

## 2-Amino-4-(piperidin-1-yl)-11*H*-pyrimido[4,5-*b*][1,5]benzodiazepin-6-ium chloride monohydrate and 2-amino-4-[methyl(2-methylphenyl)amino]-11*H*-pyrimido[4,5-*b*][1,5]benzodiazepin-6-ium chloride–benzene-1,2-diamine (1/1): complex sheets generated by multiple hydrogen bonds

Jairo Quiroga,<sup>a</sup> Jorge Trilleras,<sup>b</sup> Justo Cobo<sup>c</sup> and Christopher Glidewell<sup>d\*</sup>

<sup>a</sup>Departamento de Química, Universidad de Valle, AA 25360 Cali, Colombia,

<sup>b</sup>Departamento de Química, Universidad del Atlántico, Km 7 vía antigua Puerto Colombia, Barranquilla, Colombia,

<sup>c</sup>Departamento de Química Inorgánica y

Orgánica, Universidad de Jaén, 23071 Jaén, Spain, and

<sup>d</sup>School of Chemistry, University of St Andrews, Fife KY16 9ST, Scotland

Correspondence e-mail: cg@st-andrews.ac.uk

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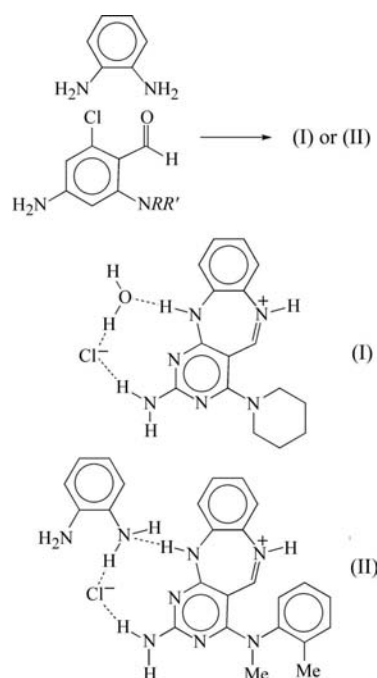
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In each of 2-amino-4-(piperidin-1-yl)-11*H*-pyrimido[4,5-*b*][1,5]benzodiazepin-6-ium chloride monohydrate, C<sub>16</sub>H<sub>19</sub>N<sub>6</sub><sup>+</sup>·Cl<sup>−</sup>·H<sub>2</sub>O, (I), and 2-amino-4-[methyl(2-methylphenyl)amino]-11*H*-pyrimido[4,5-*b*][1,5]benzodiazepin-6-ium chloride–benzene-1,2-diamine (1/1), C<sub>19</sub>H<sub>19</sub>N<sub>6</sub><sup>+</sup>·Cl<sup>−</sup>·C<sub>6</sub>H<sub>8</sub>N<sub>2</sub>, (II), the seven-membered ring in the cation adopts a boat conformation. The pyrimidine ring in (II) adopts a twist-boat conformation, but the corresponding ring in (I) is essentially planar. The amino groups of the benzene-1,2-diamine component of (II) are both pyramidal. The independent components of (I) are linked into complex sheets by a combination of N–H···O, N–H···N, N–H···Cl and O–H···Cl hydrogen bonds. In the crystal structure of (II), one N–H···N hydrogen bond and six independent N–H···Cl hydrogen bonds combine to link the components into complex sheets.

