Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

Multicentre hydrogen bonds in a 2:1 arylsulfonylimidazolone hydrochloride salt[1]

Kyung-Lae Park,[a]* Byoung-Gi Moon,[a] Sang-Hun Jung,[a] Jin-Gyu Kim[b] and Il-Hwan Suh[b]

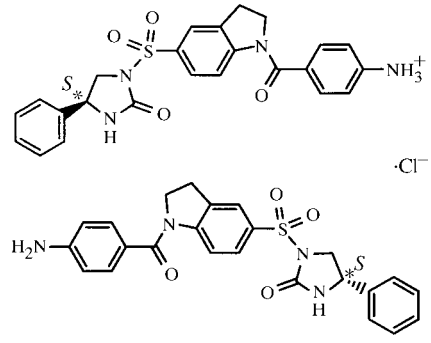
[a]College of Pharmacy, Chungnam National University, Taejeon 305-764, Korea, and [b]Department of Physics, Chungnam National University, Taejeon 305-764, Korea
Correspondence e-mail: parki@cnu.ac.kr

Received 17 May 2000
Accepted 3 July 2000

The title compound, (*S*)-(+)-4-[5-(2-oxo-4,5-dihydroimidazol-1-ylsulfonyl)indolin-1-ylcarbonyl]anilinium chloride (*S*)-(+)-1-[1-(4-aminobenzoyl)indoline-5-sulfonyl]-4-phenyl-4,5-dihydroimidazol-2-one, $C_{24}H_{23}N_4O_4S^+\cdot Cl^-\cdot C_{24}H_{22}N_4O_4S$, crystallizes in space group *C*2 from a CH_3OH/CH_2Cl_2 solution. In the crystal structure, there are two different conformers with their terminal C_6 aromatic rings mutually oriented at angles of 67.69 (14) and 61.16 (15)°. The distances of the terminal N atoms (of the two conformers) from the chloride ion are 3.110 (4) and 3.502 (4) Å. There are eight distinct hydrogen bonds, *i.e.* four N—H···Cl, three N—H···O and one N—H···N, with one N—H group involved in a bifurcated hydrogen bond with two acceptors sharing the H atom. C—H···O contacts assist in the overall hydrogen-bonding process.

Comment

In the search for new anticancer agents, the free amine of the title compound, (I), was synthesized originally as a racemic



(I)

mixture (Jung *et al.*, 1998) with only the *S* enantiomer showing improved antitumour activity (Jung, 1999, unpublished work).

[1] Internal code of the Dong-Wha Pharmaceutical Industries Co. Ltd, Korea: DW2282.

