

research papers



Acta Crystallographica Section C

Structural Chemistry

ISSN 2053-2296

(8*RS*)-4-Amino-6-(4-chlorophenyl)-8-(2,4-dichlorothiazol-5-yl)-8,9-dihydro-7*H*-pyrimido[4,5-*b*][1,4]diazepine *N,N*-dimethylformamide monosolvate: sheets built from N—H···N and C—H···O hydrogen bondsJuan Ramírez,^a Braulio Insuasty,^a Justo Cobo^b and Christopher Glidewell^{c*}^aDepartamento de Química, Universidad de Valle, AA 25360 Cali, Colombia,^bDepartamento de Química Inorgánica y Orgánica, Universidad de Jaén, 23071 Jaén, Spain, and ^cSchool of Chemistry, University of St Andrews, Fife KY16 9ST, ScotlandCorrespondence e-mail: cg@st-andrews.ac.uk

Received 24 March 2014

Accepted 19 April 2014

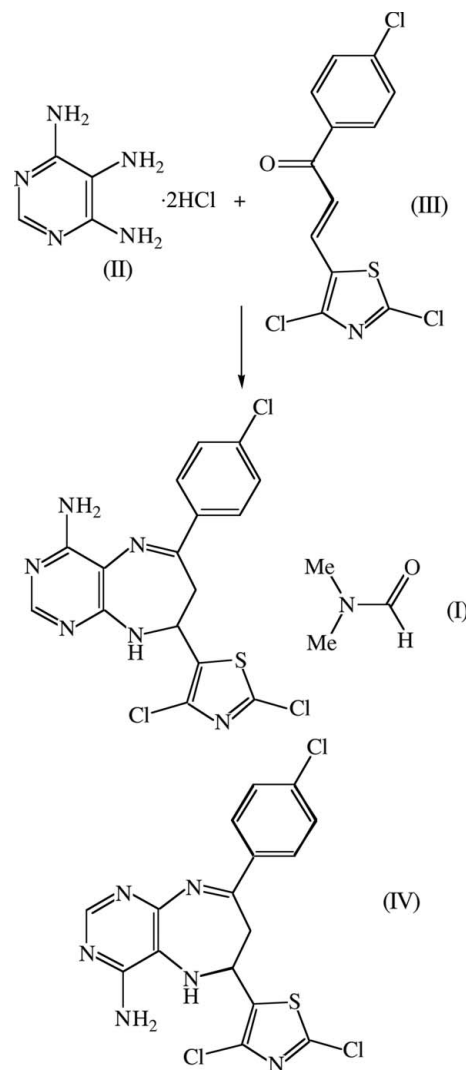
In the title compound, C₁₆H₁₁Cl₃N₆S·C₃H₇NO, the seven-membered ring adopts a conformation which is close to the twist-boat form. The molecular components are linked into sheets by a combination of two N—H···N hydrogen bonds and two C—H···O hydrogen bonds. Comparisons are made with other aminopyrimidine derivatives.

Keywords: crystal structure; biological properties; pharmacological properties; pyrimido[4,5-*b*][1,4]diazepine; hydrogen bonding.

1. Introduction

Seven-membered nitrogen-containing heterocyclic compounds, such as 1,4-diazepines, are important structural units in drug discovery due to their wide spectrum of biological and pharmacological properties (Sternbach, 1971), including antimicrobial (Parmar *et al.*, 2012), anti-HIV (Fader *et al.*, 2011, 2013) and anticancer activity (Smith *et al.*, 2006), while compounds such as pyrimido[1,4]diazepines have shown important antitumour activity (Insuasty, Orozco, Lizarazo *et al.*, 2008; Insuasty, Orozco, Quiroga *et al.*, 2008; Insuasty *et al.*, 2010; Deng *et al.*, 2013). Continuing our work on the synthesis of diverse pyrimido[4,5-*b*][1,4]diazepines from α,β -unsaturated carbonyl (chalcone-type) derivatives, in order to explore their antitumour activities, we have now prepared (8*RS*)-4-amino-6-(4-chlorophenyl)-8-(2,4-dichlorothiazol-5-yl)-8,9-dihydro-7*H*-pyrimido[4,5-*b*][1,4]diazepine, the structure of which is reported here as its monosolvate, (I) (Fig. 1), with *N,N*-dimethylformamide (DMF).

The fused heterocyclic component of (I) was prepared by the thermal reaction of 4,5,6-triaminopyrimidine as its dihydrochloride salt, (II), and the chalcone derivative 1-(4-chlorophenyl)-3-(2,4-dichlorothiazol-5-yl)propan-1-one, (III) (see Scheme), which had itself been prepared by the base-catalysed condensation reaction between 4-chloroacetophenone and 2,4-dichlorothiazole-5-carbaldehyde; crystallization from DMF yielded monosolvate (I).



The purposes of the present study were threefold: firstly, to establish the regiochemistry of the reaction between (II) and (III) to form the title pyrimidodiazepine, rather than the alternative isomeric form (IV) (see Scheme); secondly, to compare the geometry of the fused pyrimidine ring in (I) with those of other unfused but heavily substituted pyrimidines; and thirdly, to compare the supramolecular assembly in (I) with that in simpler aminopyrimidines.

2. Experimental**2.1. Synthesis and crystallization**

For the synthesis of (8*RS*)-4-amino-6-(4-chlorophenyl)-8-(2,4-dichlorothiazol-5-yl)-8,9-dihydro-7*H*-pyrimido[4,5-*b*]-

Table 1

Experimental details.

