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Four 2-amino-6-aryl-4-methoxy-11*H*-pyrimido[4,5-*b*][1,4]benzodiazepines: similar molecular structures but different crystal structures

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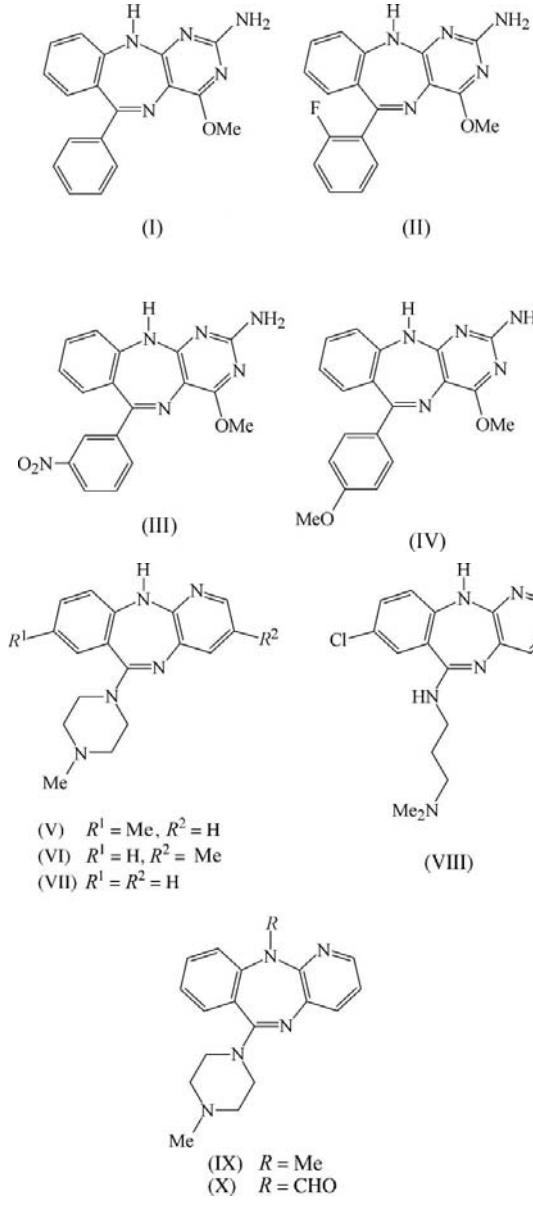
2-Amino-4-methoxy-6-phenyl-11*H*-pyrimido[4,5-*b*][1,4]-benzodiazepine, $C_{18}H_{15}N_5O$, (I), and its 6-(2-fluorophenyl)-, 6-(3-nitrophenyl)- and 6-(4-methoxyphenyl)- analogues, *viz*. $C_{18}H_{14}FN_5O$, (II), $C_{18}H_{14}N_6O_3$, (III), and $C_{19}H_{17}N_5O_2$, (IV), respectively, all adopt molecular conformations which are almost identical, containing boat-shaped seven-membered rings. In each structure, paired N—H···N hydrogen bonds link the molecules into centrosymmetric dimers. In each of (I)–(III), the dimers are further linked, forming a different three-dimensional framework in each case, while in compound (IV) the dimers are linked into sheets. The significance of this study lies in the observation of different crystal structures in four compounds whose molecular structures are very similar.

Comment

Pyrimidine-fused compounds are of considerable interest in medicinal chemistry as they have shown a wide variety of biological properties (Wang *et al.*, 2004; McGuigan *et al.*, 2004; Gangjee *et al.*, 2004). We report here the structures of four different 2-amino-4-methoxy-11*H*-pyrimido[4,5-*b*][1,4]benzodiazepines, compounds (I)–(IV) (Fig. 1), containing differently substituted 6-aryl groups, all of which have been prepared using a synthetic strategy based on a nitrosation–aminolysis–nitroso reduction sequence followed by a Bischler–Napieralski cyclocondensation (Cobo *et al.*, 2008). The structure of compound (II) has been very briefly reported, as a proof of constitution associated with the synthetic report (Cobo *et al.*, 2008), but without any information on, or discussion of, either the molecular conformation or the hydrogen bonding. In the earlier report, the site occupancies for the disordered F atoms (see *Experimental*) were fixed at 0.75 and 0.25; these occupancies have now been refined to values of 0.774 (5) and 0.226 (5).



