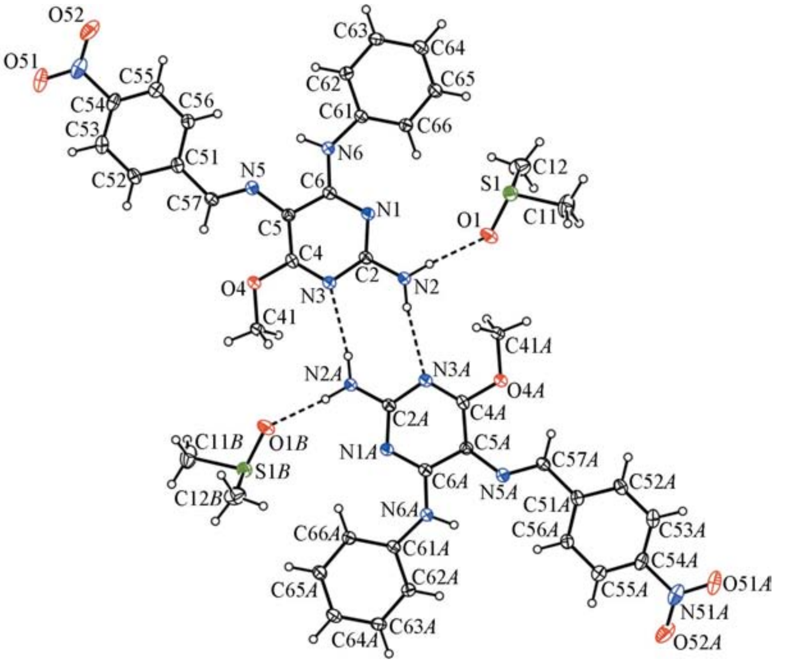

Figure 1
The molecular components of (I), showing the atom-labelling scheme and the formation of a centrosymmetric four-component aggregate containing pendent dimethyl sulfoxide units. Displacement ellipsoids are drawn at the 30% probability level and atoms marked with *A* or *B* are at the symmetry position (1 − *x*, 1 − *y*, 1 − *z*).

more significantly, by the necessity to locate the neighbouring methyl group containing atom C67 away from the C51–C56 ring, in particular away from atom H56. The location of the C61–C66 ring in (I) may be a consequence of the intramolecular N—H···N interaction.

The Schiff base frameworks of (I) and (II) can be regarded as chain-extended homologues of 4-nitroaniline, but, despite the near planarity of these frameworks in both compounds, the bond distances provide no evidence for any significant polarization of the electronic structure, with its concomitant development of quinonoid character in the nitroaryl ring, The distances in both (I) and (II) show no significant deviations from the expected values for unperturbed systems (Allen *et al.*, 1987). Although the development of such quinonoid character is particularly marked in 4-nitroaniline itself (Qian *et al.*, 2006), it is scarcely apparent in the homologous 4-amino-4′-nitrobiphenyl, although more developed in the similarly substituted biphenyl analogues where the two rings are separated by acetylene spacer units (Graham *et al.*, 1989).

In each compound, the two independent components are linked within the selected asymmetric units (Figs. 1 and 2) by a fairly short, and nearly linear, N—H···O hydrogen bond (Table 2). Despite this, the further linking of these bimolecular aggregates differs significantly between the two compounds. In (I), paired N—H···N hydrogen bonds, having one of the pyrimidine N atoms as the acceptor, form a centrosymmetric $R_2^2(8)$ (Bernstein *et al.*, 1995) motif, but there are no further direction-specific intermolecular interactions. The hydrogen-bonded structure thus consists of a four-component aggregate (Fig. 1) whose overall graph-set descriptor is $D_3^3(9)[R_2^2(8)]$. By contrast, the structure of (II) contains no N—H···N hydrogen bonds, and solvent atom O1 acts as a double acceptor in N—H···O hydrogen bonds (Table 2). The reference atom O1 at (*x*, *y*, *z*) accepts hydrogen bonds from atoms N2 at (*x*, *y*, *z*), *via* H21, and at (1 − *x*, 2 − *y*, 1 − *z*), *via* H22. The combined effect of the three independent N—H···O hydrogen bonds is the formation of a $C_3^3(12)[R_2^2(8)][R_4^2(8)]$ chain of rings running parallel to the [010] direction, in which the $R_2^2(8)$ rings formed by paired amide units are centred at $(\frac{1}{2}, n+\frac{1}{2}, \frac{1}{2})$, and the $R_4^2(8)$ rings are centred at $(\frac{1}{2}, n, \frac{1}{2})$ (in both cases, *n* represents an integer; Fig. 3). There are no direction-specific interactions between the four-component aggregates in (I), or between the chains in (II). The only C—H···π interaction observed is the intramolecular contact in (II) (Table 2).

