

Different hydrogen-bonding modes in
two closely related oximesGrzegorz Dutkiewicz,^a H. S. Yathirajan,^b
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Two closely related oximes, namely 1-chloroacetyl-3-ethyl-2,6-diphenylpiperidin-4-one oxime, C₂₁H₂₃ClN₂O₂, (I), and 1-chloroacetyl-2,6-diphenyl-3-(propan-2-yl)piperidin-4-one oxime, C₂₂H₂₅ClN₂O₂, (II), despite their identical sets of hydrogen-bond donors and acceptors, display basically different hydrogen-bonding patterns in their crystal structures. While the molecules of (I) are organized into typical centrosymmetric dimers, created by oxime–oxime O–H⋯N hydrogen bonds, in the structure of (II) there are infinite chains of molecules connected by O–H⋯O hydrogen bonds, in which the carbonyl O atom from the chloroacetyl group acts as the hydrogen-bond acceptor. Despite the differences in the hydrogen-bond schemes, the –OH groups are always in typical *anti* positions (C–N–O–H torsion angles of *ca* 180°). The oxime group in (I) is disordered, with the hydroxy groups occupying two distinct positions and C–C–N–O torsion angles of approximately 0 and 180° for the two alternatives. This disorder, even though the site-occupancy factor of the less occupied position is as low as *ca* 0.06, is also observed at lower temperatures, which seems to favour the statistical and not the dynamic nature of this phenomenon.

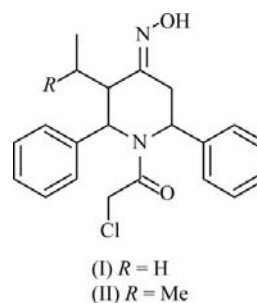
Comment

The oxime functional group, R₁R₂C=N–OH, despite its good hydrogen-bonding functionalities, is far less well explored in crystal engineering (*i.e.* constructing crystals of chosen architecture and properties) than, for instance, carboxyl or amide groups. The hydrogen-bonded structures of oximes were studied by, for example, Bertolasi *et al.* (1982), and more recently by Bruton *et al.* (2003). The results of these studies show that in cases when there are no competing hydrogen-bond acceptors, the main structural motifs are created by O–H⋯N oxime-to-oxime hydrogen bonds, and these can be either the R₂²(6) ring motif (Etter *et al.*, 1990; Bernstein *et al.*, 1995) or the C(3) chain motif (Fig. 1). Both

these motifs are found in 274 structures (organics only, coordinates determined, no repetitions) deposited in the Cambridge Structural Database (Version of November 2009; Allen, 2002), with a *ca* 4:1 preference for the ring motif (Bruton *et al.*, 2003). The presence of additional substituents capable of donating or accepting a hydrogen bond can of course change this simple pattern. For instance, it is known that when there are both oxime and carboxyl groups, the mixed ‘carboxime’ R₂²(7) motif is almost exclusively formed (see, for example, Desiraju, 1995; Maurin *et al.*, 1995; Kubicki *et al.*, 2000).

There are some examples of oxime crystal structures in which the oxime function adopts two alternative configurations with more or less equal probability, for instance, in violuric acid [pyrimidine-2,4,5,6(1*H*,3*H*)-tetrone 5-oxime; Nichol & Clegg, 2005], indan-1,2,3-trione monooxime (Ivanova *et al.*, 2002), or in a series of three *trans*-2,6-diaryl derivatives of oximes of *N*-hydroxy-4-piperidone (Díaz *et al.*, 1997). In the majority of cases, the disorder affects the whole N–OH fragment and both alternative positions are similarly occupied, but this is not always the case. Ciunik (1996) has shown, by careful study of the low-temperature crystal structures of 1-(3,4-di-*O*-acetyl-2-deoxy-2-hydroxyimino- α -*D*-erythro-pentopyranosyl)pyrazole and 2-benzoyloxycyclohexanone oxime, that the distributions of the electron densities in these structures can be accurately described by the assumption that there are only *ca* 3–5% of molecules with an alternative configuration of the oxime group.

The crystal structures of 1-chloroacetyl-3-ethyl-2,6-diphenylpiperidin-4-one oxime, (I), and 1-chloroacetyl-2,6-diphenyl-3-(propan-2-yl)piperidin-4-one oxime, (II), provide an example of two very closely related oximes with one additional hydrogen-bond-accepting carbonyl group, but where different structural motifs are formed.



