Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

2-[4-Phenyl-5-(2-pyridyl)-4*H*-1,2,4-triazol-3-yl]nicotinic acid: a case of solvent-dependent polymorphism

Liliana Mazur,[a] Anna E. Koziol[a]* and Bozena Modzelewska-Banachiewicz[b]

[a]Department of Crystallography, Faculty of Chemistry, Maria Curie-Sklodowska University, 20031 Lublin, Poland, and [b]Department of Organic Chemistry, Faculty of Pharmacy, Nicolaus Copernicus University, 85067 Bydgoszcz, Poland
Correspondence e-mail: anna.koziol@poczta.umcs.lublin.pl

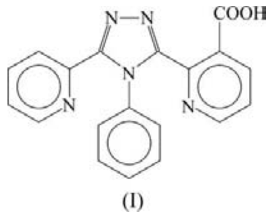
Received 14 July 2008
Accepted 16 September 2008
Online 25 September 2008

The title compound, $C_{19}H_{13}N_5O_2$, crystallizes in two monoclinic forms depending on the solvent used. From methanol or acetone, a yellow form [(I*a*), m.p. 533 K] in the space group $P2_1$ is obtained, while with ethanol as the solvent, an orange form [(I*b*), m.p. 541 K] in the space group *Cc* results. The conformers observed in the two polymorphs differ primarily in the relative orientation of pyridine/phenyl and triazole rings. Molecules of both polymorphs form chains through carboxyl O—H···N hydrogen bonding; however, in each crystal structure, a different group acts as acceptor, *viz.* a triazole and a pyridyl N atom for (I*a*) and (I*b*), respectively. This is the first case of polymorphism observed for crystals of a 3,4,5-trisubstituted 1,2,4-triazole derivative.

Comment

The phenomenon of polymorphism plays a vital role in the manufacture of pharmaceuticals, as well as in other biological and chemical fields. Polymorphic solids of the same chemical compound differ in internal solid-state structure and, as a consequence, possess different chemical and physical properties, including thermodynamic, spectroscopic, kinetic or mechanical properties. These properties can have a direct impact on a substance's stability, solubility, bioavailability or activity. However, polymorphism is not very well understood either at the crystallographic or at the molecular level. Its occurrence is unpredictable and may be caused by small differences in crystallization temperature, pressure, acidity or the nature of the mother liquor from which the substance was crystallized (solvent-dependent polymorphism) (Bernstein, 2002).

The present study is a continuation of our investigations on the structural characterization of aromatic derivatives of 4*H*-1,2,4-triazole (Mazur *et al.*, 2004*a*,*b*, 2007). The conformational flexibility of these molecules, arising from a potential rotation between aryl and triazole rings, gives the possibility of the formation of polymorphic forms. However, thus far, no polymorphs have been found for 3,4,5-trisubstituted 1,2,4-triazole derivatives, both aromatic and aliphatic.



(I)

We report here the crystal structures of two polymorphic forms of 2-[4-phenyl-5-(2-pyridyl)-4*H*-1,2,4-triazol-3-yl]nicotinic acid, *viz.* (I*a*) and (I*b*). The molecular structures observed in (I*a*) and (I*b*) (Fig. 1) are composed of a central 1,2,4-triazole ring, substituted at C5 by a 3-carboxy-2-pyridyl group, at C3 by a 2-pyridyl group and at N4 by a phenyl group. The interatomic distances within the triazole rings are not equal, ranging from 1.300 (2) to 1.389 (2) Å (Tables 1 and 3). The C3—N4 and N4—C5 bond lengths indicate single-bond char-

