Table 2. *Intramolecular bond distances* (Å) *and angles* (°) *for the three independent molecules* (*A*, *B and C*) *with e.s.d.'s in parentheses*

	A	*B*	*C*
Cl(1)—C(1)	1·739 (9)	1·745 (10)	1·747 (11)
Cl(2)—C(8)	1·752 (13)	1·752 (12)	1·801 (11)
Cl′—C(8)	1·792 (11)	1·798 (12)	1·724 (11)
O(1)—C(7)	1·223 (12)	1·221 (14)	1·226 (13)
N(1)—C(4)	1·407 (12)	1·410 (14)	1·398 (13)
N(1)—C(7)	1·339 (14)	1·345 (14)	1·341 (14)
C(1)—C(2)	1·364 (17)	1·390 (15)	1·379 (17)
C(1)—C(6)	1·376 (16)	1·377 (15)	1·363 (15)
C(2)—C(3)	1·395 (17)	1·398 (17)	1·369 (17)
C(3)—C(4)	1·372 (16)	1·362 (15)	1·378 (14)
C(4)—C(5)	1·373 (15)	1·388 (14)	1·390 (14)
C(5)—C(6)	1·372 (15)	1·367 (14)	1·377 (15)
C(5)—C(8)	1·507 (14)	1·492 (13)	1·507 (14)
C(7)—C(8)	1·529 (14)	1·563 (15)	1·526 (15)
C(8)—C(9)	1·518 (17)	1·480 (19)	1·484 (19)
C(8)—C(9′)	1·499 (18)	1·547 (19)	1·501 (18)
C(4)—N(1)—C(7)	112·2 (8)	112·5 (9)	112·1 (9)
Cl(1)—C(1)—C(6)	119·4 (8)	120·2 (8)	118·8 (8)
Cl(1)—C(1)—C(2)	117·9 (8)	116·6 (8)	117·8 (8)
C(2)—C(1)—C(6)	122·5 (10)	123·0 (10)	123·1 (10)
C(1)—C(2)—C(3)	121·2 (12)	118·7 (10)	119·2 (11)
C(2)—C(3)—C(4)	115·6 (11)	118·0 (11)	118·7 (10)
N(1)—C(4)—C(3)	128·2 (9)	129·0 (10)	130·2 (9)
C(3)—C(4)—C(5)	122·7 (9)	122·2 (10)	121·1 (9)
N(1)—C(4)—C(5)	108·9 (8)	108·6 (9)	108·5 (8)
C(4)—C(5)—C(8)	108·7 (8)	109·8 (8)	109·0 (8)
C(4)—C(5)—C(6)	121·2 (9)	120·6 (9)	119·9 (9)
C(6)—C(5)—C(8)	129·9 (9)	129·4 (9)	130·8 (9)
C(1)—C(6)—C(5)	116·4 (10)	117·2 (10)	117·6 (9)
O(1)—C(7)—N(1)	125·2 (9)	127·7 (11)	126·6 (10)
N(1)—C(7)—C(8)	107·6 (8)	107·3 (9)	108·4 (8)
O(1)—C(7)—C(8)	127·0 (9)	124·9 (10)	124·8 (9)
C(5)—C(8)—C(7)	102·1 (7)	101·7 (8)	101·3 (8)
Cl′—C(8)—C(7)	105·3 (7)	104·5 (7)	112·4 (7)
Cl′—C(8)—C(5)	112·9 (7)	111·4 (7)	116·6 (7)
Cl(2)—C(8)—C(7)	109·1 (7)	108·4 (7)	104·1 (7)
Cl(2)—C(8)—C(5)	114·3 (7)	116·7 (7)	112·0 (7)
Cl(2)—C(8)—Cl′	112·0 (6)	112·5 (6)	109·3 (6)
C(7)—C(8)—C(9)	110·5 (9)	110·7 (9)	112·2 (9)
C(7)—C(8)—C(9′)	109·6 (9)	110·3 (9)	109·4 (9)
C(5)—C(8)—C(9′)	112·8 (9)	112·2 (9)	110·6 (9)
C(5)—C(8)—C(9)	111·6 (9)	112·2 (9)	112·3 (9)
Cl′—C(8)—C(9′)	113·2 (8)	115·3 (8)	106·2 (8)
Cl(2)—C(8)—C(9)	109·0 (8)	106·8 (9)	113·8 (9)
C(9)—C(8)—C(9′)	110·0 (9)	109·4 (9)	110·5 (10)

C(7), C(8) least-squares planes make a dihedral angle of 4·6 (9)° in *A* and 6·0 (9)° in *C* respectively. The angles between plane normals of the six- and five-membered rings are 3·4 (4) for *A*, 0·8 (4) for *B* and 4·3 (3)° for *C*.