Compounds (I)–(IV) have very similar constitutions, differing only by a single substituent and its location in the pendent aryl ring. The molecules have very similar conformations (Fig. 1) which lack any internal symmetry, so that the molecules are chiral; the reference molecules were selected so that they all have the same hand. The compounds all crystallize in space group $P2_1/n$, and their unit-cell dimensions are similar. In addition, the atomic coordinates for corresponding atoms are similar in compounds (I)–(III), whereas the atomic coordinates for compound (IV) are approximately related to those in (I)–(III) by the relationship $(1 - x, 1 - y, z)$, suggesting an approximate relationship equivalent to a twofold rotation around the z axis or, equivalently, a mirror reflection across the [001] plane. However, there are some

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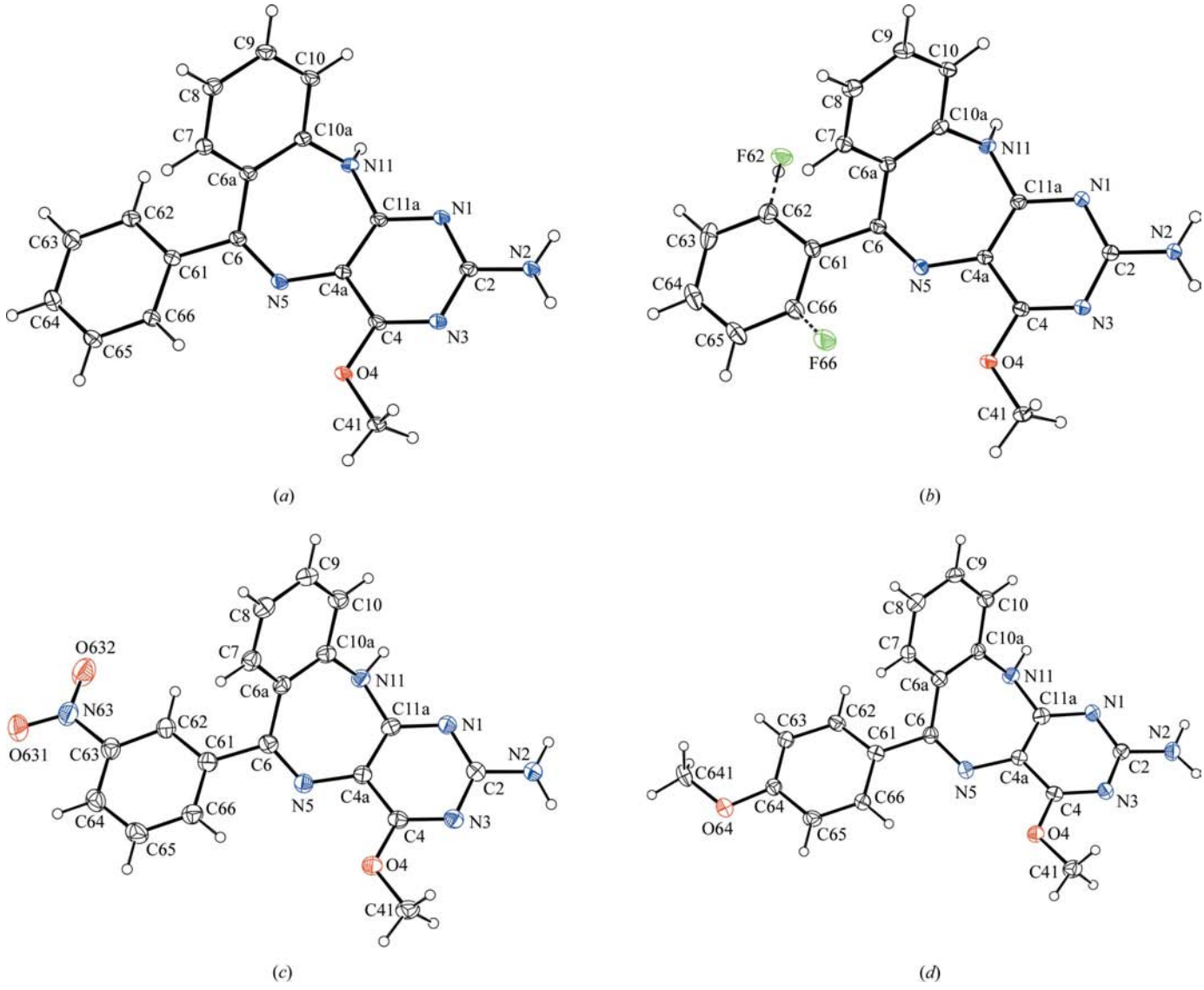

Figure 1
The molecular structures of (*a*) compound (I), (*b*) (II), (*c*) (III) and (*d*) (IV), showing the atom-labelling schemes. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radius. The refined occupancies of the F-atom sites in compound (II) are 0.774 (5) for F62 and 0.226 (5) for F66.

differences in the patterns of supramolecular aggregation manifested by the intermolecular hydrogen bonds, so that no two of these compounds are strictly isostructural.