Crystal data	
Chemical formula	C ₁₆ H ₁₁ Cl ₃ N ₆ S·C ₃ H ₇ NO
<i>M_r</i>	498.82
Crystal system, space group	Triclinic, <i>P</i> $\bar{1}$
Temperature (K)	120
<i>a</i> , <i>b</i> , <i>c</i> (Å)	9.2934 (6), 10.968 (1), 11.7071 (10)
α , β , γ (°)	69.610 (8), 87.450 (6), 74.688 (6)
<i>V</i> (Å ³)	1077.34 (17)
<i>Z</i>	2
Radiation type	Mo <i>K</i> α
μ (mm ⁻¹)	0.55
Crystal size (mm)	0.32 × 0.21 × 0.07
Data collection	
Diffractometer	Bruker–Nonius KappaCCD area-detector diffractometer
Absorption correction	Multi-scan (<i>SADABS</i> ; Sheldrick, 2003)
<i>T_{min}</i> , <i>T_{max}</i>	0.884, 0.962
No. of measured, independent and observed [<i>I</i> > 2 σ (<i>I</i>)] reflections	23893, 4908, 3534
<i>R_{int}</i>	0.065
(<i>sin</i> θ / λ) _{max} (Å ⁻¹)	0.650
Refinement	
<i>R</i> [<i>F</i> ² > 2 σ (<i>F</i> ²)], <i>wR</i> (<i>F</i> ²), <i>S</i>	0.042, 0.090, 1.06
No. of reflections	4908
No. of parameters	282
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{\text{max}}$, $\Delta\rho_{\text{min}}$ (e Å ⁻³)	0.32, -0.42

Computer programs: *COLLECT* (Nonius, 1999), *DIRAX/LSQ* (Duisenberg *et al.*, 2000), *EVALCCD* (Duisenberg *et al.*, 2003), *SIR2004* (Burla *et al.*, 2005), *SHELXL97* (Sheldrick, 2008) and *PLATON* (Spek, 2009).

[1,4]diazepine, equimolar quantities (0.5 mmol of each) of 4,5,6-triaminopyrimidine dihydrochloride, (II) (see Scheme), and chalcone (III) were dissolved in methanol (10 ml), and the mixture was heated under reflux for 24 h. The resulting solution was allowed to cool to ambient temperature, and it was then neutralized with aqueous ammonia solution (6 *M*). The neutralized mixture was then extracted exhaustively with dichloromethane, the combined extracts were dried and the solvent was removed under reduced pressure. The compound was purified by column chromatography on silica using dichloromethane–methanol (30:1 *v/v*) as eluent (yield 68%; m.p. 511–513 K). MS (EI, 70 eV), *m/z* (%): 428/426/424 (10/29/30, *M*⁺), 391/389 (58/80), 247/245 (31/100), 218 (15), 149 (16). Analysis found: C 45.2, H 2.8, N 19.9%; C₁₆H₁₁Cl₃N₆S requires: C 45.1, H 2.6, N 19.7%. Slow evaporation, at ambient temperature and in air, of a solution in DMF gave pale-yellow crystals of the title solvate, (I), suitable for single-crystal X-ray diffraction.

2.2. Refinement

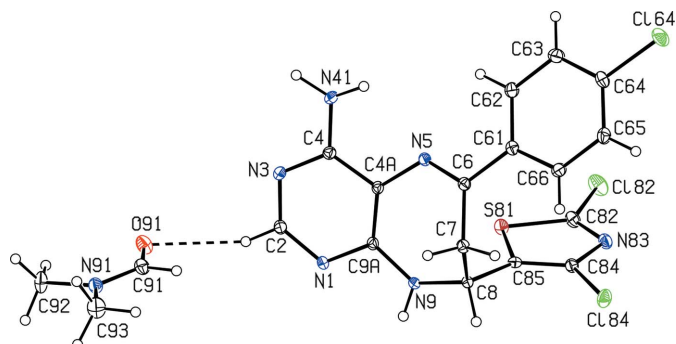
Crystal data, data collection and structure refinement details are summarized in Table 1. All H atoms were located in difference maps and then treated as riding atoms. C-bound H atoms were treated as riding in geometrically idealized positions, with C–H = 0.95 (aromatic, heteroaromatic and formyl), 0.98 (CH₃), 0.99 (CH₂) or 1.00 Å (aliphatic C–H), and with $U_{\text{iso}}(\text{H}) = kU_{\text{eq}}(\text{C})$, where $k = 1.5$ for the methyl groups, which were permitted to rotate but not to tilt, and 1.2

for all other C-bound H atoms. N-bound H atoms were permitted to ride at the positions located in difference maps, with $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{N})$, giving the N–H distances shown in Table 2. Six low-angle reflections (0 $\bar{1}$ 1, $\bar{1}$ 01, $\bar{1}$ 10, 111, $\bar{1}$ 11 and $\bar{1}$ 11), which had been totally or partially attenuated by the beam stop, were omitted from the final refinements. When the common site-occupancy factor for the atoms of the DMF component was permitted to vary, the refined value was 1.004 (4), confirming the full occupancy of the solvent site.

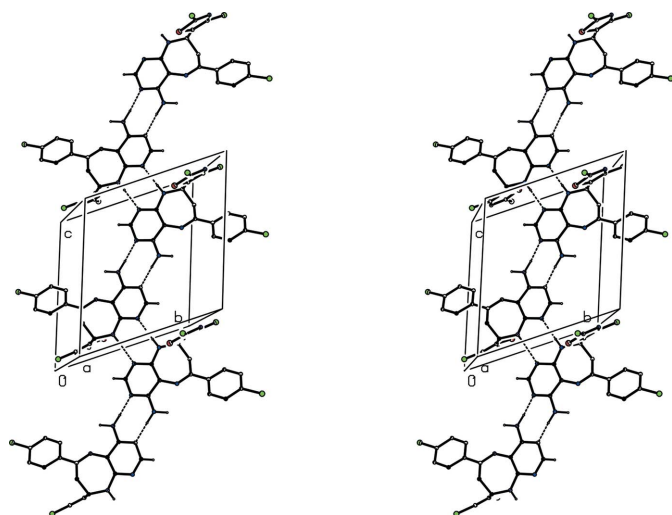
3. Results and discussion

The molecular constitution of the heterocyclic component confirms that the reaction between precursors (II) and (III) produces the fused diazepine (8*RS*)-4-amino-6-(4-chlorophenyl)-8-(2,4-dichlorothiazol-5-yl)-8,9-dihydro-7*H*-pyrimido[4,5-*b*][1,4]diazepine, as shown in the Scheme as a component of compound (I), rather than the alternative isomer (IV). The heterocyclic component of (I) contains a stereogenic centre at atom C8, and the reference molecule was selected to be one having the *R* configuration at atom C8. However, the centrosymmetric space group confirms that the compound crystallizes as a racemic mixture. In addition, the asymmetric unit was selected such that the two molecular components were linked within the asymmetric unit by the shorter of the two C–H···O hydrogen bonds (Table 2).

