The structure was solved by direct methods and refined by full-matrix least-squares techniques. All H atoms were located from a difference Fourier map and refined isotropically.

Programs used: data collection, cell refinement and data reduction: *XSCANS* (Siemens, 1994); structure solution and molecular graphics: *SHELXTL/PC* (Sheldrick, 1990); structure refinement: *SHELXL93* (Sheldrick, 1993); geometrical calculations *PARST* (Nardelli, 1983).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: MU1336). Services for accessing these data are described at the back of the journal.

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1-(*p*-Chlorophenyl)-5-oxo-3-(2-thienyl)-pyrrolidine-2-carboxylic Acid

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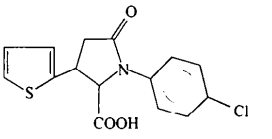
Abstract

The chlorophenyl and thiophene rings of the title molecule, $C_{15}H_{12}ClNO_3S$, are individually planar. The pyrrolidine ring is in a half-chair conformation. The thiophene ring is disordered. The structure is stabilized by a three-dimensional network of C—H···O and O—H···O hydrogen bonds.

Comment

In recent work, we have observed that *N*-phenyl γ-lactam derivatives exhibited Gram-positive and Gram-negative antibacterial activities (Ray, Kar, Roy & Brahma, 1995). The bioactivity of the γ-lactam derivatives depends on the ability of several proteins to inhibit the cross-linking of the bacterial cell wall (Baldwin, Lynch & Pitlick, 1991) and this property is controlled by substituents in the γ-lactam ring (Baldwin, Chan, Gallecher & Otsnka, 1984). In connection with our studies on the synthesis of novel γ-lactam analogues with potential as biological surrogates, we introduced a thiophene ring which can help in activating the γ-lactam system (Roy, Ray & Kar, 1997). The crystal structure determination of the title compound, (I), one of these derivatives, was carried out in order to elucidate the molecular conformation.



(I)

In general, the bond lengths and angles observed in this structure agree with those in related structures (Sivakumar, Fun, Ray, Roy & Nigam, 1995*a*,*b*), but the unusually long C12—C15 [1.596 (4) Å] and C13—C15 [1.522 (6) Å] distances are probably systematically in error because of the disorder of the thiophene ring (as explained below).

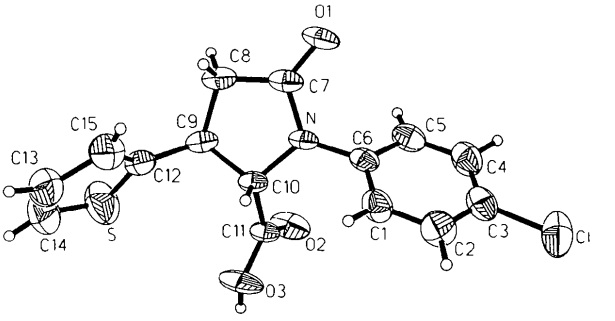


Fig. 1. The structure of title compound showing 50% probability displacement ellipsoids and the atom-numbering scheme. Only the major conformer is shown.

The pyrrolidine ring is in a half-chair conformation, with asymmetry parameter $\Delta C_2(C7) = 0.005\,(2)°$ (Nardelli, 1983*a*). The deviations of atoms C9 and C10 from the plane defined by N, C7 and C8 are −0.204 (4) and 0.260 (3) Å, respectively. The chloro-

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phenyl and thiophene rings are planar, with a dihedral of 73.5 (1)° between them. The best plane through the pyrrolidine ring makes an angle of 112.0 (2)° with the thiophene ring and an angle of 55.0 (2)° with the chlorophenyl ring.

In the crystal, the molecules form a C—H···O hydrogen-bonded network along the **c** direction [C1···O1(x, y, $z+1$) 3.275 (5), H1···O1 2.41 (4) Å and C1—H1···O1 167 (3)°] and an O—H···O hydrogen-bonded network along the **a** direction [O3···O1($x-\frac{1}{2}$, $\frac{1}{2}-y$, $z+1$) 2.659 (4), H3O···O1 1.84 (5) Å and O3—H3O···O1 174 (5)°]. Other short intermolecular contacts are C8···O2($x+\frac{1}{2}$, $\frac{3}{2}-y$, z) of 3.128 (5) Å and C10···O2($x+\frac{1}{2}$, $\frac{3}{2}-y$, z) of 3.101 (4) Å.

