

2-Amino-4-(2-methoxyphenyl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile and 2-amino-4-(2-methoxyphenyl)-7,7-dimethyl-3-nitro-4,6,7,8-tetrahydro-5H-chromen-5-one hemihydrate

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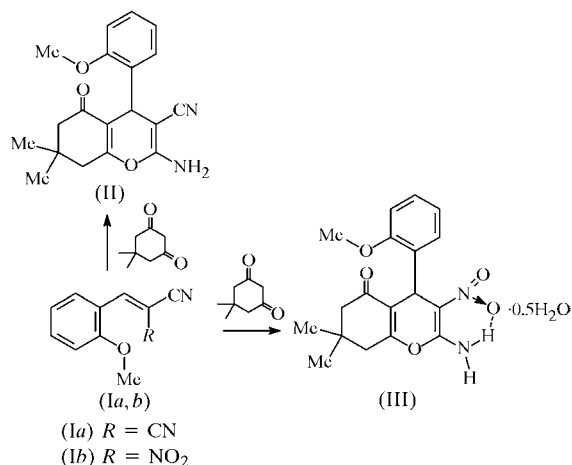
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Calculations of the conformational preferences of the methoxyphenyl substituent with respect to the pyran ring have been carried out for the two title compounds, C₁₉H₂₀N₂O₃, (II), and C₁₈H₂₀N₂O₅·0.5H₂O, (III). In both molecules, the heterocyclic ring adopts a flattened boat conformation and the fused cyclohexenone ring adopts a 'sofa' conformation. The dihedral angles between these two flat fragments are 14.5 (1) and 9.3 (1)° in (II) and (III), respectively. In both molecules, the methoxy group of the pseudo-axial aryl substituent is *syn* with respect to the pyran ring. The dihedral angles between the 2-methoxyphenyl rings and the flat parts of the pyran rings are 86.3 (1) and 87.0 (1)°, respectively. In the crystal structure of (II), intermolecular N—H···N and N—H···O hydrogen bonds link molecules into a three-dimensional framework. In the crystal structure of (III), a strong intramolecular N—H···O hydrogen bond links the flat conjugated H—N=C=C—N—O fragment into a six-membered ring. In (III), the water molecule lies on a twofold axis and forms bifurcated O—H···O hydrogen bonds with the NO₂ group of the molecule. Also in (III), hydrogen bonds link the organic and water molecules into infinite tapes along the *c* axis.

Comment

The present investigation is a continuation of our systematic work that includes the syntheses and structural studies of unsaturated nitriles as potential non-linear optical materials (Nesterov *et al.*, 2000, 2001*a,b*) and heterocyclic compounds that may be obtained using such nitriles (Nesterov & Viltch-

inskaia, 2001; Nesterov *et al.*, 2004; Nesterova *et al.*, 2004). Some 4*H*-pyran derivatives are potential bioactive compounds and can be used as calcium antagonists (Suarez *et al.*, 2002). Such heterocyclic compounds have structures similar to those of the well known 1,4-dihydropyridines (Triggle *et al.*, 1980; Bossert *et al.*, 1981, 1989; Kokubun & Reuter, 1984), which exhibit high bioactivities. Thus, there has been a growing interest in the structures of 4*H*-pyran derivatives (Florencio & Garcia-Blanco, 1987; Bellanato *et al.*, 1988; Lokaj *et al.*, 1990; Marco *et al.*, 1993; Suarez *et al.*, 2002).



Syntheses and X-ray structural investigations have been carried out for compounds (II) and (III) (Figs. 1 and 2). Most of the geometric parameters are very similar to the standard values (Allen *et al.*, 1987) and very close to our and literature data for similar 4*H*-pyran derivatives (Kislyi *et al.*, 1999; Suarez *et al.*, 2002; Nesterov *et al.*, 2004).