In (I), the difference Fourier maps show relatively large peaks in the vicinity of the oxime group, and this was the main

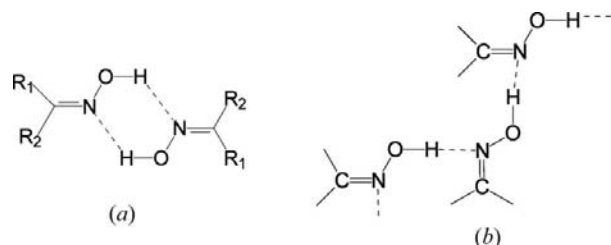


Figure 1

The two most common hydrogen-bond motifs in the crystal structures of oximes: (a) the ring R₂²(6) motif and (b) the chain C(3) motif.

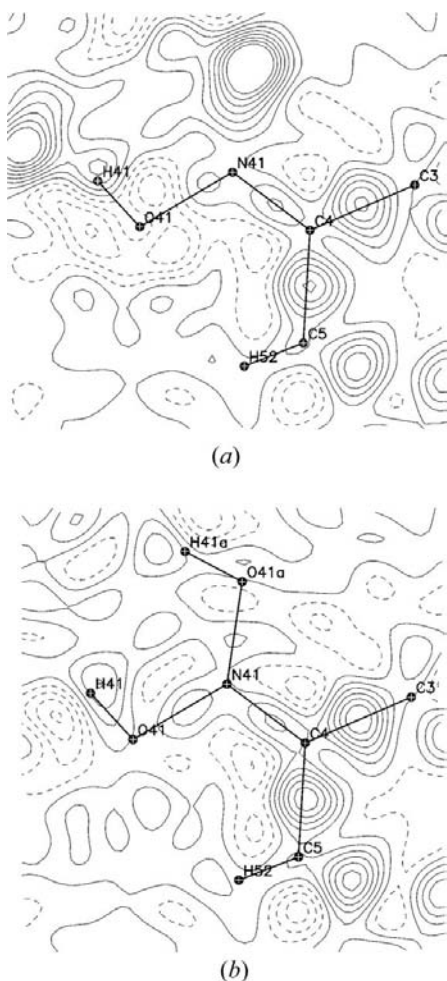


Figure 2

The residual density maps in the oxime group region in the structure of (I) at 100 K, shown (a) without and (b) with the minor conformation taken into account. Contours representing a surplus (solid lines) and a deficit (dashed lines) of residual electron density are drawn at the $0.1 \text{ e } \text{Å}^{-3}$ level (Farrugia, 1999).

reason for repeating the data collection for this compound at a lower temperature. These features are also observed at 100 K, and it turns out that the oxime group is slightly disordered over two positions, with site-occupancy factors of 0.943 (3) and 0.057 (3) at 100 K, and of 0.937 (3) and 0.063 (3) at room temperature. It might be noted that in this case only the hydroxy group is described as disordered and the position of the N atom is described as unique; no strange features with regard to the displacement parameters or geometries are observed. The stability of the occupancies over this temperature range suggests that the disorder is of a statistical rather than a dynamic nature. Fig. 2 compares the difference Fourier maps calculated for (I) at 100 K before (Fig. 2a) and after (Fig. 2b) taking this slight disorder into account.

Figs. 3 and 4 show perspective views of the molecules of (I) and (II), respectively. The bond lengths and angles in both compounds are very similar; when comparing the two room-temperature structures, the vast majority of these data differ by less than 3σ . The geometric parameters even produce quite good results in the normal probability plot test (Abrahams &

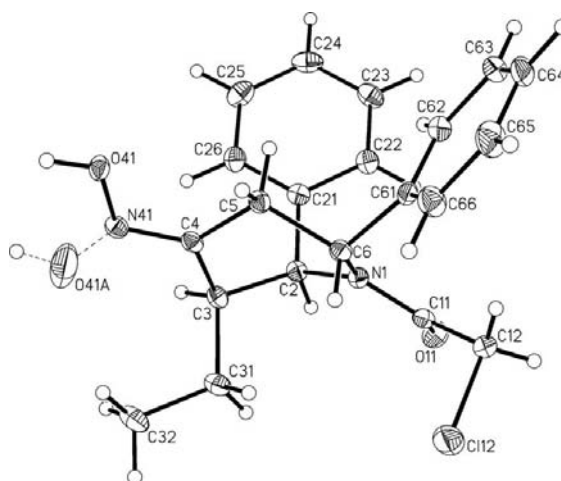


Figure 3

Anisotropic displacement ellipsoid representation of the molecular structure of (I) at 100 K, 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. The bond to the alternative position of atom O41 is shown as a dashed line.