The overall molecular conformations are dominated by the seven-membered rings, for which the ring-puckering parameters (Cremer & Pople, 1975) indicate (Table 1) an almost ideal boat form (Evans & Boeyens, 1989) in each compound, with a local pseudo-mirror plane containing atoms N11 and H11 and the mid-point of the N5—C6 bond, as demonstrated by the atom displacements from the mean planes for this ring. The orientation of the pendent aromatic ring, as indicated by the torsion angle N5—C6—C61—C62 (Table 1), is similar in each compound. The nitro and methoxy substituents on the pendent aryl ring and on the fused pyrimidyl ring are both almost coplanar with the rings concerned, as indicated by both the relevant torsion angles and the displacements of the substituent atoms from the ring planes. The conformational similarity between compounds (I)–(IV) in terms of the ring-puckering parameters, the out-of-plane atom displacements and the torsion angles is striking. The bond lengths and angles present no unusual features.

A search of the Cambridge Structural Database (CSD, Version 5.29 of January 2008; Allen, 2002) found no examples of pyrimido[4,5-*b*][1,4]benzodiazepines. However, the structures of several pyrido[2,3-*b*][1,4]diazepines, (V)–(X), which are very closely related to compounds (I)–(IV), have recently been reported. In each of compounds (V) (CSD refcode INEMOD; Spirlet *et al.*, 2003), (VI) (ZAYPOE; Dupont *et al.*, 1995), (VII) (KOYTIB; Dupont *et al.*, 1992) and (VIII) (IDIMOX; Dupont *et al.*, 2002), the conformation of the seven-membered ring is almost identical to those found in (I)–(IV), as also are those in the N^{11}-substituted compounds (IX)

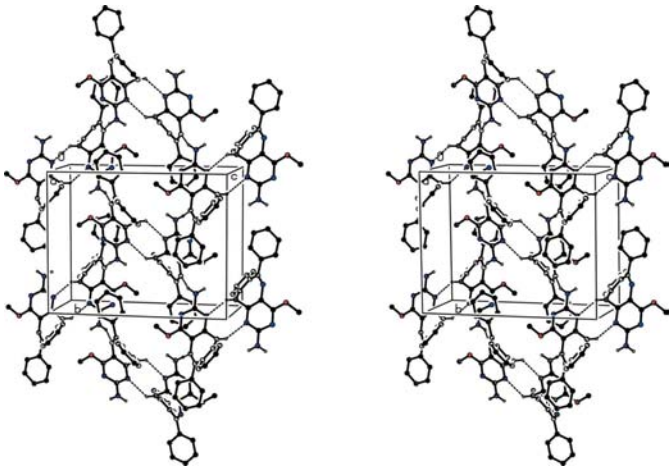

Figure 2
A stereoview of part of the crystal structure of (I), showing the formation of a sheet of alternating $R_2^2(8)$ and $R_6^6(36)$ rings parallel to $(10\bar{1})$ formed by two independent N—H···N hydrogen bonds. For the sake of clarity, H atoms bonded to C atoms have been omitted. Entirely analogous sheets can be identified in the structures of (II) and (III).

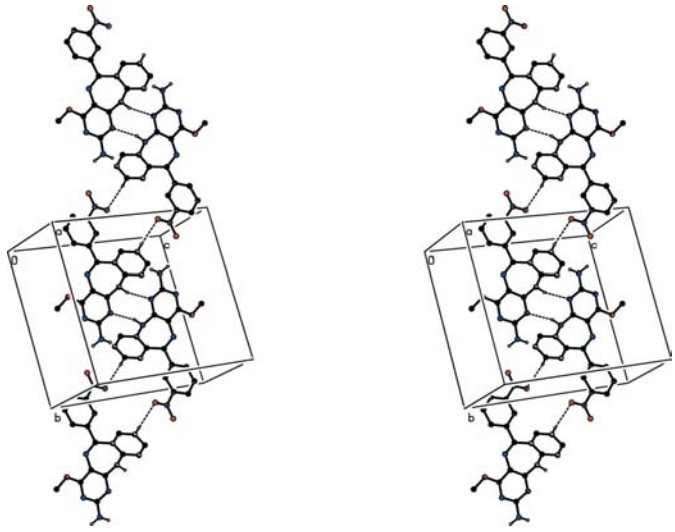

Figure 3
A stereoview of part of the crystal structure of (III), showing the formation of a chain of alternating $R_2^2(8)$ and $R_2^2(20)$ rings along $[1\bar{1}0]$ formed by N—H···N and C—H···O hydrogen bonds. For the sake of clarity, H atoms bonded to C atoms and not involved in the motif shown have been omitted.