The X-ray analyses show that the molecules of (II) and (III) have slightly different conformations. The pyran ring in both structures adopts a flattened boat conformation, with a deviation of atoms O1 and C4 from the C2/C3/C5/C10 plane [planar within 0.008 (2) and 0.001 (2) Å] of 0.151 (2) and 0.203 (2) Å in (II), and −0.108 (2) and −0.218 (2) Å in (III),

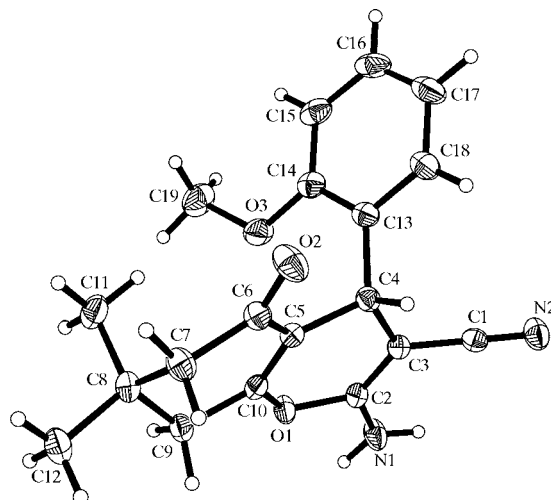


Figure 1

A view of (II), showing the atom numbering used. The non-H atoms are shown with displacement ellipsoids drawn at the 50% probability level.

respectively. The bending of the ring along the lines $O1 \cdots C4$, $C2 \cdots C10$ and $C3 \cdots C5$ is, respectively, equal to 16.6 (2), 12.4 (2) and 13.2 (2) $^\circ$ in (II), and 15.2 (2), 9.0 (2) and 14.5 (2) $^\circ$ in (III). According to our previous work and literature data, the pyran ring is flexible but usually adopts a flattened boat conformation. In both molecules, the fused cyclohexenone ring adopts a sofa conformation; atom C8 deviates from the $C7/C6/C5/C10/C9$ plane [planar within 0.030 (1) and 0.024 (1) \AA] by 0.636 (1) and -0.666 (2) \AA for (II) and (III), respectively. The dihedral angles between these two flat fragments are 14.5 (1) and 9.3 (1) $^\circ$ in (II) and (III), respectively. In both molecules, the methoxy substituent of the aryl group is *anti* relative to the H atom bonded to C4 [$H4A-C4-C13-C14 = -167$ and 178° , and $C4-C13-C14-O3 = 1.9$ (2) and 2.1 (3) $^\circ$]. The phenyl substituents occupy pseudo-axial positions and form dihedral angles with the flat moieties of the pyran rings of 86.3 (1) and 87.0 (1) $^\circ$ in (II) and (III), respectively. Such mutual orientation of these fragments and the flatness of the heterocyclic rings leads to $O \cdots C$ intramolecular steric interactions [$O3 \cdots C5 = 2.911$ (3) \AA and $O3 \cdots C10 = 3.109$ (3) \AA in (II), and $O3 \cdots C2 = 3.074$ (3) \AA , $O3 \cdots C3 = 3.006$ (3) \AA , $O3 \cdots C5 = 2.969$ (3) \AA and $O3 \cdots C10 = 3.018$ (3) \AA in (III)]. These distances are shorter than the sum of the van der Waals radii of O and C (Rowland & Taylor, 1996), especially in the case of (II). Such steric hindrance causes elongation of the $C4-C13$ bond lengths to 1.525 (2) and 1.527 (3) \AA , respectively, in comparison with neighboring Csp^3-Csp^2 distances that are equal to standard values (Allen *et al.*, 1987).

As was described previously for related compounds (Kislyi *et al.*, 1999; Nesterov *et al.*, 2001, 2004; Nesterova *et al.*, 2004), there is conjugation [especially in (III)] between the donor (NH_2) and acceptor [CN in (II) and NO_2 in (III)] groups *via* the $C2=C3$ double bond (Tables 1 and 3). Thus, in both molecules, the $C2-N1$ distances are shorter than the average conjugated $C-N$ single bond (1.370 \AA) found in the Cambridge Structural Database (Allen, 2002). In contrast, the $C2=C3$ bond lengths are elongated in comparison with the $C5=C10$ bond length and the standard value (Allen *et al.*,