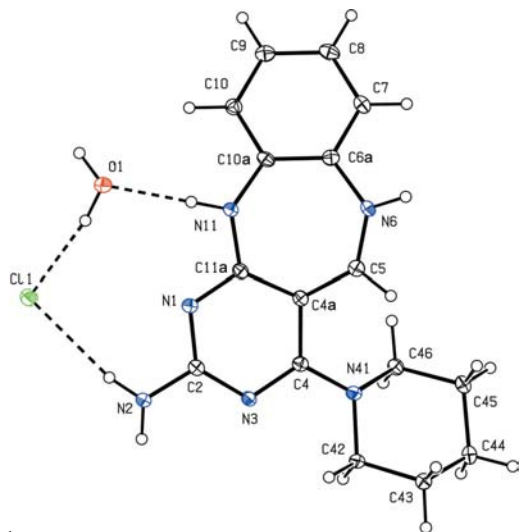
### Comment

Pyrimidine-fused compounds belong to the so-called bicyclic privileged structures, which may be useful in the field of medicinal chemistry (Horton *et al.*, 2003). They have shown a wide variety of biological properties (Gangjee *et al.*, 2004; McGuigan *et al.*, 2004; Wang *et al.*, 2004). We report here the structures of two *N*<sup>4</sup>-substituted 11*H*-pyrimido[4,5-*b*][1,5]benzodiazepine-2,4-diamines, namely 2-amino-4-(piperidin-1-yl)-11*H*-pyrimido[4,5-*b*][1,5]benzodiazepin-6-ium chloride monohydrate, (I) (Fig. 1), and 2-amino-4-[methyl(2-methylphenyl)amino]-11*H*-pyrimido[4,5-*b*][1,5]benzodiazepin-6-ium chloride–benzene-1,2-diamine (1/1), (II) (Fig. 2). Compounds (I) and (II) were both prepared rapidly and in satisfactory yield by means of a cyclocondensation reaction between benzene-1,2-diamine and a 2,4-diamino-6-chloro-5-formylpyrimidine, mediated by microwave radiation under solvent-free conditions. The pyrimidine components employed in the syntheses of (I) and (II) differ in the nature of the 4-amino substituent: a piperidine unit in the precursor for (I) and a (2-methylphenyl)amino unit in the precursor for (II) (see scheme). Both products are fused pyrimidobenzodiazepinium chloride salts, with an additional water molecule present in (I) and a molecule of benzene-1,2-diamine present in (II).



The presence of three independent components in each structure provides considerable flexibility in the choice of the asymmetric units. However, for both structures it is possible to specify rather compact asymmetric units in which the independent components are linked by multiple hydrogen bonds (Figs. 1 and 2, and Table 2). In compound (I), the three components are linked within the selected asymmetric unit by a combination of N–H···O, O–H···Cl and N–H···Cl hydrogen bonds in a cyclic  $R_3^2(10)$  motif (Bernstein *et al.*, 1995), while in (II), the components within the selected asymmetric unit are linked by a combination of three independent N–H···Cl hydrogen bonds and one N–H···N hydrogen bond to form edge-fused  $R_2^1(7)$  and  $R_3^2(10)$  rings. It may be noted that the  $R_3^2(10)$  rings in (I) and (II) differ only in the notional replacement of the water O atom in (I) by an amino N atom in (II).

The pyrimidine ring in (I) is effectively planar, but that in (II) adopts an approximate twist-boat conformation, with a ring-puckering amplitude of 0.129 (2) Å and ring-puckering



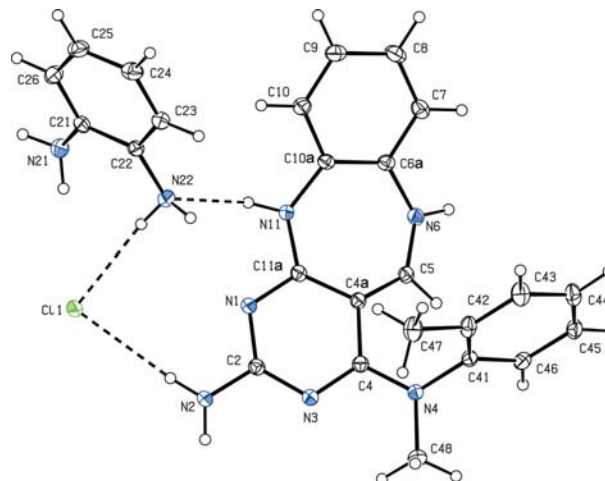
**Figure 1**

The independent components of (I), showing the atom-labelling scheme and the hydrogen bonds (dashed lines) within the selected asymmetric unit. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

angles (Cremer & Pople, 1975) of  $\theta = 81.7(9)^\circ$  and  $\varphi = 221.6(10)^\circ$ . The idealized ring-puckering angles for a twist-boat form are  $\theta = 90^\circ$  and  $\varphi = (60k + 30)^\circ$ , where  $k$  represents an integer. The seven-membered rings adopt very similar boat-type conformations in which the ring atoms C5, N6, N11 and C11a are essentially coplanar, with atoms C4a, C6a and C10a all displaced to the same side of the plane defined by atoms C5/N6/N11/C11a.

