A hydrogen-bonded ribbon in 6-amino-3-methyl-5-nitroso-2-(pyrrolidin-1-yl)pyrimidin-4(3H)-one monohydrate and hydrogen-bonded sheets in 6-amino-2-dimethylamino-3-methyl-5-nitrosopyrimidin-4(3H)-one monohydrate

Fabían Orozco,[a]‡ Braulio Insuasty,[a] Justo Cobo[b] and Christopher Glidewell[c]*

[a]Departamento de Química, Universidad de Valle, AA 25360 Cali, Colombia, [b]Departamento de Química Inorgánica y Orgánica, Universidad de Jaén, 23071 Jaén, Spain, and [c]School of Chemistry, University of St Andrews, Fife KY16 9ST, Scotland

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

In each of 6-amino-3-methyl-5-nitroso-2-(pyrrolidin-1-yl)pyrimidin-4(3H)-one monohydrate, $C_9H_{13}N_5O_2 \cdot H_2O$, (I), and 6-amino-2-dimethylamino-3-methyl-5-nitrosopyrimidin-4(3H)-one monohydrate, $C_7H_{11}N_5O_2 \cdot H_2O$, (II), the interatomic distances indicate significant polarization of the electronic structures of the pyrimidinone molecules. In each compound, the organic component contains an intramolecular N—H⋯O hydrogen bond. The molecular components in (I) are linked by a combination of two-centre O—H⋯O, O—H⋯N and N—H⋯O hydrogen bonds and a three-centre O—H⋯(NO) hydrogen bond to form a broad ribbon containing five distinct ring motifs. In compound (II), three intermolecular hydrogen bonds, one each of the O—H⋯O, O—H⋯N and N—H⋯O types, link the molecules into sheets containing equal numbers of centrosymmetric $R_4^4(10)$ and $R_{10}^8(34)$ rings.

Comment

We report here the crystal structures of 6-amino-3-methyl-5-nitroso-2-(pyrrolidin-1-yl)pyrimidin-4(3H)-one monohydrate, (I), and 6-amino-2-dimethylamino-3-methyl-5-nitrosopyrimidin-4(3H)-one monohydrate, (II) (Figs. 1 and 2), and compare them with those of 6-amino-3-methyl-2-morpholino-5-nitrosopyrimidin-4(3H)-one, (III) (Orozco et al., 2008), and of the amino acid derivatives, (IV)–(VIII) (Low et al., 1997, 1999, 2000). Our interest in the structures of this class of compounds

‡ Permanent address: Departamento de Química, Pontificia Universidad Javeriana, Kr 7 No. 43-82, Bogotá DC, Colombia.

was aroused by the observation that the structures of amino acid derivatives (IV)–(VIII) are all characterized by short intermolecular O—H⋯O hydrogen bonds, with the carboxyl group as donor and the nitrosyl O atom as acceptor, and in which the O⋯O distances are all ca 2.50 Å. At the same time, the intramolecular bond distances show a number of unusual values, and a combination of database analysis and molecular modelling led to an interpretation of the relationship between the unusual intramolecular bond lengths and the very short intermolecular hydrogen bonds in terms of highly polarized electronic structures (Low et al., 2000).

(I)

(II)

(III)

(IV) $R = CH_2COOH \cdot 2H_2O$
(V) $R = CH(COOH)CH_2CH_2SCH_3$
(VI) $R = CH(COOH)CH(CH_3)_2$
(VII) $R = CH(COOH)CH_2OH \cdot H_2O$
(VIII) $R = CH(COOH)CH(OH)CH_3$