The corresponding bond lengths and angles for the three independent molecules are similar. The molecular parameters for the six- and five-membered rings agree well with those of other structures (Codding, Lee & Richardson, 1984; Vega, Jimenez-Garay, Lopez-Castro & Marquez, 1980).

The packing of the molecule in the unit cell is shown in Fig. 2. The molecules are held together by normal van der Waals forces.

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Structure of Ranitidine Hydrochloride

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Abstract. *N*-(2-{[5-(Dimethylaminomethyl)-2-furanyl]methylthio}ethyl)-*N*′-methyl-2-nitro-1,1-ethenediamine hydrochloride, $C_{13}H_{23}N_4O_3S^+.Cl^-$, M_r = 350·86, monoclinic, $P2_1/n$, a = 18·798 (3), b = 12·980 (3), c = 7·204 (1) Å, β = 95·09 (1)°, V = 1750·9 (5) Å^3, Z = 4, D_m = 1·330 (2), D_x = 1·331 g cm^{-3}, λ(Cu $K\alpha$) = 1·5418 Å, μ = 32·00 cm^{-1}, $F(000)$ = 744, T = 293 K, final R = 0·047 for 2599 observed independent reflections. The N atom of the dimethylamino group is protonated and is hydrogen bonded to the Cl^- ion. The structure of the *N*-ethyl-*N*′-methyl-2-nitro-1,1-ethenediamine moiety takes conformations, where amine NH, ethene CH and nitro O atoms are disordered. The ranitidine molecule, as a whole, takes an open conformation, where the side chain is folded in a spiral-shaped fashion.

Introduction. H_2-receptor antagonists could become excellent drugs for the treatment of peptic ulcers and

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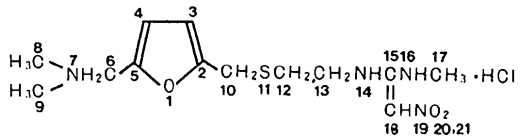
related disorders because they powerfully inhibit gastric acid secretion through the H_2 receptor (Black, Duncan, Durant, Ganellin & Parsons, 1972). Ranitidine is an potent H_2-receptor antagonist, and has been used as a therapeutic drug (Brogden, Carmine, Heel, Speight & Avery, 1982).

As part of structural studies of H_2-receptor antagonists (Shibata, Kagawa, Morisaka, Ishida & Inoue, 1983; Shibata, Kokubo, Morimoto, Morisaka, Ishida & Inoue, 1983; Ishida, In, Shibata, Doi, Inoue & Yanagisawa, 1987; In, Ishida, Doi, Inoue & Shibata, 1988), the present paper deals with the crystal structure of ranitidine hydrochloride (I).



(I)

Experimental. Crystals were grown as plates from an acetonitrile solution of ranitidine hydrochloride. Crystal density was measured by the flotation method using a C_6H_6–CCl_4 mixture. A single crystal with dimensions of approximately $0{\cdot}3 \times 0{\cdot}3 \times 0{\cdot}2$ mm was mounted on a Rigaku AFC-5 diffractometer with graphite-monochromated Cu $K\alpha$ radiation. Unit-cell dimensions were determined by a least-squares fit of 2θ values of 25 reflections in the 2θ range 42–60°. Intensities were measured by the θ–2θ scan technique with a scan rate of 4° min^{-1} in 2θ and a scan width of $\Delta(2\theta) = (1{\cdot}0 + 0{\cdot}15\tan\theta)°$. Background intensities were measured for 5 s at each end of a scan. Four standard reflections (12 0 0, 060, 004, $\bar{5}43$) were remeasured after every 100 reflections, and showed no significant variation. 2992 independent reflections within $\theta_{max} = 65{\cdot}0°$ [$(\sin\theta)/\lambda = 0{\cdot}588$ Å^{-1}] were collected (h −22–22, k 0–15, l 0–8), and corrected for Lorentz and polarization effects; no absorption or extinction corrections were carried out.

