

1,3-Benzothiazole-6-carboxamidinium chloride dihydrate

Dubravka Matković-Čalogović,^{a*} Zora Popović,^a Vesna Tralić-Kulenović,^b Livio Racanè^b and Grace Karminski-Zamola^c

^aLaboratory of General and Inorganic Chemistry, Department of Chemistry, Faculty of Science, University of Zagreb, Ul. kralja Zvonimira 8, 10000 Zagreb, Croatia,

^bFaculty of Textile Technology, University of Zagreb, Pierottijeva 6, 10000 Zagreb, Croatia, and ^cFaculty of Chemical Engineering and Technology, University of Zagreb, Marulićev trg 19, 10000 Zagreb, Croatia

Correspondence e-mail: dubravka@chem.pmf.hr

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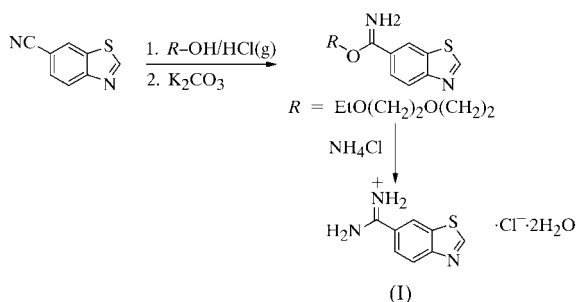
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The title compound, $C_8H_8N_3S^+ \cdot Cl^- \cdot 2H_2O$, has been synthesized and characterized both spectroscopically and structurally. The structure consists of 1,3-benzothiazole-6-carboxamidinium cations, chloride anions and water molecules, all interconnected by hydrogen bonds into a three-dimensional network. The 1,3-benzothiazole moiety is inclined to the 6-amidine group by $36.71(9)^\circ$.

Comment

Small and simple heterocyclic structures often exhibit complex biological properties. Substituted benzothiazoles show anti-tumor (Goldfarb *et al.*, 1999), anti-infective and antifungal (Sener *et al.*, 2000), and antihelminthic activities (Nadkarn *et al.*, 2000). In order to find new potent antitumor benzothiazole compounds (Racanè *et al.*, 2001), we have introduced an amidine group into the benzothiazole moiety. This report describes the synthesis and crystal structure of a new cationic compound, namely 1,3-benzothiazole-6-carboxamidinium chloride dihydrate, (I). Substituted benzothiazoles that are not bound to a metal are rare.



As depicted in the *Scheme*, the starting compound was 6-cyanobenzothiazole (Boggust & Cocker, 1949). The conversion of the cyano function into the amidine function

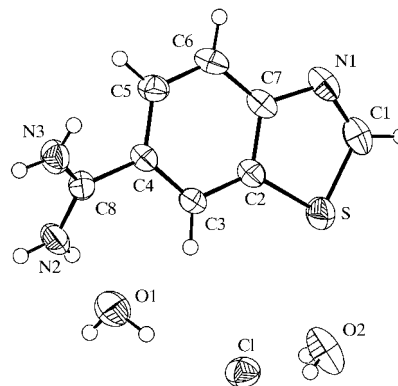


Figure 1

A view of (I), with the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level.

was achieved using the Pinner method (Boyd, 1991). The imidoyl ether hydrochloride that was generated as an intermediate product was converted into the free base with potassium carbonate and was then converted with ammonium chloride into (I).

The structure comprises 1,3-benzothiazole-6-carboxamidinium cations, chloride anions and water molecules (Fig. 1); pertinent bond lengths and angles are given in Table 1. The 1,3-benzothiazole moiety is planar, with the largest deviation from the plane being that of atom C6 [$0.023(2) \text{ \AA}$]. However, the entire 1,3-benzothiazole-6-carboxamidinium cation is not planar, since the plane through the 6-amidine group is inclined to that through the 1,3-benzothiazole moiety by $36.71(9)^\circ$. The differences in the C—C bonds within the benzene ring are usual for such fused rings. The bond angle around the S atom is within the range found in the five-membered rings of other substituted benzothiazole derivatives (Davidović *et al.*, 1999; Popović *et al.*, 2001, 2002). The hydrogen-bond pattern is very interesting, since all N—H and O—H donor atoms are