(Ia) $R_2N = (CH_2)_4N$
(IIa) $R_2N = Me_2N$

(IIIa)
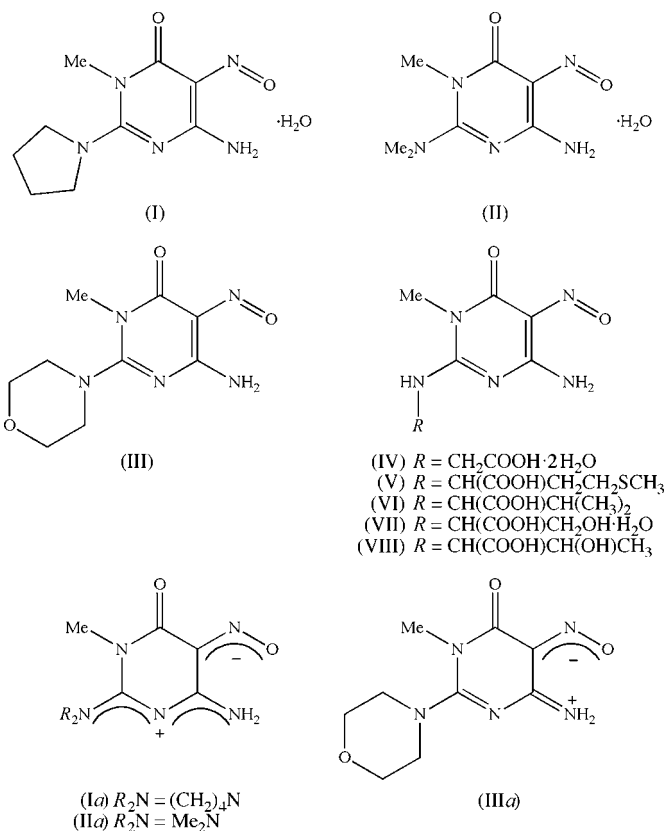
Although the pyrimidinone ring in (III) is effectively planar (Orozco et al., 2008), the rings in both (I) and (II) show a modest distortion towards a twist-boat conformation. The ring-puckering parameters (Cremer & Pople, 1975) are $\theta = 99.5(1)°$ and $\varphi = 273.9(10)°$ for (I), and $\theta = 87.1(10)°$ and $\varphi = 100.2(11)°$ for (II); the ideal values, for rings having all bond distances equal, are $\theta = 90°$ and $\varphi = (60k + 30)°$, where k represents an integer. In both compounds, ring atoms N2 and C5 are displaced to one side of the mean ring plane, and atoms N3 and C6 are displaced to the opposite side. While the ring-atom displacements are modest, in the range 0.04–0.07 Å, the displacements of the exocyclic substituent atoms are much greater, with the maximum displacement being experienced by atom C31 in each case [0.453 (2) Å in (I) and 0.619 (2) Å in (II)]. The twist-boat conformation is not uncommon amongst highly substituted pyrimidines of this general type (Quesada et al., 2002; Melguizo et al., 2003). The boat conformation has also been observed (Quesada et al., 2004), as well as the expected planar forms.
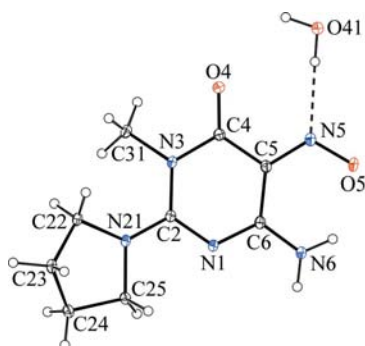
organic compounds

Figure 1
The molecular components of compound (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii. The hydrogen bond linking the two components within the selected asymmetric unit is indicated by a dashed line.
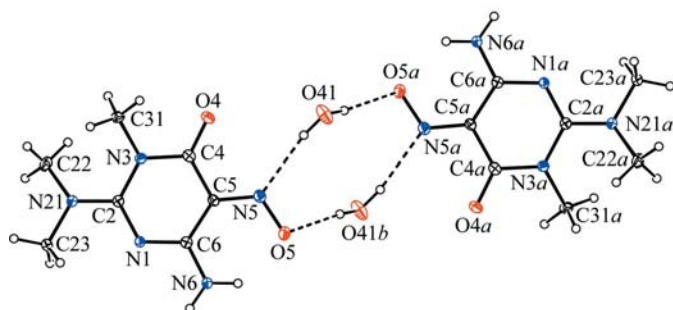