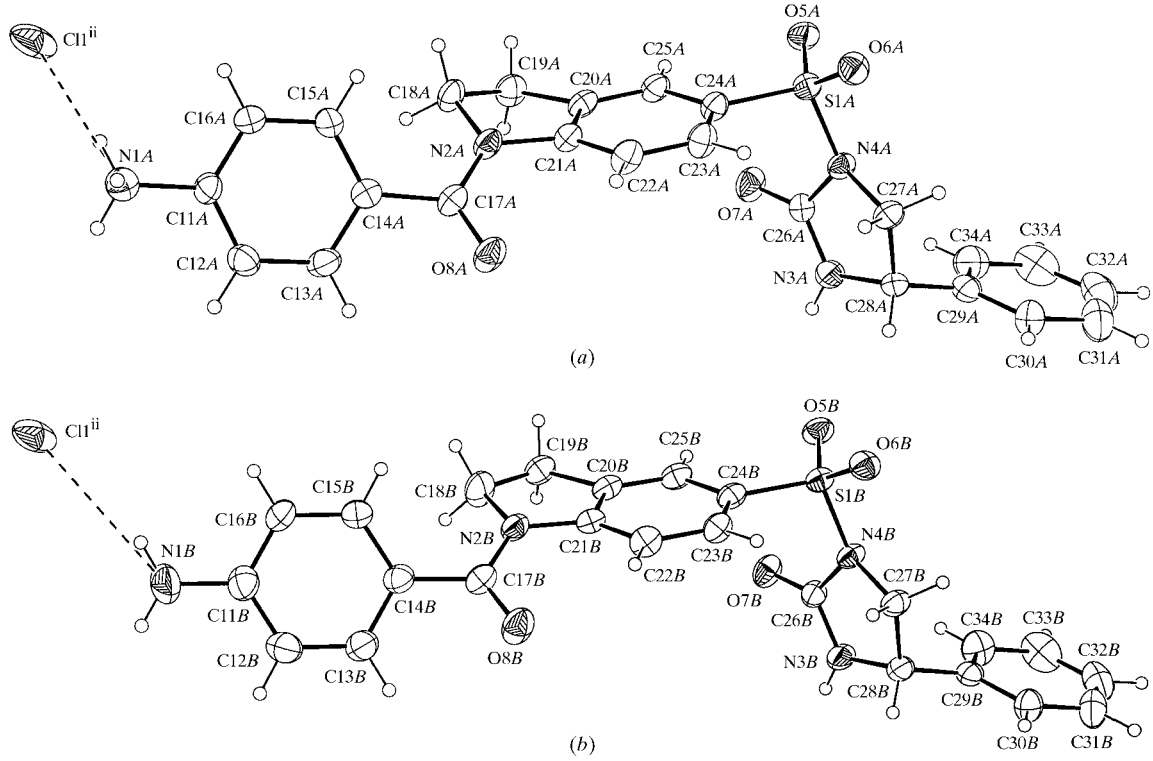


Figure 1
The molecular structure and atomic numbering scheme of (*a*) molecule *A* and (*b*) molecule *B*. Displacement ellipsoids are drawn at the 30% probability level for all non-H atoms. The interactions of the Cl1^{ii} ion [symmetry code: (ii) $1-x, 1+y, -z$] with N1*A* and N1*B* are highlighted with dashed lines.

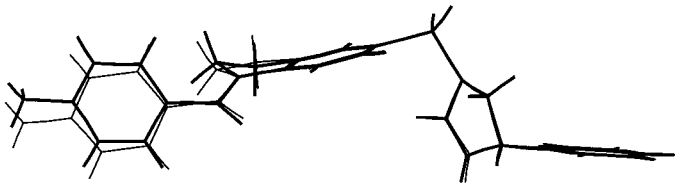


Figure 2
Illustration of the conformational differences of the two conformers, with molecule *A* (thick lines) overlayed on molecule *B* (thin lines).

Treatment of the free amine with anhydrous HCl/CH_3OH solvent and recrystallization from a CH_3OH/CH_2Cl_2 solution unexpectedly produced single crystals of the 2:1 hydrochloride salt. A 1:1 salt, however, could also be formed, but only as an amorphous powder. Attempts to obtain a stoichiometric single crystal of the 1:1 salt from various solvents have thus far failed. The present X-ray crystallographic study was undertaken in order to elucidate the structural characteristics of the 2:1 hydrochloride salt.

In the crystal structure, there exist two conformationally different molecules (*A* and *B*; see Fig. 1). The Cl1$\cdots$N1*A*/*B* distances are 3.110 (4) and 3.502 (4) Å in *A* and *B*, respectively. In addition, the bond lengths of the terminal amine N1*A*/*B* atom to the aromatic ring differ [N1*A*—C11*A* 1.475 (4) Å and N1*B*—C11*B* 1.388 (5) Å], indicating that molecule *A* is protonated as NH_3^+ and molecule *B* exists in the free NH_2 amine form. In the solid-state IR spectrum, both NH_3^+ and NH_2 stretching vibrations were identified; difference Fourier synthesis also verified the existence of three and two H atoms at N1*A* and N1*B*, respectively. The torsion angles between the three aromatic rings differ in molecules *A* and *B*, as depicted in Fig. 2. The major differences are observed in the orientation of the terminal aniline group in comparison with the rest of the molecule. The angles of the N-substituted C_6 ring to the terminal phenyl-ring plane are 67.69 (14)° in *A* and 61.16 (15)° in *B*, while the indoline groups are oriented at angles of 68.22 (13) and 60.38 (14)° to the former plane in *A* and *B*, respectively. In the indoline group, both conformers differ (torsion angles in Table 1), with the C18*B* atom lying closer to the indoline ring plane in *B* [C18*A*—C19*A*—C20*A*—C25*A* −161.6 (4)° and C18*B*—C19*B*—C20*B*—C25*B* −173.7 (4)°].

