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Two thiosemicarbazones derived from salicylaldehyde: very specific hydrogen-bonding interactions of the N—H···S═C type

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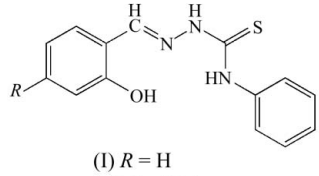
The molecular structures of two salicylaldehyde thiosemicarbazone derivatives, namely salicylaldehyde 4-phenylthiosemicarbazone, $C_{14}H_{13}N_3OS$, (I), and 4-methoxysalicylaldehyde 4-phenylthiosemicarbazone, $C_{15}H_{15}N_3O_2S$, (II), both of potential pharmacological interest, are found in the keto (thione) tautomeric form. The first compound represents a second triclinic polymorph of composition β-$C_{14}H_{13}N_3OS$. Although both polymorphs crystallize in the same space group ($P\overline{1}$), the α-polymorph [Seena, Kurup & Suresh (2008). *J. Chem. Crystallogr.* **38**, 93–96] differs from the β form in its unit-cell volume at 293 K. The molecules in the crystal structures of (I) and (II) are linked into centrosymmetric $R_2^2(8)$ dimers by hydrogen bonds of the N—H···S═C type. These dimers are connected through π–π stacking and T-shaped C—H···π interactions into three-dimensional networks.

Comment

Thiosemicarbazones are a class of organic molecules belonging to the large family of thiourea derivatives (Casas *et al.*, 2000). Widespread interest in the chemistry of thiosemicarbazones is associated with their broad spectrum of biological activities, with potential uses in antibacterial, antiviral and antitumour treatments (Bharti *et al.*, 2002; Smee & Sidwell, 2003; Hu *et al.*, 2006; Oliveira *et al.*, 2008). Many of their properties are a function of the parent aldehyde or ketone, and these properties can therefore be elegantly tuned by the appropriate choice of parent. From a structural perspective, thiosemicarbazones attract attention as interesting ligands due to their tendency to undergo tautomerism and form planar, highly rigid, Schiff bases capable of imposing a variety of mixed-donor coordination environments about metal cations. Thiosemicarbazones derived from salicylaldehyde can exist in several tautomeric forms but the most interesting are those denoted *A* and *B* in the scheme below. Such molecular isomerization can result in different binding modes. In form *A*, the molecule can act as a monoanionic ligand after losing the H atom from the hydroxyl group, or as a dianionic ligand after losing H atoms from the mercapto and hydroxyl groups of form *B*.

(*A*) Keto (thione) form (*B*) Enol (thiol) form



(I) R = H
(II) R = OMe

We present here the crystal structures of two closely related thiosemicarbazones derived from salicylaldehyde, *viz.* salicylaldehyde 4-phenylthiosemicarbazone, (I), and 4-methoxysalicylaldehyde 4-phenylthiosemicarbazone, (II). The structure of (I) has been reported previously (Seena *et al.*, 2008). The compound crystallized in the same space group ($P\overline{1}$) and we refer to it as the α-polymorph (obtained from ethanol). We have now obtained a second triclinic polymorph of (I), denoted the β-polymorph (obtained from methanol). Although both polymorphs crystallize in space group No. 2, they have different unit-cell volumes at 293 K and their unit-cell parameters are different [in particular, V = 2002.1 (5) Å^3 for the α-polymorph and V = 1339.6 (1) Å^3 for the β-polymorph]. These two forms of (I) have different numbers of

