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Anomeric effect and hydrogen-bonded supramolecular motif in 5-(3-fluoro-4-methoxyphenyl)-1-[(3-fluoro-4-methoxyphenyl)aminomethyl]-1,3,5-triazinane-2-thione

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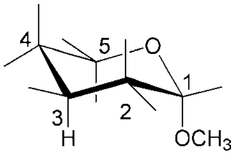
In the title compound, $C_{18}H_{20}F_2N_4O_2S$, the triazinane-2-thione ring adopts an envelope conformation, the ring substituents lie on the same side of the mean plane of the heterocyclic ring and the *exo* lp—N—C—N_{triaz} unit (lp is a lone pair and triaz is the triazinane ring) exhibits an antiperiplanar orientation, which is shown to be governed by strong anomeric effects. Molecules are linked into a complex three-dimensional framework by a combination of two N—H···S hydrogen bonds, three C—H···F hydrogen bonds and a π–π stacking interaction.

Comment

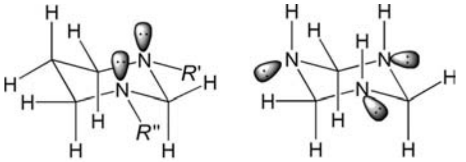
The anomeric effect is well recognized as one of the most important factors in the conformational analysis of systems containing geminal heteroatoms. It generally manifests itself as the propensity of an electronegative substituent at atom C1 of a pyranose ring to occupy an axial orientation (Scheme 1; Edward, 1955), despite unfavourable steric interaction with H atoms at C3 and C5. Similar conformational preferences have also been found in many heterocycles. This axial conformational preference is now termed the generalized anomeric effect. The effect is not restricted to heterocyclic systems, and evidence for its existence in acyclic compounds has also been found (Narasimhamurthy *et al.*, 1990; Christen *et al.*, 1996; Gobbato *et al.*, 1997). Thus, the term 'anomeric effect' has been generalized to refer to the conformational preference of an lp—*X*—*Z*—*Y* moiety for an antiperiplanar orientation of the lone pair (lp) to the *Z*—*Y* bond, where *X* represents an atom possessing lone pairs, *Z* is usually a C atom and *Y* denotes an atom more electronegative than *Z*.



Scheme 1

Several theoretical models have been proposed to account for the origin of this effect. Although dipolar electrostatic interactions were first considered as its origin (Edward, 1955; Perrin *et al.*, 1994; Pinto *et al.*, 1988), they failed to explain the structural changes observed in the axial conformation, such as the decrease in the *X*—*Z* bond length, the increase in the *Z*—*Y* bond length and the opening of the *X*—*Z*—*Y* angle. To explain these conformational preferences and changes in bond parameters, a stereoelectronic model (SM) has been proposed (Wiberg & Rablen, 1993). The SM considers that the stabilization of the antiperiplanar conformation results from the delocalization of one of the lps on *X* to the *Z*—*Y* σ^* antibonding orbital, which takes place when the lp—*X*—*Y*—*Z* fragment adopts an antiperiplanar orientation. This stereoelectronic interaction is denoted as $n(X) \rightarrow \sigma^*(Y—Z)$ and its validity has been well examined by X-ray analysis (Uehara *et al.*, 1999; Ellenik & Magnusson, 1994; Juaristi & Cuevas, 1993; Kakanejadifard & Farnia, 1997; Zhang *et al.*, 2009). If we concentrate on the N—C—N fragment, many experimental results have indicated that lp—N—C—N is in an antiperiplanar conformation, and the $n(\mathrm{N}) \rightarrow \sigma^*(\mathrm{C—N})$ interaction is the dominant factor in determining the conformational preference.

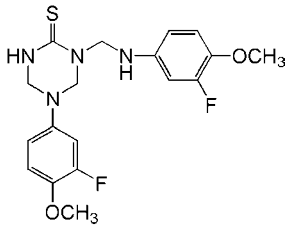
On the other hand, some N—C—N-containing compounds have been studied using both the quantum theory of atoms in molecules and X-ray analysis (Eskandari *et al.*, 2007; Dong *et al.*, 1999; Fun & Kia, 2008). The results show that the lp—N—C—N units in 1,3-diazacyclohexanes and 1,3,5-triazinane prefer the *gauche* orientation (Scheme 2). Thus, the conformational preferences of these N—C—N units are not in line with the SM of the anomeric effect. In contrast, these variations can be explained on the basis of the steric interactions.