The carbonyl plane is twisted from the phenyl plane in both conformations [C13*A*—C14*A*—C17*A*—O8*A* −31.4 (5)° and C13*B*—C14*B*—C17*B*—O8*B* −30.0 (6)°]. The longer Csp^2—Csp^2 bond lengths [C14*A*—C17*A* 1.503 (5) Å and C14*B*—C17*B* 1.485 (5) Å] arise from the deviation from coplanarity of the amide carbonyl and phenyl-ring systems. The two amide groups of each molecule show a characteristic feature in both conformations. The former C—N bonds are shorter than the normal amide C—N bonds [N2*A*—C17*A* 1.368 (5) Å and N2*B*—C17*B* 1.382 (5) Å] attached to the indoline ring. The lengths of the two amide C—N bonds of the imidazolone ring differ, with the short N3*A*—C26*A* [1.314 (5) Å] and N3*B*—C26*B* [1.318 (5) Å] bonds having double-bond character compared with the longer N4*A*—C26*A* [1.402 (4) Å] and N4*B*—C26*B* [1.402 (4) Å] bonds on the opposite side of the urea group.

The hydrogen-bonding parameters listed in Table 2 reveal the differences in the intermolecular relationships of the two molecules on packing. The distance of the terminal N atom to the central Cl1 ion shows remarkable inequality, with N1$A^{ii}\cdots$Cl1 [3.110 (4) Å; symmetry code: (ii) $1-x$, $-1+y$, $-z$] substantially shorter than N1$B^{ii}\cdots$Cl1 [3.502 (4) Å]. The former constitutes a hydrogen bond, whereas the latter resides at the edge of conventional hydrogen bonds. All imidazolone NH groups in *A* and *B* act as donors to the Cl1 ion, forming hydrogen bonds of similar strength and geometry [N3$A^{i}\cdots$Cl1 3.106 (3) Å and N3*B*$\cdots$Cl1 3.103 (3) Å; symmetry code: (i) x, y, $1+z$]. Thus, the Cl ion is a fourfold acceptor, accepting two from the N1A^{ii} and N1B^{ii} terminal amines and two from the N3A^{i} and N3*B* atoms of the imidazolone groups of molecules *A* and *B*. The N1A^{ii}, N3A^{i} and N3*B* atoms and the Cl1 ion are almost coplanar and perpendicular to the *c* axis, resulting in a 'hydrogen-bonding channel' parallel to the *c* axis. The increased anisotropy of the N3*A* and N3*B* atoms may be due to the inherent loose packing through this channel with the Cl ion as an acceptor of hydrogen in the centre showing a synchronous positional disorder and atomic mobility in this direction.