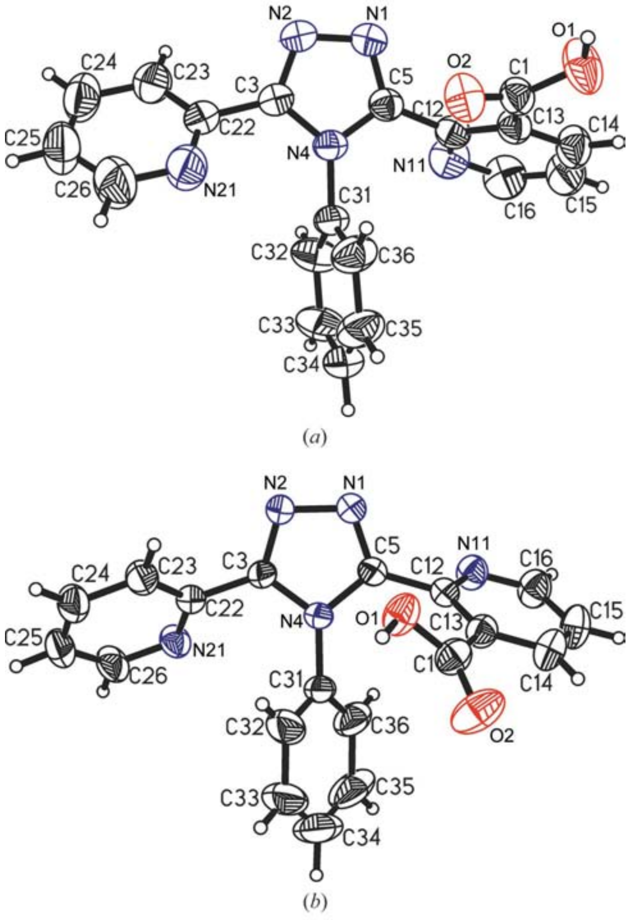


Figure 1
Molecules of the title compound, showing the atom-numbering schemes: (*a*) polymorphic form (I*a*) and (*b*) form (I*b*). Displacement ellipsoids are drawn at the 50% probability level.

doi:10.1107/S0108270108029806

acter, whereas the N1—C5 and N2—C3 distances are indicative of significant double-bond character. The substituent atoms C22 and C31 in both polymorphs, as well as atom C12 in (I*b*), are almost coplanar with the central triazole ring, whereas atom C12 in (I*a*) is displaced from the triazole plane by 0.151 (2) Å. This out-of-plane deformation may result from intermolecular interactions. The N21—C22 bonds in the pyridyl groups and N1—N2 bonds in the triazole rings are also influenced by intermolecular contacts. All four rings in both polymorphic forms are almost perfectly planar. As in all similar compounds reported in the Cambridge Structural Database (CSD, Version 5.29; Allen, 2002; refcodes AYEFOZ, FAXRAY, FAXSON, HIYFAW, IWOROB, MATKOH, MEGWIF, MEGXAY, NIFJUH, NUBCES, QAYVOB, QUIWVOH, TAWMAG and VERYEX), these aromatic rings are not coplanar (Fig. 2). The interplanar angles between the triazole and its substituent rings are in the range 40.7 (2)–83.0 (2)° (Table 5). Moreover, the relative orientation of the N atoms of the 2-pyridyl substituents at C3 and C5 is opposite for forms (I*a*) and (I*b*). Molecule (I*a*) possesses *transoidally* oriented pyridyl groups, while (I*b*) is a *cisoid* conformer (Fig. 2). Besides the orientation of the rings, another significant difference between polymorphic conformers is observed, which is the relative orientation of the N11-pyridyl ring and the COOH group (substituted at the C13 position). The O1—C1—C13—C12 torsion angles indicate that the protonated carboxyl O1 atom is oriented *trans* in (I*a*) and *cis* in (I*b*) with respect to pyridyl C12 atom (Fig. 2). All these conformational differences are accompanied by different intermolecular O—H···N hydrogen-bond patterns.