and (X) (SONBOM and SONBIG, respectively; Dupont *et al.*, 1991).

Despite the similarity in the unit-cell dimensions of compounds (I)–(IV) and the close similarity of their molecular structures, these compounds differ in both their crystal structures and in the patterns of the hydrogen bonding. In each compound, paired N—H···N hydrogen bonds, with atom N11 as the donor and pyrimidine atom N1 as the acceptor, generate centrosymmetric $R_2^2(8)$ motifs (Bernstein *et al.*, 1995), centred for the sake of convenience at $(\frac{1}{2}, \frac{1}{2}, \frac{1}{2})$ in each case. However, the subsequent linking of the dimeric units is different in each case, leading to the formation of different three-dimensional hydrogen-bonded framework structures in each of (I)–(III), and to a two-dimensional network in (IV).

In each of (I)–(III), a second N—H···N hydrogen bond (Table 2) links the $R_2^2(8)$ dimers into a sheet. Amino atom N2 in the molecule at (x, y, z), which forms part of the dimer centred at $(\frac{1}{2}, \frac{1}{2}, \frac{1}{2})$, acts as hydrogen-bond donor to ring atom N5 in the molecule at $(\frac{1}{2} - x, \frac{1}{2} + y, \frac{1}{2} - z)$, which forms part of the dimer centred at (0, 1, 0). In this manner, the dimer centred at $(\frac{1}{2}, \frac{1}{2}, \frac{1}{2})$ is directly linked to the four dimers centred at (0, 0, 0), (0, 1, 0), (1, 0, 1) and (1, 1, 1), so forming a sheet parallel to $(10\bar{1})$ built solely from N—H···N hydrogen bonds and consisting of $R_2^2(8)$ rings alternating with $R_6^6(32)$ rings (Fig. 2).

These sheets are then linked to form a three-dimensional framework by the co-operative action of C—H···N and C—H···π(arene) hydrogen bonds in (I) and by just a single C—H···π(arene) hydrogen bond in (II). In each of (I) and (II) these additional hydrogen bonds form a chain running parallel to [010] in which alternate molecules form parts of adjacent $(10\bar{1})$ sheets. The final two hydrogen bonds in the structure of (III) link the $(10\bar{1})$ sheets into a continuous framework structure *via* two distinct motifs. Aryl atom C8 in the molecule at (x, y, z) acts as donor to nitro atom O632 in the molecule at $(2 - x, -y, 1 - z)$, so forming a centrosymmetric $R_2^2(20)$ motif centred at $(1, 0, \frac{1}{2})$. This motif links the $R_2^2(8)$ dimers into a chain running parallel to $[1\bar{1}0]$ and containing $R_2^2(8)$ rings centred at $(\frac{1}{2} + n, \frac{1}{2} - n, \frac{1}{2})$ (where n represents zero or an integer) alternating with $R_2^2(20)$ rings centred at $(n, 1 - n, \frac{1}{2})$ (where n represents zero or an integer) (Fig. 3). The combination of a chain along $[1\bar{1}0]$ and a sheet parallel to $(10\bar{1})$ is sufficient to generate a three-dimensional framework structure. Finally, aryl atom C65 at (x, y, z) acts as donor to the ring C6a/C7–C10/C10a in the molecule at $(\frac{3}{2} - x, -\frac{1}{2} + y, \frac{1}{2} - z)$, so forming a chain running parallel to the [010] direction and consisting of molecules related by the 2_1 screw axis along $(\frac{3}{4}, y, \frac{1}{4})$, where successive molecules are components of two different $(10\bar{1})$ sheets (Fig. 4).