The diazepine ring of (I) adopts a conformation close to the twist-boat form (Evans & Boeyens, 1989), with ring-puckering parameters (Cremer & Pople, 1975) calculated for the atom sequence N5–C4a–C9a–N9–C8–C7–C6 of $Q = 0.739$ (2) Å, $\varphi_2 = 12.8$ (2)° and $\varphi_3 = 117.3$ (4)°. On the other hand, the pyrimidine ring is effectively planar, with a maximum deviation from the mean plane of the six ring atoms of 0.031 (3) Å for atom C4. This contrasts with the behaviour often observed in highly substituted pyrimidines, particularly in those having three adjacent substituents at positions 4, 5 and 6, where markedly nonplanar ring conformations are often adopted, with boat forms most commonly observed (Melguizo *et al.*, 2003; Quesada *et al.*, 2004; Cobo *et al.*, 2008). The geometry at amino atom N41 is slightly pyramidal, with a sum of the interbond angles of 353.7°, but, despite this slightly pyramidal

**Figure 1**

The molecular components of (I), showing the atom-labelling scheme and the C–H···O hydrogen bond (dashed line) within the selected asymmetric unit. Displacement ellipsoids are drawn at the 30% probability level.


Figure 2

A stereoview of part of the crystal structure of (I), showing the formation of a chain of centrosymmetric $R_2^2(8)$ rings running parallel to the [001] direction. Hydrogen bonds are shown as dashed lines. For the sake of clarity, the DMF solvent molecules and H atoms bonded to C atoms have been omitted.

geometry, atom N41 does not act as an acceptor of hydrogen bonds. The closest H atom which might participate in an intermolecular interaction with atom N41 is atom H65 at $(-x + 1, -y + 2, -z + 1)$, at a distance of 3.10 Å, far too long to be regarded as structurally significant. The bond distances present no unusual features.

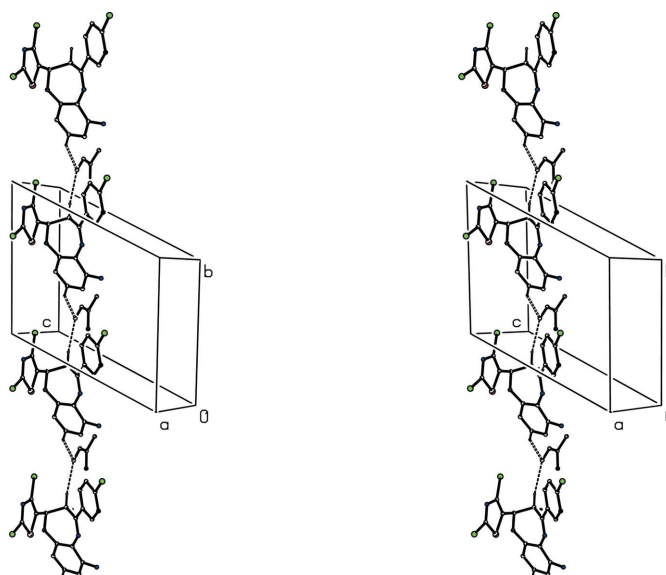
The heterocyclic component of (I) participates in two intermolecular N—H...N hydrogen bonds (Table 2), which lead to the formation of a chain of centrosymmetric $R_2^2(8)$ (Bernstein *et al.*, 1995) rings running parallel to the [001] direction (Fig. 2). The rings containing inversion-related pairs of atoms N1 as hydrogen-bond acceptors are centred at $(\frac{1}{2}, \frac{1}{2}, n)$, while those containing inversion-related pairs of atoms N3 as hydrogen-bond acceptors are centred at $(\frac{1}{2}, \frac{1}{2}, \frac{1}{2} + n)$, where n represents an integer in both cases. The formation of this chain of rings utilizes only two of the three available N—H bonds. The third bond of this type does not participate in the formation of intermolecular hydrogen bonds, but merely forms a rather short intramolecular contact to atom N5, which likewise does not participate in any intermolecular hydrogen bonds. The N—H...N angle associated with this intra-

Table 2

Hydrogen-bond geometry (Å, °).

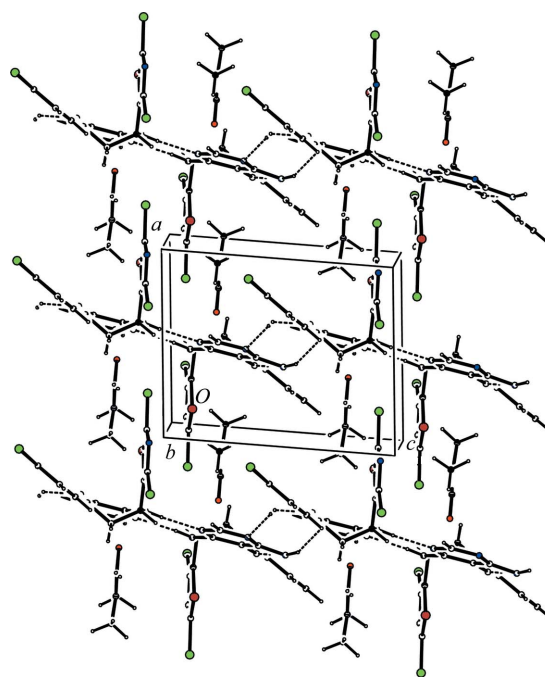
$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
N9—H9...N1 ⁱ	0.86	2.07	2.924 (3)	176
N41—H41A...N3 ⁱⁱ	0.99	2.09	3.024 (3)	156
N41—H41B...N5	0.98	2.26	2.689 (3)	105
C2—H2...O91	0.95	2.41	3.265 (3)	149
C7—H7B...O91 ⁱⁱⁱ	0.99	2.57	3.497 (3)	156
C8—H8...Cl84 ^{iv}	1.00	2.81	3.756 (3)	158
C62—H62...N5	0.95	2.44	2.763 (3)	100
C92—H92A...O91	0.98	2.39	2.809 (4)	105

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


Figure 3

A stereoview of part of the crystal structure of (I), showing the formation of a $C_2^1(9)$ chain running parallel to the [010] direction. Hydrogen bonds are shown as dashed lines. For the sake of clarity, H atoms not involved in the motif shown have been omitted.

molecular contact is only 105° (Table 2), so this contact cannot be regarded as having any structural significance (*cf.* Wood *et al.*, 2009). Thus, the only acceptors in the N—H...N hydrogen bonds are the two N atoms of the pyrimidine ring, and none of the other N atoms present acts as a hydrogen-bond acceptor.