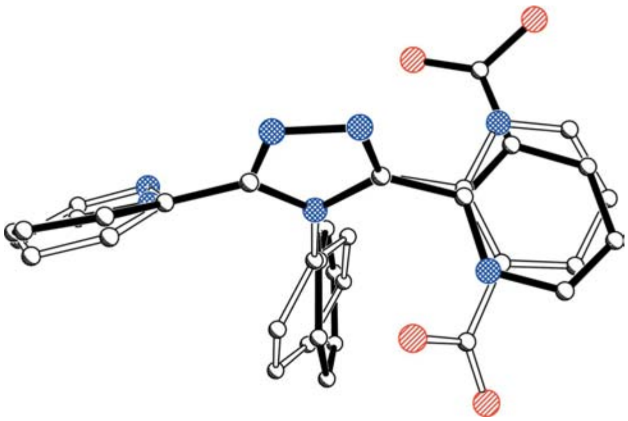


Figure 2
Molecular fit of the triazole atoms of the (I*a*) (filled bonds) and (I*b*) (empty bonds) conformers, showing the differing orientations of the substituent rings and the carboxyl groups.

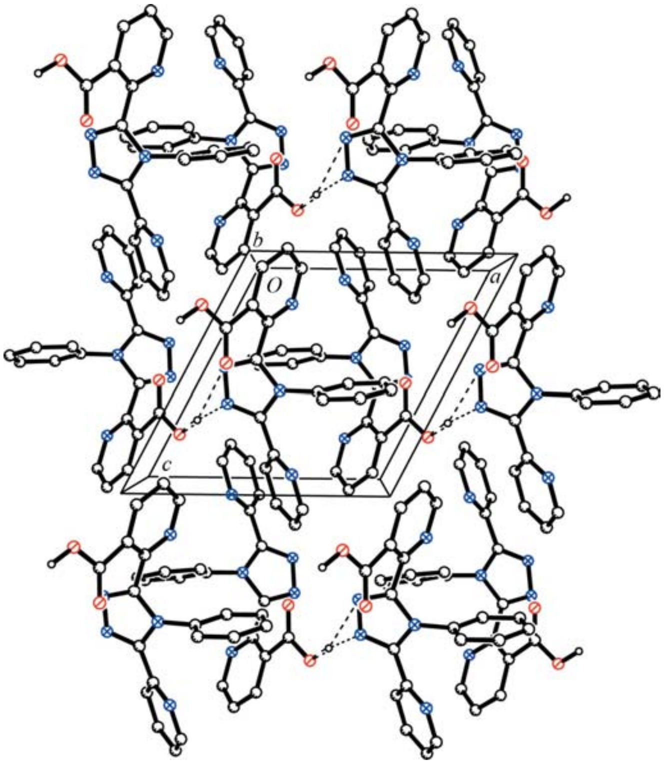


Figure 3
The molecular arrangement of polymorph (I*a*), viewed along the *b* axis. Dashed lines indicate hydrogen bonds and H atoms have been omitted (except for those forming O—H···N bonds).

Substantial differences in the molecular packing of the polymorphs are observed (Figs. 3 and 4). The molecules of yellow phase (I*a*) are linked by strong O1—H1O···N2^{i} [symmetry code: (i) $2 - x$, $y + \frac{1}{2}$, $1 - z$] hydrogen bonds (Table 2) forming a *C*(8) chain (Bernstein *et al.*, 1995) parallel to the *b* axis (Fig. 5). These chains are enforced by weaker multicentre C—H···O/N intermolecular interactions, giving a complex three-dimensional framework.

In the structure of orange polymorph (I*b*), the carboxyl O1—H1O bond participates in the formation of a strong hydrogen bond with pyridyl N21 atom of the second molecule transformed by the *c*-glide plane (Table 4 and Fig. 5). The resulting infinite chain (running along the *c* axis) is described