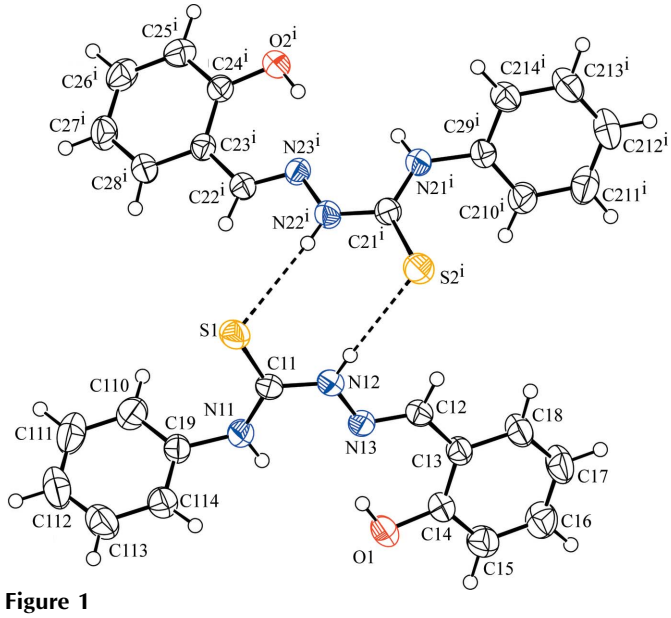


Figure 1
A view of the molecular structure of the centrosymmetric dimer of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii. Hydrogen bonds are indicated by dashed lines. [Symmetry code: (i) 1 + x, y, z.]

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molecules in the asymmetric unit (three and two, respectively). The asymmetric unit of (I) consists of two crystallographically independent molecules, (I*a*) and (I*b*) (Fig. 1). The molecular structures of (I) (in both polymorphs) and (II) (Fig. 2) are very similiar, but not equal. The crystal structures are characterized by a great variety of interactions, especially of the N—H···S type, and these will be discussed later.

The atom-labelling schemes are almost the same. In the following discussion, the order of the compounds for a given value is (I*a*) and (I*b*) of (I), then (II). Selected bond lengths and bond angles for (I) and (II) are given in Tables 1 and 3. Similar to many uncomplexed and unprotonated thiosemicarbazones (Soriano-García *et al.*, 1986; Dinçer *et al.*, 2005; Seena *et al.*, 2008), a *trans* configuration of atom S1 with respect to atom N3 is observed [S1—C1—N2—N3 = −178.51 (10), −178.04 (10) and 176.30 (9)°] and atom N1 is in a *cis* configuration with respect to atom N3. The C—S bond lengths do not differ significantly from that found in thiourea (Truter, 1967). This bond, together with the C1—N2 and C1—N1 bond lengths (Tables 1 and 3), indicate that the molecules in the crystal structures of (I) and (II) are in the keto (thione) form. This is also in agreement with the absence of a strong band in the IR spectra centred at 2500 cm^{-1} [ν(S—H) stretching mode].

The molecular structures of (I) and (II) consist of three structural fragments, *viz.* salicyl and phenyl parts separated by the central thiosemicarbazone part. The salicyl–thiosemicarbazone parts of the molecules are almost planar. Maximum deviations from the plane in molecule (I*a*) are −0.214 (1), 0.183 (1) and −0.138 (2) Å for N11, O1 and C17, respectively [−0.192 (1), 0.107 (1) and 0.097 (1) Å for N21, N22 and O2 in (I*b*), and 0.285 (2), −0.140 (2), −0.092 (1) Å for N1, C15 and C1 in (II)]. The dihedral angle between the planes of the salicyl–thiosemicarbazone parts and the phenyl ring on atom N1 of 64.44 (4)° [and 53.07 (4) and 52.16 (5)°] indicates nonplanarity of the ligands, although the thiosemicarbazone parts themselves are planar. Such an arrangement allows delocalization of the π-electrons in the N1—C1—N2—N3—C2 groups. The salicylaldimine parts of the molecules in the crystal structures of (I) and (II) are characterized by a six-membered pseudo-aromatic ring (N3—

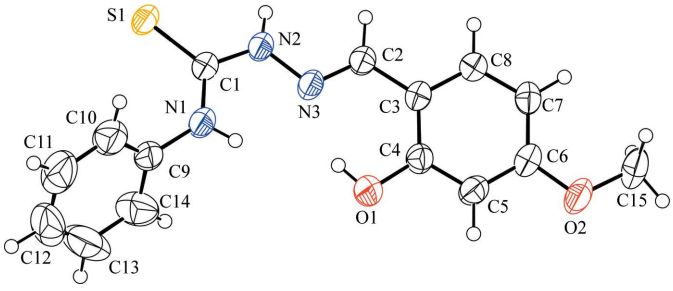


Figure 2
A view of the molecular structure of (II), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

