

Dithioether ligands containing a 2,6-disubstituted pyridine linker with two thioether-heterocycle arms

Archimede Rotondo,* Giuseppe Bruno, Francesco Nicoló, Giuseppe Tresoldi and Santo Di Pietro

Dipartimento di Chimica Inorganica, Chimica Analitica e Chimica Fisica, Università di Messina, Salita Sperone 31, 98166 Messina, Italy
Correspondence e-mail: arotondo@unime.it

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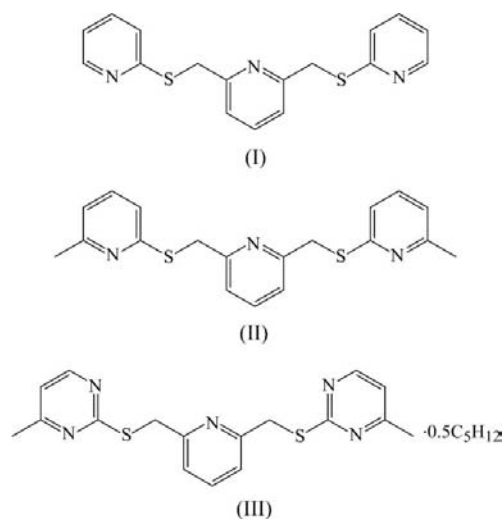
The structure of 2,6-bis(2-pyridylsulfanylmethyl)pyridine (pytmp), (I), $C_{17}H_{15}N_3S_2$, presents a twisted conformation, with the three planar moieties almost perpendicular to each other. The structures of two related derivatives, namely 2,6-bis(6-methyl-2-pyridylsulfanylmethyl)pyridine (mpytmp), (II), $C_{19}H_{19}N_3S_2$, and 2,6-bis(4-methyl-2-pyrimidylsulfanylmethyl)pyridine (mprtmp) *n*-pentane hemisolvate, (III), $C_{17}H_{17}N_5S_2 \cdot 0.5C_5H_{12}$, present extended planar fragments with just one quasi-perpendicular arylsulfanylmethyl side arm, such that the molecules are folded in an L-shaped conformation. All three conformations appear different from those adopted by similar compounds, demonstrating the great flexibility of such species, although such differences in conformational behaviour might drive specific coordination modes.

Comment

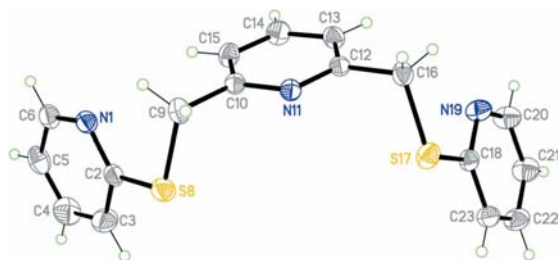
The coordination chemistry of chelate ligands containing mixed functionalities in transition metal complexes is an active area of research. In particular, the chemistry of hemilabile ligands, which contain both inert and labile groups, has received considerable attention (Slone *et al.*, 1999; Vagg, 1987; Heard, 2007). Some years ago, while studying thioether ligands with aromatic N-heterocycles, we found that these usually *N,N'*-bidentate donors often show *N,S*-chelation towards congested ruthenium substrates (Scopelliti *et al.*, 2001; Tresoldi *et al.*, 2008). The resultant complexes display dynamic stereochemical rearrangements, which involve inversion at the S atom coordinated to ruthenium (Tresoldi *et al.*, 2002), restricted rotation of the pendant ring (Baradello *et al.*, 2004), and exchange between *N,N'*-chelation, *N,S*-chelation with the formation of a five-membered ring and *N,S*-chelation with the formation of a four-membered ring (Tresoldi *et al.*, 2002). However, species containing the last coordination type are, generally, low-concentration isomers in mixtures containing five-membered *N,S*-chelate species. Furthermore, the ex-

change processes between four- and five-membered *N,S*-chelated species show high energy barriers (Tresoldi *et al.*, 2008).