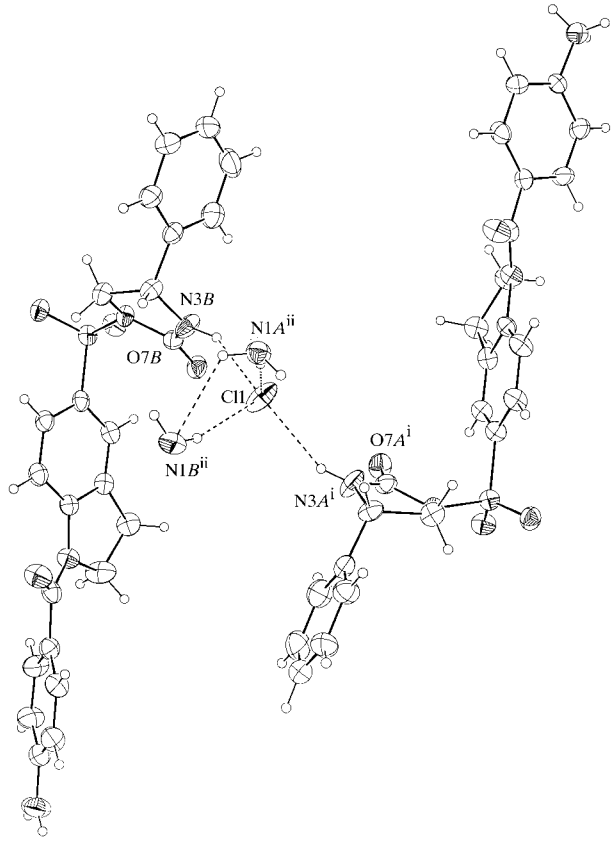


Figure 3
A view of the intermolecular hydrogen bonds around the Cl ion. Displacement ellipsoids are drawn at the 30% probability and the interactions are indicated with dashed lines connecting H and acceptor atoms [symmetry codes: (i) x, y, $1+z$; (ii) $1-x$, $-1+y$, $-z$].

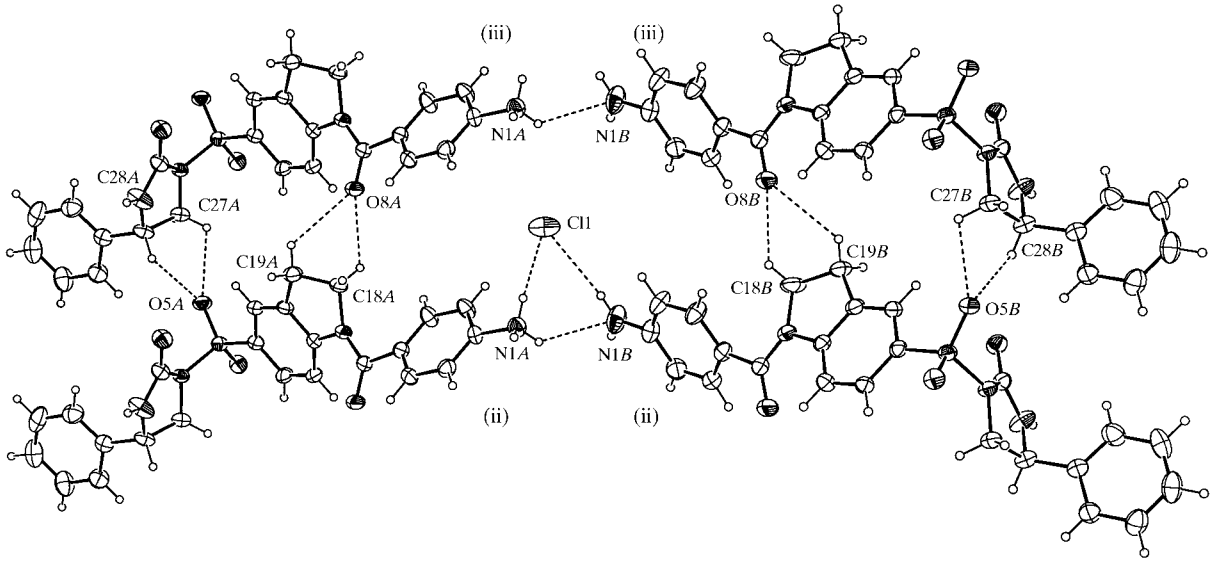


Figure 4
Intermolecular C—H···O and N—H···Cl/N—H···N interactions between the conformers are depicted with displacement ellipsoids drawn at the 30% probability level [symmetry codes: (ii) $1-x, -1+y, -z$; (iii) $1-x, y, -z$].

As well as the four hydrogen bonds to the Cl1 ion, four more hydrogen bonds involving the N—H groups and O atoms of the imidazolone contribute to crystalline cohesion. N1A^{iii} donates its H1A^{iii} and H1C^{iii} atoms to the carbonyl O7A^{i} and the O7B atom of the imidazolone, and N1B^{iii} interacts with the neighbouring N1A^{iii} and O7B atoms [symmetry code: (iii) $1-x, y, -z$]. The O7B and N1B^{iii} acceptors share H1C^{iii} from N1A^{iii}, thus building a three-centre hydrogen bond, and O7B is an acceptor of two H atoms from N1A^{iii} and N1B^{iii}. In Fig. 3, all the hydrogen bonds around the Cl ion are shown explicitly. Furthermore, additional multi-centre interactions involving aliphatic C—H groups of A and B are present. These are depicted in Fig. 4 and listed in Table 2.