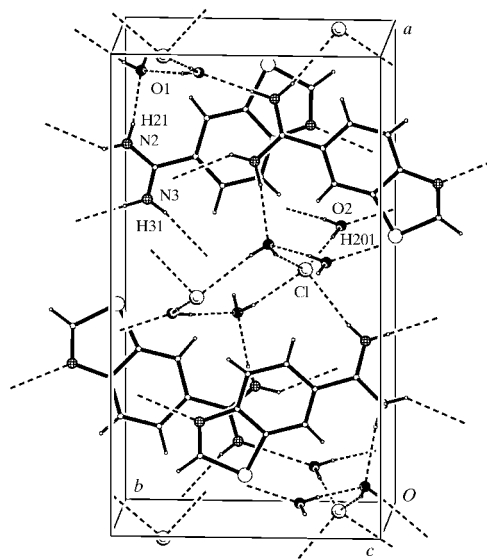


Figure 2

The packing of the ions and molecules in the unit cell. Hydrogen bonds are indicated by dashed lines.

involved in the hydrogen bonding to the acceptor atoms, *i.e.* endocyclic N atoms, Cl ions and water O atoms. Water molecules have an important role since they form six out of the eight hydrogen bonds that interconnect the ions and molecules into a three-dimensional network (Fig. 2 and Table 2).

Experimental

A solution of 6-cyanobenzothiazole (4 g, 25 mmol) in dry 2-(2-ethoxyethoxy)ethanol (60 ml) was cooled to 278 K and saturated with HCl. The flask was then stoppered and the contents stirred at room temperature for 2 d (until IR spectra indicated the disappearance of the nitrile peak). Excess HCl was removed from the suspension with a stream of N₂. The reaction mixture was poured into dry ether (400 ml), and crystals of the imidoyl ether hydrochloride were filtered off, washed with dry ether and dried under reduced pressure over KOH. The imidoyl ether hydrochloride was poured into cold water (150 ml) containing 20% K₂CO₃ (20 ml) and the free base was extracted with CHCl₃. The solvent was evaporated and the oil residue was dissolved in ethanol (100 ml). A solution of NH₄Cl (1.4 g, 26 mmol) in water (25 ml) was added to the ethanol solution and the mixture was heated under reflux for 5 h. After filtration (charcoal), the hot reaction mixture was left to stand at room temperature for 4 d. Compound (I) separated as colourless crystals [m.p. = 548 K, yield = 3.94 g (68%)]. Spectroscopic analysis, IR (KBr, cm⁻¹): 3265, 3080 (NH), 1679 (C=N); ¹H NMR (300 MHz, DMSO-*d*₆): δ 9.67 (*s*, 1H, H-2), 9.41 (*br s*, 4H, H-NH, disappeared with D₂O), 8.74 (*d*, 1H, *J*_{7,5} = 1.7 Hz, H-7), 8.31 (*d*, 1H, *J*_{4,5} = 8.6 Hz, H-4), 7.95 (*dd*, 1H, *J*_{5,4} = 8.6 Hz, *J*_{5,4} = 1.8 Hz, H-5); ¹³C NMR (75 MHz, DMSO-*d*₆): δ 166.2 (*s*), 161.3 (*d*), 156.5 (*s*), 134.5 (*s*), 126.4 (*d*), 125.7 (*s*), 124.2 (*d*), 123.8 (*d*). Analysis, calculated for C₈H₈ClN₃S·2H₂O: C 38.48, H 4.84, N 16.83, Cl 14.20%; found: C 38.67, H 4.48, N 17.03, Cl 14.64%.