Scheme 2

However, despite these two different conformations and two interpretations for lp—N—C—N fragments, no studies of the anomeric effect, to our knowledge, have involved the 5-aryl-1-[(arylamino)methyl]-1,3,5-triazinane-2-thiones. Unlike the previously studied N—C—N units, the N(thioureido)—C—N(arylamine) fragments in 5-aryl-1-[(arylamino)methyl]-1,3,5-triazinane-2-thiones have two environmentally diverse N atoms. The concrete role they play in the conformational effect is our chief concern. Therefore, we report here the results of our studies of the anomeric effects and supramolecular structure of one such compound, the title compound, (I) (Fig. 1).

In (I), the triazinane-2-thione ring adopts an envelope conformation. Atom N1 is the flap atom, displaced by 0.636 (3) Å from the plane of the other five atoms. The N3 anilinomethyl and N1 phenyl groups lie on the same side of the mean plane of the heterocyclic ring. The conformation is similar to those in our previously reported compounds (Zhang *et al.*, 2008). However, the N4 *p*-orbital containing the lone electron pair is aligned with the N3—C4 bond, and thus the associated σ^* orbital as well, allowing for hyperconjugation and commensurate shortening of the N4—C4 bond, which is different from observations made with other N-containing heterocycles (Eskandari *et al.*, 2007; Dong *et al.*, 1999; Fun & Kia, 2008). This shows that the orientation of the N4 *p*-orbital containing the lp is not caused coincidentally by the crystal packing or by intramolecular π–π or C—H$\cdots\pi$ interactions, but suggests the existence of anomeric effects in the *exo* N3—C4—N4 fragment. This can be further confirmed by some correlative geometric parameters (Table 1).



(I)

In (I), the *endo* residues, *viz.* N1—C1—N2 and N1—C2—N3, are similar in chemical environment to the *exo* N3—C4—N4 fragment, and their bond lengths are consistent with the usual value for N—Csp^3 bonds (1.44–1.47 Å; Glidewell *et al.*, 2003; Nesterov *et al.*, 2003; Akkurt *et al.*, 2007; Ma *et al.* 1996). Therefore, the *endo* fragments in (I) were selected as the model fragments. As shown in Table 1, the N4—C4 bond is much shorter than the corresponding N1—C1 and N1—C2 bonds, while the C4—N3 bond is much longer than the C1—N2 and C2—N3 bonds. The observed conformation, the remarkable lengthening of the N3—C4 bond and the significant shortening of the N4—C4 bond all point to the conclusion that there is a strong anomeric effect in the *exo* N3—C4—N4 unit. The existence of the anomeric effect was also further verified *via* the opening of the N4—C4—N3 angle relative to the N1—C1—N2 and N1—C2—N3 angles (Table 1). This interaction is best rationalized in terms of the 'negative hyperconjugation' of the N4 *p*-electron pair with the adjacent antibonding orbital of C4—N3, and it is this interaction that requires the N3—C4 bond to be aligned with the N4 *p*-orbital containing the lone electron pair.