The structure was solved by direct methods using *MULTAN*87 (Debaerdemaeker, Germain, Main, Tate & Woolfson, 1987) and successive Fourier syntheses, and refined by the block-diagonal least-squares procedure. 2599 observed reflections [$|F_o| \geq 2\sigma(|F_o|)$] were included in the refinement; the function minimized was $\sum w(|F_o| - |F_c|)^2$. Ideal positions of all the H atoms were calculated on the basis of stereochemical considerations, and were verified on the difference Fourier map calculated using the anisotropic non-H atoms; H atoms of the disordered moiety were not clearly revealed. The H-atom parameters were included in subsequent refinement cycles with isotropic thermal factors. The weighting scheme used in the last cycle was $w = 1{\cdot}0/[\sigma(F_o)^2 + 0{\cdot}03850|F_o| - 0{\cdot}00042|F_o|^2]$. The number of observations per refined parameter is 2599/369 = 7·04 and $S = 1{\cdot}003$. The final R and wR values are 0·047 and 0·044, respectively. $(\Delta/\sigma)_{max} = 0{\cdot}10$ for non-H positional parameters. $\Delta\rho = -0{\cdot}25$–$0{\cdot}28$ e Å^{-3}. The atomic scattering factors were taken from *International Tables for X-ray Crystallography* (1974). For all crystallographic computations, *The Universal Crystallographic Computing System* (1979) was used. All the computations were performed on a Micro VAX II computer at the Computation Center, Osaka University of Pharmaceutical Sciences. The final atomic parameters are listed in Table 1.*

Table 1. *Fractional atomic coordinates and equivalent isotropic temperature factors* (Å^2) *for non-H atoms with e.s.d.'s in parentheses*

$B_{eq} = (4/3)\sum_i\sum_j \beta_{ij}\mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	B_{eq}
O(1)	0·53063 (9)	−0·1186 (1)	0·6527 (2)	3·87 (8)
C(2)	0·5792 (1)	−0·0450 (2)	0·6221 (4)	4·1 (1)
C(3)	0·6232 (2)	−0·0799 (3)	0·4956 (4)	5·1 (1)
C(4)	0·6004 (2)	−0·1822 (3)	0·4483 (4)	4·8 (1)
C(5)	0·5448 (1)	−0·2030 (2)	0·5475 (4)	3·9 (1)
C(6)	0·5002 (2)	−0·2936 (2)	0·5692 (4)	4·2 (1)
N(7)	0·5172 (1)	−0·3473 (2)	0·7521 (3)	4·3 (1)
C(8)	0·5035 (2)	−0·2850 (3)	0·9160 (4)	5·8 (2)
C(9)	0·5904 (2)	−0·3892 (3)	0·7673 (5)	6·1 (2)
C(10)	0·5776 (2)	0·0497 (2)	0·7370 (4)	4·8 (1)
S(11)	0·59686 (4)	0·02448 (7)	0·9820 (1)	4·95 (4)
C(12)	0·6866 (2)	−0·0236 (3)	0·9875 (4)	5·8 (2)
C(13)	0·7434 (2)	0·0532 (3)	0·9413 (4)	6·2 (2)
N(14)	0·7301 (2)	0·1650 (3)	0·9415 (5)	3·6 (2)
N(14′)*	0·7473 (2)	0·1144 (3)	1·1102 (5)	3·6 (2)
C(15)	0·7192 (1)	0·2171 (2)	1·1021 (3)	3·5 (1)
N(16)	0·6940 (3)	0·3212 (4)	1·0996 (6)	4·8 (2)
N(16′)	0·6991 (2)	0·2667 (3)	0·9249 (5)	3·7 (2)
C(17)	0·6743 (2)	0·3661 (3)	0·9164 (5)	6·5 (2)
C(18)	0·7384 (3)	0·1736 (5)	1·2703 (6)	3·8 (2)
C(18′)	0·7072 (3)	0·2650 (4)	1·2623 (6)	3·4 (2)
N(19)	0·7179 (1)	0·2160 (2)	1·4387 (3)	4·3 (1)
O(20)	0·6847 (2)	0·2880 (3)	1·4625 (5)	4·8 (2)
O(20′)	0·6961 (3)	0·2734 (4)	1·5711 (5)	6·7 (2)
O(21)	0·7413 (3)	0·1548 (4)	1·5816 (5)	5·6 (2)
O(21′)	0·7426 (2)	0·1341 (3)	1·4682 (5)	4·7 (2)
Cl	0·91226 (4)	0·02006 (6)	0·2349 (1)	4·72 (3)