The pattern of the bond distances (Table 1) in the fused tricyclic cores are very similar for (I) and (II), and a number of general comments can be made. Firstly, the bond distances in the C6a/C7–C10/C10a carbocyclic rings span only very small ranges, *ca* 0.015 Å, indicating the occurrence of unperturbed benzenoid delocalization within this ring in both compounds. Secondly, the bond distances in the pyrimidine rings are typical of their types and again are consistent with aromatic-type delocalization in these rings. Thirdly, in the seven-membered rings, there is not even approximate equivalence between the distances in the two halves of the ring (defined by the local pseudo-mirror through atom C4a and the mid-point of the C6a–C10a bond), as expected for a simple benzodiazepinium cation and, in particular, there are some marked differences in the C–N distances. Thus, the C5–N6 bond is markedly shorter than the N6–C6a bond in both compounds, consistent with C5–N6 being a localized double bond. Hence, it may be concluded that there is no electronic delocalization between the fused rings, nor around the periphery, so that the outer rings both behave as closed  $6\pi$  systems, while the central ring contains a localized double bond.

In the benzene-1,2-diamine component of (II), the N atoms are both markedly pyramidal, with angle sums at N21 and N22 of 340.1 and 336.1°, respectively, and the C–N distances in this component (Table 1) are typical of those in aryl–NH<sub>2</sub> fragments containing pyramidal N atoms (Allen *et al.*, 1987). All of the amino-group H atoms lie on the same side of the

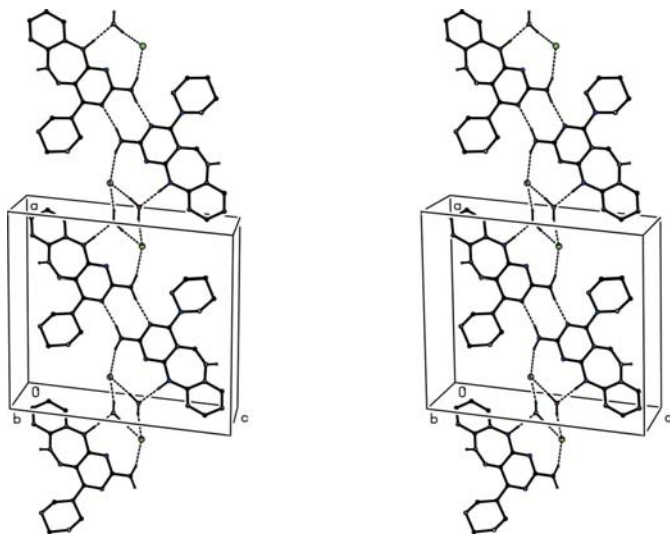


**Figure 2**

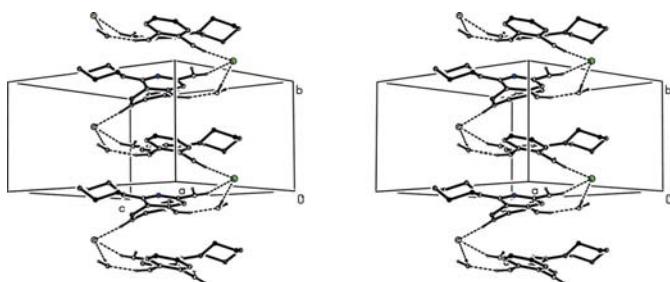
The independent components of (II), showing the atom-labelling scheme and the hydrogen bonds (dashed lines) within the selected asymmetric unit. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

aryl ring plane, and the C–C–N–H torsion angles (Table 1) indicate that this component has approximate mirror symmetry, with the mirror normal to the ring plane and passing through the mid-points of the C21–C22 and C24–C25 bonds. By contrast, in pure benzene-1,2-diamine [Cambridge Structural Database (Allen, 2002) refcode BAGFIY; Stalhandske, 1981], where again the amino groups are pyramidal with angle sums at the N atoms of 341 and 335°, the H atoms of the two amino groups lie on opposite sides of the ring plane, so that the molecule has approximate twofold rotation symmetry, with the axis passing through the mid-points of the bonds corresponding to C21–C22 and C24–C25 in (II).