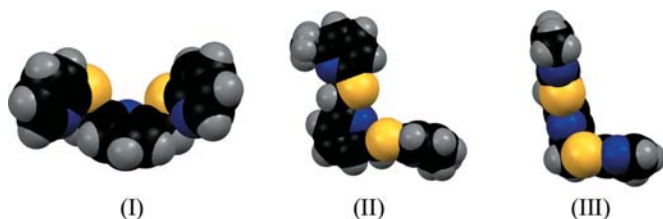
With the aim of favouring the formation of four-membered *N,S*-chelated species and as an extension of our stereodynamic studies, we embarked on a programme which uses dithioether ligands containing a 2,6-disubstituted pyridine linker with two thioether-heterocycle arms to prepare fluxional transition metal complexes. These dithioether compounds can also be used as antiviral compounds (Joseph-McCarthy *et al.*, 2001; Tsang *et al.*, 2001). Furthermore, compounds bearing S and N donor atoms tend to form a great variety of structurally interesting supramolecular entities, in particular with group 11 metals (Peng *et al.*, 2006; Han *et al.*, 2005; Amoores *et al.*, 2005; Li *et al.*, 2004; Park *et al.*, 2005). Since the flexible backbone of these dithioethers allows great structural diversity, we first investigated the Cambridge Structural Database (CSD, Version 5.30; Allen, 2002) in order to understand the influence of the chemical nature of the outer rings on the structural and conformational properties of the dithioether ligands. It must be mentioned that the X-ray determination of 2,6-bis(2-pyrimidylsulfanylmethyl)pyridine (prttmp) has already been reported (Peng *et al.*, 2006). We prepared the dithioethers by the reaction of the pyridine- or pyrimidinethiolate, formed *in situ* from KOH and the appropriate thiol, and 2,6-bis(chloromethyl)pyridine in butan-1-ol at high temperature. In this way, we were able to obtain the new ligand 2,6-bis(6-methyl-2-pyridylsulfanylmethyl)pyridine (mpytmp). Colourless crystals of the title compounds 2,6-bis(2-pyridylsulfanylmethyl)pyridine (pytmp), (I), 2,6-bis(6-methyl-2-pyridylsulfanylmethyl)pyridine (mpytmp), (II), and 2,6-bis(4-methyl-2-pyrimidylsulfanylmethyl)pyridine (mprtmp) *n*-pentane hemisolvate, (III), were obtained by slow evaporation of solvent mixtures and we present here their crystallographic characterization.



In (I), the pytmp molecule exists in a closed conformation (Figs. 1 and 2). Indeed, the approximately planar 2-pyridylsulfanylmethyl groups [maximum deviation from the mean N1/C2–C6/S8/C9 plane of 0.176 (2) Å for atom C3 and from the mean C16/S17/N19/C18–C23 plane of 0.106 (1) Å for atom


Figure 1

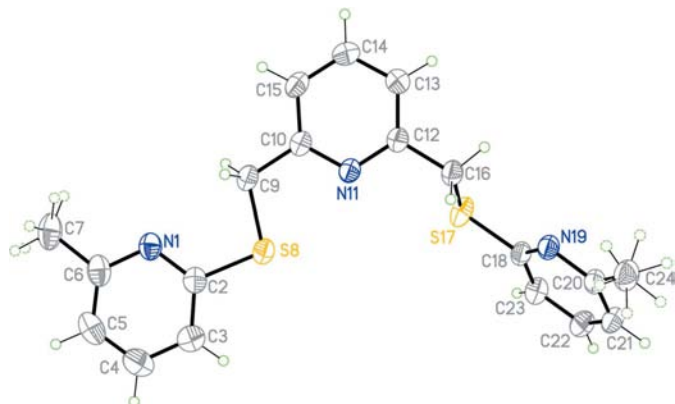
The molecular structure of (I), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 40% probability level and H atoms are shown as small spheres of arbitrary radii.


Figure 2

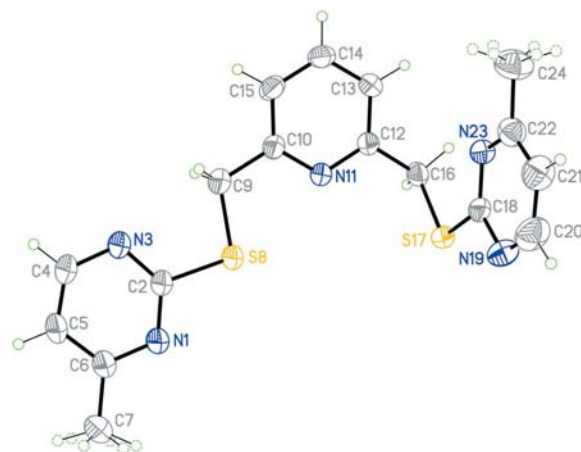
Space-filling views of the molecular conformations of (I), (II) and (III).