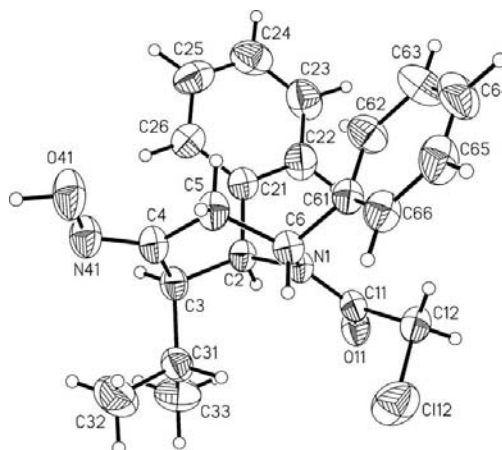
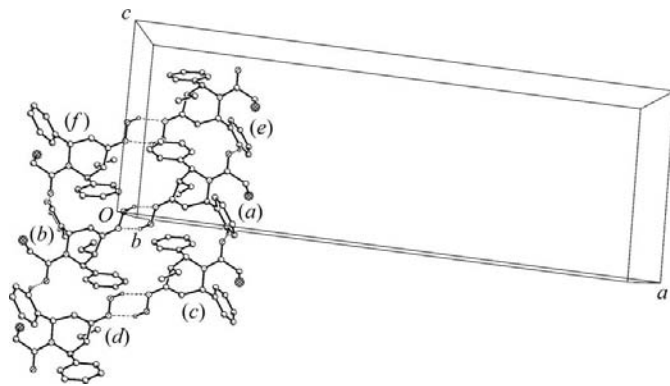


Figure 4

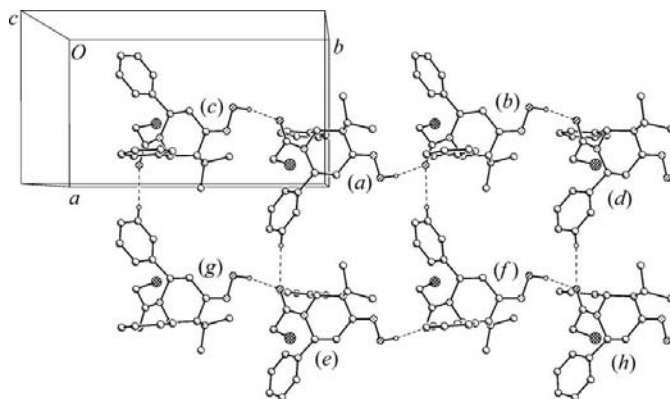
Anisotropic displacement ellipsoid representation of the molecular structure of (II), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

Keve, 1971; *International Tables for X-ray Crystallography*, 1974) which, in a sense, describes the deviation from a statistical distribution of the differences between the structures under consideration. In the case of (I) and (II), the correlation coefficient R^2 between the set of experimental differences between the geometric parameters and the theoretical values for a pure statistical distribution is 0.91 for the bond lengths and is even better – as high as 0.967 – for the angles.

The conformations of the piperidine rings in (I) and (II) are best described as distorted twist-boat. The distortions from the ideal conformation are quite severe, as can be seen from the large values of the asymmetry parameters (Duax & Norton, 1975), which quantitatively describe the distortion from ideal symmetry of a certain conformation. A twisted boat should have C_s symmetry, and the values of the $\Delta C_s^{2,3}$ parameter are 13.9° for (I) and 18.1° for (II) (this is the best approximate

**Figure 5**

The hydrogen-bonded 'ladder' of molecules of (I), as viewed approximately along the [010] direction. Hydrogen bonds are shown as dashed lines. [Symmetry codes: (a) x, y, z ; (b) $-x, 2 - y, -z$; (c) $x, 2 - y, -\frac{1}{2} + z$; (d) $-x, y, -\frac{1}{2} - z$; (e) $x, 2 - y, \frac{1}{2} + z$; (f) $-x, y, \frac{1}{2} - z$.]