In addition to the three hydrogen bonds within the selected asymmetric unit of (I), the crystal structure of (I) contains three further hydrogen bonds, one each of the N–H···N, O–H···Cl and N–H···Cl types, linking the three-component aggregates comprising the asymmetric units to form complex sheets. The formation of the sheets is most simply analysed in terms of two one-dimensional substructures. The first substructure in (I) is a chain of edge-fused rings running parallel to the [100] direction. Pairs of symmetry-related N–H···N hydrogen bonds link pairs of cations related by inversion, *via* a centrosymmetric  $R_2^2(8)$  motif, while O–H···Cl hydrogen bonds link pairs of water molecules and pairs of chloride ions in a centrosymmetric  $R_4^2(8)$  motif. Within the chain of rings, the  $R_2^2(8)$  rings are centred at  $(n + \frac{1}{2}, \frac{1}{2}, \frac{1}{2})$ , where  $n$  represents an integer, and the  $R_4^2(8)$  rings are centred at  $(n, \frac{1}{2}, \frac{1}{2})$ , where  $n$  again represents an integer, and these two centrosymmetric motifs are linked by the  $R_3^2(10)$  ring within the asymmetric unit, giving a continuous chain of edge-fused rings parallel to [100] (Fig. 3). In the second substructure in (I), atom N6 in the cation at  $(x, y, z)$  acts as hydrogen-bond donor to the chloride ion at  $(\frac{3}{2} - x, -\frac{1}{2} + y, \frac{1}{2} - z)$ , so linking the three-component aggregates related by the  $2_1$  screw axis along  $(\frac{3}{4}, y, \frac{1}{4})$  into a  $C_2^3(9)C_2^1(10)[R_3^2(10)]$  chain of rings running parallel to the [010] direction (Fig. 4). The combination of [100] and [010]



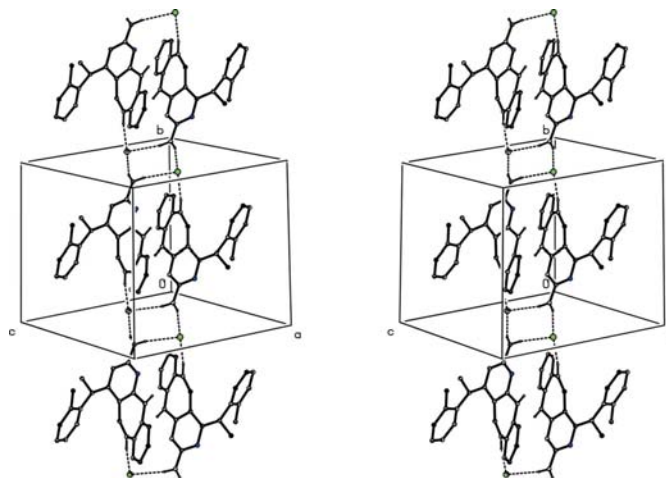
**Figure 3**  
A stereoview of part of the crystal structure of (I), showing the formation of a hydrogen-bonded chain along [100] and containing three types of edge-fused ring. Hydrogen bonds are shown as dashed lines. For the sake of clarity, H atoms bonded to C atoms have been omitted.