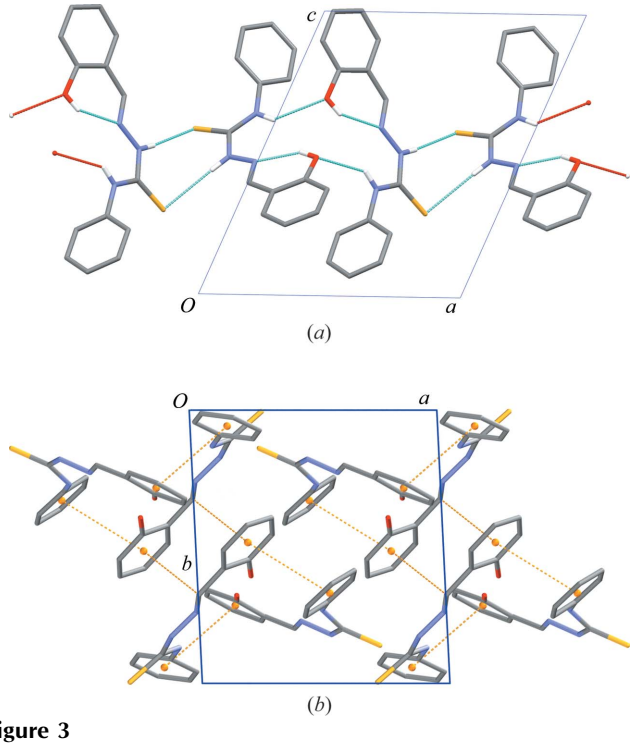


Figure 3
The crystal packing of (I), viewed down (*a*) the *b* axis and (*b*) the *c* axis. Hydrogen bonds and π–π stacking interactions are indicated by dashed lines.

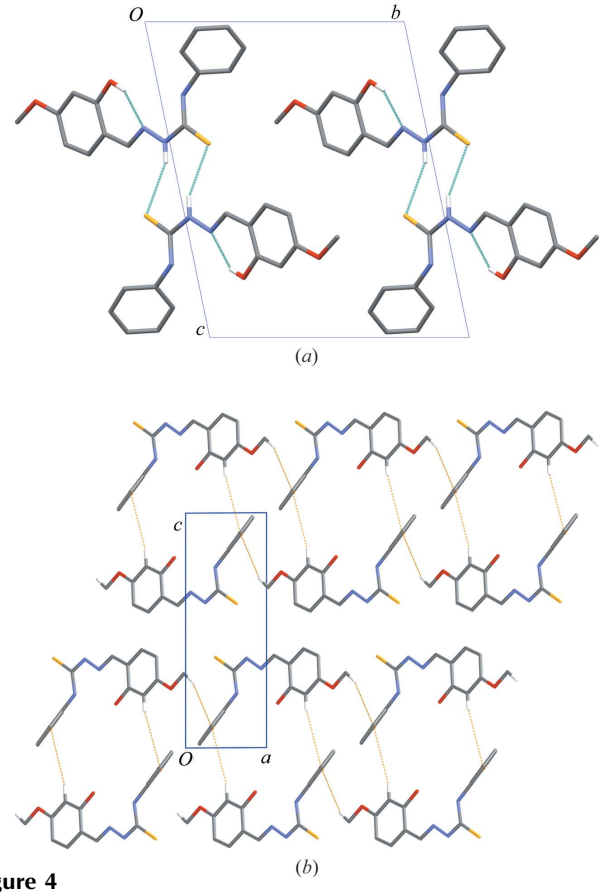
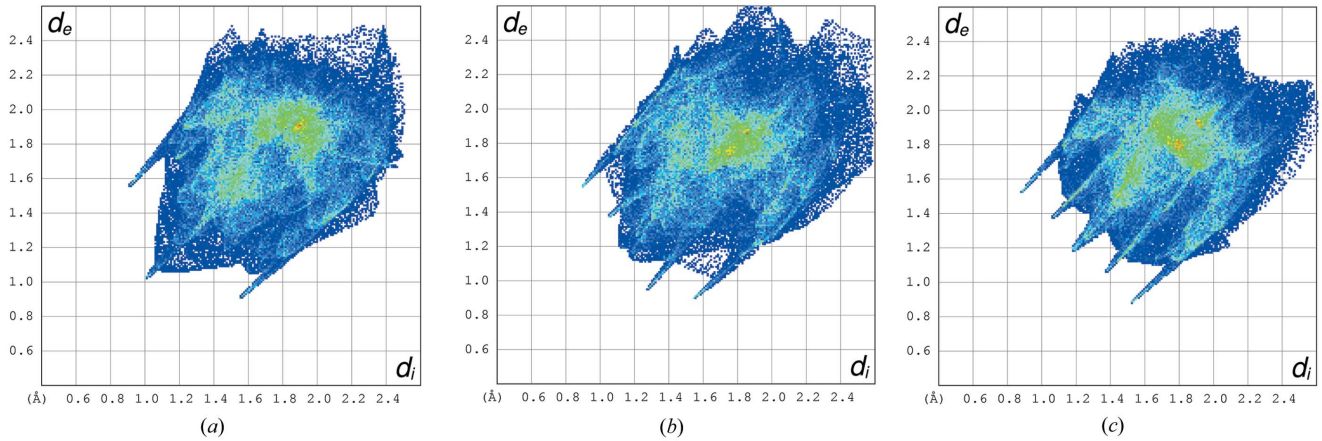