Figure 4

Part of the crystal structure of (I), viewed approximately along the [010] direction, showing the location of the DMF components between the chains of rings parallel to [001]. Hydrogen bonds are shown as dashed lines.

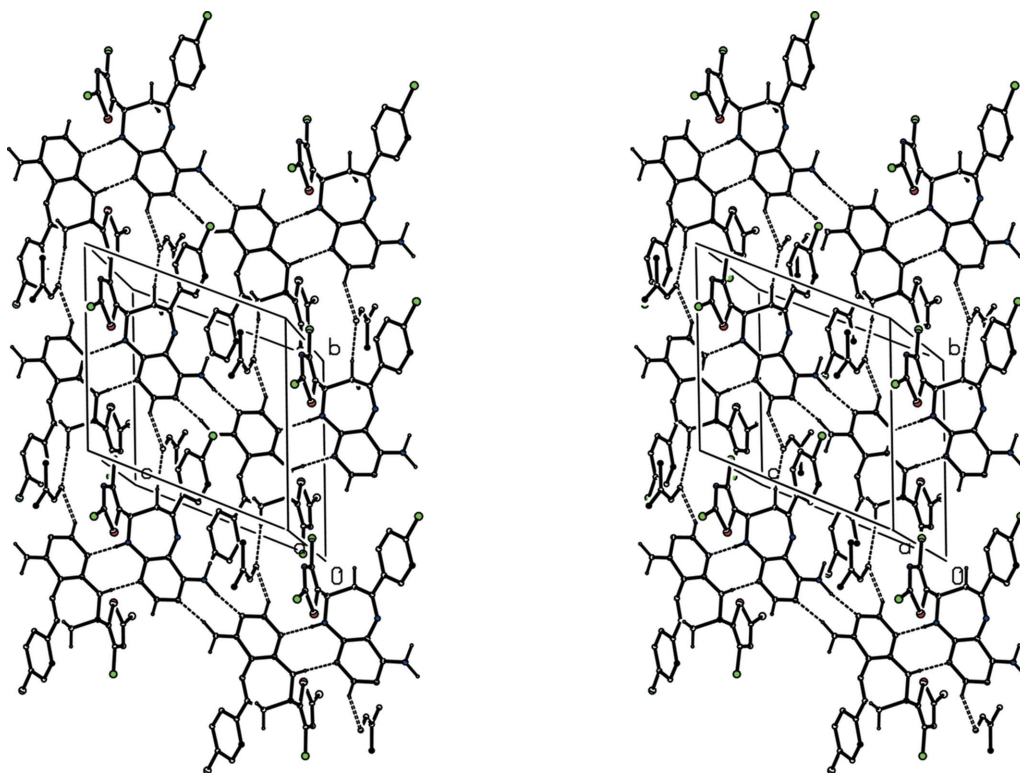


Figure 5

A stereoview of part of the crystal structure of (I), showing the formation of a sheet parallel to (100) containing four types of hydrogen-bonded ring. Hydrogen bonds are shown as dashed lines. For the sake of clarity, H atoms bonded to the C atoms which are not involved in the motifs shown have been omitted.

One chain of $R_2^2(8)$ rings passes through each unit cell, but chains of this type which are related by translation along the [010] direction are linked by means of two C—H \cdots O hydrogen bonds involving the O atom of the DMF component as a double acceptor (Table 2). These two hydrogen bonds generate a $C_2^1(9)$ chain running parallel to the [010] direction (Fig. 3), such that the DMF components lie between the chains of rings (Fig. 4). The combination of the chains along [010] and [001] generates a sheet lying parallel to (100) (Fig. 5) in which rings of types $R_5^4(18)$ and $R_6^4(24)$ can be identified, in addition to the two types of $R_2^2(8)$ ring discussed above.

There are a number of other short intra- and intermolecular contacts within the crystal structure of (I) (Table 2). However, those involving atoms C62 and C92 both have very small D—H \cdots A angles and so are unlikely to have any structural significance (Wood *et al.*, 2009). In addition, the contact involving atom C92 lies wholly within the DMF component, while the C92—H92A bond forms part of a methyl group which is likely to be undergoing very rapid rotation about the adjacent C—N bond, even in the solid state at low temperature (Riddell & Rogerson, 1996, 1997). The C—H \cdots Cl contact involving atom C8 has an H \cdots Cl distance which is only slightly less than the sum of the van der Waals radii of 2.84 Å (Bondi, 1964; Rowland & Taylor, 1996) and, in addition, it is well established (Brammer *et al.*, 2001; Thallypally & Nangia, 2001) that Cl atoms bonded to C atoms are extremely poor acceptors of hydrogen bonds, even from good donors

such as N and O atoms; hence, this contact is unlikely to have any structural significance. There are no intermolecular Cl \cdots Cl contact distances within the sum of the van der Waals radii (3.50 Å; Bondi, 1964; Rowland & Taylor, 1996).

Chains of $R_2^2(8)$ rings are a common hydrogen-bonding motif in aminopyrimidines (Rodríguez *et al.*, 2008), but disruption of such chain formation can result either from steric hindrance arising from bulky substituents or from the presence of an alternative hydrogen-bond acceptor which effectively competes with the pyrimidine ring N atoms. In the first of these circumstances, the supramolecular aggregation may be restricted to the formation of a simple dimer (Quesada *et al.*, 2004), or to the formation of a linear tetramer (Bowes *et al.*, 2003) where each of these aggregates can be regarded as a short fragment of a continuous chain. In the presence of alternative hydrogen-bond acceptors, such as O atoms, chains containing combinations of $R_2^2(8)$ and $R_4^4(16)$ rings (Quesada *et al.*, 2002), or $R_2^2(8)$ and $R_4^4(18)$ rings (Bowes *et al.*, 2003), and sheets containing $R_2^2(8)$ and $R_6^6(40)$ rings (Bowes *et al.*, 2003), have all been observed. In every case, the $R_2^2(8)$ motif is present, as in (I) described here, but different additional ring motifs always occur in the presence of hydrogen-bond acceptors other than the N atoms of pyrimidine rings.

The authors thank the Centro de Instrumentación Científico-Técnica of the Universidad de Jaén and the staff for the data collection. Financial support from COLCIENCIAS, the

Universidad del Valle, the Consejería de Economía, Innovación, Ciencia y Empleo (Junta de Andalucía, Spain) and the Universidad de Jaén is gratefully acknowledged.