The molecules of (I) are linked into a complex three-dimensional framework by six weak intermolecular interactions, two N—H$\cdots$S hydrogen bonds, three C—H$\cdots$F hydrogen bonds (Table 2) and one π–π stacking interaction. However, the structure can be easily analyzed as an edge-fused dimer. Thioureido atom N2 in the molecule at (x, y, z) acts as a hydrogen-bond donor to thiocarbonyl atom S1 in the molecule at ($1 - x$, $1 - y$, $-z$), so generating by inversion a dimer centred at ($\frac{1}{2}$, $\frac{1}{2}$, 0) and characterized by the usual $R_2^2(8)$ (Bernstein *et al.*, 1995) graph-set motif (Fig. 2). Such dimers, as the backbone building units, are further linked into a two-dimensional network by N—H$\cdots$S and C—H$\cdots$F hydrogen bonds (Table 2). Imino atom N4 in the molecule at (x, y, z), part of the dimer centred at ($\frac{1}{2}$, $\frac{1}{2}$, 0), acts as a hydrogen-bond donor to atom S1 in the molecule at ($x - 1$, y, z), part of the dimer centred at ($-\frac{1}{2}$, $\frac{1}{2}$, 0). Meanwhile, phenyl atom C10 and methyl atom C18 in the molecule at ($1 - x$, $1 - y$, $-z$) act as hydrogen-bond donors to, respectively, atoms F1 and F2 in the molecule at ($-x$, $1 - y$, $-z$), so generating by inversion and translation a multiple hydrogen-bonded chain parallel to [100] (Fig. 2). Chains of this type are laterally linked into a sheet by another C—H$\cdots$F interaction (Table 2). Methyl atom C11 in the molecule at (x, y, z) acts as a hydrogen-bond donor, *via* atom H11*B*, to atom F2 in the molecule at ($-x$, $-y$, $1 - z$), thus forming by inversion and translation a hydrogen-bonded sheet parallel to (011) (Fig. 2). Two such sheets, related to one another by a 2_1 screw axis along (x, $\frac{1}{2}$, $\frac{1}{2}$), pass through each unit cell, and adjacent sheets are linked through a π–π stacking interaction to build up a three-dimensional framework. The

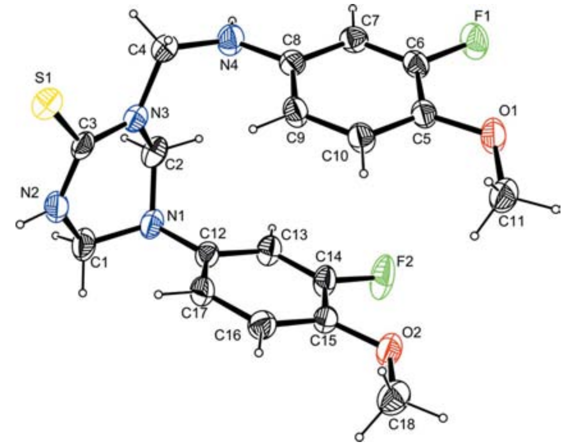


Figure 1
The molecular structure of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

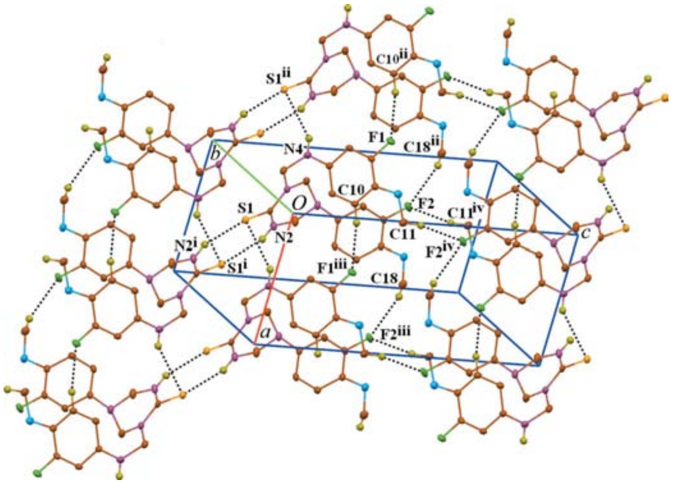


Figure 2
Part of the crystal structure of (I), showing the formation of a sheet parallel to (011). For the sake of clarity, H atoms not involved in the motif shown have been omitted. Intermolecular interactions are represented by dashed lines. Selected atoms are labelled. [Symmetry codes: (i) $-x + 1$, $-y + 1$, $-z$; (ii) $x - 1$, y, z; (iii) $x + 1$, y, z; (iv) $-x$, $-y$, $-z + 1$.]

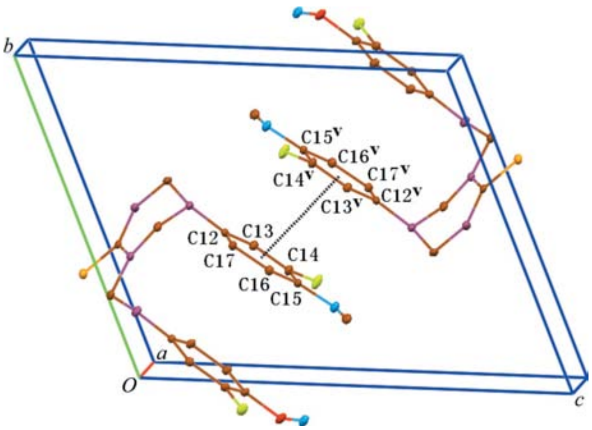


Figure 3
Part of the crystal structure of compound (I), showing the π–π stacking interaction that links the (011) sheets. For the sake of clarity, all H atoms have been omitted. [Symmetry code: (v) $1 - x, 1 - y, 1 - z$.]