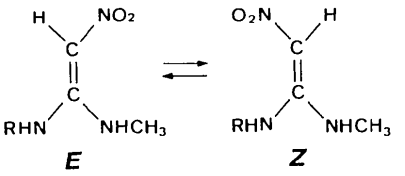
* Primed atoms are disordered.

Discussion. The molecular conformation of ranitidine drawn by *ORTEP*II (Johnson, 1976) is shown in Fig. 1. Bond lengths, bond angles and some torsion angles for non-H atoms are given in Table 2.

As is shown in Fig. 1, the structure of the *N*,*N*′-dimethyl-2-nitro-1,1-ethenediamine moiety is disordered, where each of the N(14), N(16), C(18), O(20) and O(21) atoms occupies two different positions having the same electron densities, thus for-

* Lists of structure factors, anisotropic thermal parameters, selected torsion angles and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 52917 (12 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

ming two orientations of this fragment with respect to the remaining structure. The formation of this disordered structure, which is partially stabilized by two N—H···O intramolecular hydrogen bonds [N(14′)···O(21′) = 2·601 (6) and N(16)···O(20) = 2·671 (6) Å], probably results from the chemical behaviour of the enamine structure involved in the ranitidine molecule, because an equimolar mixture of *E*/*Z* enamine isomers exists in solution (Cholerton, Hunt, Klinkert & Martin-Smith, 1984):



The disordered atoms in the *N*,*N*′-dimethyl-2-nitro-1,1-ethenediamine moiety form a plane consisting of three trigonally arranged lozenges; the fluctuation of each atom from the best-fit plane is in the range −0·147 (4) [C(13)] to 0·177 (6) Å [C(18)]. The dihedral angles of this plane to the disordered nitro group and furan ring are 9·9 (3) and 63·4 (1)°, respectively.

The N(7) atom of the dimethylamino group is protonated by HCl, and is vertically located above the furan ring. The methylthioethyl side chain takes the most frequently observed conformation (Shibata, Kokubo, Morimoto, Morisaka, Ishida & Inoue, 1983; Ishida, In, Shibata, Doi, Inoue & Yanagisawa, 1987), in which the torsion angles about C(2)—C(10), C(10)—S(11) and S(11)—C(12) bonds are in the *gauche* region. Thus, the ranitidine molecule, as a whole, has an open conformation with a spirally coiled side chain. Such an open conformation is thought also to exist in solution (Sega, Moimas, Decorte, Toso & Sunjic, 1982; Gaggelli, Marchettini, Sega & Valensin, 1988), although the ranitidine molecule in its hydrogen oxalate crystal (Kojic-Prodic, Ruzic-Toros & Toso, 1982) takes a folded conformation.

Bond lengths and angles are in agreement with the related H_2-antagonists within their e.s.d.'s. One N—O bond distance in the disordered nitro group is shorter than the other, showing the localized π-bonding system.

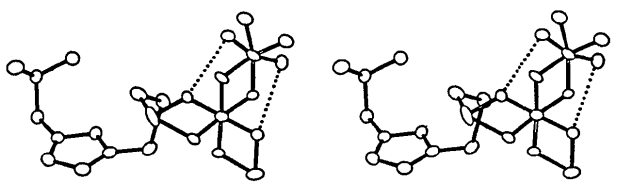


Fig. 1. A stereoscopic view of the ranitidine molecule. Dotted lines represent intramolecular hydrogen bonds.