Supporting information for this paper is available from the IUCr electronic archives (Reference: SF3229).

References

- Bernstein, J., Davis, R. E., Shimon, L. & Chang, N.-L. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 1555–1573.
- Bondi, A. (1964). *J. Phys. Chem.* **68**, 441–452.
- Bowes, K. F., Glidewell, C., Low, J. N., Melguizo, M. & Quesada, A. (2003). *Acta Cryst.* **C59**, o4–o8.
- Brammer, L., Bruton, E. A. & Sherwood, P. (2001). *Cryst. Growth Des.* **1**, 277–290.
- 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., Trilleras, J., Quiroga, J., Marchal, A., Nogueras, M., Low, J. N. & Glidewell, C. (2008). *Acta Cryst.* **B64**, 596–609.
- Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.
- Deng, X., Elkins, J. M., Zhang, J., Yang, Q., Erazo, T., Gomez, N., Choi, H. G., Wang, J., Dzamko, N., Lee, J.-D., Sim, T. & Kim, N. (2013). *Eur. J. Med. Chem.* **70**, 758–767.
- 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.
- Evans, D. G. & Boeyens, J. C. A. (1989). *Acta Cryst.* **B45**, 581–590.
- Fader, L. D. *et al.* (2011). *Bioorg. Med. Chem. Lett.* **21**, 398–404.
- Fader, L. D. *et al.* (2013). *Bioorg. Med. Chem. Lett.* **23**, 3401–3405.
- Insuasty, B., García, A., Quiroga, J., Abonía, R., Nogueras, M. & Cobo, J. (2010). *Eur. J. Med. Chem.* **45**, 2841–2846.
- Insuasty, B., Orozco, F., Lizarazo, C., Quiroga, J., Abonía, R., Hursthouse, M., Nogueras, M. & Cobo, J. (2008). *Bioorg. Med. Chem.* **16**, 8492–8500.
- Insuasty, B., Orozco, F., Quiroga, J., Abonía, R., Nogueras, M. & Cobo, J. (2008). *Eur. J. Med. Chem.* **43**, 1955–1962.
- Melguizo, M., Quesada, A., Low, J. N. & Glidewell, C. (2003). *Acta Cryst.* **B59**, 263–276.
- Nonius (1999). *COLLECT*. Nonius BV, Delft, The Netherlands.
- Parmar, N. J., Barad, H. A., Pansuriya, B. R., Teraiya, S. B., Gupta, V. K. & Kant, R. (2012). *Bioorg. Med. Chem. Lett.* **22**, 3816–3821.
- Quesada, A., Marchal, A., Melguizo, M., Low, J. N. & Glidewell, C. (2004). *Acta Cryst.* **B60**, 76–89.
- Quesada, A., Marchal, A., Melguizo, M., Nogueras, M., Sánchez, A., Low, J. N., Cannon, D., Farrell, D. M. M. & Glidewell, C. (2002). *Acta Cryst.* **B58**, 300–315.
- Riddell, F. G. & Rogerson, M. (1996). *J. Chem. Soc. Perkin Trans. 2*, pp. 493–504.
- Riddell, F. G. & Rogerson, M. (1997). *J. Chem. Soc. Perkin Trans. 2*, pp. 249–256.
- Rodríguez, R., Nogueras, M., Cobo, J., Low, J. N. & Glidewell, C. (2008). *Acta Cryst.* **C64**, o376–o378.
- Rowland, R. S. & Taylor, R. (1996). *J. Phys. Chem.* **100**, 7384–7391.
- Sheldrick, G. M. (2003). *SADABS*. University of Göttingen, Germany.
- Sheldrick, G. M. (2008). *Acta Cryst.* **A64**, 112–122.
- Smith, L. *et al.* (2006). *Bioorg. Med. Chem. Lett.* **16**, 5102–5106.
- Spek, A. L. (2009). *Acta Cryst.* **D65**, 148–155.
- Sternbach, L. H. (1971). *Angew. Chem. Int. Ed. Engl.* **10**, 34–43.
- Thallypally, P. K. & Nangia, A. (2001). *CrystEngComm*, **3**, 114–119.
- Wood, P. A., Allen, F. H. & Pidcock, E. (2009). *CrystEngComm*, **11**, 1563–1571.

supplementary materials

Acta Cryst. (2014). **C70**, 536-540 [doi:10.1107/S2053229614008936]

(8*RS*)-4-Amino-6-(4-chlorophenyl)-8-(2,4-dichlorothiazol-5-yl)-8,9-dihydro-7*H*-pyrimido[4,5-*b*][1,4]diazepine *N,N*-dimethylformamide monosolvate: sheets built from N—H⋯N and C—H⋯O hydrogen bonds

Juan Ramírez, Braulio Insuasty, Justo Cobo and Christopher Glidewell

Computing details

Data collection: *COLLECT* (Nonius, 1999); cell refinement: *DIRAX/LSQ* (Duisenberg *et al.*, 2000); data reduction: *EVALLCCD* (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* (Sheldrick, 2008) and *PLATON* (Spek, 2009).

(8*RS*)-4-Amino-6-(4-chlorophenyl)-8-(2,4-dichlorothiazol-5-yl)-8,9-dihydro-7*H*-pyrimido[4,5-*b*][1,4]diazepine *N,N*-dimethylformamide monosolvate

Crystal data

$C_{16}H_{11}Cl_3N_6S \cdot C_3H_7NO$
 $M_r = 498.82$
 Triclinic, $P\bar{1}$
 Hall symbol: -P 1
 $a = 9.2934$ (6) Å
 $b = 10.968$ (1) Å
 $c = 11.7071$ (10) Å
 $\alpha = 69.610$ (8)°
 $\beta = 87.450$ (6)°
 $\gamma = 74.688$ (6)°
 $V = 1077.34$ (17) Å³

$Z = 2$
 $F(000) = 512$
 $D_x = 1.538$ Mg m⁻³
 Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
 Cell parameters from 4914 reflections
 $\theta = 2.9$ – 27.5 °
 $\mu = 0.55$ mm⁻¹
 $T = 120$ K
 Plate, pale yellow
 $0.32 \times 0.21 \times 0.07$ mm