Experimental

The synthesis of the title compound was carried out by a novel one-step condensation of *p*-chloroaminomalonate with thiophenylacryloyl chloride through an intermolecular Michael addition followed by intramolecular amidification and hydrolysis of the diester (Kar, Chatterjee & Ray, 1993). Single crystals were grown by slow evaporation of a 2-propanol solution of the compound.

Crystal data

$C_{15}H_{12}ClNO_3S$
M_r = 321.77
Orthorhombic
$Pna2_1$
a = 10.758 (1) Å
b = 23.899 (2) Å
c = 5.900 (1) Å
V = 1516.9 (3) Å^3
Z = 4
D_x = 1.409 Mg m^{-3}
D_m not measured
Mo $K\alpha$ radiation
λ = 0.71073 Å
Cell parameters from 39 reflections
θ = 5.41–12.49°
μ = 0.397 mm^{-1}
T = 293 (2) K
Rectangular
0.48 × 0.28 × 0.16 mm
Colourless

Data collection

Siemens *P*4 diffractometer
$\theta/2\theta$ scans
Absorption correction: none
2574 measured reflections
2235 independent reflections
1206 reflections with $I > 2\sigma(I)$
R_{int} = 0.027
θ_{max} = 27.49°
$h = -1 \rightarrow 13$
$k = -1 \rightarrow 31$
$l = -1 \rightarrow 7$
3 standard reflections
every 97 reflections
intensity decay: <3%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.038
$wR(F^2)$ = 0.082
S = 0.816
2235 reflections
235 parameters
All H atoms refined
$w = 1/[\sigma^2(F_o^2) + (0.0293P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.14 e Å^{-3}
$\Delta\rho_{min}$ = −0.18 e Å^{-3}
Extinction correction: none
Scattering factors from *International Tables for Crystallography* (Vol. C)
Absolute configuration: Flack (1983)
Flack parameter = 0.03 (12)

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

C15—C13	1.522 (6)	C7—C8	1.493 (5)
C15—C12	1.596 (4)	C8—C9	1.533 (5)
O1—C7	1.226 (4)	C9—C12	1.503 (5)
O2—C11	1.177 (4)	C9—C10	1.552 (5)
O3—C11	1.312 (5)	C10—C11	1.519 (4)
N—C7	1.366 (5)	C12—S	1.645 (4)
N—C6	1.432 (4)	C13—C14	1.313 (7)
N—C10	1.462 (5)	C14—S	1.618 (6)
C13—C15—C12	98.2 (3)	N—C10—C11	111.2 (3)
C7—N—C6	123.3 (3)	N—C10—C9	102.3 (3)
C7—N—C10	112.6 (3)	C11—C10—C9	112.2 (3)
C6—N—C10	121.2 (3)	O2—C11—O3	124.5 (3)
C1—C6—N	119.6 (4)	O2—C11—C10	124.0 (3)
C5—C6—N	120.7 (4)	O3—C11—C10	111.5 (3)
O1—C7—N	123.9 (3)	C9—C12—C15	124.1 (3)
O1—C7—C8	127.5 (4)	C9—C12—S	121.6 (3)
N—C7—C8	108.6 (3)	C15—C12—S	114.2 (3)
C7—C8—C9	105.3 (3)	C14—C13—C15	117.6 (5)
C12—C9—C8	115.9 (3)	C13—C14—S	115.6 (5)
C12—C9—C10	113.2 (3)	C14—S—C12	94.4 (3)
C8—C9—C10	103.2 (3)		

The structure was solved by direct methods and refined by full-matrix least-squares techniques. All H atoms except H15 (attached to C15) were located from a difference Fourier map and refined isotropically. The refinement at this stage did not lead to good convergence (R = 0.086 and wR = 0.197) and the difference Fourier map showed an electron cloud of approximately 1.55 e Å^{-3} near C15. Based on our earlier experiences with γ-lactam derivatives (Sivakumar, Fun, Ray, Roy & Nigam, 1995*a*,*b*), this was interpreted in terms of disorder involving formal rotation of the thiophene ring through 180° about the C9—C12 single bond so that the S and C15 atoms interchange their positions. Hence, it was decided to refine the structure on this basis (with S′ coinciding with C15 and C15′ with S); this model gave very good convergence and the final R values reported above. The populations were 63 and 37% for the major and minor conformations, respectively.

Programs used: data collection, cell refinement and data reduction: *XSCANS* (Siemens, 1994); structure solution and molecular graphics: *SHELXTL/PC* (Sheldrick, 1990); structure refinement: *SHELXL*93 (Sheldrick, 1993); geometrical calculations: *PARST* (Nardelli, 1983*b*).