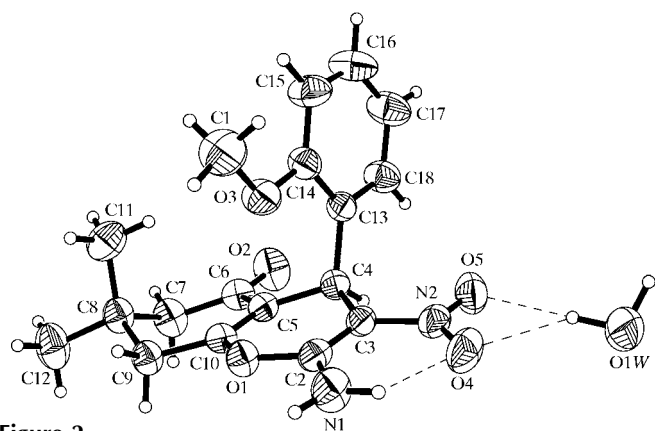


Figure 2

A view of (III), showing the atom numbering used. The non-H atoms are shown with displacement ellipsoids drawn at the 50% probability level. Dashed lines indicate the intramolecular $N-H \cdots O$ hydrogen bond and the $O-H \cdots O$ bifurcated hydrogen bonds.

1987). Variations of the other bond lengths in the flat fragments are less distinct in (II). However, in (III), the $C3-N2$ distance is considerably shorter than usual for $C-NO_2$ bonds (1.468 \AA ; Allen *et al.*, 1987) and the $N2-O4$ distance is distinctly longer than the standard value (Allen *et al.*, 1987).

In the crystal structure of (II), both H atoms of the NH_2 group participate in intermolecular $N-H \cdots N$ and $N-H \cdots O$ hydrogen bonds that link the molecules into a three-dimensional framework (Fig. 3 and Table 2). In (III), a strong intramolecular $N-H \cdots O$ hydrogen bond links the flat conjugated $H-N-C=C-N-O$ fragment into a six-membered ring. The water molecule lies on a twofold axis and forms bifurcated $O-H \cdots O$ hydrogen bonds with the NO_2 group of the molecule. In the crystal structure, hydrogen bonds link the organic and water molecules into infinite tapes along the c axis (Fig. 4 and Table 4).

Analysis of the crystal packing shows that in (III) there is only one intermolecular steric contact [$O4 \cdots O4^{iii} = 2.894$ (2) \AA ; symmetry code: (iii) $-x, -y + 2, -z$], which is equal to the sum of the van der Waals radii of the O atoms (Rowland & Taylor, 1996). The other geometric parameters in (II) and (III) have standard values (Allen *et al.*, 1987).

Using computational methods (*GAUSSIAN03*; Frisch *et al.*, 2003), we explored the conformational preferences of the methoxyphenyl substituent with respect to the pyran ring in molecules (II) and (III). This was performed first at the AM1 level by minimizing the conformer found in the crystal and then rotating the $H4-C4-C13-C14$ angle by 10° increments and minimizing the conformations encountered until the original conformer was generated once again. For the molecules of both (II) and (III), two minima were found. The first has the methoxy substituent on the benzene ring *syn* to the pyran ring ($H4-C4-C13-C14$ angle close to -180°), similar

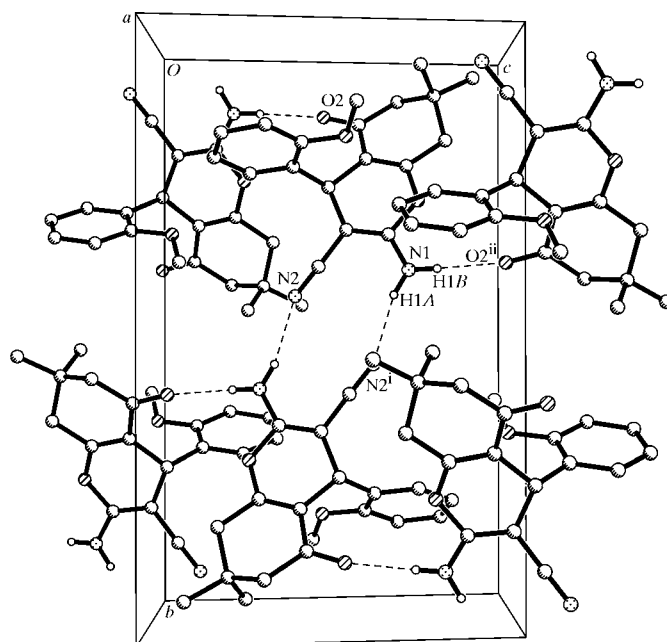


Figure 3

A projection of the crystal packing of (II) along the a axis. [Symmetry codes: (i) $-x + 1, -y + 1, -z + 1$; (ii) $x + \frac{1}{2}, -y + \frac{1}{2}, z + \frac{1}{2}$]