Crystal data

C₈H₈N₃S⁺·Cl⁻·2H₂O
M_r = 249.72
 Orthorhombic, *Pna*2₁
a = 16.9296 (9) Å
b = 9.3433 (5) Å
c = 7.3389 (15) Å
V = 1160.9 (3) Å³
Z = 4
D_x = 1.429 Mg m⁻³

Mo *Kα* radiation
 Cell parameters from 60 reflections
 θ = 12.5–17.8°
 μ = 0.49 mm⁻¹
T = 293 (2) K
 Block, colourless
 0.47 × 0.42 × 0.22 mm

Data collection

Philips PW1100 diffractometer
 (updated by Stoe)
 ω scans
 Absorption correction: ψ scan
 (*X-RED*; Stoe & Cie, 1995)
*T*_{min} = 0.792, *T*_{max} = 0.893
 4203 measured reflections
 3377 independent reflections
 2945 reflections with *I* > 2σ(*I*)

*R*_{int} = 0.034
 θ _{max} = 30.0°
h = -23 → 23
k = -13 → 13
l = -10 → 10
 4 standard reflections
 frequency: 90 min
 intensity decay: 4%

Refinement

Refinement on *F*²
R [*F*² > 2σ(*F*²)] = 0.032
wR (*F*²) = 0.081
S = 1.06
 3377 reflections
 185 parameters
 All H-atom parameters refined
 $w = 1/[\sigma^2(F_o^2) + (0.0471P)^2 + 0.0723P]$
 where $P = (F_o^2 + 2F_c^2)/3$

(Δ/σ)_{max} < 0.001
 $\Delta\rho$ _{max} = 0.25 e Å⁻³
 $\Delta\rho$ _{min} = -0.20 e Å⁻³
 Extinction correction: *SHELXL97*
 Extinction coefficient: 0.083 (4)
 Absolute structure: Flack (1983)
 Flack parameter = 0.02 (6)

Table 1

Selected geometric parameters (Å, °).

S—C1	1.7292 (19)	N1—C1	1.297 (3)
S—C2	1.7283 (16)	N1—C7	1.393 (2)
C1—S—C2	88.43 (9)	N1—C7—C2	114.67 (15)
S—C2—C3	128.93 (12)	N1—C7—C6	125.70 (15)
S—C2—C7	109.79 (12)	N2—C8—N3	121.80 (16)
S—C1—N1	117.76 (13)	N2—C8—C4	118.81 (15)
C1—N1—C7	109.34 (14)	N3—C8—C4	119.38 (15)

Table 2

Hydrogen-bonding geometry (Å, °).

<i>D</i> —H... <i>A</i>	<i>D</i> —H	H... <i>A</i>	<i>D</i> ... <i>A</i>	<i>D</i> —H... <i>A</i>
N2—H21...O1	0.85 (2)	2.11 (2)	2.950 (3)	171 (2)
N2—H22...N1 ⁱ	0.84 (3)	2.37 (3)	3.078 (2)	142 (2)
N3—H31...Cl ⁱⁱ	0.81 (3)	2.49 (3)	3.3023 (18)	171 (3)
N3—H32...O2 ⁱ	0.82 (3)	1.96 (3)	2.778 (2)	179 (4)
O1—H101...Cl ⁱⁱⁱ	0.91 (4)	2.27 (3)	3.159 (2)	165 (3)
O1—H102...Cl ^{iv}	0.73 (5)	2.41 (4)	3.136 (2)	170 (3)
O2—H201...Cl	0.77 (4)	2.41 (4)	3.183 (3)	177.4 (17)
O2—H202...O1 ^v	0.79 (3)	2.07 (3)	2.859 (3)	175 (3)

Symmetry codes: (i) *x*, 1 + *y*, *z*; (ii) 1 - *x*, 1 - *y*, *z* - ½; (iii) ½ - *x*, ½ + *y*, *z* - ½; (iv) ½ + *x*, ½ - *y*, *z*; (v) ½ - *x*, *y* - ½, *z* - ½.

H atoms were found in a difference Fourier map and refined isotropically, giving C—H distances in the range 0.91 (3)–0.96 (2) Å, O—H distances in the range 0.73 (5)–0.91 (4) Å and N—H distances in the range 0.81 (3)–0.85 (2) Å.

Data collection: *STADIA* (Stoe & Cie, 1995); cell refinement and data reduction: *X-RED* (Stoe & Cie, 1995); structure solution: *SHELXS97* (Sheldrick, 1990); structure refinement: *SHELXL97* (Sheldrick, 1997); molecular graphics: *PLATON98* (Spek, 2003).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: GG1150). Services for accessing these data are described at the back of the journal.

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