Figure 2
The molecular components of compound (II), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii. The hydrogen bonds linking the components into centrosymmetric four-molecule aggregates are indicated by dashed lines. Atoms labelled with the suffixes a and b are at the symmetry position $(1 - x, -y, 1 - z)$.
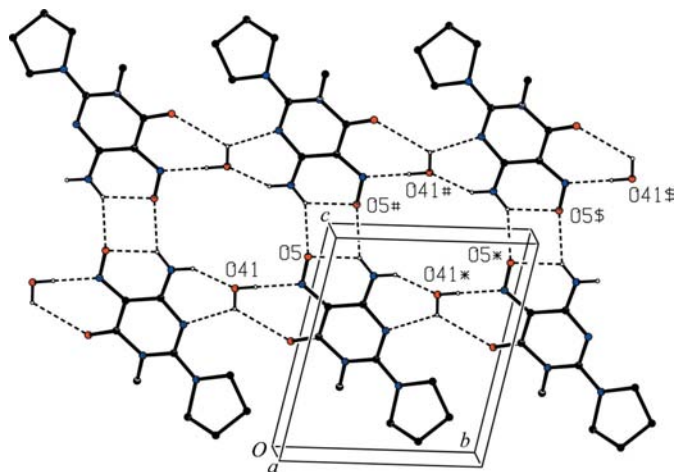

Figure 3
Part of the crystal structure of (I), showing the formation of a hydrogen-bonded ribbon running parallel to the [010] direction and containing five distinct types of ring. For the sake of clarity, H atoms bonded to C atoms have been omitted. Atoms labelled with an asterisk (*), a hash symbol (#) or a dollar sign ($) are at the symmetry positions $(x, 1 + y, z)$, $(1 - x, -y, 2 - z)$ and $(1 - x, 1 - y, 2 - z)$, respectively.

2008). Of the amino acid derivatives, (IV) crystallizes as a dihydrate (Low *et al.*, 1997) and (VII) as a monohydrate (Low *et al.*, 2000), while (V), (VI) and (VIII) all crystallize in the unsolvated forms (Low *et al.*, 1999, 2000).

In each of (I) and (II), the organic components contain an intramolecular N—H⋯O hydrogen bond forming an $S(6)$ motif (Bernstein *et al.*, 1995) (Table 2), but the remaining details of the hydrogen bonding are very different in the two compounds. In (I), the water molecule acts as a single acceptor, in an N—H⋯O hydrogen bond, and as a triple donor, forming a two-centre O—H⋯N hydrogen bond within the selected asymmetric unit (Fig. 1) and a three-centre O—H⋯(N,O) hydrogen bond, which serves to link two pyrimidinone molecules related by translation (Fig. 3). The hydrogen bonds involving the water molecules, together with the intramolecular N—H⋯O hydrogen bond, thus generate a chain of edge-fused $S(6)$, $R_2^2(6)$ and $R_2^2(7)$ rings running parallel to the [010] direction. Pairs of antiparallel chains, related to one another by inversion, are linked by an intermolecular N—H⋯O hydrogen bond involving only the organic components, so generating a broad ribbon. The central core of this ribbon consists of $R_2^2(4)$ rings centred at $(\frac{1}{2}, n, 1)$, where n represents an integer, alternating with $R_6^6(14)$ rings centred at $(\frac{1}{2}, n + \frac{1}{2}, 1)$, where n again represents an integer. This central core is flanked by two outer strips, each containing $S(6)$, $R_2^2(6)$ and $R_2^2(7)$ rings, so that, overall, the ribbon contains five different ring motifs (Fig. 3).

The hydrogen bonding in (II) is simpler than that in (I) (Table 2). In particular, the water molecule does not act as an acceptor of hydrogen bonds. As a double donor, it forms only two-centre hydrogen bonds, one each of the O—H⋯N and O—H⋯O types, which link a pair of organic components which are related to one another by inversion, thus forming a centrosymmetric four-molecule aggregate centred at $(\frac{1}{2}, 0, \frac{1}{2})$