C16] are both almost perpendicular with respect to the 2,6-dimethylpyridine core [angles between the mean planes = 75.88 (2) and 70.25 (3)°, respectively]. This arrangement, with a pseudo- C_s symmetry (Figs. 1 and 2, and Table 1), is also stabilized by dipolar intramolecular interactions between the methylene groups and the nearby pyridine N atoms ($C9 \cdots N1 = 2.91 \text{ \AA}$, $H9A \cdots N1 = 2.39 \text{ \AA}$ and $C9-H9A \cdots N1 = 113^\circ$, and $C16 \cdots N19 = 2.93 \text{ \AA}$, $H16B \cdots N19 = 2.44 \text{ \AA}$ and $C16-H16B \cdots N19 = 111^\circ$). The overall three-dimensional packing is stabilized by hydrophobic interactions and by a weak dipolar intermolecular interaction aligning molecules along the crystallographic screw b axis [$C9 \cdots S17^i = 3.76 \text{ \AA}$ and $C9-H9B \cdots S17^i = 144^\circ$; symmetry code: (i) $-x + \frac{3}{2}, y + \frac{1}{2}, -z + \frac{1}{2}$] (Fig. 5).

In the structure of (II), the central pyridyl ring of the mpytmp molecule is roughly coplanar with one of the side arms [Fig. 3; angle between mean planes = 6.90 (3)°], so that an extended part of the molecule is roughly planar, with a maximum overall deviation from the N1/C2–C6/S8/C9/C10/C15 mean plane (excluding C7) of 0.405 (2) Å for atom C4. Because of steric hindrance, the other (6-methyl-2-pyridyl)sulfanylmethyl group is tilted out of this plane; the angle between the N1/C2–C6/S8/C9/C10/C15 (excluding C7) and C16/S17/N19/C18–C23 mean planes is 64° (see also the comparison of selected parameters in Table 1). The crystal packing is mainly supported by nonpolar interactions, such as head-to-tail π – π staggered stacking between homologous extended N1/C2–C6/S8/C9/C10/C15 planar moieties related by the the symmetry code ($-x + 1, -y + 1, -z + 1$) [an interplanar distance of 3.503 (3) Å, a centroid-to-centroid distance of 4.234 (3) Å, and an angle between the line linking the two inversion-related centroids and the planes of 34 (s.u.?)°]. The whole crystal packing is made up of stacked L-shaped molecules (Fig. 2) filling the three-dimensional space (Fig. 6).


Figure 3

The molecular structure of (II), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 40% probability level and H atoms are shown as small spheres of arbitrary radii.


Figure 4

The molecular structure of (III), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 40% probability level and H atoms are shown as small spheres of arbitrary radii.

The asymmetric unit of (III) is composed of one mprtmp molecule (Fig. 4) and half of an n -pentane molecule disordered around the crystallographic inversion centre. Again, the mprtmp molecule shows an extended planar moiety for atoms N1/C2/N3/C4–C6/S8/C9/C10/C15 (excluding C7) [maximum deviation from the mean plane of 0.259 (3) Å for atom C9], whereas the other ‘arm’ is out of the plane (angle between the mean planes of the extended group and C16/S17/C18/N19/C20–C22/N23 = 80°; see also dihedral angles in Table 1). This time, the mutual orientation of the planar fragments is different from (II), as can be deduced from the selected dihedral angles, but again the conformation of the molecule resembles an L-shaped building block (Fig. 2) for the crystal packing.