**Figure 6**

A fragment of the hydrogen-bonded layer of molecules of (II), viewed approximately along the [001] direction. Hydrogen bonds are shown as dashed lines. [Symmetry codes: (a) x, y, z ; (b) $\frac{3}{2} - x, \frac{1}{2} + y, \frac{3}{2} - z$; (c) $\frac{3}{2} - x, -\frac{1}{2} + y, \frac{3}{2} - z$; (d) $x, 1 + y, z$; (e) $1 + x, y, z$; (f) $\frac{3}{2} - x, \frac{1}{2} + y, \frac{3}{2} - z$; (g) $\frac{3}{2} - x, -\frac{1}{2} + y, \frac{3}{2} - z$; (h) $1 + x, 1 + y, z$.]

symmetry which can be found). Both phenyl substituents are in axial positions (see Table 1 for the torsion angles), the chloroacetyl groups occupy (pseudo-)equatorial positions, the ethyl [in (I)] and 2-propyl [in (II)] groups are axial, and the position of the oxime function is closer to equatorial. The phenyl rings are planar to a good approximation. Interestingly, in all three cases, the largest deviation from the mean plane of the phenyl ring at C2 is at least twice as large as that for the phenyl ring at C6. These mean planes make dihedral angles of 60.71 (9)° in (I) and 72.09 (6)° in (II). The acetyl groups are also planar to within 3σ , and their planes are almost perpendicular to the phenyl ring planes [dihedral angles in the range 74.53 (10)–87.36 (11)°]. The C–Cl bond from the chloroacetyl group is almost perpendicular to the plane of the rest of the group, and the Cl atom is *ca* 1.65 Å out of the plane.

These very closely related molecules turn out to show different organizations in their crystal structures. In both cases, the main driving force of the packing is provided by the relatively strong hydrogen bonds. Also in both cases, there are, along with the oxime function, which can act as both hydrogen-bond donor and acceptor, additional relatively good

hydrogen-bond acceptors, namely the carbonyl C=O groups. As discussed above, the geometric features of both molecules are almost identical, so for instance, there are no additional steric hindrances which might influence the hydrogen bonding. And still, despite all these similarities, the hydrogen-bond patterns are essentially different in the two structures. The molecules of (I) are connected into centrosymmetric pairs by means of relatively short O–H...N hydrogen bonds (Tables 2 and 3). The graph set connected with this motif is $R_2^2(6)$, typical for oxime functions and mostly preferred in the absence of other hydrogen-bond donors and/or acceptors. Interestingly, the disorder present in the structure does not influence the hydrogen-bond motif. A relatively short and linear C66–H66...O11(carbonyl) interaction connects neighbouring dimers into a kind of 'ladder', forming $C(7)$ chains and large $R_4^4(32)$ rings (Fig. 5). In (II), by contrast, there are no oxime-to-oxime bonds. The hydrogen-bonded chains along the [010] direction are created by means of N–H...O-(carbonyl) hydrogen bonds. These $C(9)$ chains are connected into layers parallel to (001) by weak C–H...O(carbonyl) hydrogen bonds (Table 4 and Fig. 6), which form $C(8)$ chains on their own, and also a second-order $R_4^4(38)$ ring. In this case, there are far fewer weak intermolecular contacts, and not even the N atom of the oxime group is involved in any such contacts.

Experimental

1-Chloroacetyl-3-ethyl-2,6-diphenylpiperidin-4-one (17.75 g, 50 mmol) for (I) or 1-chloroacetyl-2,6-diphenyl-3-(propan-2-yl)piperidin-4-one (18.49 g, 50 mmol) for (II), sodium acetate trihydrate (20.4 g, 150 mmol), hydroxylamine hydrochloride (4.02 g, 60 mmol) and ethanol (50 ml) were placed in a round-bottomed flask. The reaction mixture was refluxed for about half an hour and the progress of the reaction was monitored by thin-layer chromatography. After completion of the reaction, the resulting substance was poured into water, filtered off and dried. The crude products obtained were subjected to column chromatography on silica gel (100–200 mesh) using a benzene–ethyl acetate mixture (9:1 v/v) as eluent. Crystals of (I) and (II) were grown from absolute ethanol [m.p. 460 K for (I) and 458 K for (II)].