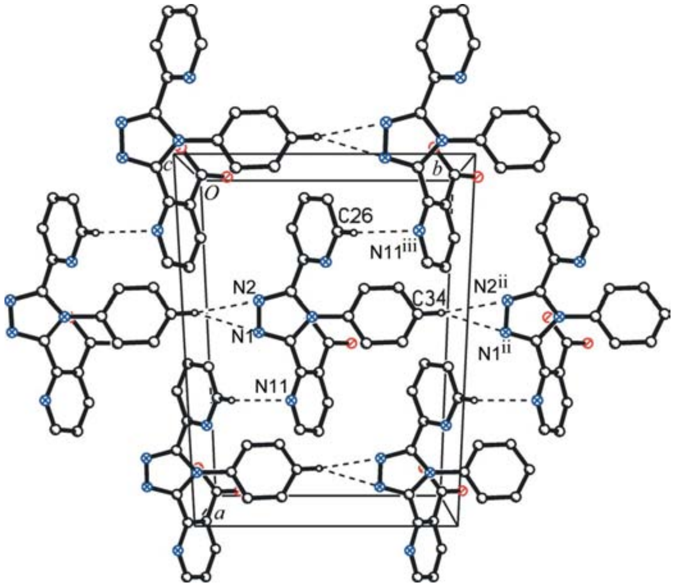


Figure 4
The arrangement of molecules of polymorph (I*b*), viewed along the *c* axis, showing a layer formed by C—H···N hydrogen bonds (dashed lines) (other H atoms have been omitted). [Symmetry codes: (ii) x, $y + 1$, z; (iii) $x - \frac{1}{2}$, $y + \frac{1}{2}$, z.]

by a *C*(10) motif. Moreover, short directional contacts between carbonyl atom O2 and the triazole atoms of the ring at (x, $1 - y$, $z - \frac{1}{2}$) are observed (Fig. 6), which might be attractive in nature (Desiraju & Steiner, 1999). In addition to these interactions, there are also numerous weak C—H···N-type hydrogen bonds between adjacent molecular columns. Atom C26 acts as a hydrogen-bond donor to pyridyl atom N11 (Fig. 4) in the molecule at ($x - \frac{1}{2}$, $y + \frac{1}{2}$, z). Simultaneously, the phenyl C34—H34 group participates in the formation of a three-centre hydrogen bond with triazole atoms N1 and N2 of the next molecule, repeated by translation along the [010] direction. Propagation of these hydrogen bonds then links all molecules into (001) sheets.

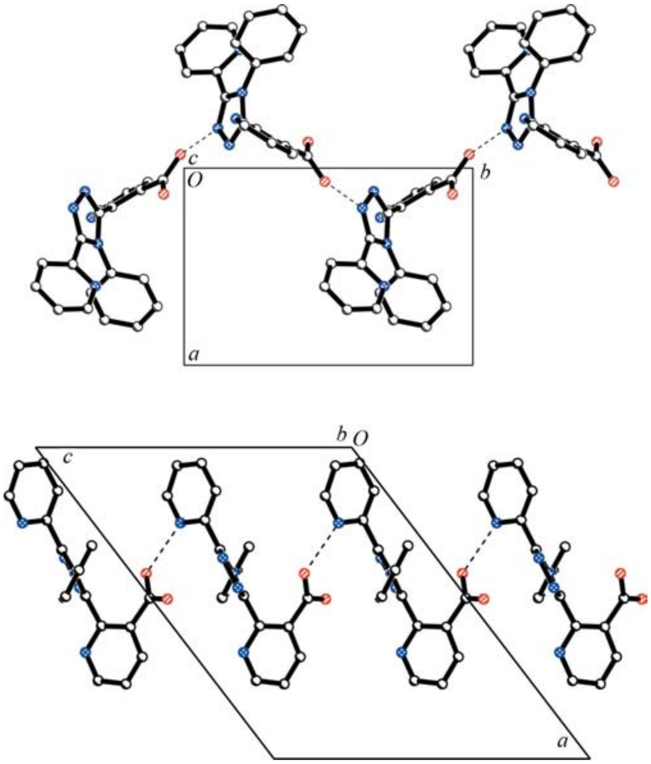


Figure 5
The chains formed by the O—H···N intermolecular hydrogen bonds in the forms (I*a*) (top) and (I*b*) (bottom). H atoms have been omitted.