Because of some weak dipolar intermolecular interactions [$C15 \cdots N1^i = 3.70 \text{ \AA}$, $H15 \cdots N1^i = 2.79 \text{ \AA}$ and $C15-H15 \cdots N1 = 165^\circ$; $C15 \cdots S8^i = 3.83 \text{ \AA}$, $H15 \cdots S8^i = 3.19 \text{ \AA}$ and $C15-H15 \cdots S8^i = 128^\circ$; $C14 \cdots S17^i = 3.86 \text{ \AA}$, $H14 \cdots S17^i = 3.17 \text{ \AA}$ and $C15-H15 \cdots S8^i = 132^\circ$; symmetry code: (i) $x - 1, y, z$], the mprtmp units of (III) are arrayed along the crystallographic a axis. The L-shaped conformation allows a brick-

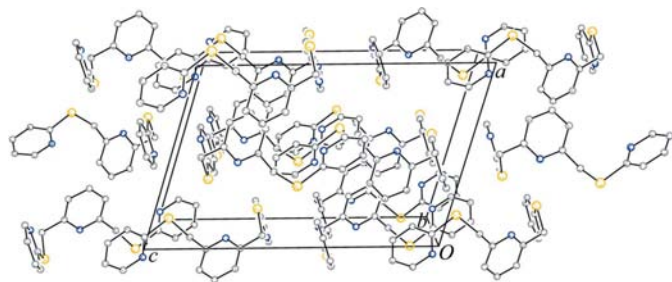


Figure 5
The crystal packing of (I). S atoms are shown with larger radii.

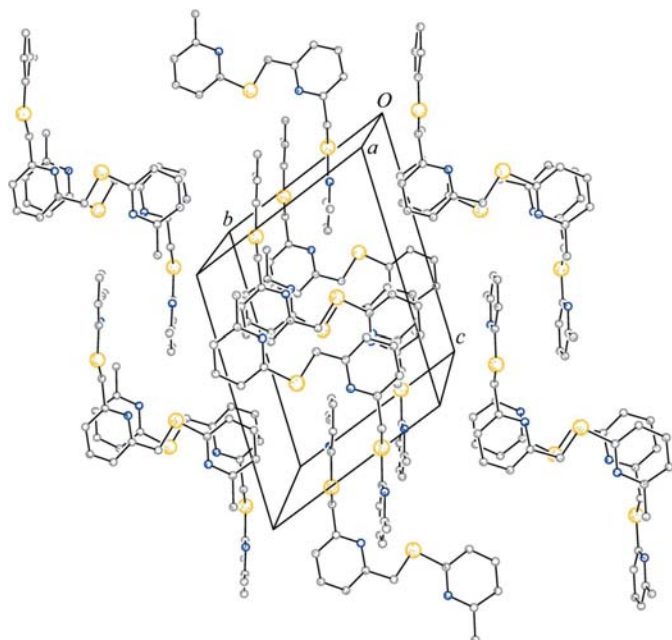


Figure 6
The crystal packing of (II). S atoms are shown with larger radii.

like filling of the other two space directions, further supported by π - π staggered interactions between the single pyridyl fragments related by the symmetry code $(-x + 2, -y, -z + 2)$ [with a mean interplanar distance of 3.472 (3) Å, a centroid-to-centroid distance of 3.521 (3) Å, and an angle between the line linking the two inversion-related centroids and the planes of 1.3 (2)°]. Channels of *n*-pentane solvent run along the crystallographic *a* axis (Fig. 7).

It is well known that 2,6-bis(arylsulfanylmethyl)pyridines, because of the orientation of the S-atom lone pairs, drastically change their conformation to bind to transition metals (Teixidor *et al.*, 2001). The conformations of (I)–(III) seem to be unique among uncoordinated 2,6-bis(arylsulfanylmethyl)pyridines (Luo *et al.*, 2006; Sillanpää *et al.*, 1994). This is likely allowed by the presence of *ortho* aromatic N atoms over the pendant side chains. However, the large deviation from the quasi- C_2 symmetric conformation of the very similar prtmp (Peng *et al.*, 2006; comparable with Luo *et al.*, 2006) confirms the high flexibility of such substrates, the major conformations of which are established only by weak inter- and intramolecular forces.

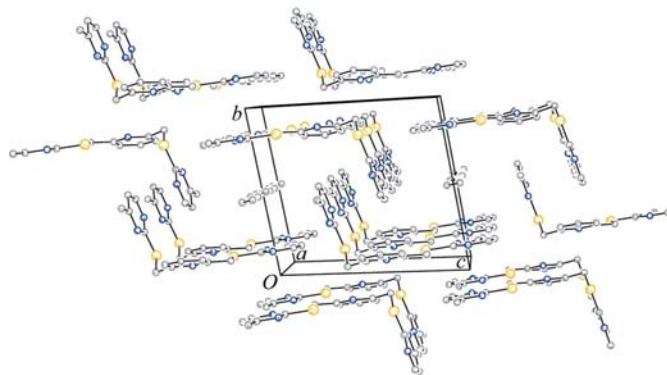


Figure 7
The crystal packing of (III). S atoms are shown with larger radii. The *n*-pentane solvent molecules are embedded in channels along the crystallographic *a* axis.