Compound (I) at 293 K

Crystal data

$C_{21}H_{23}ClN_2O_2$	$V = 3777.6 (6) \text{ \AA}^3$
$M_r = 370.86$	$Z = 8$
Monoclinic, $C2/c$	Mo $K\alpha$ radiation
$a = 34.176 (3) \text{ \AA}$	$\mu = 0.22 \text{ mm}^{-1}$
$b = 9.1227 (9) \text{ \AA}$	$T = 293 \text{ K}$
$c = 12.1235 (11) \text{ \AA}$	$0.3 \times 0.15 \times 0.1 \text{ mm}$
$\beta = 91.962 (8)^\circ$	

Data collection

Oxford Xcalibur diffractometer with a Sapphire2 (large Be window) detector	8775 measured reflections
Absorption correction: multi-scan (CrysAlis Pro; Oxford Diffraction, 2009)	3304 independent reflections
$T_{\min} = 0.993, T_{\max} = 1.000$	1743 reflections with $I > 2\sigma(I)$
	$R_{\text{int}} = 0.051$

Table 1Selected torsion angles ($^{\circ}$).

The second line, where present, refers to the minor-occupancy part.

	(I) at 293 K	(II)
C6–N1–C2–C3	–43.5 (3)	–46.09 (16)
N1–C2–C3–C4	62.2 (2)	60.54 (15)
C2–C3–C4–C5	–27.1 (3)	–25.49 (18)
C3–C4–C5–C6	–27.6 (3)	–25.9 (2)
C4–C5–C6–N1	47.2 (3)	41.84 (18)
C5–C6–N1–C2	–10.3 (3)	–5.19 (17)
C2–N1–C11–O11	12.5 (4)	4.2 (2)
C2–N1–C11–C12	–166.4 (2)	–176.33 (12)
O11–C11–C12–C12	–94.6 (3)	–97.36 (14)
N1–C11–C12–C12	84.4 (3)	83.14 (15)
C6–N1–C2–C21	87.4 (2)	84.39 (14)
C11–N1–C2–C3	126.5 (2)	120.23 (13)
N1–C2–C21–C26	–142.4 (2)	–124.11 (14)
C3–C2–C21–C26	–15.6 (3)	2.1 (2)
N1–C2–C21–C22	40.5 (3)	57.69 (17)
C3–C2–C21–C22	167.3 (2)	–176.11 (13)
C21–C2–C3–C4	–66.0 (2)	–66.15 (15)
N1–C2–C3–C31	–62.4 (3)	–65.77 (14)
C4–C3–C31–C32	73.0 (3)	41.4 (2)
C2–C3–C4–N41	149.7 (2)	149.75 (15)
C31–C3–C4–C5	97.3 (2)	98.83 (16)
C5–C4–N41–O41	–2.5 (3)	–3.7 (2)
	179.10 (18)	
C3–C4–N41–O41	–179.10 (18)	–178.61 (13)
	2.6 (12)	
N41–C4–C5–C6	155.7 (2)	159.26 (16)
C2–N1–C6–C61	–130.9 (2)	–127.67 (13)
C4–C5–C6–C61	172.20 (19)	167.98 (13)
N1–C6–C61–C62	45.7 (3)	50.09 (19)
C5–C6–C61–C62	–76.7 (3)	–74.41 (17)

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.050$

$wR(F^2) = 0.079$

$S = 1.00$

3304 reflections

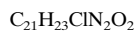
297 parameters

1 restraint

H atoms treated by a mixture of independent and constrained refinement

$\Delta\rho_{\max} = 0.21 \text{ e } \text{\AA}^{-3}$

$\Delta\rho_{\min} = -0.29 \text{ e } \text{\AA}^{-3}$

Compound (I) at 100 K**Crystal data**

$M_r = 370.86$

Monoclinic, $C2/c$

$a = 33.849 \text{ (3) } \text{\AA}$

$b = 9.025 \text{ (1) } \text{\AA}$

$c = 11.980 \text{ (1) } \text{\AA}$

$\beta = 92.51 \text{ (1)}^{\circ}$

$V = 3656.2 \text{ (6) } \text{\AA}^3$

$Z = 8$

Mo $K\alpha$ radiation

$\mu = 0.23 \text{ mm}^{-1}$

$T = 100 \text{ K}$

$0.3 \times 0.15 \times 0.1 \text{ mm}$

Data collection

Oxford Xcalibur diffractometer with an Eos detector

Absorption correction: multi-scan

(CrysAlis PRO; Oxford

Diffraction, 2009)

$T_{\min} = 0.957, T_{\max} = 1.000$

14395 measured reflections

3729 independent reflections

3245 reflections with $I > 2\sigma(I)$

$R_{\text{int}} = 0.013$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.030$

$wR(F^2) = 0.078$

$S = 1.08$

3729 reflections

312 parameters

1 restraint

H atoms treated by a mixture of independent and constrained refinement

$\Delta\rho_{\max} = 0.31 \text{ e } \text{\AA}^{-3}$

$\Delta\rho_{\min} = -0.26 \text{ e } \text{\AA}^{-3}$

Table 2Hydrogen-bond geometry ($\text{\AA}, ^{\circ}$) for (I) at 293 K.