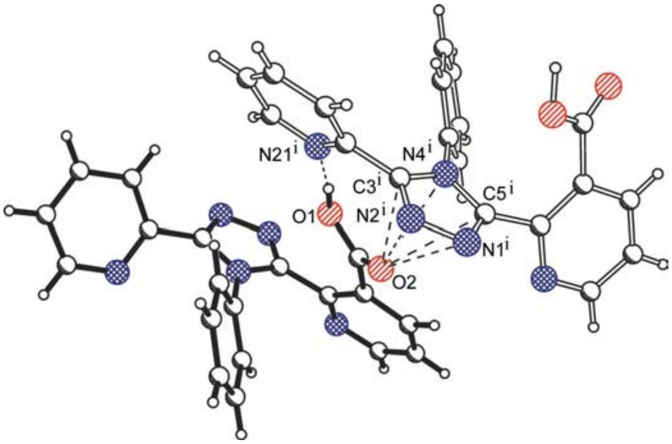


Figure 6
Intermolecular O—H···N hydrogen bonding and the accompanying carbonyl–triazole contacts in polymorph (I*b*). [Symmetry code: (i) $x, 1 - y, z - \frac{1}{2}$.]

The two crystalline forms (I*a*) and (I*b*) are obtained from different solvents. It seems that the polarity of solvents and their ability to form solute–solvent aggregates of different structure results in variation of intermolecular contacts during the formation of the solid. In the case of (I*b*), ethanol (or water) molecules promote formation of C—H···N hydrogen bonds and electrostatic C═O···triazole interactions which are of a more hydrophobic nature. Thus, the crystals of polymorph (I*b*) have higher melting point (by 8 K) and density (by 0.056 Mg m^{-3}).

Experimental

Plate-shaped yellow single crystals of polymorph (I*a*) were obtained by recrystallization of the title compound from methanol and acetone solutions at room temperature. Prismatic orange crystals of the second polymorph (I*b*) were obtained by recrystallization from 95% ethanol. The melting points determined on a Boëtius microscope were 533 and 541 K for forms (I*a*) and (I*b*), respectively.

Compound (I*a*)

Crystal data

$C_{19}H_{13}N_5O_2$
$M_r = 343.34$
Monoclinic, $P2_1$
$a = 9.032$ (3) Å
$b = 11.758$ (2) Å
$c = 9.208$ (2) Å
$\beta = 117.11$ (2)°
$V = 870.4$ (4) Å^3
$Z = 2$
Cu *Kα* radiation
$\mu = 0.73$ mm^{-1}
$T = 295$ (2) K
0.58 × 0.42 × 0.36 mm

Data collection

Kuma KM-4 four-circle diffractometer
3798 measured reflections
3577 independent reflections
2628 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.026$
3 standard reflections every 100 reflections intensity decay: 0.8%

Table 1
Selected geometric parameters (Å, °) for (I*a*).

N1—C5	1.300 (2)	C3—N4	1.364 (2)
N1—N2	1.379 (2)	N4—C5	1.367 (2)
N2—C3	1.309 (2)	N21—C22	1.320 (3)
O2—C1—C13—C12	24.4 (3)	O1—C1—C13—C12	−154.5 (2)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O1—H1O···N2^i	1.02 (3)	1.61 (3)	2.628 (2)	172 (3)
C25—H25···O2^{ii}	0.93	2.69	3.474 (3)	143
C34—H34···O2^{iii}	0.93	2.75	3.657 (3)	164
C33—H33···N1^{iii}	0.93	2.69	3.520 (3)	149

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

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.037$
$wR(F^2) = 0.104$
$S = 1.05$
3577 reflections
239 parameters
1 restraint
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{\max} = 0.17$ e Å^{-3}
$\Delta\rho_{\min} = -0.15$ e Å^{-3}
Absolute structure: Flack (1983)
Flack parameter: 0.3 (2)

Compound (I*b*)

Crystal data

$C_{19}H_{13}N_5O_2$
$M_r = 343.34$
Monoclinic, *Cc*
$a = 16.384$ (5) Å
$b = 9.725$ (4) Å
$c = 13.181$ (3) Å
$\beta = 127.36$ (4)°
$V = 1669.3$ (13) Å^3
$Z = 4$
Cu *Kα* radiation
$\mu = 0.76$ mm^{-1}
$T = 295$ (2) K
0.46 × 0.30 × 0.26 mm

Data collection

Kuma KM-4 four-circle diffractometer
6411 measured reflections
3504 independent reflections
2716 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.028$
3 standard reflections every 100 reflections intensity decay: 0.1%

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.040$
$wR(F^2) = 0.109$
$S = 1.05$
3504 reflections
239 parameters
2 restraints
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{\max} = 0.17$ e Å^{-3}
$\Delta\rho_{\min} = -0.20$ e Å^{-3}
Absolute structure: Flack (1983)
Flack parameter: −0.1 (3)

Table 3
Selected geometric parameters (Å, °) for (I*b*).