Despite the nonplanarity of the pyrimidinone rings, the bond distances in (I) and (II) (Table 1) provide evidence for polarization of the electronic structure, but in a manner which differs slightly from that in (III). The key indicators for compounds of this type have been identified (Low *et al.*, 2000) as: (i) the C—N distances in the sequence N21—C2—N1—C6—N6; (ii) the similarity of the distances C4—C5 and C5—C6; (iii) the distances C5—N5 and N5—O5 and, perhaps most importantly, the difference between these distances. On this basis, the extent of the polarization can be identified as greatest in (II) and least in (III), with the extent of the delocalization greater in (I) and (II) than in (III), all indicating the importance of the polarized forms (Ia) and (IIa) in addition to the localized forms (I) and (II), compared with form (IIIa) (Orozco *et al.*, 2008). Accordingly, in both (I) and (II), hydrogen bonds involving atom N6 as the donor or atom O5 as the acceptor can be regarded as charge-assisted hydrogen bonds (Gilli *et al.*, 1994). In (II), where all of the intermolecular hydrogen bonds are of the two-centre type, those involving atoms N6 or O5 exhibit almost linear D—H⋯A fragments.

Compounds (I) and (II) both crystallize as monohydrates, while (III) crystallizes in the unsolvated form (Orozco *et al.*,
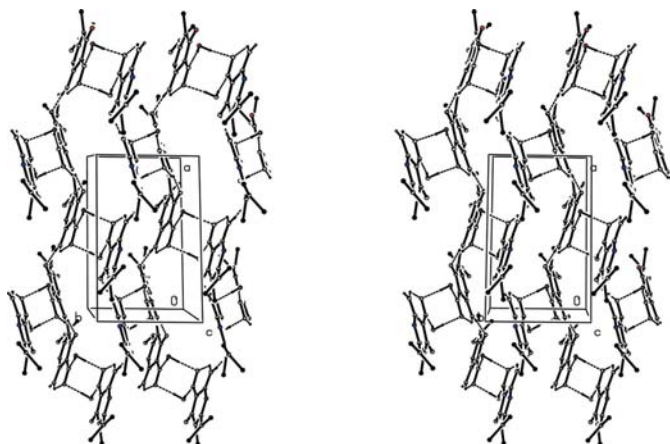
Figure 4
A stereoview of part of the crystal structure of (II), showing the formation of a hydrogen-bonded sheet parallel to (10$\bar{1}$) and containing three types of ring. For the sake of clarity, H atoms bonded to C atoms have been omitted.

and containing an $R_4^4(10)$ motif (Fig. 2). This aggregate can conveniently be regarded as the basic building block for the supramolecular structure. The intermolecular N—H···O hydrogen bond links the four-molecule aggregate centred at ($\frac{1}{2}$, 0, $\frac{1}{2}$) to four similar aggregates centred at (0, $\frac{1}{2}$, 0), (0, $-\frac{1}{2}$, 0), (1, $\frac{1}{2}$, 1) and (1, $-\frac{1}{2}$, 1), so generating a sheet parallel to (10$\bar{1}$) and containing $S(6)$, $R_4^4(10)$ and $R_{10}^8(34)$ rings (Fig. 4). Thus, although there are fewer independent hydrogen bonds in the structure of (II) than in (I), the hydrogen-bonded supramolecular structure of (II) is two-dimensional, as opposed to the one-dimensional hydrogen-bonded structure of (I).

In each of (I) and (II), the water component is firmly embedded in the hydrogen-bonded structure. By contrast, (III) contains no water component and its very simple hydrogen-bonded structure is built from just two inter-molecular N—H···O hydrogen bonds, in which the ketonic and morpholine O atoms are the acceptors, giving a sheet containing only $S(6)$ and $R_4^4(26)$ rings. Had the morpholine O atom not been available to accept a hydrogen bond in the structure of (III), then, without further reorganization, the hydrogen-bonded structure would consist of simple $C(6)$ chains, with one of the amino N—H bonds finding no acceptor site. This suggests that the presence of water in (I) and (II), *versus* its absence in (III), may be connected with the overall ratio of hydrogen-bond donors and acceptors.

Three-dimensional hydrogen-bonded structures are formed by each of (IV)–(VI) and (VIII), despite the fact that, whereas (IV) crystallizes as a dihydrate (Low *et al.*, 1997), the other three compounds all crystallize in the solvent-free forms (Low *et al.*, 1999, 2000), while the monohydrate, (VII), forms only a two-dimensional hydrogen-bonded structure (Low *et al.*, 2000). The contrast between the two-dimensional structure of (VII) and the three-dimensional structures of (V) and (VI) is both striking and unexpected in view of the considerably greater number of potential hydrogen-bonding donor and acceptor sites available in the asymmetric unit of (VII) compared with (V) and (VI).