Table 2. *Bond distances* (Å) *and angles* (°) *for non*-H *atoms with e.s.d.'s in parentheses*

O(1)—C(2)	1·353 (3)	N(14)—C(15)	1·371 (5)
O(1)—C(5)	1·372 (3)	N(14′)—C(15)	1·434 (5)
C(2)—C(3)	1·362 (4)	C(15)—N(16)	1·431 (6)
C(2)—C(10)	1·483 (4)	C(15)—N(16′)	1·449 (5)
C(3)—C(4)	1·427 (4)	C(15)—C(18)	1·357 (6)
C(4)—C(5)	1·344 (4)	C(15)—C(18′)	1·347 (5)
C(5)—C(6)	1·461 (4)	N(16)—C(17)	1·460 (6)
C(6)—N(7)	1·500 (4)	N(16′)—C(17)	1·373 (6)
N(7)—C(8)	1·473 (4)	C(18)—N(19)	1·416 (6)
N(7)—C(9)	1·476 (4)	C(18′)—N(19)	1·419 (5)
C(10)—S(11)	1·800 (3)	N(19)—O(20)	1·145 (5)
S(11)—C(12)	1·795 (4)	N(19)—O(20′)	1·305 (5)
C(12)—C(13)	1·519 (5)	N(19)—O(21)	1·343 (5)
C(13)—N(14)	1·473 (5)	N(19)—O(21′)	1·172 (4)
C(13)—N(14′)	1·449 (5)		

C(2)—O(1)—C(5)	107·9 (2)	C(13)—N(14)—C(15)	121·7 (2)
O(1)—C(2)—C(3)	109·4 (2)	C(13)—N(14′)—C(15)	119·0 (2)
O(1)—C(2)—C(10)	116·5 (2)	N(14)—C(15)—N(16)	121·9 (3)
C(3)—C(2)—C(10)	133·8 (2)	N(14)—C(15)—C(18)	120·0 (3)
C(2)—C(3)—C(4)	106·4 (2)	N(14′)—C(15)—N(16′)	120·9 (2)
C(3)—C(4)—C(5)	106·9 (2)	N(14′)—C(15)—C(18′)	118·9 (3)
O(1)—C(5)—C(4)	109·4 (2)	N(16)—C(15)—C(18)	117·8 (3)
O(1)—C(5)—C(6)	116·3 (2)	N(16′)—C(15)—C(18′)	120·0 (3)
C(4)—C(5)—C(6)	134·3 (2)	C(15)—N(16)—C(17)	116·5 (2)
C(5)—C(6)—N(7)	112·9 (2)	C(15)—N(16′)—C(17)	121·2 (2)
C(6)—N(7)—C(8)	114·2 (2)	C(15)—C(18)—N(19)	122·2 (2)
C(6)—N(7)—C(9)	111·2 (2)	C(15)—C(18′)—N(19)	122·7 (2)
C(8)—N(7)—C(9)	111·8 (2)	C(18)—N(19)—O(20)	129·7 (3)
C(2)—C(10)—S(11)	112·6 (1)	C(18)—N(19)—O(21)	109·4 (3)
C(10)—S(11)—C(12)	101·1 (1)	C(18′)—N(19)—O(20′)	111·7 (3)
S(11)—C(12)—C(13)	116·4 (1)	C(18′)—N(19)—O(21′)	126·2 (3)
C(12)—C(13)—N(14)	121·6 (2)	O(20)—N(19)—O(21)	120·9 (3)
C(12)—C(13)—N(14′)	99·2 (2)	O(20′)—N(19)—O(21′)	122·1 (3)

O(1)—C(2)—C(10)—S(11)	62·6 (2)	C(10)—S(11)—C(12)—C(13)	67·6 (3)
O(1)—C(5)—C(6)—N(7)	−72·4 (2)	S(11)—C(12)—C(13)—N(14)	15·8 (3)
C(5)—C(6)—N(7)—C(8)	63·6 (3)	S(11)—C(12)—C(13)—N(14′)	72·5 (2)
C(5)—C(6)—N(7)—C(9)	−64·0 (2)	C(12)—C(13)—N(14)—C(15)	65·8 (4)
C(2)—C(10)—S(11)—C(12)	62·8 (2)	C(12)—C(13)—N(14′)—C(15)	−108·8 (4)

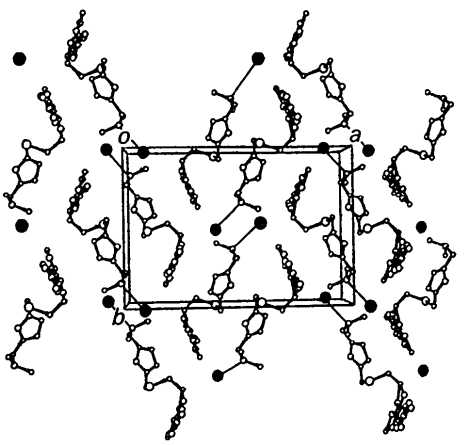


Fig. 2. Crystal structure of ranitidine hydrochloride, viewed along the *c* axis. Filled circles show the Cl^- ions, and the thin lines represent the hydrogen bonds between the N(7) and Cl^- atoms.