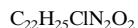
$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
O41–H41 \cdots N41 ⁱ	0.82	2.11	2.842 (2)	149
O41A–H41A \cdots N41 ⁱ	0.82	2.07	2.81 (3)	151
C66–H66 \cdots O11 ⁱⁱ	0.92 (2)	2.50 (2)	3.380 (4)	162 (2)

Symmetry codes: (i) $-x, -y + 2, -z$; (ii) $x, -y + 2, z - \frac{1}{2}$.**Table 3**Hydrogen-bond geometry ($\text{\AA}, ^{\circ}$) for (I) at 100 K.

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
O41–H41 \cdots N41 ⁱ	0.84	2.05	2.7991 (13)	148
O41A–H41A \cdots N41 ⁱ	0.84	2.00	2.76 (2)	150
C66–H66 \cdots O11 ⁱⁱ	0.956 (17)	2.451 (17)	3.3550 (17)	157.6 (13)

Symmetry codes: (i) $-x, -y + 2, -z$; (ii) $x, -y + 2, z - \frac{1}{2}$.**Table 4**Hydrogen-bond geometry ($\text{\AA}, ^{\circ}$) for (II).

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
O41–H41 \cdots O11 ⁱⁱⁱ	0.94 (3)	1.83 (3)	2.7449 (16)	165 (2)
C65–H65 \cdots O11 ^{iv}	0.97 (2)	2.47 (2)	3.375 (2)	153.9 (18)

Symmetry codes: (iii) $-x + \frac{3}{2}, y + \frac{1}{2}, -z + \frac{3}{2}$; (iv) $x + 1, y, z$.**Compound (II)****Crystal data**

$M_r = 384.89$

Monoclinic, $P2_1/n$

$a = 9.469 \text{ (1) } \text{\AA}$

$b = 16.658 \text{ (2) } \text{\AA}$

$c = 12.653 \text{ (2) } \text{\AA}$

$\beta = 90.29 \text{ (1)}^{\circ}$

$V = 1995.8 \text{ (4) } \text{\AA}^3$

$Z = 4$

Cu $K\alpha$ radiation

$\mu = 1.84 \text{ mm}^{-1}$

$T = 295 \text{ K}$

$0.4 \times 0.2 \times 0.2 \text{ mm}$

Data collection

Oxford SuperNova diffractometer (single source at offset) with an Atlas detector

Absorption correction: multi-scan

(CrysAlis PRO; Oxford

Diffraction, 2009)

$T_{\min} = 0.448, T_{\max} = 1.000$

10226 measured reflections

3877 independent reflections

3643 reflections with $I > 2\sigma(I)$

$R_{\text{int}} = 0.016$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.045$

$wR(F^2) = 0.120$

$S = 1.05$

3877 reflections

322 parameters

H atoms treated by a mixture of independent and constrained refinement

$\Delta\rho_{\max} = 0.25 \text{ e } \text{\AA}^{-3}$

$\Delta\rho_{\min} = -0.24 \text{ e } \text{\AA}^{-3}$

Methyl H atoms in (I) and (II) and disordered hydroxy H atoms in (I) were positioned geometrically in idealized positions, with $C-H = 0.96 \text{ \AA}$ and $O-H = 0.82 \text{ (298 K)}$ or 0.84 \AA (100 K), and refined as rigid groups, with $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{O})$ or $1.5U_{\text{eq}}(\text{methyl C})$. All other H atoms in both (I) and (II) were found in subsequent difference Fourier maps and refined isotropically. For (I), at both temperatures, a bond-length restraint of $1.41 \text{ (1) } \text{\AA}$ was applied to the N41–O41A bond involving the minor disorder component.

For all three data sets, data collection: *CrysAlis Pro* (Oxford Diffraction, 2009); cell refinement: *CrysAlis Pro*; data reduction:

CrysAlis Pro; program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1993); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *Stereochemical Workstation Operation Manual* (Siemens, 1989); 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: DN3141). Services for accessing these data are described at the back of the journal.

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