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2-(Methoxycarbonyl)-4-methylthiophen-3-aminium chloride monohydrate: the first crystal structure of a 3-aminothiophene-2-carboxylic acid ester

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Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.002 Å
R factor = 0.040
wR factor = 0.114
Data-to-parameter ratio = 18.5

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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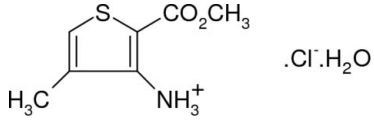
In the crystal structure of the title compound, $C_7H_{10}NO_2S^+\cdot Cl^-\cdot H_2O$, a weak N—H···O intramolecular hydrogen bond is observed without the formation of a conjugated π-electron system. The three-dimensional network is sustained *via* extensive hydrogen bonding involving the ions and the water molecule.

Comment

3-Aminothiophene-2-carboxylic acid derivatives, bioisosteres of anthranilic acid derivatives, are very important building blocks in medicinal chemistry. They are extensively used as starting materials to synthesize various thiophene-containing structures with potential activities in the fields of oncology (Wyne *et al.*, 2004; Andersen *et al.*, 2002; Benish *et al.*, 2002; Levin *et al.*, 2000), neuroscience (Rault *et al.*, 1996) or cardiovascular disease (Eto *et al.*, 2004; Inoue *et al.*, 2004; Larsen *et al.*, 2003; Weinstock & Franz, 2002; Nakashima *et al.*, 1999). The chemical stability of many compounds of this family is limited. It must be pointed out that *o*-aminothiophenecarboxylic acids are not stable because of spontaneous decarboxylation. Among 3-aminothiophene-2-carboxylates, the title compound, (I), is the most important because it serves as starting material to produce carticaine (Malamed *et al.*, 2000; Donaldson *et al.*, 1987; Vree & Gielen, 2005), the local anaesthetic of choice in dentistry. Currently, the industrial synthesis of the title compound remains a subject of research because of the difficulties encountered in isolating the base or one of its salts with high yield and purity (Kadushkin *et al.*, 2002). In the course of our studies aimed at the synthesis of new thiophene compounds with potential biological activity, the title compound was needed but was hygroscopic when prepared according to the literature method (Barker *et al.*, 2002). Its degree of hydration could not be determined. In order to overcome these difficulties, a new process in water was developed, leading to a stable monohydrate salt.



(I)

Fig. 1 shows a view of the asymmetric unit, which consists of one cation, one chloride ion and one water molecule. In the cation, the ester group is coplanar with the thiophene ring [dihedral angle 2.75 (6)°]; thus one O atom of the ester group (O7) lies in the proximity of one H atom (H10*A*) of the protonated amino group (N10). The intramolecular contact

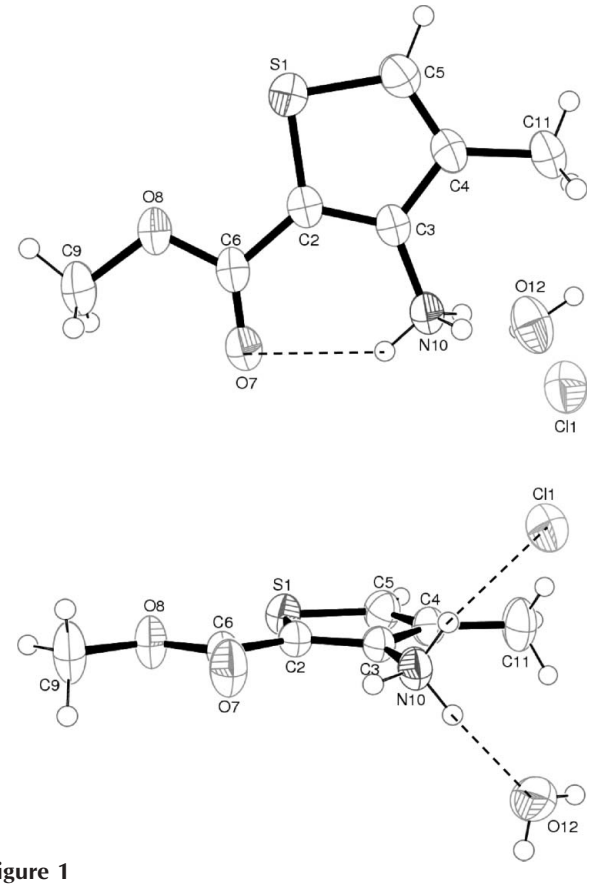


Figure 1
Two views of the title compound, showing the atom-numbering scheme. Displacement ellipsoids are shown at the 50% probability level. H atoms are drawn as small circles of arbitrary radii. Dashed lines indicate hydrogen bonds.

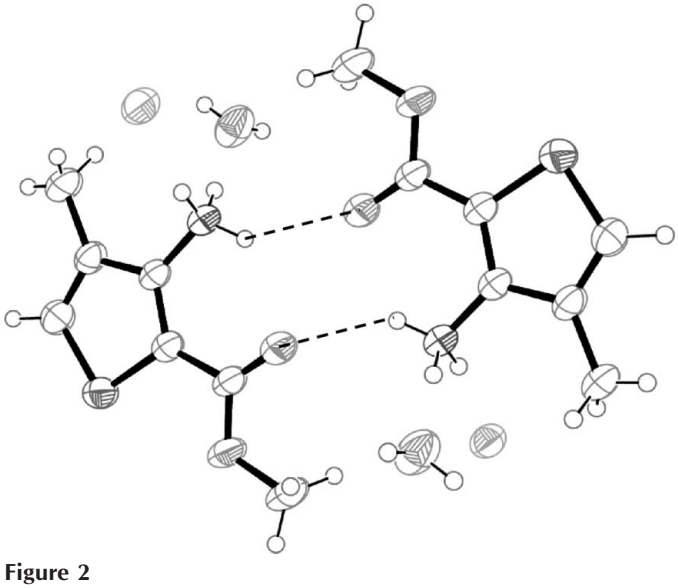


Figure 2
A view of the dimer, showing the N—H···O hydrogen bonds (dashed lines).