The linking of the $R_2^2(8)$ rings in (IV) again generates a sheet parallel to $(10\bar{1})$, just as in (III), but now the dimers are linked by a C—H···π(arene) hydrogen bond rather than by an N—H···N hydrogen bond (Fig. 5). Indeed, neither of the N—H bonds of the amino group plays any role in the hydrogen bonding, as there are no potential hydrogen-bond acceptors within 2.60 Å of the amino H atoms in (IV). There are no direction-specific interactions of any kind between adjacent sheets, so that the hydrogen-bonded structure of (IV) is strictly two-dimensional. It is striking that in neither compound does pyrimidine atom N3 play any role in the hydrogen bonding.

Thus, although the unit-cell dimensions of compounds (I)–(IV) are similar and their molecular constitutions and conformations are almost identical, unexpectedly the crystal structures, dominated by multiple hydrogen bonds, are somewhat different.

It is of interest briefly to compare the hydrogen-bonded structures of (I)–(IV) with those found in compounds (V)–(VIII). This comparison is of particular interest in view of the

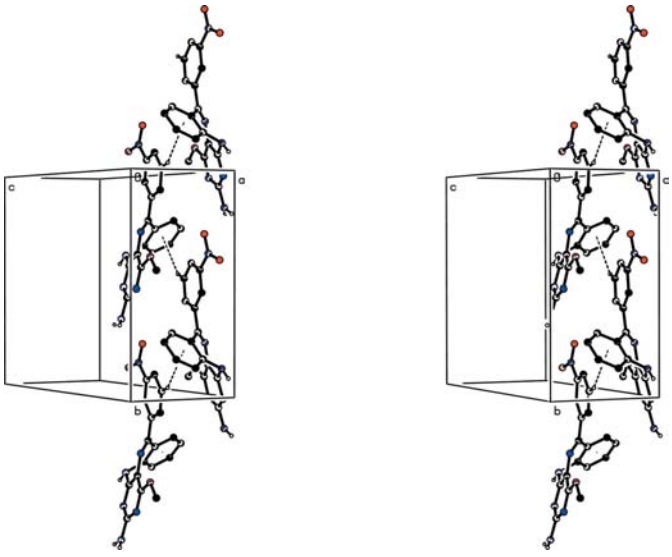

Figure 4
A stereoview of part of the crystal structure of (III), showing the formation of a chain along [010] formed by C—H···π(arene) hydrogen bonds. For the sake of clarity, H atoms bonded to C atoms and not involved in the motif shown have been omitted.

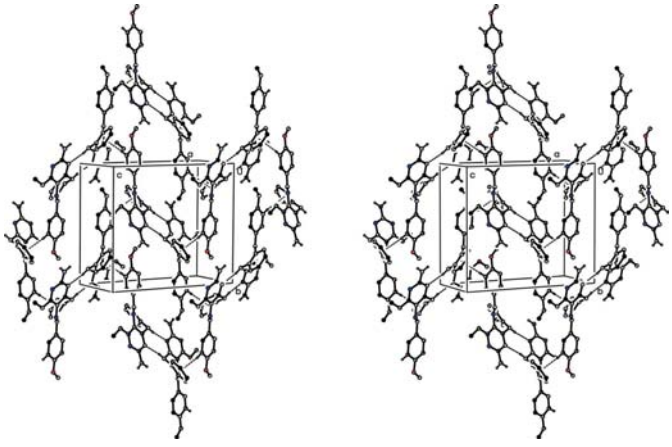

Figure 5
A stereoview of part of the crystal structure of (IV), showing the formation of a sheet parallel to (10$\bar{1}$) using a combination of N—H···N and C—H···π(arene) hydrogen bonds. For the sake of clarity, H atoms bonded to C atoms and not involved in the motif shown have been omitted.

nonparticipation in the hydrogen-bonded structures of (I)–(IV) by atom N3, the sole point of difference in the fused tricyclic systems of (I)–(IV) on the one hand and (V)–(VIII) on the other.

In both (V) and (VI), paired N—H···N hydrogen bonds having the pyridine N atom as acceptor generate centrosymmetric $R_2^2(8)$ dimers, exactly as in (I)–(IV). In (V) these dimers are linked into chains of centrosymmetric rings by pairs of symmetry-related C—H···π(arene) hydrogen bonds, but there are no direction-specific interactions between the dimers in (VI). In neither compound do the two N atoms of the pendent piperidine substituent play any part in the hydrogen bonding. By contrast, there are two independent N—H···N