Experimental

The free amine of the title compound was synthesized and purified as reported previously (Jung *et al.*, 1998) from (*S*)-phenylglycinol (converted into its hydrochloride in CH_3OH saturated with HCl gas). After treatment of this CH_3OH/HCl solution with ethyl acetate, an amorphous powder of the hydrochloride salt was obtained. The elemental analysis and IR spectrum showed that all terminal amine groups are protonated in the 1:1 hydrochloride salt. [Elemental analysis, calculated for $C_{24}H_{23}N_4O_4S^+\cdot Cl^-$: C 57.77, H 4.65, N 11.23%; found: C 57.0 (5), H 4.4 (3), N 10.86 (8)%. IR spectrum (ν_{max}, KBr, cm^{-1}): 3200, 2800.] The amorphous salt was then treated in CH_3OH/CH_2Cl_2 (7:1) co-solvent and slow evaporation produced single crystals of (I) suitable for X-ray measurements. The elemental analysis and IR spectrum revealed (I) to have NH_2, NH and NH_3^+ groups. [Elemental analysis, calculated for $C_{24}H_{23}N_4O_4S^+\cdot Cl^-\cdot C_{24}H_{22}N_4O_4S$: C 59.96, H 4.72, N 11.65; found: C 59.87 (5), H 4.45 (11), N 11.46 (13)%. IR spectrum (ν_{max}, KBr, cm^{-1}): 3330, 3200, 2800.]

Crystal data

$C_{24}H_{23}N_4O_4S^+\cdot Cl^-\cdot C_{24}H_{22}N_4O_4S$
M_r = 961.49
Monoclinic, $C2$
a = 28.945 (3) Å
b = 6.5473 (9) Å
c = 27.526 (2) Å
β = 117.622 (7)°
V = 4621.9 (9) Å^3
Z = 4
D_x = 1.382 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 25 reflections
θ = 11.42–14.21°
μ = 0.237 mm^{-1}
T = 294 (2) K
Prism, pale brown
0.43 × 0.40 × 0.33 mm

Table 1
Selected geometric parameters (Å, °).

	Molecule *A*	Molecule *B*
S1—N4	1.660 (3)	1.670 (3)
S1—C24	1.763 (3)	1.748 (3)
N1—C11	1.475 (4)	1.388 (5)
N2—C17	1.368 (5)	1.382 (5)
N3—C26	1.314 (5)	1.318 (5)
N3—C28	1.452 (5)	1.452 (4)
N4—C26	1.402 (4)	1.402 (4)
N4—C27	1.457 (4)	1.454 (4)
O7—C26	1.230 (4)	1.229 (4)
O8—C17	1.221 (4)	1.222 (4)
C14—C17	1.503 (5)	1.485 (5)
N2—C18—C19	103.4 (3)	105.3 (3)
C21—N2—C17—O8	−7.0 (6)	−4.1 (6)
C18—N2—C17—C14	−26.8 (5)	−22.9 (6)
C21—N2—C17—C14	169.7 (3)	176.1 (3)
C13—C14—C17—O8	−31.4 (5)	−30.0 (6)
C17—N2—C18—C19	−141.4 (4)	−153.4 (3)
C21—N2—C18—C19	24.3 (4)	9.8 (4)
N2—C18—C19—C20	−24.8 (4)	−9.3 (4)
C18—C19—C20—C21	18.2 (4)	5.9 (4)
C18—C19—C20—C25	−161.6 (4)	−173.7 (4)
C18—N2—C21—C20	−13.5 (4)	−6.4 (4)
C18—N2—C21—C22	162.7 (4)	170.9 (4)

Data collection

Enraf–Nonius CAD-4 diffractometer	5916 reflections with $I > 2\sigma(I)$
ω–2θ scans	$R_{int} = 0.030$
Absorption correction: ψ scan (North *et al.*, 1968)	$\theta_{max} = 25.17^\circ$
$T_{min} = 0.905$, $T_{max} = 0.926$	$h = 0 \rightarrow 34$
8420 measured reflections	$k = -7 \rightarrow 7$
4537 independent reflections (plus 3715 Friedel-related reflections)	$l = -32 \rightarrow 29$
	3 standard reflections
	frequency: 300 min
	intensity decay: 1%