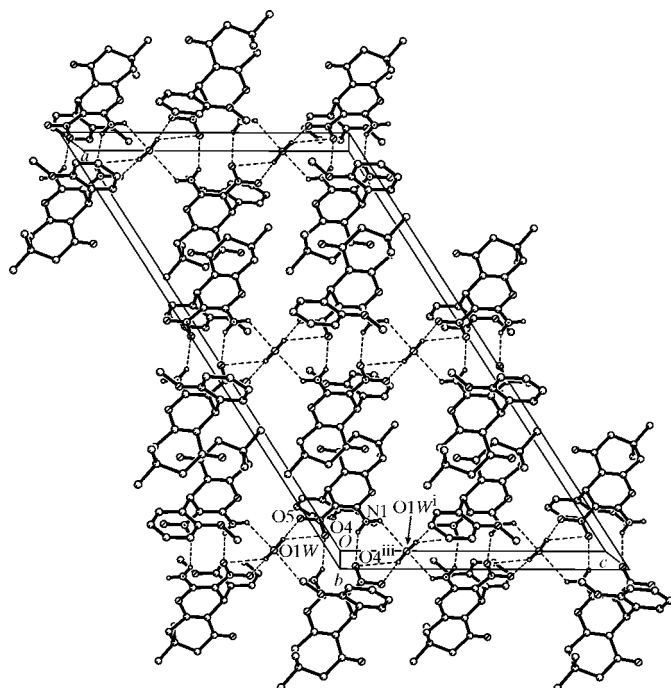


Figure 4
A projection of the crystal packing of (III) along the *b* axis. [Symmetry code: (iii) $-x, -y + 2, -z$.]

to the configuration observed in the crystal structures (Figs. 1 and 2). The second has the methoxy substituent on the benzene ring *anti* to the pyran ring (H4–C4–C13–C14 angle close to 0°). For compound (II) at the AM1 level, the *anti* conformation is predicted to be the global minimum, being $1.8 \text{ kcal mol}^{-1}$ more stable than the *syn* minimum and $6.4 \text{ kcal mol}^{-1}$ more stable than the highest energy conformation. A frequency calculation confirmed that the highest energy conformation corresponds to an energy maximum. In contrast, higher level restricted Hartree–Fock calculations on the two minima of (II) [basis set 6-311++G(*d,p*)] predict that the *syn* conformer observed in the crystal is more stable than the *anti* conformer by $0.9 \text{ kcal mol}^{-1}$. AM1 calculations on (III) gave similar results, with the *anti* conformer predicted to be more stable than the *syn* by $0.5 \text{ kcal mol}^{-1}$ and also more stable than the highest energy conformation by $5.1 \text{ kcal mol}^{-1}$. A frequency calculation confirmed that the highest energy conformation corresponds to an energy maximum. Similar to the results with (II), the higher level *ab initio* calculations (same basis set used) predict the conformer observed in the crystal of (III) to be the minimum energy conformer: the *syn* conformer is predicted to be $2.2 \text{ kcal mol}^{-1}$ more stable than the *anti*.

Experimental

Compounds (II) and (III) were obtained by the reaction of (2-methoxybenzylidene)malononitrile, (1a), or *trans*-1-cyano-2-(2-methoxyphenyl)-1-nitroethylene, (1b), with 5,5-dimethylcyclohexane-1,3-dione (dimedone) according to literature procedures (Kislyi *et al.*, 1999; Nesterov & Viltchinskaja, 2001). The precipitates were isolated and recrystallized from acetonitrile for (II) and from ethanol for (III) [m.p. 474 K and yield 96% for (II), and m.p. 435 K (hemihydrate) and

yield 71% for (III)]. Both compounds were characterized by ^1H and ^{13}C NMR spectroscopy. The crystals were grown by slow isothermic evaporation of a solution in acetonitrile for (II) and ethanol for (III).