C12–C17 rings in the molecules at (x, y, z) and $(1 - x, 1 - y, 1 - z)$ are strictly parallel, with an interplanar spacing of 3.556 (1) Å; the ring-centroid separation is 3.644 (1) Å, corresponding to a ring-centroid offset of 0.797 (1) Å (Fig. 3). Propagation of the motif by the space group symmetry links each (011) sheet to the two neighbouring sheets, so linking all of the sheets into a complex three-dimensional framework.

In conclusion, analysis of the X-ray crystallographic structural parameters in (I) has revealed that there is only a stereoelectronic interaction in the *exo* N(thioureido)—C—N(arylamine) fragment, where arylamine atom N4 acts as an lp donor to the thioureido N3—C4 σ^* antibonding orbital, and that the supramolecular structure exhibits a complex three-dimensional packing arrangement *via* a combination of two N—H···S hydrogen bonds, three C—H···F hydrogen bonds and a π–π stacking interaction.

Experimental

The method used for the preparation of (I) will be reported elsewhere (Zhang *et al.*, 2009). After cooling of a dimethylformamide solution of (I) to ambient temperature, slow evaporation of the solvent yielded crystals suitable for single-crystal X-ray diffraction.

Crystal data

$C_{18}H_{20}F_2N_4O_2S$
$M_r = 394.44$
Triclinic, $P\overline{1}$
$a = 6.6019$ (8) Å
$b = 11.1195$ (13) Å
$c = 13.9076$ (17) Å
$\alpha = 106.693$ (1)°
$\beta = 102.362$ (1)°
$\gamma = 103.715$ (1)°
$V = 905.31$ (19) Å^3
$Z = 2$
Mo $K\alpha$ radiation
$\mu = 0.22$ mm^{-1}
$T = 296$ K
0.31 × 0.28 × 0.23 mm

Data collection

Bruker SMART CCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
$T_{min} = 0.935$, $T_{max} = 0.951$
6772 measured reflections
3341 independent reflections
2683 reflections with $I > 2\sigma(I)$
$R_{int} = 0.015$

Table 1
Selected geometric parameters (Å, °).

C4—N4	1.422 (2)	C1—N2	1.467 (2)
C4—N3	1.490 (2)	C2—N1	1.445 (3)
C3—N2	1.339 (2)	C2—N3	1.478 (2)
C1—N1	1.442 (2)		
N4—C4—N3	112.62 (16)	N1—C2—N3	110.60 (16)
N1—C1—N2	110.71 (16)		

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

D—H···A	D—H	H···A	D···A	D—H···A
N2—H2···S1^{i}	0.86	2.68	3.469 (2)	152
N4—H4···S1^{ii}	0.86	2.69	3.456 (2)	148
C10—H10···F1^{iii}	0.93	2.53	3.434 (3)	165
C11—H11B···F2^{iv}	0.96	2.59	3.535 (3)	169
C18—H18C···F2^{iii}	0.96	2.51	3.292 (3)	139

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

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.038$
$wR(F^2) = 0.098$
$S = 1.04$
3341 reflections
246 parameters
H-atom parameters constrained
$\Delta\rho_{max} = 0.30$ e Å^{-3}
$\Delta\rho_{min} = -0.24$ e Å^{-3}

All H atoms were placed in idealized positions and allowed to ride on their parent atoms, with C—H = 0.93 (aromatic), 0.97 (CH_2) or 0.96 Å (CH_3) and N—H = 0.86 Å, and with $U_{iso}(H) = 1.2U_{eq}$(C,N) or $1.5U_{eq}$(methyl C).

Data collection: *SMART* (Bruker, 1997); cell refinement: *SAINT* (Bruker, 1997); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *SHELXTL* (Sheldrick, 2008); software used to prepare material for publication: *SHELXTL*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: DN3126). Services for accessing these data are described at the back of the journal.

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