The principal differences between the hydrogen-bonded structures of (I) and (II) arise from the nature of the hydrogen bonds deployed and from the role of the dimethyl sulfoxide components. The formation of an N—H···N hydrogen bond with pyrimidine ring atom N3, as found in (I), is not feasible in (II) because N3 now carries a H atom; the alternative ring site N1 is very effectively shielded in (II) by the adjacent amine and methyl substituents, while Schiff base atom N5 is shielded by the C61–C66 aryl ring, so that formation of N—H···N hydrogen bonds is wholly impeded. On the other hand, in (II) not only are there three N—H bonds readily available as donors, but also atom O4 is available as a hydrogen-bond acceptor. Finally, the dimethyl sulfoxide component acts only as a single acceptor of hydrogen bonds in (I), and thus it plays only a marginal role in the supramolecular aggregation, possibly by simply filling space which would otherwise be empty. In contrast, this component acts as a double acceptor in (II), where it plays a key role in the chain formation, by acting

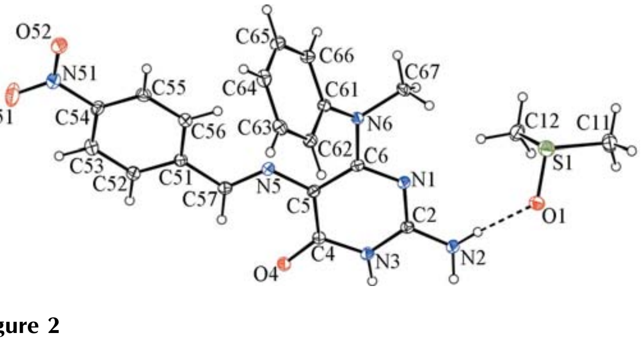

Figure 2
The molecular components of (II), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level.

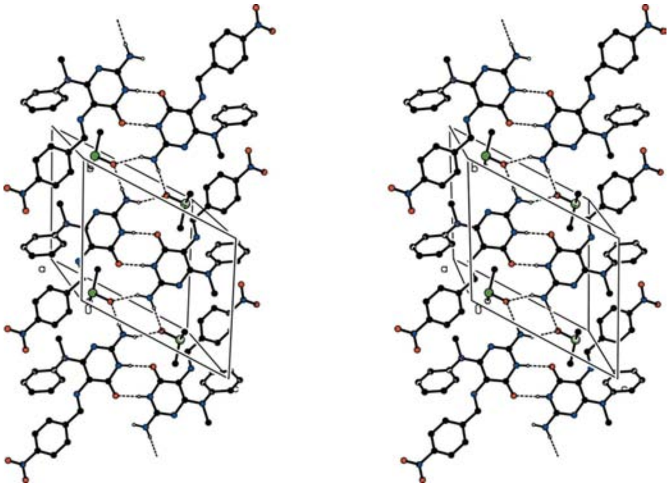

Figure 3
A stereoview of part of the crystal structure of (II), showing the formation of a hydrogen-bonded chain along [010] containing $R_2^2(8)$ and $R_4^2(8)$ rings. For the sake of clarity, H atoms bonded to C atoms have been omitted.

as the sole link between $R_2^2(8)$ dimer units built from paired N—H···O=C hydrogen bonds.

Experimental

For the synthesis of (I), a mixture of 2,5-amino-6-anilino-4-methoxypyrimidine (0.856 mmol) and 4-nitrobenzaldehyde (0.860 mmol) was added to a mixture of methanol (10 ml) and acetic acid (0.5 ml), and the resulting solution was stirred overnight (*ca* 12 h) at ambient temperature. The resulting orange product, *viz.* 2-amino-6-anilino-4-methoxy-5-[(*E*)-4-nitrobenzylideneamino]pyrimidine, was collected by filtration, washed several times with water and then dried (yield 99%, m.p. 487–489 K). For the synthesis of (II), a mixture of 2,5-diamino-6-[methyl(phenyl)amino]pyrimidin-4(3*H*)-one (0.822 mmol) and 4-nitrobenzaldehyde (0.827 mmol) was added to a mixture of methanol (10 ml) and acetic acid (0.5 ml), and the resulting solution was stirred overnight (*ca* 12 h) at ambient temperature. The resulting dark-red product, *viz.* 2-amino-6-[methyl(phenyl)amino]-5-[(*E*)-4-nitrobenzylideneamino]pyrimidin-4(3*H*)-one, was collected by filtration, washed several times with water and then dried (yield 83%, m.p. 510–512 K). Recrystallization of both compounds from dimethyl sulfoxide gave crystals of the monosolvates suitable for single-crystal X-ray diffraction.