Data collection

Bruker Nonius KappaCCD area-detector diffractometer
 Radiation source: Bruker Nonius FR591 rotating anode
 Graphite monochromator
 Detector resolution: 9.091 pixels mm⁻¹
 φ and ω scans
 Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)

$T_{\min} = 0.884$, $T_{\max} = 0.962$
 23893 measured reflections
 4908 independent reflections
 3534 reflections with $I > 2\sigma(I)$
 $R_{\text{int}} = 0.065$
 $\theta_{\max} = 27.5$ °, $\theta_{\min} = 3.0$ °
 $h = -11 \rightarrow 12$
 $k = -14 \rightarrow 14$
 $l = -15 \rightarrow 15$

Refinement

Refinement on F^2

Least-squares matrix: full

$R[F^2 > 2\sigma(F^2)] = 0.042$

$wR(F^2) = 0.090$

$S = 1.06$

4908 reflections

282 parameters

0 restraints

Primary atom site location: structure-invariant
direct methods

Secondary atom site location: difference Fourier
map

Hydrogen site location: inferred from
neighbouring sites

H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.0223P)^2 + 1.1607P]$

where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{\max} = 0.001$

$\Delta\rho_{\max} = 0.32 \text{ e } \text{\AA}^{-3}$

$\Delta\rho_{\min} = -0.42 \text{ e } \text{\AA}^{-3}$

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (\AA^2)

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
N1	0.5182 (2)	0.48915 (19)	0.85559 (17)	0.0162 (4)
C2	0.5061 (3)	0.4323 (2)	0.7753 (2)	0.0179 (5)
H2	0.4724	0.3528	0.8052	0.021*
N3	0.5353 (2)	0.47220 (19)	0.65761 (18)	0.0187 (4)
C4	0.5846 (3)	0.5849 (2)	0.6165 (2)	0.0165 (5)
C4a	0.5935 (3)	0.6615 (2)	0.6908 (2)	0.0146 (4)
N5	0.6443 (2)	0.77628 (19)	0.63120 (17)	0.0163 (4)
C6	0.6114 (3)	0.8819 (2)	0.6622 (2)	0.0157 (5)
C7	0.5115 (3)	0.8931 (2)	0.7653 (2)	0.0168 (5)
H7A	0.4150	0.8776	0.7506	0.020*
H7B	0.4913	0.9854	0.7678	0.020*
C8	0.5844 (3)	0.7896 (2)	0.8893 (2)	0.0149 (4)
H8	0.5269	0.8166	0.9548	0.018*
N9	0.5744 (2)	0.65510 (18)	0.90431 (17)	0.0159 (4)
H9	0.5427	0.6131	0.9731	0.019*
C9a	0.5616 (2)	0.6067 (2)	0.8136 (2)	0.0147 (4)
N41	0.6270 (2)	0.6210 (2)	0.50087 (18)	0.0209 (4)
H41A	0.6028	0.5786	0.4448	0.025*
H41B	0.6364	0.7137	0.4674	0.025*
C61	0.6783 (3)	0.9934 (2)	0.5919 (2)	0.0170 (5)
C62	0.7680 (3)	0.9815 (2)	0.4950 (2)	0.0219 (5)
H62	0.7829	0.9033	0.4736	0.026*
C63	0.8352 (3)	1.0813 (2)	0.4300 (2)	0.0257 (6)
H63	0.8956	1.0723	0.3643	0.031*
C64	0.8131 (3)	1.1952 (2)	0.4624 (2)	0.0220 (5)
Cl64	0.90541 (9)	1.31785 (7)	0.38615 (7)	0.03536 (18)
C65	0.7248 (3)	1.2111 (2)	0.5555 (2)	0.0226 (5)
H65	0.7104	1.2899	0.5760	0.027*
C66	0.6563 (3)	1.1109 (2)	0.6199 (2)	0.0208 (5)
H66	0.5937	1.1222	0.6838	0.025*
S81	0.89137 (7)	0.66025 (6)	0.89844 (6)	0.02024 (14)
C82	1.0130 (3)	0.7462 (2)	0.9184 (2)	0.0219 (5)
N83	0.9541 (2)	0.8612 (2)	0.93179 (19)	0.0210 (4)
C84	0.8012 (3)	0.8852 (2)	0.9247 (2)	0.0178 (5)
C85	0.7439 (3)	0.7908 (2)	0.9062 (2)	0.0151 (5)

Cl82	1.20168 (7)	0.67929 (7)	0.92165 (7)	0.03491 (17)
Cl84	0.69444 (7)	1.03173 (6)	0.94045 (6)	0.02664 (15)
N91	0.0742 (2)	0.2713 (2)	0.76010 (19)	0.0215 (4)
C91	0.2073 (3)	0.2935 (2)	0.7662 (2)	0.0244 (5)
H91	0.2080	0.3804	0.7652	0.029*
O91	0.3290 (2)	0.21251 (17)	0.77315 (18)	0.0285 (4)
C92	0.0625 (3)	0.1403 (3)	0.7639 (3)	0.0323 (6)
H92A	0.1628	0.0793	0.7717	0.048*
H92B	0.0109	0.1506	0.6885	0.048*
H92C	0.0059	0.1026	0.8339	0.048*
C93	-0.0644 (3)	0.3766 (3)	0.7439 (3)	0.0350 (7)
H93A	-0.0434	0.4560	0.7525	0.053*
H93B	-0.1331	0.3437	0.8058	0.053*
H93C	-0.1102	0.4011	0.6624	0.053*

