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N-Amidinio-3,5,5-trimethyl-2-pyrazoline-1-carboxamidine chloride (BPC-151), an oral hypoglycaemic agent

Maria Gdaniec,[a] Franciszek Saczewski[b] and Zdzislaw Brzozowski[b]*

[a]Faculty of Chemistry, Adam Mickiewicz University, 60-780 Poznań, Poland, and [b]Department of Chemical Technology of Drugs, Medical University of Gdańsk, 80-416 Gdańsk, Poland

Correspondence e-mail: magdan@amu.edu.pl

Key indicators

Single-crystal X-ray study
T = 130 K
Mean σ(C–C) = 0.002 Å
R factor = 0.030
wR factor = 0.079
Data-to-parameter ratio = 11.8

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

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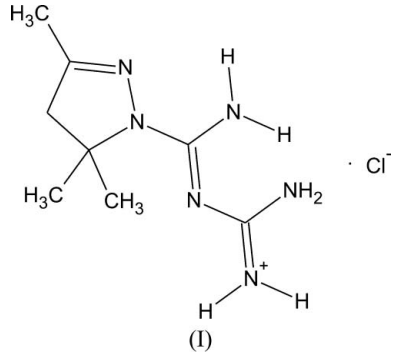
In the title compound, $C_8H_{17}N_6^+\cdot Cl^-$, the biguanidinium unit is non-planar and the bridging N atom is unprotonated. The ions are connected by hydrogen bonds into a two-dimensional network.

Comment

Diabetes mellitus is a chronic disease that is growing in prevalence worldwide. Biguanide agents such as metformin (Campbell *et al.*, 1996) have many characteristics that are ideal for treating type 2 diabetes, including weight loss, insulin sensitization, positive lipid effect, mild hypotensive effect and low incidence of hypoglycaemia. These drugs are therefore considered to be the first-line medications. Recently, pharmacophoric features of biguanide (Bharatam *et al.*, 2005) have attracted attention due to misleading information found in the medicinal chemistry literature regarding its tautomeric structure (Glennon *et al.*, 2003; Rahman *et al.*, 2003). Previously in our laboratories, a series of biguanide derivatives have been synthesized and the title compound, (I), (BPC-151) has been selected as a useful oral hypoglycemic agent (Brzozowski *et al.*, 1979, 1981; Negwer, 1987). Here we report the crystal structure of (I) because the tautomeric structure of this compound also needs clarification.



(I)

The asymmetric unit of (I) consists of a monoprotonated cation and a chloride anion (Fig. 1). The bridging N atom of the biguanidinium fragment, N8, is not protonated, a feature typical of all biguanidinium monocations in the crystalline state (Cambridge Structural Database, Version 5.27, plus January 1st 2006 update; Allen, 2002). The biguanidinium unit is non-planar, but the C—N bond lengths, which are in the range 1.3207 (18)–1.3502 (17) Å (Table 1), suggest some degree of delocalization of π-electron density through this fragment. There is an intramolecular N11—H112···N7 interaction (Table 2), leading to pyramidalization of the N7 amino group (sum of bond angles at N7 = 351°). Intermolecular hydrogen bonds between cation and anion assemble the

component species in (I) into a strongly corrugated two-dimensional network parallel to (100), as shown in Fig. 2.

Experimental

The title compound was prepared according to a known procedure (Brzozowski *et al.*, 1979). Crystals of (I) for X-ray analysis were obtained by recrystallization from an aqueous solution.

Crystal data

$C_8H_{17}N_6^+\cdot Cl^-$
M_r = 232.73
Monoclinic, $P2_1/c$
a = 8.5463 (7) Å
b = 10.5588 (9) Å
c = 13.2894 (11) Å
β = 95.150 (7)°
V = 1194.38 (17) Å^3
Z = 4
D_x = 1.294 Mg m^{-3}
Mo $K\alpha$ radiation
μ = 0.30 mm^{-1}
T = 130 K
Block, colourless
0.20 × 0.10 × 0.10 mm

Data collection

Kuma KM-4-CCD κ-geometry diffractometer
ω scans
Absorption correction: none
6642 measured reflections
2425 independent reflections
2047 reflections with $I > 2\sigma(I)$
R_{int} = 0.015
θ_{max} = 26.4°

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.030
$wR(F^2)$ = 0.079
S = 1.06
2425 reflections
205 parameters
All H-atom parameters refined
$w = 1/[\sigma^2(F_o^2) + (0.0446P)^2 + 0.2097P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.24 e Å^{-3}
$\Delta\rho_{min}$ = −0.21 e Å^{-3}
Extinction correction: *SHELXL97*
Extinction coefficient: 0.018 (2)

Table 1
Selected bond lengths (Å).