Figure 4
The crystal packing of (II), viewed down (*a*) the *a* axis and (*b*) the *b* axis. Hydrogen bonds and C—H···π interactions are indicated by dashed lines.



(*a*) (*b*) (*c*)

Figure 5
Two-dimensional fingerprint plots for (*a*) the α-polymorph of (I), (*b*) the β-polymorph of (I) and (*c*) (II).

C2—C3—C4—O1—H1O). Rings are formed by an intramolecular hydrogen bond [*S*(6)] which is enhanced by π-electron delocalization, as can be seen easily from the bond lengths within the rings (Tables 1 and 3). Such resonance-assisted hydrogen bonds seem to be the general features of the crystal structures of thiosemicarbazones and Schiff bases derived from salicylaldehyde (Soriano-García *et al.*, 1986; Popović *et al.*, 2002). The C4—O1 bond lengths (Tables 1 and 3) are comparable with those found in phenols (Allen *et al.*, 1987). In contrast, C2—N3 is assigned as a double bond. The endocyclic bond distances and angles found in the phenyl rings, with the exception of that at C3, do not differ from those in normal sp^2-hybridized moieties. The measured collapse of the C4—C3—C8 angles together with the good electron-donor properties of the O atom may be a consequence of the conjugation of the phenyl ring with the thiosemicarbazone parts of the molecules.

The crystal packings are characterized by a great variety of hydrogen bonds (presented in Tables 2 and 4). A close inspection of the unit cells (Figs. 3 and 4) and two-dimensional fingerprint plots derived from Hirshfeld surfaces (McKinnon *et al.*, 2004) of both polymorphs of (I) and (II) revealed very specific N—H···S hydrogen bonding (spikes centred around 2.6 Å). This type of structural motif [denoted $R_2^2(8)$; Etter *et al.*, 1990] is very common in the crystal structures of thiosemicarbazones (Soriano-García *et al.*, 1986; Sampath *et al.*, 2003; Dinçer *et al.*, 2005).

Figs. 5(*a*) and 5(*b*) unambiguously show that different intermolecular interactions are present in the α- and β-polymorphs, which result in different packing modes. In the α-polymorph, the shortest contacts correspond to the very close H···H contacts [H25···H25^{i} and H3···H27^{ii} are 2.25 (4) and 2.25 (6) Å; symmetry codes: (i) $-x, -y, 2-z$; (ii) $1-x, -y, 1-z$]. In plots of (I) and (II) (Figs. 5*b* and 5*c*) 'wings' are more pronounced, which indicate aromatic interactions [π···π stacking: C14···C214 and C114···C24 distances are 3.237 (2) and 3.267 (2) Å, respectively, in (I)] and there are T-shaped C—H···π contacts between the molecules in (II) [C12···H5^{iii} and C10···H15*B*^{iv} = 2.93 and 2.86 Å, respectively; symmetry codes: (iii) $2-x, -y, -z$; (iv) $-2+x, 1+y, z$)].