Atomic displacement parameters (\AA^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
N1	0.0165 (10)	0.0174 (9)	0.0169 (10)	-0.0083 (8)	0.0023 (8)	-0.0061 (8)
C2	0.0176 (12)	0.0178 (11)	0.0198 (12)	-0.0068 (9)	0.0017 (9)	-0.0070 (10)
N3	0.0235 (11)	0.0192 (10)	0.0169 (10)	-0.0088 (8)	0.0025 (8)	-0.0087 (8)
C4	0.0152 (11)	0.0176 (11)	0.0173 (11)	-0.0038 (9)	0.0014 (9)	-0.0075 (9)
C4a	0.0147 (11)	0.0154 (10)	0.0145 (11)	-0.0049 (9)	-0.0008 (9)	-0.0052 (9)
N5	0.0177 (10)	0.0170 (9)	0.0151 (9)	-0.0073 (8)	0.0006 (8)	-0.0046 (8)
C6	0.0142 (11)	0.0175 (11)	0.0148 (11)	-0.0048 (9)	-0.0013 (9)	-0.0043 (9)
C7	0.0159 (12)	0.0156 (11)	0.0189 (11)	-0.0041 (9)	0.0013 (9)	-0.0062 (9)
C8	0.0150 (11)	0.0160 (10)	0.0163 (11)	-0.0066 (9)	0.0033 (9)	-0.0074 (9)
N9	0.0199 (10)	0.0172 (9)	0.0132 (9)	-0.0098 (8)	0.0038 (8)	-0.0052 (8)
C9a	0.0117 (11)	0.0167 (11)	0.0177 (11)	-0.0048 (9)	0.0010 (9)	-0.0077 (9)
N41	0.0300 (12)	0.0227 (10)	0.0152 (10)	-0.0120 (9)	0.0041 (9)	-0.0095 (8)
C61	0.0159 (12)	0.0163 (11)	0.0175 (11)	-0.0042 (9)	-0.0016 (9)	-0.0040 (9)
C62	0.0285 (14)	0.0158 (11)	0.0227 (12)	-0.0079 (10)	0.0035 (11)	-0.0070 (10)
C63	0.0321 (15)	0.0236 (12)	0.0231 (13)	-0.0107 (11)	0.0091 (11)	-0.0088 (11)
C64	0.0226 (13)	0.0171 (11)	0.0248 (13)	-0.0083 (10)	0.0013 (10)	-0.0031 (10)
Cl64	0.0460 (4)	0.0246 (3)	0.0392 (4)	-0.0209 (3)	0.0158 (3)	-0.0088 (3)
C65	0.0259 (14)	0.0185 (11)	0.0254 (13)	-0.0083 (10)	0.0005 (11)	-0.0083 (10)
C66	0.0253 (13)	0.0199 (12)	0.0184 (12)	-0.0069 (10)	0.0026 (10)	-0.0078 (10)
S81	0.0156 (3)	0.0179 (3)	0.0274 (3)	-0.0032 (2)	0.0014 (2)	-0.0091 (2)
C82	0.0154 (12)	0.0229 (12)	0.0251 (13)	-0.0054 (10)	-0.0011 (10)	-0.0050 (10)
N83	0.0193 (11)	0.0237 (10)	0.0206 (10)	-0.0099 (8)	-0.0001 (8)	-0.0053 (9)
C84	0.0177 (12)	0.0169 (11)	0.0196 (12)	-0.0056 (9)	0.0020 (9)	-0.0067 (9)
C85	0.0152 (11)	0.0162 (10)	0.0133 (11)	-0.0033 (9)	0.0031 (9)	-0.0051 (9)
Cl82	0.0139 (3)	0.0363 (4)	0.0479 (4)	-0.0036 (3)	0.0003 (3)	-0.0088 (3)
Cl84	0.0276 (3)	0.0211 (3)	0.0365 (4)	-0.0056 (2)	0.0017 (3)	-0.0170 (3)
N91	0.0208 (11)	0.0197 (10)	0.0254 (11)	-0.0068 (8)	0.0026 (9)	-0.0088 (9)
C91	0.0294 (15)	0.0199 (12)	0.0253 (13)	-0.0107 (11)	0.0050 (11)	-0.0067 (11)
O91	0.0219 (10)	0.0242 (9)	0.0379 (11)	-0.0073 (8)	0.0044 (8)	-0.0085 (8)
C92	0.0330 (16)	0.0263 (13)	0.0448 (17)	-0.0139 (12)	-0.0021 (13)	-0.0164 (13)
C93	0.0248 (15)	0.0314 (15)	0.0496 (18)	-0.0031 (12)	0.0020 (13)	-0.0183 (14)

Geometric parameters (Å, °)

N1—C2	1.319 (3)	C63—C64	1.390 (3)
N1—C9a	1.372 (3)	C63—H63	0.9500
C2—N3	1.332 (3)	C64—C65	1.368 (4)
C2—H2	0.9500	C64—Cl64	1.745 (2)
N3—C4	1.354 (3)	C65—C66	1.390 (3)
C4—N41	1.344 (3)	C65—H65	0.9500
C4—C4a	1.422 (3)	C66—H66	0.9500
C4a—N5	1.402 (3)	S81—C82	1.721 (3)
C4a—C9a	1.403 (3)	S81—C85	1.727 (2)
N5—C6	1.289 (3)	C82—N83	1.296 (3)
C6—C61	1.489 (3)	C82—Cl82	1.709 (3)
C6—C7	1.509 (3)	N83—C84	1.376 (3)
C7—C8	1.545 (3)	C84—C85	1.363 (3)
C7—H7A	0.9900	C84—Cl84	1.718 (2)
C7—H7B	0.9900	N91—C91	1.333 (3)
C8—N9	1.452 (3)	N91—C93	1.453 (3)
C8—C85	1.508 (3)	N91—C92	1.455 (3)
C8—H8	1.0000	C91—O91	1.226 (3)
N9—C9a	1.364 (3)	C91—H91	0.9500
N9—H9	0.8600	C92—H92A	0.9800
N41—H41A	0.9896	C92—H92B	0.9800
N41—H41B	0.9805	C92—H92C	0.9800
C61—C66	1.399 (3)	C93—H93A	0.9800
C61—C62	1.401 (3)	C93—H93B	0.9800
C62—C63	1.380 (3)	C93—H93C	0.9800
C62—H62	0.9500		
C2—N1—C9a	117.0 (2)	C62—C63—C64	118.9 (2)
N1—C2—N3	128.1 (2)	C62—C63—H63	120.5
N1—C2—H2	115.9	C64—C63—H63	120.5
N3—C2—H2	115.9	C65—C64—C63	121.5 (2)
C2—N3—C4	115.25 (19)	C65—C64—Cl64	119.13 (19)
N41—C4—N3	116.5 (2)	C63—C64—Cl64	119.3 (2)
N41—C4—C4a	120.9 (2)	C64—C65—C66	119.3 (2)
N3—C4—C4a	122.6 (2)	C64—C65—H65	120.4
N5—C4a—C9a	129.7 (2)	C66—C65—H65	120.4
N5—C4a—C4	114.1 (2)	C65—C66—C61	121.0 (2)
C9a—C4a—C4	116.0 (2)	C65—C66—H66	119.5
C6—N5—C4a	123.5 (2)	C61—C66—H66	119.5
N5—C6—C61	116.8 (2)	C82—S81—C85	89.12 (11)
N5—C6—C7	122.4 (2)	N83—C82—Cl82	122.87 (19)
C61—C6—C7	120.87 (19)	N83—C82—S81	116.73 (19)
C6—C7—C8	111.26 (18)	Cl82—C82—S81	120.40 (14)
C6—C7—H7A	109.4	C82—N83—C84	108.1 (2)
C8—C7—H7A	109.4	C85—C84—N83	118.0 (2)
C6—C7—H7B	109.4	C85—C84—Cl84	124.08 (19)
C8—C7—H7B	109.4	N83—C84—Cl84	117.93 (17)
H7A—C7—H7B	108.0	C84—C85—C8	130.8 (2)