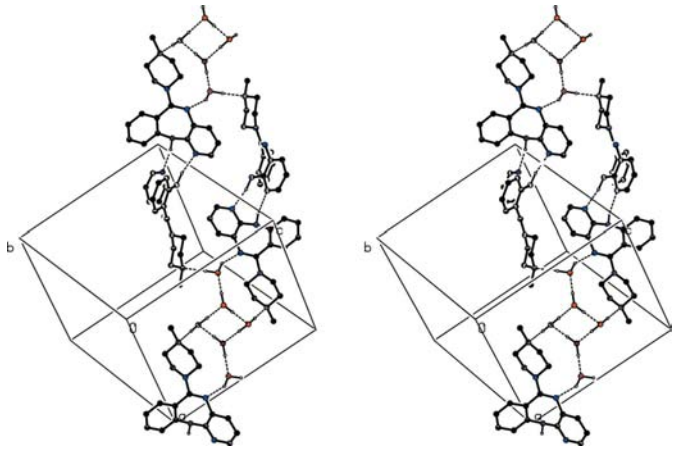

Figure 6
A stereoview of part of the crystal structure of (V) (CSD refcode KOYTIB; Dupont *et al.*, 1992), showing the formation of a chain containing four types of ring. The original atom coordinates have been used and, for the sake of clarity, H atoms bonded to C atoms have all been omitted.

hydrogen bonds in (VIII). An intramolecular hydrogen bond is formed by the two N atoms of the dimethylaminopropylamine substituent, and an intermolecular hydrogen bond utilizes the ring N—H as donor and the imine N atom of the diazepine ring as acceptor to form a simple *C*(5) chain. A single C—H···π(arene) hydrogen bond links these chains into sheets.

Compound (VII) crystallizes from acetone–methanol (50:50 *v*/*v*) as a sesquihydrate (Dupont *et al.*, 1992) with two molecules of the organic component and three water molecules in the asymmetric unit. All of the N—H and O—H bonds are involved in the hydrogen bonding, which generates a ribbon or chain of edge-fused rings running parallel to the [1$\bar{1}\bar{1}$] direction of the triclinic cell, in which there are rings of $R_2^2(8)$, $R_4^4(8)$, $R_4^4(13)$ and $R_6^6(32)$ types, the second and fourth of which are centrosymmetric (Fig. 6). Embedded within the ribbon is a homodromic (Saenger & Lindner, 1980) and centrosymmetric ring of four hydrogen-bonded water molecules.

Experimental

Samples of compounds (I)–(IV) were prepared as described previously by Cobo *et al.* (2008). Crystals suitable for single-crystal X-ray diffraction were grown by slow evaporation from methanol solutions.

Compound (I)

Crystal data

$C_{18}H_{15}N_5O$
M_r = 317.35
Monoclinic, $P2_1/n$
a = 7.022 (6) Å
b = 12.855 (9) Å
c = 16.199 (8) Å
β = 93.851 (5)°
V = 1459.0 (18) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.10 mm^{-1}
T = 120 (2) K
0.47 × 0.35 × 0.26 mm

Table 1
Conformational parameters (Å, °) for compounds (I)–(IV).

Ring-puckering angles correspond to the atom sequence N5—C4a—C11a—N11—C10a—C6a—C6.

	(I)	(II)	(III)	(IV)
Displacements from the mean plane of the seven-membered ring				
N5	0.214 (3)	0.208 (2)	0.205 (2)	0.186 (3)
C4a	−0.312 (4)	−0.307 (2)	−0.305 (3)	−0.328 (4)
C11a	−0.140 (4)	−0.137 (2)	−0.133 (3)	−0.103 (4)
N11	0.469 (3)	0.464 (2)	0.458 (2)	0.465 (3)
C10a	−0.174 (4)	−0.178 (2)	−0.176 (3)	−0.206 (4)
C6a	−0.295 (4)	−0.287 (2)	−0.285 (3)	−0.281 (4)
C6	0.239 (4)	0.236 (2)	0.236 (3)	0.267 (4)
Puckering parameters for the seven-membered ring				
φ_2	53.9 (3)	54.4 (2)	54.6 (2)	59.1 (3)
φ_3	257.9 (14)	258.4 (9)	258.0 (11)	257.7 (15)
Q_T	0.746 (3)	0.736 (2)	0.729 (3)	0.750 (4)
Torsion angles				
C4a—C4—O4—C41	−176.8 (3)	−175.2 (2)	−173.8 (3)	−175.8 (3)
N5—C6—C61—C62	−139.2 (4)	−133.4 (2)	−136.2 (3)	−147.2 (4)
C62—C63—N63—O631			−171.2 (3)	
C63—C64—O64—C641				−9.6 (6)
Displacements from the mean planes of the aryl/pyrimidyl rings				
C41	0.046 (4)	0.135 (3)	0.178 (3)	−0.112 (4)
O631			0.125 (3)	
O632			−0.252 (3)	
C641				−0.169 (5)