Compound (II)

Crystal data

$\text{C}_{19}\text{H}_{20}\text{N}_2\text{O}_3$
 $M_r = 324.37$
Monoclinic, $P2_1/n$
 $a = 8.7941$ (18) Å
 $b = 17.450$ (4) Å
 $c = 11.007$ (2) Å
 $\beta = 98.174$ (16) $^\circ$
 $V = 1671.9$ (6) Å 3
 $Z = 4$

$D_x = 1.289 \text{ Mg m}^{-3}$
Mo $K\alpha$ radiation
Cell parameters from 24 reflections
 $\theta = 11\text{--}12^\circ$
 $\mu = 0.09 \text{ mm}^{-1}$
 $T = 153$ (2) K
Prism, colorless
 $0.45 \times 0.30 \times 0.25 \text{ mm}$

Data collection

Siemens P3/PC diffractometer
 $\omega/2\theta$ scans
3105 measured reflections
2907 independent reflections
2562 reflections with $I > 2\sigma(I)$
 $R_{\text{int}} = 0.027$
 $\theta_{\text{max}} = 25.0^\circ$

$h = 0 \rightarrow 10$
 $k = 0 \rightarrow 20$
 $l = -13 \rightarrow 12$
3 standard reflections
every 97 reflections
intensity decay: 3%

Refinement

Refinement on F^2
 $R[F^2 > 2\sigma(F^2)] = 0.036$
 $wR(F^2) = 0.094$
 $S = 1.04$
2907 reflections
220 parameters
H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.05P)^2 + 0.54P]$
where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{\text{max}} < 0.001$
 $\Delta\rho_{\text{max}} = 0.22 \text{ e \AA}^{-3}$
 $\Delta\rho_{\text{min}} = -0.20 \text{ e \AA}^{-3}$

Table 1

Selected geometric parameters (Å, $^\circ$) for (II).

| | | | |
|----------------|-------------|----------|-------------|
| O1–C2 | 1.3749 (15) | C1–C3 | 1.4162 (18) |
| O1–C10 | 1.3773 (16) | C2–C3 | 1.3535 (18) |
| O2–C6 | 1.2232 (16) | C4–C13 | 1.5246 (18) |
| N1–C2 | 1.3317 (17) | C5–C10 | 1.3299 (18) |
| N2–C1 | 1.1514 (17) | C5–C6 | 1.4679 (18) |
| C2–O1–C10 | 118.38 (10) | N2–C1–C3 | 177.83 (14) |
| C14–O3–C19 | 117.19 (11) | | |
| C19–O3–C14–C15 | –15.06 (19) | | |

Table 2

Hydrogen-bond geometry (Å, $^\circ$) for (II).

| <i>D</i> –H... <i>A</i> | <i>D</i> –H | H... <i>A</i> | <i>D</i> ... <i>A</i> | <i>D</i> –H... <i>A</i> |
|---------------------------|-------------|---------------|-----------------------|-------------------------|
| N1–H1A...N2 ⁱ | 0.88 | 2.18 | 3.041 (2) | 166 |
| N1–H1B...O2 ⁱⁱ | 0.88 | 2.07 | 2.943 (2) | 173 |

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

Compound (III)

Crystal data

$\text{C}_{18}\text{H}_{20}\text{N}_2\text{O}_5 \cdot 0.5\text{H}_2\text{O}$
 $M_r = 353.37$
Monoclinic, $C2/c$
 $a = 28.461$ (5) Å
 $b = 9.456$ (2) Å
 $c = 15.860$ (3) Å
 $\beta = 122.819$ (11) $^\circ$
 $V = 3587.1$ (13) Å 3
 $Z = 8$

$D_x = 1.309 \text{ Mg m}^{-3}$
Mo $K\alpha$ radiation
Cell parameters from 24 reflections
 $\theta = 10\text{--}11^\circ$
 $\mu = 0.10 \text{ mm}^{-1}$
 $T = 298$ (2) K
Prism, colorless
 $0.40 \times 0.35 \times 0.30 \text{ mm}$