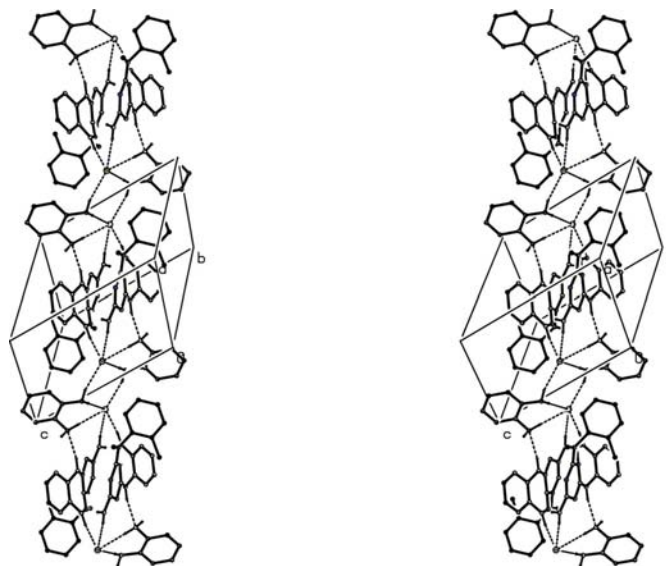
**Figure 4**  
A stereoview of part of the crystal structure of (I), showing the formation of a hydrogen-bonded  $C_3^2(9)C_1^1(10)[R_4^2(10)]$  chain of rings along [010]. Hydrogen bonds are shown as dashed lines. For the sake of clarity, H atoms bonded to C atoms have been omitted.

chains of rings generates a sheet of some complexity lying parallel to (001).

In compound (II), there are four N—H bonds exterior to the three-component aggregate comprising the selected asymmetric unit. As in (I), the hydrogen-bonded structure of (II) is two-dimensional and again it is readily analysed in terms of two substructures, one involving only the ionic components and the other involving all three components. In the first and simpler of the two substructures, the cations and anions are linked by three independent N—H...Cl hydrogen bonds involving atoms N2 and N6 as donors (Table 2) to form a chain of edge-fused centrosymmetric rings running parallel to the [010] direction, in which  $R_4^2(8)$  rings are centred at  $(\frac{1}{2}, n, \frac{1}{2})$ , alternating with  $R_4^2(20)$  rings centred at  $(\frac{1}{2}, n + \frac{1}{2}, \frac{1}{2})$ , where in both cases  $n$  represents an integer (Fig. 5). The second, more complex, substructure again contains centrosymmetric  $R_4^2(20)$  rings built from pairs of cations and anions and centred at  $(n + \frac{1}{2}, n + \frac{1}{2}, \frac{1}{2})$ , where  $n$  represents an integer. These rings alternate with centrosymmetric  $R_4^2(8)$  rings built from chloride ions and benzene-1,2-diamine molecules which are centred at  $(n, n, \frac{1}{2})$ , where  $n$  represents an integer, so forming a chain



**Figure 5**  
A stereoview of part of the crystal structure of (II), showing the formation of a hydrogen-bonded chain of edge-fused  $R_4^2(8)$  and  $R_4^2(20)$  rings along [010] and containing only the ionic components. Hydrogen bonds are shown as dashed lines. For the sake of clarity, H atoms bonded to C atoms have been omitted.



**Figure 6**  
A stereoview of part of the crystal structure of (II), showing the formation of a chain along [110] containing four types of hydrogen-bonded ring. Hydrogen bonds are shown as dashed lines. For the sake of clarity, H atoms bonded to C atoms have been omitted.

running parallel to the [110] direction (Fig. 6). The  $R_4^2(8)$  and  $R_4^2(20)$  rings in the chain along [110] are spiro-fused, in contrast with the edge-fused  $R_4^2(8)$  and  $R_4^2(20)$  rings in the chain along [010]. In addition, the chain along [110] also contains the  $R_2^1(7)$  and  $R_3^2(10)$  rings which lie within the selected asymmetric unit, so that the chain along [110] contains four distinct ring types, as opposed to just two ring types in the chain along [010]. The combination of chains of rings along [010] and [110] generates a complex sheet parallel to (001). Unlike that of (I), the structure of (II) contains a single rather weak C—H... $\pi$ (arene) hydrogen bond (Table 2) but this lies within the (001) sheet, rather than linking adjacent

sheets, so that the hydrogen-bonded structures of (I) and (II) are both strictly two-dimensional.