Experimental

For the preparation of 2,6-bis(2-pyridylsulfanylmethyl)pyridine, (I), a stirred mixture of KOH (2.17 g, 38.7 mmol) and 2-mercaptopyridine (4.30 g, 38.7 mmol) in butan-1-ol (60 ml) was heated under reflux for 1 h under N_2 . To the resulting thiolate solution, cooled to room temperature and stirred, were added slowly (over *ca* 30 min) and alternately small portions (*ca* 50 mg) of 2,6-bis(chloromethyl)pyridine (3.41 g, 19.4 mmol) and small aliquots (*ca* 1 ml) of butan-1-ol (20 ml). The solution was then heated to 363–373 K for 3 h. The solvent was removed and the residue extracted with CH_2Cl_2 (160 ml). Crystals suitable for X-ray analysis were obtained by slow evaporation from a solution in a 1:1 mixture of CH_2Cl_2 and *n*-heptane (50 ml). (I) is very soluble in $CHCl_3$ and CH_2Cl_2 , moderately soluble in acetone and sparingly soluble in diethyl ether.

2,6-Bis(6-methyl-2-pyridylsulfanylmethyl)pyridine, (II), was prepared in a similar manner to (I), using KOH (2.17 g, 38.7 mmol), 2-mercapto-6-methylpyridine (4.85 g, 38.7 mmol) and 2,6-bis(chloromethyl)pyridine (3.41 g, 19.4 mmol). The product obtained by extraction with CH_2Cl_2 and slow evaporation was an oil, which was dissolved in a mixture of diethyl ether (50 ml) and pentane (100 ml) and allowed to stand until colourless crystals of (II) suitable for X-ray analysis were formed. (II) is soluble in most common solvents.

2,6-Bis(4-methyl-2-pyrimidylsulfanylmethyl)pyridine *n*-pentane hemisolvate, (III), was prepared in a similar manner to (I), using 2-mercapto-4-methylpyrimidine hydrochloride (6.29 g, 38.7 mmol), KOH (4.34 g, 77.4 mmol) and 2,6-bis(chloromethyl)pyridine (3.41 g, 19.4 mmol). Crystals suitable for X-ray analysis were obtained by slow evaporation (*ca* 2 d) from a solution in a mixture of CH_2Cl_2 , *n*-heptane and *n*-pentane (2:1:1 *v/v*).

Spectroscopic and analytical data for compounds (I) and (II) are extensively reported in the archived CIF.

Compound (I)

Crystal data

$C_{17}H_{15}N_3S_2$	$V = 1557.7$ (3) Å ³
$M_r = 325.44$	$Z = 4$
Monoclinic, $P2_1/c$	Mo $K\alpha$ radiation
$a = 10.696$ (1) Å	$\mu = 0.34$ mm ⁻¹
$b = 9.281$ (1) Å	$T = 296$ K
$c = 16.741$ (1) Å	$0.38 \times 0.26 \times 0.14$ mm
$\beta = 110.39$ (2)°	

Data collection

Bruker APEXII CCD diffractometer
Absorption correction: multi-scan (SADABS; Bruker, 2007)
 $T_{\min} = 0.856$, $T_{\max} = 1.000$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.028$
 $wR(F^2) = 0.080$
 $S = 1.08$
3188 reflections

Compound (II)

Crystal data

$C_{19}H_{19}N_3S_2$
 $M_r = 353.49$
Triclinic, $P\bar{1}$
 $a = 7.946$ (1) Å
 $b = 9.842$ (1) Å
 $c = 12.503$ (1) Å
 $\alpha = 69.829$ (2)°
 $\beta = 75.053$ (2)°
 $\gamma = 80.807$ (2)°
 $V = 884.06$ (16) Å³
 $Z = 2$
Mo $K\alpha$ radiation
 $\mu = 0.31$ mm⁻¹
 $T = 296$ K
0.36 × 0.28 × 0.16 mm