Data collection

| | |
|--|------------------------------|
| Enraf–Nonius CAD-4 diffractometer | $\theta_{\max} = 25.0^\circ$ |
| $\omega/2\theta$ scans | $h = 0 \rightarrow 33$ |
| 3162 measured reflections | $k = 0 \rightarrow 11$ |
| 3097 independent reflections | $l = -18 \rightarrow 15$ |
| 1749 reflections with $I > 2\sigma(I)$ | 3 standard reflections |
| $R_{\text{int}} = 0.038$ | every 97 reflections |
| | intensity decay: 3% |

Refinement

| | |
|---------------------------------|--|
| Refinement on F^2 | H atoms treated by a mixture of independent and constrained refinement |
| $R[F^2 > 2\sigma(F^2)] = 0.055$ | |
| $wR(F^2) = 0.116$ | $w = 1/[\sigma^2(F_o^2) + (0.0534P)^2]$ |
| $S = 1.05$ | where $P = (F_o^2 + 2F_c^2)/3$ |
| 3097 reflections | $(\Delta/\sigma)_{\max} < 0.001$ |
| 238 parameters | $\Delta\rho_{\max} = 0.13 \text{ e } \text{\AA}^{-3}$ |
| | $\Delta\rho_{\min} = -0.16 \text{ e } \text{\AA}^{-3}$ |

Table 3

Selected geometric parameters (\AA , $^\circ$) for (III).

| | | | |
|---------------|-------------|-----------|-----------|
| O1–C2 | 1.357 (3) | N2–C3 | 1.379 (3) |
| O1–C10 | 1.391 (2) | C2–C3 | 1.386 (3) |
| O2–C6 | 1.215 (3) | C4–C13 | 1.527 (3) |
| O4–N2 | 1.262 (2) | C5–C10 | 1.330 (3) |
| O5–N2 | 1.248 (2) | C5–C6 | 1.468 (3) |
| N1–C2 | 1.309 (3) | | |
| C2–O1–C10 | 119.85 (17) | C14–O3–C1 | 118.2 (2) |
| C1–O3–C14–C15 | –5.9 (4) | | |

Table 4

Hydrogen-bond geometry (\AA , $^\circ$) for (III).

| $D-H\cdots A$ | $D-H$ | $H\cdots A$ | $D\cdots A$ | $D-H\cdots A$ |
|------------------------------------|----------|-------------|-------------|---------------|
| N1–H1B \cdots O4 | 0.86 | 2.01 | 2.602 (3) | 125 |
| N1–H1B \cdots O4 ⁱⁱⁱ | 0.86 | 2.28 | 3.052 (3) | 150 |
| N1–H1A \cdots O1W ⁱⁱⁱ | 0.86 | 2.50 | 3.115 (3) | 129 |
| O1W–H1W \cdots O5 | 0.99 (4) | 1.99 (4) | 2.980 (3) | 179 (5) |
| O1W–H1W \cdots O4 | 0.99 (4) | 2.55 (4) | 3.216 (3) | 125 (5) |

Symmetry code: (iii) $-x, -y + 2, -z$.

In both organic molecules, the H atoms were placed in geometrically calculated positions and refined using a riding model, with C–H distances of 0.95 and 0.93 \AA in (II) in (III), respectively, for aromatic H atoms, 0.98 and 0.96 \AA for methyl H atoms, 0.99 and 0.97 \AA for CH₂ H atoms, 1.0 and 0.98 \AA for CH H atoms, and 0.88 and 0.86 \AA for NH₂ groups, with $U_{\text{iso}}(\text{H})$ values of $1.2U_{\text{eq}}(\text{C,N})$ or $1.5U_{\text{eq}}(\text{methyl C})$. In (III), the H atom of the water molecule was located in a difference Fourier map and refined isotropically.

For compound (II), data collection: *P3/PC* (Siemens, 1989); cell refinement: *P3/PC*. For compound (III), data collection: *CAD-4 Software* (Enraf–Nonius, 1989); cell refinement: *CAD-4 Software*. For both compounds, data reduction: *SHELXTL-Plus* (Sheldrick, 1994);

program(s) used to solve structure: *SHELXS97* (Sheldrick, 1990); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL-Plus*; software used to prepare material for publication: *SHELXL97*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: FG1879). Services for accessing these data are described at the back of the journal.

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