Data collection

Bruker–Nonius KappaCCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
T_{min} = 0.967, T_{max} = 0.976
3338 measured reflections
3338 independent reflections
2768 reflections with $I > 2\sigma(I)$
R_{int} = 0.000

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.085
$wR(F^2)$ = 0.225
S = 1.20
3338 reflections
219 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.45 e Å^{-3}
$\Delta\rho_{min}$ = −0.59 e Å^{-3}

Compound (II)

Crystal data

$C_{18}H_{14}FN_5O$
M_r = 335.34
Monoclinic, $P2_1/n$
a = 6.9115 (10) Å
b = 12.8801 (14) Å
c = 16.560 (2) Å
β = 95.110 (10)°
V = 1468.4 (3) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.11 mm^{-1}
T = 120 (2) K
0.24 × 0.14 × 0.11 mm

Data collection

Bruker–Nonius KappaCCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
T_{min} = 0.976, T_{max} = 0.988
35898 measured reflections
3340 independent reflections
2361 reflections with $I > 2\sigma(I)$
R_{int} = 0.067

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.060
$wR(F^2)$ = 0.171
S = 1.05
3340 reflections
237 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.64 e Å^{-3}
$\Delta\rho_{min}$ = −0.56 e Å^{-3}

Table 2
Hydrogen-bond parameters (Å, °) for compounds (I)–(IV).

Cg represents the centroid of the C6a/C7–C10/C10a ring.

Compound	D—H···A	D—H	H···A	D···A	D—H···A
(I)	N2—H22···N5^{i}	0.88	2.40	3.129 (5)	141
	N11—H11···N1^{ii}	0.88	2.45	3.036 (4)	125
	C7—H7···N3^{iii}	0.95	2.57	3.503 (5)	168
	C65—H65···*Cg*^{iii}	0.95	2.65	3.500 (5)	150
(II)	N2—H22···N5^{i}	0.88	2.36	3.099 (3)	142
	N11—H11···N1^{ii}	0.88	2.48	3.069 (3)	125
	C65—H65···*Cg*^{iii}	0.95	2.75	3.562 (3)	145
(III)	N2—H22···N5^{i}	0.88	2.34	3.177 (4)	160
	N11—H11···N1^{ii}	0.88	2.33	3.186 (4)	163
	C8—H8···O632^{iv}	0.95	2.48	3.162 (4)	129
	C65—H65···*Cg*^{iii}	0.95	2.77	3.526 (4)	138
(IV)	N11—H11···N1^{ii}	0.88	2.26	3.132 (4)	171
	C65—H65···*Cg*^{i}	0.95	2.61	3.492 (4)	155

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

Compound (III)

Crystal data

$C_{18}H_{14}N_6O_3$
M_r = 362.35
Monoclinic, $P2_1/n$
a = 7.047 (4) Å
b = 13.502 (7) Å
c = 16.418 (5) Å
β = 91.22 (5)°
V = 1561.8 (13) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.11 mm^{-1}
T = 120 (2) K
0.22 × 0.15 × 0.14 mm

Data collection

Bruker–Nonius KappaCCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
T_{min} = 0.966, T_{max} = 0.985
24447 measured reflections
3467 independent reflections
1748 reflections with $I > 2\sigma(I)$
R_{int} = 0.103

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.061
$wR(F^2)$ = 0.182
S = 1.02
3467 reflections
245 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.25 e Å^{-3}
$\Delta\rho_{min}$ = −0.28 e Å^{-3}

Compound (IV)

Crystal data

$C_{19}H_{17}N_5O_2$
M_r = 347.38
Monoclinic, $P2_1/n$
a = 7.6718 (18) Å
b = 13.2928 (15) Å
c = 15.969 (2) Å
β = 95.343 (12)°
V = 1621.5 (5) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.10 mm^{-1}
T = 120 (2) K
0.17 × 0.15 × 0.08 mm

Data collection

Bruker–Nonius KappaCCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
T_{min} = 0.974, T_{max} = 0.992
22968 measured reflections
3072 independent reflections
1312 reflections with $I > 2\sigma(I)$
R_{int} = 0.179

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.069$	237 parameters
$wR(F^2) = 0.189$	H-atom parameters constrained
$S = 0.94$	$\Delta\rho_{max} = 0.30$ e Å^{-3}
3072 reflections	$\Delta\rho_{min} = -0.32$ e Å^{-3}