Data collection

Bruker APEXII CCD diffractometer
Absorption correction: multi-scan (SADABS; Bruker, 2007)
 $T_{\min} = 0.934$, $T_{\max} = 1.000$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.032$
 $wR(F^2) = 0.089$
 $S = 1.05$
3351 reflections

Compound (III)

Crystal data

$C_{17}H_{17}N_5S_2 \cdot 0.5C_5H_{12}$
 $M_r = 391.57$
Triclinic, $P\bar{1}$
 $a = 7.407$ (1) Å
 $b = 11.100$ (1) Å
 $c = 12.428$ (1) Å
 $\alpha = 95.910$ (10)°
 $\beta = 99.800$ (10)°
 $\gamma = 97.310$ (10)°
 $V = 990.6$ (2) Å³
 $Z = 2$
Mo $K\alpha$ radiation
 $\mu = 0.28$ mm⁻¹
 $T = 296$ K
0.36 × 0.3 × 0.12 mm

Data collection

Bruker APEXII CCD diffractometer
Absorption correction: multi-scan (SADABS; Bruker, 2007)
 $T_{\min} = 0.898$, $T_{\max} = 1.000$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.044$
 $wR(F^2) = 0.135$
 $S = 1.06$
3758 reflections
264 parameters

Table 1

Comparison of selected geometric parameters (Å, °) for (I), (II) and (III).

Parameters	(I)	(II)	(III)
C2—S8	1.766 (1)	1.768 (1)	1.763 (2)
S8—C9	1.809 (1)	1.797 (1)	1.781 (2)
C16—S17	1.809 (1)	1.809 (1)	1.797 (2)
S17—C18	1.768 (1)	1.765 (1)	1.759 (2)
C2—S8—C9	102.4 (1)	100.3 (1)	100.1 (1)
C18—S17—C16	103.8 (1)	101.3 (1)	102.9 (1)
N1—C2—S8—C9	-16.3 (1)	15.1 (1)	-3.8 (2)
C3—C2—S8—C9	166.19 (12)	-165.6 (1)	176.3 (2)
C2—S8—C9—C10	-92.3 (1)	175.9 (1)	172.4 (2)
C12—C16—S17—C18	93.4 (1)	-172.7 (1)	-55.4 (2)
C16—S17—C18—N19	6.4 (1)	-4.7 (1)	128.0 (2)
C16—S17—C18—C23	-174.1 (1)	175.0 (1)	-72.3 (1)

All H atoms were located in difference Fourier maps and refined in ideal positions using the riding and rigid model technique, with C—H distances ranging from 0.93 (aromatic H) to 0.97 Å (methylene H), and with $U_{iso}(H) = 1.5U_{eq}(C)$ for methyl and $1.2U_{eq}(C)$ for aromatic and methylene H atoms. In (II) and (III), dynamic or statistical disorder of the methyl groups was treated as two totally staggered conformations with site-occupancy factors of 0.5. The half *n*-pentane solvent molecule in (III) was treated as a rigid group with a site-occupancy factor of 0.5 by restraining both displacement parameters and distances. The components of the anisotropic displacement parameters in the direction of the bonds were restrained to be equal within an effective standard deviation of 0.001, and additionally the U_{ij} components were restrained to approximate isotropic behaviour. C—C bond distances were restrained to 1.540 (5) Å and 1.3 C··C distances (C25··C27, C26··C28 and C27··C29) were restrained to 2.52 (1) Å. The *n*-pentane solvent molecule is disordered about inversion centres.

For all compounds, data collection: APEX2 (Bruker, 2007); cell refinement: SAINT (Bruker, 2007); data reduction: SAINT; program(s) used to solve structure: SHELXS97 (Sheldrick, 2008); program(s) used to refine structure: SHELXL97 (Sheldrick, 2008); molecular graphics: XP (Bruker, 2007), ORTEP-3 for Windows (Farrugia, 1997) and Mercury (Macrae *et al.*, 2006); software used to prepare material for publication: WinGX (Farrugia, 1999), PARST (Nardelli, 1995), enCIFer (Allen *et al.*, 2004) and PLATON (Spek, 2009).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: KU3018). Services for accessing these data are described at the back of the journal.

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