N9—C8—C85	111.20 (18)	C84—C85—S81	108.02 (17)
N9—C8—C7	111.28 (18)	C8—C85—S81	121.12 (16)
C85—C8—C7	111.74 (18)	C91—N91—C93	122.2 (2)
N9—C8—H8	107.5	C91—N91—C92	120.6 (2)
C85—C8—H8	107.5	C93—N91—C92	117.1 (2)
C7—C8—H8	107.5	O91—C91—N91	126.2 (2)
C9a—N9—C8	126.71 (19)	O91—C91—H91	116.9
C9a—N9—H9	114.6	N91—C91—H91	116.9
C8—N9—H9	115.0	N91—C92—H92A	109.5
N9—C9a—N1	112.26 (19)	N91—C92—H92B	109.5
N9—C9a—C4a	126.9 (2)	H92A—C92—H92B	109.5
N1—C9a—C4a	120.8 (2)	N91—C92—H92C	109.5
C4—N41—H41A	120.5	H92A—C92—H92C	109.5
C4—N41—H41B	114.0	H92B—C92—H92C	109.5
H41A—N41—H41B	119.2	N91—C93—H93A	109.5
C66—C61—C62	118.1 (2)	N91—C93—H93B	109.5
C66—C61—C6	122.3 (2)	H93A—C93—H93B	109.5
C62—C61—C6	119.7 (2)	N91—C93—H93C	109.5
C63—C62—C61	121.2 (2)	H93A—C93—H93C	109.5
C63—C62—H62	119.4	H93B—C93—H93C	109.5
C61—C62—H62	119.4		
C9a—N1—C2—N3	2.3 (4)	C7—C6—C61—C62	-178.6 (2)
N1—C2—N3—C4	0.6 (4)	C66—C61—C62—C63	1.2 (4)
C2—N3—C4—N41	174.5 (2)	C6—C61—C62—C63	-178.2 (2)
C2—N3—C4—C4a	-4.8 (3)	C61—C62—C63—C64	0.2 (4)
N41—C4—C4a—N5	2.0 (3)	C62—C63—C64—C65	-1.0 (4)
N3—C4—C4a—N5	-178.7 (2)	C62—C63—C64—Cl64	176.7 (2)
N41—C4—C4a—C9a	-173.4 (2)	C63—C64—C65—C66	0.4 (4)
N3—C4—C4a—C9a	5.9 (3)	Cl64—C64—C65—C66	-177.22 (19)
C9a—C4a—N5—C6	-31.3 (4)	C64—C65—C66—C61	1.0 (4)
C4—C4a—N5—C6	154.0 (2)	C62—C61—C66—C65	-1.7 (4)
C4a—N5—C6—C61	178.1 (2)	C6—C61—C66—C65	177.6 (2)
C4a—N5—C6—C7	-1.2 (3)	C85—S81—C82—N83	0.9 (2)
N5—C6—C7—C8	65.5 (3)	C85—S81—C82—Cl82	-179.79 (17)
C61—C6—C7—C8	-113.8 (2)	Cl82—C82—N83—C84	-179.93 (18)
C6—C7—C8—N9	-76.7 (2)	S81—C82—N83—C84	-0.6 (3)
C6—C7—C8—C85	48.3 (2)	C82—N83—C84—C85	-0.1 (3)
C85—C8—N9—C9a	-100.0 (3)	C82—N83—C84—Cl84	179.64 (18)
C7—C8—N9—C9a	25.2 (3)	N83—C84—C85—C8	-177.2 (2)
C8—N9—C9a—N1	-165.0 (2)	Cl84—C84—C85—C8	3.1 (4)
C8—N9—C9a—C4a	17.7 (4)	N83—C84—C85—S81	0.7 (3)
C2—N1—C9a—N9	-178.4 (2)	Cl84—C84—C85—S81	-178.99 (14)
C2—N1—C9a—C4a	-0.9 (3)	N9—C8—C85—C84	-164.9 (2)
N5—C4a—C9a—N9	-0.3 (4)	C7—C8—C85—C84	70.1 (3)
C4—C4a—C9a—N9	174.3 (2)	N9—C8—C85—S81	17.4 (3)
N5—C4a—C9a—N1	-177.4 (2)	C7—C8—C85—S81	-107.63 (19)
C4—C4a—C9a—N1	-2.8 (3)	C82—S81—C85—C84	-0.82 (18)
N5—C6—C61—C66	-177.3 (2)	C82—S81—C85—C8	177.33 (19)

C7—C6—C61—C66	2.0 (3)	C93—N91—C91—O91	-175.8 (3)
N5—C6—C61—C62	2.0 (3)	C92—N91—C91—O91	1.3 (4)

Hydrogen-bond geometry (Å, °)

<i>D—H...A</i>	<i>D—H</i>	<i>H...A</i>	<i>D...A</i>	<i>D—H...A</i>
N9—H9...N1 ⁱ	0.86	2.07	2.924 (3)	176
N41—H41A...N3 ⁱⁱ	0.99	2.09	3.024 (3)	156
N41—H41B...N5	0.98	2.26	2.689 (3)	105
C2—H2...O91	0.95	2.41	3.265 (3)	149
C7—H7B...O91 ⁱⁱⁱ	0.99	2.57	3.497 (3)	156
C8—H8...C184 ^{iv}	1.00	2.81	3.756 (3)	158
C62—H62...N5	0.95	2.44	2.763 (3)	100
C92—H92A...O91	0.98	2.39	2.809 (4)	105

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