Experimental

Compound (I) was prepared by slight modification of the procedure described by Purohit *et al.* (1989), using methanol as the solvent instead of ethanol. White needle-like crystals were obtained directly from the reaction mixture as the first form of compound (I). The structure of this α-polymorph, obtained from ethanol, was recently published by Seena *et al.* (2008). The remaining mother liquor was kept at room temperature and after 2–3 weeks yielded the β-polymorph of compound (I) in the form of transparent prisms. The crystals were filtered off and dried over KOH. From this batch were picked single crystals suitable for X-ray diffraction. Compound (II) was prepared by adopting a similar procedure as for (I). Equimolar amounts of 4-phenylthiosemicarbazide and 4-methoxysalicylaldehyde were dissolved in methanol and stirred until white needle-like crystals started to precipitate (4–5 h). After standing overnight, the compound was filtered off and dried in a desiccator (over KOH). The mother liquor was kept at room temperature and after 6 d yielded single crystals of (II) suitable for X-ray diffraction. Elemental analysis calculated for $C_{15}H_{15}N_3O_2S$: C 59.78, H 5.02, N 13.94, S 10.64%; found: C 59.67, H 4.96, N 13.87, S 10.60%.

Compound (I)

Crystal data

$C_{14}H_{13}N_3OS$
M_r = 271.34
Triclinic, $P\overline{1}$
a = 10.6328 (3) Å
b = 11.1114 (3) Å
c = 12.8839 (10) Å
α = 75.251 (5)°
β = 65.652 (2)°
γ = 81.539 (2)°
V = 1339.56 (12) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.24 mm^{-1}
T = 293 (2) K
0.79 × 0.59 × 0.20 mm

Data collection

Oxford Diffraction Xcalibur CCD diffractometer
Absorption correction: analytical (*CrysAlis RED*; Oxford Diffraction, 2003)
T_{min} = 0.856, T_{max} = 0.936
14306 measured reflections
4676 independent reflections
4184 reflections with $I > 2\sigma(I)$
R_{int} = 0.012

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.031
$wR(F^2)$ = 0.079
S = 1.03
4676 reflections
345 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.15 e Å^{-3}
$\Delta\rho_{min}$ = −0.20 e Å^{-3}

Table 1
Selected bond lengths (Å) for (I).

C11—N11	1.3341 (17)	C21—N21	1.3361 (17)
C11—N12	1.3515 (17)	C21—N22	1.3416 (17)
C11—S1	1.6758 (14)	C21—S2	1.6827 (13)
C12—N13	1.2816 (17)	C22—N23	1.2790 (17)
C12—C13	1.447 (2)	C22—C23	1.4470 (18)
C13—C14	1.400 (2)	C23—C24	1.4019 (18)
C14—O1	1.3563 (17)	C24—O2	1.3575 (16)
C19—N11	1.4300 (17)	C29—N21	1.4251 (17)
N12—N13	1.3770 (16)	N22—N23	1.3764 (15)

Table 2
Hydrogen-bond geometry (Å, °) for (I).

D—H···A	D—H	H···A	D···A	D—H···A
N11—H11N···O2	0.86	2.37	3.0881 (16)	141
O1—H1O···N13	0.82	2.01	2.7252 (16)	145
N21—H21N···O1	0.86	2.56	3.2806 (18)	142
O2—H2O···N23	0.82	1.98	2.6984 (14)	146
N12—H12N···S2^{i}	0.86	2.58	3.4391 (12)	175
N22—H22N···S1^{ii}	0.86	2.59	3.4398 (11)	172

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

Compound (II)

Crystal data

$C_{15}H_{15}N_3O_2S$
M_r = 301.37
Triclinic, $P\overline{1}$
a = 4.73851 (17) Å
b = 11.3244 (4) Å
c = 14.0775 (5) Å
α = 78.390 (3)°
β = 89.547 (3)°
γ = 89.364 (3)°
V = 739.90 (5) Å^3
Z = 2
Mo $K\alpha$ radiation
μ = 0.23 mm^{-1}
T = 293 (2) K
0.40 × 0.35 × 0.30 mm

Data collection

Oxford Diffraction Xcalibur CCD diffractometer
8408 measured reflections
2591 independent reflections
2230 reflections with $I > 2\sigma(I)$
R_{int} = 0.015

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.030
$wR(F^2)$ = 0.087
S = 1.08
2591 reflections
192 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.16 e Å^{-3}
$\Delta\rho_{min}$ = −0.17 e Å^{-3}

H atoms were constrained to ideal geometry using an appropriate riding model, with C—H = 0.93–0.96 Å, N—H = 0.86 Å and O—H = 0.82 Å, and with U_{iso}(H) = 1.2U_{eq}(C,N) or 1.5U_{eq}(O).