## Experimental

An intimate mixture of benzene-1,2-diamine (0.2 mmol) with the appropriate  $N^4$ -substituted 2,4-diamino-6-chloropyrimidine-5-carbaldehyde (0.2 mmol) [2-amino-6-chloro-4-piperidinopyrimidine-5-carbaldehyde for (I) and 2-amino-6-chloro-4-(2-methylphenylamino)pyrimidine-5-carbaldehyde for (II)] was subjected to microwave irradiation in the absence of solvent (maximum power 300 W over 3 min at a controlled temperature of 378 K) using a focused microwave reactor (CEM Discover). After cooling to ambient temperature, the solid products were washed with ethanol and then with diethyl ether to give red crystals of (I) and (II) suitable for single-crystal X-ray diffraction. For (I), yield 70%, m.p. 524–526 K; MS (70 eV)  $m/z$  (%): 294 ( $M^+$ , 100), 293 (34), 251 (19), 237 (17), 169 (11), 84 (16), 36 (15). For (II), yield 70%, m.p. 525–527 K; MS (70 eV)  $m/z$  (%): 330 ( $M^+$ , 27), 315 (14), 108 (19), 81 (54), 69 (100), 41 (28).

## Compound (I)

### Crystal data

$C_{16}H_{19}N_6^+ \cdot Cl^- \cdot H_2O$	$V = 1582.4$ (3) Å <sup>3</sup>
$M_r = 348.84$	$Z = 4$
Monoclinic, $P2_1/n$	Mo $K\alpha$ radiation
$a = 13.7831$ (14) Å	$\mu = 0.26$ mm <sup>-1</sup>
$b = 7.5324$ (9) Å	$T = 120$ K
$c = 15.2987$ (12) Å	$0.32 \times 0.28 \times 0.10$ mm
$\beta = 94.925$ (8)°	

### Data collection

Bruker–Nonius KappaCCD area-detector diffractometer	22943 measured reflections
Absorption correction: multi-scan (SADABS; Sheldrick, 2003)	3122 independent reflections
$T_{\min} = 0.933$ , $T_{\max} = 0.975$	2253 reflections with $I > 2\sigma(I)$
	$R_{\text{int}} = 0.066$

### Refinement

$R[F^2 > 2\sigma(F^2)] = 0.044$	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.111$	$\Delta\rho_{\text{max}} = 0.26$ e Å <sup>-3</sup>
$S = 1.07$	$\Delta\rho_{\text{min}} = -0.32$ e Å <sup>-3</sup>
3122 reflections	
223 parameters	
2 restraints	

## Compound (II)

### Crystal data

$C_{19}H_{19}N_6^+ \cdot Cl^- \cdot C_6H_8N_2$	$\gamma = 107.512$ (10)°
$M_r = 475.00$	$V = 1149.0$ (3) Å <sup>3</sup>
Triclinic, $P\bar{1}$	$Z = 2$
$a = 10.9559$ (13) Å	Mo $K\alpha$ radiation
$b = 11.2372$ (13) Å	$\mu = 0.20$ mm <sup>-1</sup>
$c = 11.432$ (2) Å	$T = 120$ K
$\alpha = 102.894$ (12)°	$0.42 \times 0.35 \times 0.12$ mm
$\beta = 112.176$ (14)°	

### Data collection

Bruker–Nonius KappaCCD area-detector diffractometer	30475 measured reflections
Absorption correction: multi-scan (SADABS; Sheldrick, 2003)	4532 independent reflections
$T_{\min} = 0.941$ , $T_{\max} = 0.977$	3349 reflections with $I > 2\sigma(I)$
	$R_{\text{int}} = 0.057$

**Table 1**

Selected bond distances (Å) for (I) and (II), and selected torsion angles (°) for (II).