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2,6-Diamino-9-(carboxymethyl)purine Ethyl Ester†

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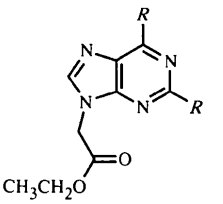
Abstract

In the crystal structure of the title compound (as its hemihydrate, $C_9H_{12}N_6O_2.0.5H_2O$), a potential intermediate for the synthesis of peptidic nucleic acids containing 2,6-diaminopurine, the asymmetric unit contains two molecules, one ordered and the other with twofold positional disorder about a pivot point near the 6-amino group, together with one water molecule. The side chain emerges at N9 with C8—N9—C10—C11 torsion angles of 93.0 (2) and 50.8 (6)/−97.0 (6)°, respectively.

Comment

Peptidic nucleic acids (PNA's) are DNA mimetics in which *N*-(2-aminoethyl)glycine units replace the conventional sugar–phosphate backbone (Hyrup & Nielsen, 1996; Egholm, Buchardt, Coull, Nielsen & Berg, 1992) and in which the DNA bases adenine (A), thymine (T), cytosine (C), guanine (G) (Egholm, Christensen *et al.*, 1993) and pseudoisocytosine (Egholm *et al.*, 1995) are attached to the peptidic backbone through methylene carbonyl linkers. PNA's bind with high affinity and specificity (Egholm, Buchardt *et al.*, 1993) to DNA targets and thus offer the possibility of inhibiting gene expression in a controlled manner (Thuong & Hélène, 1993). Our interest in modulating the affinity of PNA's for target nucleic acid sequences has prompted an investigation of PNA's containing 2,6-diaminopurine (D), which can make a three hydrogen-bond Watson–Crick base pair with T, compared with the two hydrogen-bond base pair made by A. The title compound, (1), is a potential intermediate in the synthesis of PNA's containing D.



(1) $R=NH_2$
(2) $R=Cl$
(3) $R=N_3$

We have successfully prepared (1) by two alternative routes, the first involving alkylation of 2,6-dichloropurine using ethyl bromoacetate (Chan, Schwalbe, Sood & Fraser, 1995) to give (2), followed by treatment with sodium azide at elevated temperature, resulting in substitution of both chloro groups to give (3) (Sood, Schwalbe & Fraser, 1997). Hydrogenolysis (10% Pd/C) of (3) under H_2 at room temperature for 4 d gave (1), in crystalline form, but with a very modest overall yield. The second and more direct method (Dueholm *et al.*, 1994) involved alkylation of diaminopurine using ethyl bromoacetate and sodium hydride. The reaction was regioselective, giving (1) in 79% yield with only a small amount of the corresponding N7 regioisomer. The structure determination shows that the ethyl carboxymethylene side chain is indeed attached at N9 and here we compare the crystal structure of (1) with those of other analogues.

Many geometric features of (1) (Table 1) resemble those previously found in its adenine (Flensburg & Egholm, 1994), 2,6-dichloropurine, (2) (Chan, Schwalbe, Sood & Fraser, 1995), and 2,6-diazidopurine, (3) (Sood, Schwalbe & Fraser, 1997), analogues. Two molecules of (1), along with a molecule of water, are present in the asymmetric unit: a well ordered molecule (1*A*) with an accompanying disordered molecule, either (1*B*) or (1*C*). The hydrogen-bonded 6-amino group is almost invariant in molecules (1*B*) and (1*C*) (Fig. 1). In (1*A*), atoms of the heterocycle are coplanar within 0.008 Å and the side chain emerges almost orthogonally from the heterocycle, where the torsion angle C8*A*—N9*A*—C10*A*—C11*A* is 93.0 (2)°, with the six atoms of the side chain coplanar within an r.m.s. deviation of 0.092 Å. Similarly, the side-chain atoms of (1*B*) and (1*C*) are reasonably coplanar, but with C8*B*—N9*B*—C10*B*—C11*B* and C8*C*—N9*C*—C10*C*—C11 torsion angles of 50.8 (6) and −97.0 (6)°, respectively. Compared with its adenine analogue, the N1*A*—C6*A*—C5*A* bond angle is expanded by 0.64 (15)° and the N3*A*—C2*A*—N1*A* bond angle is compressed by

† Alternative name: ethyl 2,6-diaminopurine-9-acetate.