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0486P)^2 + 1.0617P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R(F) = 0.048$	$(\Delta/\sigma)_{max} < 0.001$
$wR(F^2) = 0.116$	$\Delta\rho_{max} = 0.28$ e Å^{-3}
$S = 1.018$	$\Delta\rho_{min} = -0.18$ e Å^{-3}
8252 reflections	Absolute structure: (Flack, 1983)
605 parameters	Flack parameter = −0.07 (7)
H-atom parameters constrained	

Table 2
Hydrogen-bonding geometry and short intermolecular contacts (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N1A—H1A···O7A^{i}	0.89	1.90	2.768 (4)	166
N1A—H1B···Cl1^{ii}	0.89	2.22	3.110 (4)	174
N1A—H1C···O7B^{iii}	0.89	2.36	3.086 (4)	139
N1A—H1C···N1B	0.89	2.51	3.008 (4)	116
N1B—H1D···O7B^{iii}	0.86	2.23	2.980 (4)	145
N1B—H1E···Cl1^{ii}	0.86	2.66	3.502 (4)	166
N3A—H3A···Cl1^{iv}	0.86	2.32	3.106 (3)	153
N3B—H3B···Cl1	0.86	2.33	3.103 (3)	150
C18A—H18A···O8A^{v}	0.97	2.55	3.018 (4)	109
C19A—H19B···O8A^{v}	0.97	2.85	3.336 (5)	112
C27A—H27A···O5A^{vi}	0.97	2.48	2.935 (4)	109
C28A—H28A···O5A^{vi}	0.98	2.64	3.158 (5)	113
C18B—H18C···O8B^{v}	0.97	2.44	3.123 (5)	127
C19B—H19D···O8B^{v}	0.97	2.78	3.351 (5)	118
C27B—H27C···O5B^{vi}	0.97	2.46	2.919 (4)	109
C28B—H28B···O5B^{vi}	0.98	2.57	3.095 (5)	113

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

The H atoms were treated using a riding model (C—H = 0.93–0.98 Å and N—H = 0.86–0.89 Å). The absolute structure was inferred not only from the absolute configuration of (*S*)-phenylglycinol used as starting material in the synthesis, but also determined by refining an enantiomorph-sensitive parameter to −0.07 (7) (Flack, 1983) using all 3715 Friedel pairs.

Data collection: *CAD*-4 *EXPRESS* (Enraf–Nonius, 1994); cell refinement: *CAD*-4 *EXPRESS*; data reduction: *XCAD*4 (Harms & Wocadlo, 1995); program(s) used to solve structure: *WinGX* (Farrugia, 1998); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*-3 *for Windows* (Johnson *et al.*, 1998); software used to prepare material for publication: *WinGX*.

KP, BM and SJ acknowledge a grant (HMP-98-DA-7-0015) from the Good Health R & D Project, Ministry of Health & Welfare, Korea.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GG1010). Services for accessing these data are described at the back of the journal.

References

Enraf–Nonius (1994). *CAD*-4 *EXPRESS*. Enraf–Nonius, Delft, The Netherlands.
Farrugia, L. J. (1998). *WinGX*. Version 1.61 for Windows. University of Glasgow, Scotland.
Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.
Harms, K. & Wocadlo, S. (1995). *XCAD*4. University of Marburg, Germany.
Johnson, C. K., Burnett, M. N. & Farrugia, L. J. (1998). *ORTEP*-3 *for Windows*. University of Glasgow, Scotland.
Jung, S.-H. (1999). Unpublished work.
Jung, S.-H., Lee, H.-S., Song, J.-S., Kim, H.-M., Han, S.-B., Lee, C.-W., Lee, M.-S., Choi, D.-R., Lee, J.-A., Chung, Y.-H., Yoon, S.-J., Moon, E.-Y., Hwang, H.-S., Seong, S.-K. & Lee, D.-K. (1998). *Bioorg. Med. Chem. Lett.* **8**, 1547–1550.
North, A. C. T., Phillips, D. C. & Mathews, F. S. (1968). *Acta Cryst.* A**24**, 351.
Sheldrick, G. M. (1997). *SHELXL*97. University of Göttingen, Germany.