All H atoms were located in difference maps and then treated as riding atoms, with C—H = 0.95 (aromatic) or 0.98 Å (CH_3) and N—H = 0.88 Å, and with $U_{iso}(H) = kU_{eq}$(carrier), where $k = 1.5$ for the methyl groups and 1.2 for all other H atoms. Compound (I) was handled as a nonmerohedral twin using the HKLF5 option in *SHELXL97* (Sheldrick, 2008), with a twinning matrix ($\bar{1}$,0,0/0,$\bar{1}$,0/0.310,0,1), giving twin fractions of 0.847 (4) and 0.153 (4). In compound (II), the F atom was disordered over two sites bonded to atoms C62 and C66, with occupancies of 0.775 (5) and 0.225 (5), respectively; restraints were applied to ensure similarity of the C—F distances and C—C—F angles in the two orientations. For compound (IV), the merging index was 0.179, but this occurred for a weak data set with only 42.7% of the reflections having $I > 2\sigma(I)$, despite data collection at 120 K.

For all compounds, data collection: *COLLECT* (Nonius, 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, 2003); 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: SK3273). Services for accessing these data are described at the back of the journal.

References

Allen, F. H. (2002). *Acta Cryst.* B**58**, 380–388.
Bernstein, J., Davis, R. E., Shimoni, L. & Chang, N.-L. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 1555–1573.
Burla, M. C., Caliandro, R., Camalli, M., Carrozzini, B., Cascarano, G. L., De Caro, L., Giacovazzo, C., Polidori, G. & Spagna, R. (2005). *J. Appl. Cryst.* **38**, 381–388.
Cobo, J., Nogueras, M., Low, J. N. & Rodríguez, R. (2008). *Tetrahedron Lett.* **49**, 7271–7273.
Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.
Duisenberg, A. J. M., Hooft, R. W. W., Schreurs, A. M. M. & Kroon, J. (2000). *J. Appl. Cryst.* **33**, 893–898.
Duisenberg, A. J. M., Kroon-Batenburg, L. M. J. & Schreurs, A. M. M. (2003). *J. Appl. Cryst.* **36**, 220–229.
Dupont, L., Englebert, S., Dideberg, O., Liégeois, J. F. & Delarge, J. (1991). *Acta Cryst.* C**47**, 2690–2693.
Dupont, L., Englebert, S., Dideberg, O., Liégeois, J. F. & Delarge, J. (1992). *Acta Cryst.* C**48**, 1322–1324.
Dupont, L., Eyrolles, L., Evrard, G., Delarge, J. & Liégeois, J.-F. (2002). *Acta Cryst.* E**58**, o69–o71.
Dupont, L., Liégeois, J.-F., Rogister, F. & Delarge, J. (1995). *Acta Cryst.* C**51**, 1889–1891.
Evans, D. G. & Boeyens, J. C. A. (1989). *Acta Cryst.* B**45**, 581–590.
Ferguson, G. (1999). *PRPKAPPA*. University of Guelph, Canada.
Gangjee, A., Zeng, Y., McGuire, J. J., Mehraein, F. & Kisliuk, R. L. (2004). *J. Med. Chem.* **47**, 6893–6901.
McArdle, P. (2003). *OSCAIL for Windows*. Version 10. Crystallography Centre, Chemistry Department, NUI Galway, Ireland.
McGuigan, C., Pathirana, R. N., Snoeck, R., Andrei, G., DeClercq, E. & Balzarini, J. (2004). *J. Med. Chem.* **47**, 1847–1851.
Nonius (1999). *COLLECT*. Nonius BV, Delft, The Netherlands.
Saenger, W. & Lindner, K. (1980). *Angew. Chem. Int. Ed. Engl.* **19**, 398–399.
Sheldrick, G. M. (2003). *SADABS*. Version 2.10. University of Göttingen, Germany.
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.
Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.
Spirlet, M.-R., Graulich, A. & Liégeois, J.-F. (2003). *Acta Cryst.* E**59**, o1990–o1991.
Wang, S., Folkes, A., Chuckowree, I., Cockcroft, X., Sohal, S., Miller, W., Milton, J., Wren, S. P., Vicker, N., Depledge, P., Scott, J., Smith, L., Jones, H., Mistry, P., Faint, R., Thompson, D. & Cocks, S. (2004). *J. Med. Chem.* **47**, 1329–1338.