For both compounds, data collection: *CrysAlis CCD* (Oxford Diffraction, 2003); cell refinement: *CrysAlis RED* (Oxford Diffraction, 2003); data reduction: *CrysAlis RED*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *ORTEP-3* (Farrugia, 1997) and *Mercury* (Macrae *et al.*, 2006); software used to prepare material for publication: *PLATON* (Spek, 2003).

Table 3
Selected bond lengths (Å) for (II).

C1—N1	1.3331 (18)	C3—C4	1.4000 (19)
C1—N2	1.3441 (17)	C4—O1	1.3551 (17)
C1—S1	1.6768 (13)	C9—N1	1.4249 (19)
C2—N3	1.2797 (17)	N2—N3	1.3812 (15)
C2—C3	1.4514 (17)		

Table 4
Hydrogen-bond geometry (Å, °) for (II).

D—H···A	D—H	H···A	D···A	D—H···A
O1—H1O···N3	0.82	1.94	2.6642 (15)	146
C13—H13···O1^{i}	0.93	2.54	3.387 (2)	151
C14—H14···O1^{ii}	0.93	2.67	3.487 (3)	147
N2—H2N···S1^{iii}	0.86	2.58	3.3862 (12)	156

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

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: AV3157). Services for accessing these data are described at the back of the journal.

References

Allen, F. H., Kennard, O., Watson, D. G., Brammer, L., Orpen, A. G. & Taylor, R. (1987). *J. Chem. Soc. Perkin Trans. 2*, pp. S1–19.
Bharti, N., Husain, K., Garza, M. T. G., Cruz-Vega, D. E., Castro-Garza, J., Mata-Cardenas, B. D., Naqvi, F. & Azam, A. (2002). *Bioorg. Med. Chem. Lett.* **12**, 3475–3478.
Casas, J. S., García-Tasende, M. S. & Sordo, J. (2000). *J. Coord. Chem. Rev.* **209**, 197–261.
Dinçer, M., Özdemir, N., Çukurovalı, A. & Yılmaz, İ. (2005). *Acta Cryst.* E**61**, o880–o883.
Etter, M. C., MacDonald, J. C. & Bernstein, J. (1990). *Acta Cryst.* B**46**, 256–262.
Farrugia, L. J. (1997). *J. Appl. Cryst.* **30**, 565.
Hu, W., Zhou, W., Xia, C. & Wen, X. (2006). *Bioorg. Med. Chem. Lett.* **16**, 2213–2218.
Macrae, C. F., Edgington, P. R., McCabe, P., Pidcock, E., Shields, G. P., Taylor, R., Towler, M. & van de Streek, J. (2006). *J. Appl. Cryst.* **39**, 453–457.
McKinnon, J. J., Spackman, M. A. & Mitchell, A. S. (2004). *Acta Cryst.* B**60**, 627–668.
Oliveira, R. B., Souza-Fagundes, E. M., Soares, R. P. P., Andrade, A. A., Krettli, A. U. & Zani, C. L. (2008). *Eur. J. Med. Chem.* **43**, 1983–1988.
Oxford Diffraction (2003). *CrysAlis CCD* and *CrysAlis RED*. Versions 1.170. Oxford Diffraction Ltd, Abingdon, England.
Popović, Z., Pavlović, G., Matković-Čalogović, D., Roje, V. & Leban, I. (2002). *J. Mol. Struct.* **615**, 23–31.
Purohit, S., Koley, A. P., Prasad, L. S., Manoharan, P. T. & Ghosh, S. (1989). *Inorg. Chem.* **28**, 3735–3742.
Sampath, N., Malathy Sony, S. M., Ponnuswamy, M. N. & Nethaji, M. (2003). *Acta Cryst.* C**59**, o346–o348.
Seena, E. B., Kurup, P. M. R. & Suresh, E. (2008). *J. Chem. Crystallogr.* **38**, 93–96.
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.
Smee, D. F. & Sidwell, R. W. (2003). *Antiviral Res.* **57**, 41–52.
Soriano-García, M., Valdés-Martínez, J., Toscano, R. A., Gómez-Lara, J. & Villalobos-Peñaloza, M. (1986). *Acta Cryst.* C**42**, 623–625.
Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.
Truter, M. R. (1967). *Acta Cryst.* **22**, 556–559.