Compound (I)

Crystal data

$C_{18}H_{16}N_6O_3\cdot C_2H_6OS$
M_r = 442.50
Triclinic, $P\overline{1}$
a = 8.0386 (8) Å
b = 10.6862 (14) Å
c = 12.8856 (13) Å
α = 71.007 (11)°
β = 74.463 (9)°
γ = 88.672 (12)°
V = 1005.9 (2) Å^3
Z = 2
Mo $K\alpha$ radiation
μ = 0.20 mm^{-1}
T = 120 (2) K
0.45 × 0.32 × 0.08 mm

Data collection

Bruker–Nonius KappaCCD diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
$T_{\min}$ = 0.944, $T_{\max}$ = 0.984
29080 measured reflections
4614 independent reflections
2569 reflections with $I > 2\sigma(I)$
$R_{\rm int}$ = 0.089

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.057
$wR(F^2)$ = 0.154
S = 1.05
4614 reflections
283 parameters
H-atom parameters constrained
$\Delta\rho_{\max}$ = 0.38 e Å^{-3}
$\Delta\rho_{\min}$ = −0.47 e Å^{-3}

Compound (II)

Crystal data

$C_{18}H_{16}N_6O_3\cdot C_2H_6OS$
M_r = 442.50
Triclinic, $P\overline{1}$
a = 10.2601 (8) Å
b = 10.4555 (6) Å
c = 11.4537 (14) Å
α = 113.230 (7)°
β = 112.295 (8)°
γ = 96.709 (8)°
V = 992.0 (2) Å^3
Z = 2
Mo $K\alpha$ radiation
μ = 0.21 mm^{-1}
T = 120 (2) K
0.35 × 0.26 × 0.08 mm

Data collection

Bruker–Nonius KappaCCD diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
$T_{\min}$ = 0.941, $T_{\max}$ = 0.984
29046 measured reflections
4556 independent reflections
2896 reflections with $I > 2\sigma(I)$
$R_{\rm int}$ = 0.074

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.057
$wR(F^2)$ = 0.161
S = 1.07
4556 reflections
283 parameters
H-atom parameters constrained
$\Delta\rho_{\max}$ = 0.40 e Å^{-3}
$\Delta\rho_{\min}$ = −0.66 e Å^{-3}

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

	(I)	(II)
N1—C6—N6—C61	5.2 (4)	−140.1
C6—N6—C61—C62	179.6 (3)	34.1 (4)
C6—C5—N5—C57	176.2 (2)	−178.0 (3)
C5—N5—C57—C51	178.7 (2)	176.8 (2)
N5—C57—C51—C52	172.1 (2)	165.6 (3)
C53—C54—N51—O51	5.1 (4)	3.4 (4)
N3—C4—O4—C41	−5.0 (4)	–

Table 2
Hydrogen bonds and short intramolecular contacts (Å, °) for (I) and (II).

Cg represents the centroid of the C61–C66 ring.

Compound	*D*—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
(I)	N2—H21···O1	0.88	2.11	2.966 (3)	163
	N2—H22···N3$^{\rm i}$	0.88	2.32	3.186 (3)	170
	N6—H6···N5	0.88	2.11	2.598 (3)	114
(II)	N2—H21···O1	0.88	2.07	2.949 (3)	175
	N2—H22···O1$^{\rm ii}$	0.88	2.15	2.935 (3)	148
	N3—H3···O4$^{\rm i}$	0.88	1.86	2.739 (3)	176
	C56—H56···*Cg*	0.95	2.46	3.397 (4)	168

Symmetry codes: (i) $-x+1, -y+1, -z+1$; (ii) $-x+1, -y+2, -z+1$.

Crystals of (I) and (II) are triclinic; for each, the space group $P\bar{1}$ was chose and confirmed by the structure analysis. All H atoms were located in difference maps and then treated as riding atoms in geometrically idealized positions, with C—H distances of 0.95 (aromatic and methylidene) or 0.98 Å (methyl) and N—H distances of 0.88 Å, and with $U_{iso}(H) = kU_{eq}$(carrier), where $k = 1.5$ for the methyl groups and $k = 1.2$ for all other H atoms.

For both compounds, 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: *OSCAIL* (McArdle, 2003) and *SHELXL97* (Sheldrick, 2008); molecular graphics: *PLATON* (Spek, 2009); software used to prepare material for publication: *SHELXL97* and *PRPKAPPA* (Ferguson, 1999).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK3294). Services for accessing these data are described at the back of the journal.

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