Experimental

To a suspension of 6-amino-2-methylsulfanyl-3-methyl-5-nitroso-pyrimidin-4(3*H*)-one (25 mmol) in methanol (80 ml), the appropriate secondary amine (100 mmol), *viz.* pyrrolidine for (I) and dimethyl-amine for (II), was added dropwise with magnetic stirring. The reactions proceeded for 6 h with a change of colour from blue to violet and the liberation of methanethiol. The resulting solid products were collected by filtration and washed with cold ethanol, and then recrystallized from dimethylformamide–water (3:1 *v/v*) to give red–violet crystals suitable for single-crystal X-ray diffraction. Analysis for (I): 87% yield, m.p. 484 K; MS (70 eV) *m/z* (%): 223 (M^+, 100), 209 (4), 150 (20), 123 (17), 97 (24). Analysis for (II): 52% yield, m.p. 504 K; MS (70 eV) *m/z* (%): 197 (M^+, 90), 183 (32), 152 (56), 92 (100), 42 (73).

Compound (I)

Crystal data

$C_9H_{13}N_5O_2 \cdot H_2O$	$\gamma = 64.436\,(16)°$
$M_r = 241.26$	$V = 523.46\,(19)$ Å^3
Triclinic, $P\bar{1}$	$Z = 2$
$a = 7.9734\,(18)$ Å	Mo $K\alpha$ radiation
$b = 8.452\,(2)$ Å	$\mu = 0.12$ mm^{-1}
$c = 8.9099\,(2)$ Å	$T = 120$ K
$\alpha = 75.158\,(9)°$	$0.41 \times 0.18 \times 0.15$ mm
$\beta = 84.727\,(7)°$	

Data collection

Bruker–Nonius KappaCCD area-detector diffractometer	12137 measured reflections
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)	2051 independent reflections
	1629 reflections with $I > 2\sigma(I)$
$T_{min} = 0.953$, $T_{max} = 0.983$	$R_{int} = 0.054$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.046$	155 parameters
$wR(F^2) = 0.116$	H-atom parameters constrained
$S = 1.05$	$\Delta\rho_{max} = 0.26$ e Å^{-3}
2051 reflections	$\Delta\rho_{min} = -0.28$ e Å^{-3}

Compound (II)

Crystal data

$C_7H_{11}N_5O_2 \cdot H_2O$	$V = 951.34\,(19)$ Å^3
$M_r = 215.22$	$Z = 4$
Monoclinic, $P2_1/n$	Mo $K\alpha$ radiation
$a = 11.8125\,(6)$ Å	$\mu = 0.12$ mm^{-1}
$b = 7.1372\,(7)$ Å	$T = 120$ K
$c = 11.8588\,(19)$ Å	$0.16 \times 0.16 \times 0.12$ mm
$\beta = 107.910\,(4)°$	

Data collection

Bruker–Nonius KappaCCD area-detector diffractometer	9096 measured reflections
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)	1873 independent reflections
	1304 reflections with $I > 2\sigma(I)$
$T_{min} = 0.971$, $T_{max} = 0.986$	$R_{int} = 0.049$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.046$	139 parameters
$wR(F^2) = 0.109$	H-atom parameters constrained
$S = 1.05$	$\Delta\rho_{max} = 0.22$ e Å^{-3}
1873 reflections	$\Delta\rho_{min} = -0.27$ e Å^{-3}

organic compounds

Table 1
Selected bond distances (Å) for compounds (I)–(III).

Δ represents the bond-length difference $d(C5-N5) - d(N5-O5)$.