Fig. 2 shows the crystal packing viewed along the *c* axis. The Cl^- ions lie between neighboring dimethyl amino groups and are hydrogen bonded to the N(7) atom [N(7)(x, y, z)···Cl^-($x-\frac{1}{2}$, $-y-\frac{1}{2}$, $z+\frac{1}{2}$) = 2·982 (2), H···Cl^- = 1·94 (4) Å, ∠N—H···Cl^- =

176 (3)°]. In the crystal packing, intermolecular hydrogen bonds are also formed for the atomic pairs N(14)···O(21) and N(16′)···O(20′): N(14)(x, y, z)···O(21)(x, y, $z-1$) = 2·623 (6) and N(16′)(x, y, z)···O(20′)(x, y, $z-1$) = 2·546 (6) Å.

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Structure of a Cyclic Kynurenine Derivative

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Abstract. (2-Oxo-2,3,4,5-tetrahydro-1*H*-1-benzazepin-1-yl)ethanoic acid, $C_{12}H_{13}NO_3$, $M_r = 219{\cdot}2$, orthorhombic, *Pbca*, $a = 15{\cdot}230$ (1), $b = 10{\cdot}196$ (1), $c = 28{\cdot}267$ (2) Å, $U = 4389{\cdot}4$ (1) Å^3, D_m (flotation) = 1·32 (1), $D_x = 1{\cdot}327$ Mg m^{-3}, $Z = 16$, λ(Cu $K\alpha$) = 1·5418 Å, $\mu = 0{\cdot}70$ mm^{-1}, $F(000) = 1856$, $T = 294$ (1) K, final $R = 0{\cdot}061$ for 2772 observed data. The two independent molecules adopt essentially similar conformations. The seven-membered heterocyclic rings are in a boat form, and the aromatic rings are planar within the limits of experimental error. The carboxylate group of one of the molecules assumes two orientations in the crystal with occupancies of 0·34 (1) and 0·66 (1).

Introduction. As part of a program in which we are defining conformational detail for a number of cyclic derivatives of kynurenine (I), a major metabolic and oxidative degradation product of the amino acid tryptophan, we report here the structure of (2-oxo-2,3,4,5-tetrahydro-1*H*-1-benzazepin-1-yl)-ethanoic acid (II). Because of the structural similarities of these kynurenine derivatives to the biologically active seven-membered nitrogen heterocycles, they are of considerable pharmacological interest. Their relationship to the biologically active 1,4-benzodiazepines, which exhibit anxiolytic effects on the central nervous system (Hoffmeister & Stille, 1981), has rendered the cyclic kynurenines of particular interest as potential sources of *natural* anxiolytic agents.

Experimental. (II) was synthesized by standard base-catalysed hydrolysis of benzyl (2-oxo-2,3,4,5-tetrahydro-1*H*-1-benzazepin-1-yl)ethanoate obtained from 2-oxo-2,3,4,5-tetrahydro-1*H*-1-benzazepine (Tomita, Minami & Uyeo, 1969). A colourless triangular platelet of side *ca* 0·63 mm and 0·13 mm thick, crystallized from aqueous ethanol, was aligned on a Rigaku-AFC diffractometer; cell parameters determined by least squares from 2θ values for 25 strong reflections ($35° < 2\theta < 75°$); Cu $K\alpha$ radiation (graphite crystal monochromator, $\lambda = 1{\cdot}5418$ Å); ω–2θ scan, scan rate 4° min^{-1}, scan range ($\Delta\omega$) (1·2 + 0·5 tan θ)°, $2\theta_{max} = 130°$, 10 s stationary background counts; three standard reflections monitored

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