distance between O7 and H10*A* is 2.18 (2) Å, indicating the formation of a weak intramolecular hydrogen bond. With this hydrogen bond, the six atoms O7, C6, C2, C3, N10 and H10*A* form a six-membered pseudo-ring. Since the hydrogen bond closing the ring is a weak one, the observed lengths of the single and double bonds in the pseudo-ring (Table 1) are close to the typical values (Glusker *et al.*, 1994), which excludes the formation of a weak conjugated π-electron system inside this pseudo-ring.

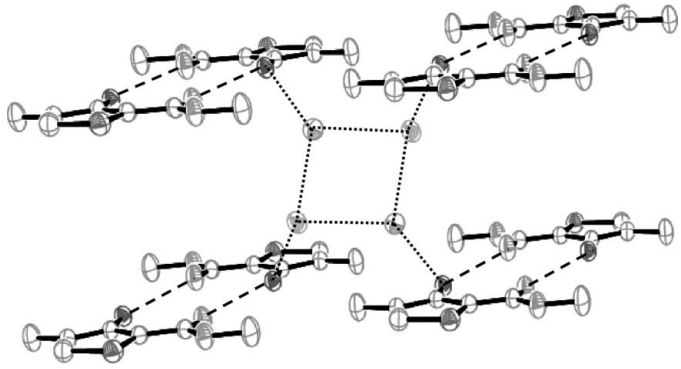


Figure 3
A packing diagram of the title compound, showing the stacking of the dimers along the *a* axis. N—H···O, N—H···Cl and O—H···Cl hydrogen bonds are shown as dashed lines. H atoms have been omitted for clarity.

In the crystal packing, the three-dimensional network is sustained *via* extensive hydrogen bonding involving the ions and the water molecule (Table 2). The cations are linked into centrosymmetric dimers by a pair of intermolecular N—H···O hydrogen interactions (Fig. 2). The dimers are stacked in columns along the *a* axis through N—H···O and N—H···Cl hydrogen interactions (Fig. 3). Both H atoms of the water molecule are engaged in hydrogen bonds with adjacent chloride anions.

Experimental

Methyl-3-amino-4-methylthiophene-2-carboxylate (10 g) was added to hydrochloric acid (100 ml, 6 *N*) and the mixture was refluxed. After 1 h, all the starting material was dissolved and reflux was continued for 3 h. The reaction mixture was left to cool; crystals suitable for X-ray analysis appeared after 10 h at room temperature.

Crystal data

$C_7H_{10}NO_2S^+\cdot Cl^-\cdot H_2O$
M_r = 225.69
Triclinic, $P\overline{1}$
a = 7.1872 (8) Å
b = 7.5620 (10) Å
c = 10.9203 (13) Å
α = 107.887 (10)°
β = 97.596 (10)°
γ = 106.276 (9)°
V = 526.49 (11) Å^3
Z = 2
D_x = 1.424 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 25 reflections
θ = 18–25°
μ = 0.54 mm^{-1}
T = 293 (2) K
Prism, colourless
0.57 × 0.45 × 0.18 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: Gaussian (*JANA98* (Petříček & Dušek, 1998))
T_{min} = 0.585, T_{max} = 0.803
3215 measured reflections
3065 independent reflections
2509 reflections with $I > 2\sigma(I)$
R_{int} = 0.014
θ_{max} = 30.0°
$h = -10 \rightarrow 10$
$k = -10 \rightarrow 10$
$l = 0 \rightarrow 15$
3 standard reflections
frequency: 60 min
intensity decay: 33%

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0708P)^2 + 0.0703P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)] = 0.040$	$(\Delta/\sigma)_{max} < 0.001$
$wR(F^2) = 0.114$	$\Delta\rho_{max} = 0.48$ e Å^{-3}
$S = 1.07$	$\Delta\rho_{min} = -0.33$ e Å^{-3}
3065 reflections	
166 parameters	
All H-atom parameters refined	

Table 1
Selected bond lengths (Å).

C2—C3	1.3713 (19)	C3—N10	1.4506 (19)
C2—C6	1.463 (2)	C6—O7	1.2082 (19)

Table 2
Hydrogen-bond geometry (Å, °).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N10—H10*A*···O7	0.89 (2)	2.18 (2)	2.8489 (18)	132 (2)
N10—H10*A*···O7^{i}	0.89 (2)	2.24 (2)	3.0064 (19)	145 (2)
N10—H10*B*···O12	0.94 (2)	1.76 (2)	2.692 (2)	171 (2)
N10—H10*C*···Cl1	0.93 (2)	2.15 (2)	3.0624 (15)	168 (2)
O12—H12*B*···Cl1^{ii}	0.81 (3)	2.33 (4)	3.1187 (17)	165 (3)
O12—H12*A*···Cl1^{iii}	0.84 (4)	2.38 (4)	3.202 (2)	169 (3)

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

All H atoms were located in a difference Fourier map and refined freely. The very high intensity decay during data collection was satisfactorily corrected on the basis of standard reflections, using a linear model.

Data collection: *CAD-4*/*PC Software* (Enraf–Nonius, 1996); cell refinement: *CAD-4*/*PC Software*; data reduction: *JANA98* (Petříček & Dušek, 1998); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1990); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3* (Farrugia, 1997); software used to prepare material for publication: *SHELXL97*.

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