N1—C5	1.302 (3)	C3—N4	1.368 (2)
N1—N2	1.389 (2)	N4—C5	1.365 (2)
N2—C3	1.306 (3)	N21—C22	1.344 (3)
C12—C13—C1—O2	154.8 (2)	C12—C13—C1—O1	−27.2 (3)

Table 4
Hydrogen-bond geometry (Å, °) for (I*b*).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O1—H1O···N21$^{\rm i}$	1.06 (4)	1.61 (4)	2.660 (3)	172 (4)
C34—H34···N1$^{\rm ii}$	0.93	2.65	3.541 (4)	160
C34—H34···N2$^{\rm ii}$	0.93	2.68	3.582 (4)	164
C26—H26···N11$^{\rm iii}$	0.93	2.66	3.522 (3)	155
C23—H23···N11$^{\rm iv}$	0.93	2.57	3.484 (3)	169

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

Table 5
Angles (°) between triazole and aryl ring planes.

	(I*a*)	(I*b*)
Triazole/pyridyl N11–C16	74.3 (2)	61.0 (2)
Triazole/pyridyl N21–C26	40.7 (2)	55.9 (2)
Triazole/phenyl C31–C36	83.0 (2)	54.7 (2)
Phenyl/pyridyl N11–C16	70.8 (2)	61.1 (2)
Phenyl/pyridyl N21–C26	80.5 (2)	55.7 (2)

In the absence of significant anomalous scattering, it was impossible to establish unambiguously the absolute structures of both polymorphs crystallizing in the noncentrosymmetric space groups. Nevertheless, the enantiomer selected in each case gave a value of the Flack parameter closest to zero. H atoms bonded to the O1 atoms were located in difference Fourier maps and their positions were refined with their isotropic displacement parameters fixed at 0.1 Å^2. All remaining H atoms were positioned geometrically and constrained, with C—H distances of 0.93 Å. The displacement parameters of the H atoms were set at $U_{\rm iso}({\rm H}) = 1.2U_{\rm eq}({\rm C})$.

For both compounds, data collection: *KM-4 Software* (Kuma, 1998); cell refinement: *KM-4 Software*; data reduction: *KM-4 Software*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *SHELXTL/PC* (Sheldrick, 2008); software used to prepare material for publication: *SHELXL97* and *enCIFer* (Allen *et al.*, 2004).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SQ3157). Services for accessing these data are described at the back of the journal.

References

Allen, F. H. (2002). *Acta Cryst.* B**58**, 380–388.
Allen, F. H., Johnson, O., Shields, G. P., Smith, B. R. & Towler, M. (2004). *J. Appl. Cryst.* **37**, 335–338.
Bernstein, J. (2002). *Polymorphism in Molecular Crystals*. Oxford: Oxford Science Publications, Clarendon Press.
Bernstein, J., Davis, R. E., Shimoni, L. & Chang, N. L. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 1555–1573.
Desiraju, G. R. & Steiner, T. (1999). *The Weak Hydrogen Bond in Structural Chemistry and Biology*. Oxford University Press.
Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.
Kuma (1998). *KM-4 Software*. Version 10.3. Kuma Diffraction, Wroclaw, Poland.
Mazur, L., Koziol, A. E. & Modzelewska-Banachiewicz, B. (2004*a*). *Acta Cryst.* E**60**, o2244–o2246.
Mazur, L., Koziol, A. E. & Modzelewska-Banachiewicz, B. (2004*b*). *Acta Cryst.* E**60**, o2287–o2289.
Mazur, L., Koziol, A. E. & Modzelewska-Banachiewicz, B. (2007). *Acta Cryst.* E**63**, o3455.
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.