Parameter	(I)	(II)	(III)†
N1—C2	1.326 (2)	1.320 (3)	1.315 (3)
C2—N3	1.376 (2)	1.377 (3)	1.376 (3)
N3—C4	1.401 (2)	1.388 (3)	1.415 (3)
C4—C5	1.446 (2)	1.438 (3)	1.447 (3)
C5—C6	1.429 (3)	1.438 (3)	1.435 (3)
C6—N1	1.338 (2)	1.333 (3)	1.357 (3)
C2—N21	1.325 (2)	1.328 (3)	1.358 (3)
C4—O4	1.209 (2)	1.226 (2)	1.221 (3)
C5—N5	1.336 (2)	1.332 (3)	1.358 (3)
N5—O5	1.273 (2)	1.278 (2)	1.275 (3)
C6—N6	1.313 (2)	1.311 (3)	1.316 (3)
Δ	0.063 (3)	0.054 (3)	0.083 (3)

† Data for (III) are taken from Orozco *et al.* (2008).

Table 2
Hydrogen-bonding parameters (Å, °) for compounds (I) and (II).

Compound	$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
(I)	N6—H6$A\cdots$O5	0.88	2.00	2.630 (2)	128
	N6—H6$A\cdots$O5^i	0.88	2.25	2.989 (2)	142
	N6—H6$B\cdots$O41^{ii}	0.88	1.99	2.808 (2)	154
	O41—H41$A\cdots$N5	0.86	2.00	2.860 (2)	177
	O41—H41$B\cdots$O4†	0.86	2.48	2.946 (2)	114
	O41—H41$B\cdots$N1^{iii}	0.86	2.57	3.082 (2)	119
(II)	N6—H6$A\cdots$O5	0.88	1.97	2.641 (2)	132
	N6—H6$B\cdots$O4^{iv}	0.88	2.01	2.874 (2)	168
	O41—H41$A\cdots$N5	0.86	2.15	2.995 (2)	168
	O41—H41$B\cdots$O5^v	0.86	2.08	2.921 (2)	166

† The O4$\cdots$H41$B\cdots$N1^{iii} angle is 125°. Symmetry codes: (i) $1-x, -y, 2-z$; (ii) $x, 1+y, z$; (iii) $x, -1+y, z$; (iv) $-\frac{1}{2}+x, \frac{1}{2}-y, -\frac{1}{2}+z$; (v) $1-x, -y, 1-z$.

All H atoms were located in difference maps and then treated as riding atoms. H atoms bonded to C or N atoms were allowed to ride in geometrically idealized positions, with C—H = 0.98 (CH$_3$) or 0.99 Å (CH$_2$) and N—H = 0.88 Å, and with U_{iso}(H) = kU_{eq}(C,N), where k = 1.5 for the methyl groups, which were permitted to rotate but not to tilt, and 1.2 otherwise. Water H atoms were permitted to ride at the positions deduced from the difference maps, with O—H = 0.86 Å and U_{iso}(H) = 1.5U_{eq}(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*.

References

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.

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.

Gilli, P., Bertolasi, V., Ferretti, V. & Gilli, G. (1994). *J. Am. Chem. Soc.* **116**, 909–915.

Low, J. N., Ferguson, G., López, R., Arranz, P., Cobo, J., Melguizo, M., Nogueras, M. & Sánchez, A. (1997). *Acta Cryst.* C**53**, 890–892.

Low, J. N., Godino, M. L., López, R., Pérez, A., Melguizo, M. & Cobo, J. (1999). *Acta Cryst.* C**55**, 1727–1730.

Low, J. N., López, M. D., Arranz Mascarós, P., Cobo Domingo, J., Godino, M. L., López Garzón, R., Gutiérrez, M. D., Melguizo, M., Ferguson, G. & Glidewell, C. (2000). *Acta Cryst.* B**56**, 882–892.

Melguizo, M., Quesada, A., Low, J. N. & Glidewell, C. (2003). *Acta Cryst.* B**59**, 263–276.

Nonius (1999). *COLLECT*. Nonius BV, Delft, The Netherlands.

Orozco, F., Insuasty, B., Low, J. N., Cobo, J. & Glidewell, C. (2008). *Acta Cryst.* C**64**, o220–o225.

Quesada, A., Marchal, A., Melguizo, M., Low, J. N. & Glidewell, C. (2004). *Acta Cryst.* B**60**, 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.* B**58**, 300–315.

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. (2009). *Acta Cryst.* D**65**, 148–155.