N2—C6	1.3502 (17)	N8—C9	1.3332 (17)
C6—N8	1.3207 (18)	C9—N10	1.3238 (19)
C6—N7	1.3448 (18)	C9—N11	1.3353 (18)

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

D—H···A	D—H	H···A	D···A	D—H···A
N10—H102···Cl1	0.866 (19)	2.355 (19)	3.1767 (14)	158.4 (16)
N10—H101···Cl1^{i}	0.812 (19)	2.43 (2)	3.2271 (14)	168.8 (17)
N11—H111···Cl1	0.785 (19)	2.56 (2)	3.2965 (16)	156.3 (17)
N7—H72···Cl1^{ii}	0.90 (2)	2.29 (2)	3.1687 (13)	165.0 (16)
N11—H112···N7	0.832 (19)	2.386 (18)	2.891 (2)	119.8 (15)

Symmetry codes: (i) $-x+2, y-\frac{1}{2}, -z+\frac{1}{2}$; (ii) $-x+2, -y+2, -z+1$.

All H atoms were located in electron-density difference maps and their positional and displacement parameters included in the refinement [C—H = 0.948 (16)–1.009 (16); N—H 0.785 (19)–0.866 (19).]

Data collection: *CrysAlis CCD* (Oxford Diffraction, 2004); cell refinement: *CrysAlis CCD*; data reduction: *CrysAlis RED* (Oxford Diffraction, 2004); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *Stereochemical Workstation Operation Manual* (Siemens, 1989) and *Mercury* (Version 1.4; Bruno *et al.*, 2002); software used to prepare material for publication: *SHELXL97*.

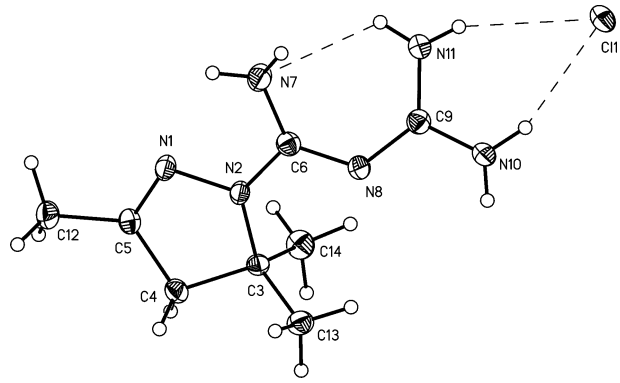


Figure 1
The molecular structure of (I), with 50% probability displacement ellipsoids. Hydrogen bonds are shown as dashed lines.

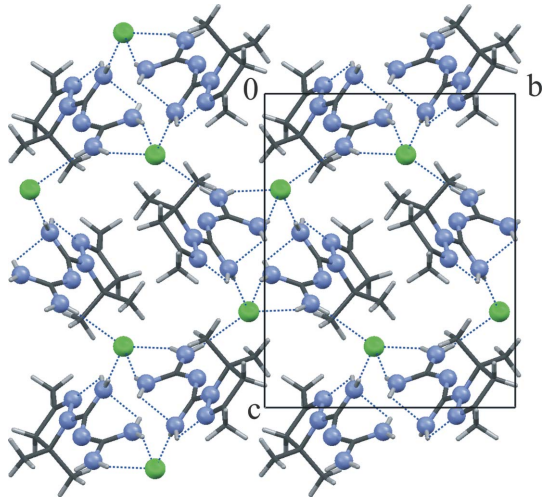


Figure 2
The two-dimensional network of hydrogen-bonded ions in (I). Hydrogen bonds are shown as dashed lines.

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