	(I)	(II)
N1–C2	1.345 (3)	1.342 (2)
C2–N3	1.338 (3)	1.334 (2)
N3–C4	1.331 (4)	1.316 (3)
C4–C4a	1.428 (3)	1.432 (3)
C4a–C5	1.389 (3)	1.389 (3)
C5–N6	1.307 (3)	1.298 (2)
N6–C6a	1.418 (3)	1.412 (2)
C6a–C7	1.378 (3)	1.374 (3)
C7–C8	1.377 (3)	1.374 (3)
C8–C9	1.373 (3)	1.375 (3)
C9–C10	1.377 (3)	1.366 (3)
C10–C10a	1.380 (3)	1.377 (3)
C10a–N11	1.401 (3)	1.397 (2)
N11–C11a	1.348 (3)	1.347 (2)
C11a–N1	1.308 (3)	1.315 (2)
C4a–C11a	1.426 (3)	1.416 (3)
C6a–C10a	1.388 (3)	1.381 (3)
C2–N2	1.329 (3)	1.319 (2)
C4–N4		1.350 (2)
C4–N41	1.350 (3)	
C21–N21		1.391 (3)
C22–N22		1.404 (2)
C22–C21–N21–H21A		39
C22–C21–N21–H21B		171
C21–C22–N22–H22A		–32
C21–C22–N22–H22B		–159

**Table 2**

Hydrogen-bond parameters (Å, °) for (I) and (II).

Cg1 is the centroid of the C41–C46 ring.

Compound	$D-H \cdots A$	$D-H$	$H \cdots A$	$D \cdots A$	$D-H \cdots A$
(I)	N2–H2A <sup>i</sup> ···C11	0.88	2.59	3.422 (2)	159
	N11–H11 <sup>i</sup> ···O1	0.88	1.92	2.782 (3)	167
	O1–H1A <sup>i</sup> ···C11	0.88 (3)	2.29 (3)	3.151 (2)	165 (3)
	O1–H1B <sup>i</sup> ···C11 <sup>i</sup>	0.89 (2)	2.19 (2)	3.078 (2)	171 (3)
	N2–H2B <sup>ii</sup> ···N3 <sup>ii</sup>	0.88	2.33	3.198 (3)	169
(II)	N6–H6 <sup>iii</sup> ···C11 <sup>iii</sup>	0.88	2.41	3.281 (2)	169
	N2–H2A <sup>i</sup> ···C11	0.88	2.65	3.521 (2)	171
	N11–H11 <sup>i</sup> ···N22	0.88	2.09	2.922 (3)	158
	N21–H21A <sup>i</sup> ···C11	0.88	2.60	3.477 (2)	179
	N22–H22A <sup>i</sup> ···C11	0.88	2.51	3.380 (2)	172
	N2–H2B <sup>iv</sup> ···C11 <sup>iv</sup>	0.88	2.37	3.209 (2)	161
	N6–H6 <sup>ii</sup> ···C11 <sup>ii</sup>	0.92	2.14	3.050 (2)	172
	N21–H21B <sup>v</sup> ···C11 <sup>v</sup>	0.88	2.56	3.418 (2)	167
	C9–H9 <sup>vi</sup> ···Cg1 <sup>vi</sup>	0.95	2.96	3.770 (3)	144

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

### Refinement

$R[F^2 > 2\sigma(F^2)] = 0.042$	309 parameters
$wR(F^2) = 0.103$	H-atom parameters constrained
$S = 1.06$	$\Delta\rho_{\text{max}} = 0.37$ e Å <sup>-3</sup>
4532 reflections	$\Delta\rho_{\text{min}} = -0.26$ e Å <sup>-3</sup>

All H atoms were located in difference maps. H atoms bonded to C atoms were then treated as riding in geometrically idealized positions, with C–H = 0.95 (aromatic or alkenyl), 0.98 (CH<sub>3</sub>) or 0.99 Å (CH<sub>2</sub>), 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 H atoms bonded to C atoms. H atoms bonded to N atoms were treated as riding at the positions located in difference maps, with  $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{N})$ , giving N–H distances in the range 0.88–0.92 Å. The

coordinates of the H atoms of the water molecule in (I) were refined subject to a distance restraint O–H = 0.89 (2) Å, with  $U_{\text{iso}}(\text{H}) = 1.5U_{\text{eq}}(\text{O})$ .

For both 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: *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: SK3368). Services for accessing these data are described at the back of the journal.

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