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1-Methyl-1*H*-imidazo[4,5-*f*]quinolin-6-ium chloride monohydrate

Viktor Kettmann,[a]* Jan Lokaj,[b] Viktor Milata,[b] Jozef Salonˇ[b] and Mohamed Mahmoud Mohamed Hasan[b]

[a]Faculty of Pharmacy, Comenius University, Odbojarov 10, Bratislava 83232, Slovak Republic, and [b]Faculty of Chemical Technology, Slovak Technical University, Radlinskeho 9, Bratislava 81237, Slovak Republic
Correspondence e-mail: kettmann@fpharm.uniba.sk

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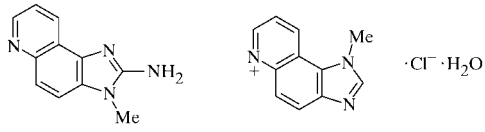
The title compound, $C_{11}H_{10}N_3^+\cdot Cl^-\cdot H_2O$, belongs to the N1-methyl-substituted imidazo[4,5-*f*]quinoline family, in which the heterocyclic ring is protonated at the pyridine rather than at the imidazole N atom. The molecule as a whole is almost exactly planar. The molecular structure has been compared with that of the 2-amino analogue described in the literature, and it was found that the extra amino group of the latter is involved in conjugation with the adjacent double bond, *i.e.* the conjugation does not extend over the entire heterocyclic system. The cation of the title compound forms a strong hydrogen bond with the Cl^- anion and the anions are interconnected by the water solvent molecule.

Comment

Imidazoquinolines, produced in cooked meats, have long been known as strong mutagens and carcinogens (Nagao *et al.*, 1977; Weissberger & Taylor, 1981). On the other hand, in the last few years, some derivatives incorporating the imidazoquinoline nucleus have been reported to possess antimutagenic/antitumour activity (Lankaputhra & Shah, 1998; Bishop *et al.*, 2001). It is obvious that the mutagenicity/antimutagenicity depends sensitively on the substitution pattern of the imidazoquinoline nucleus; for example, 2-amino-3-methyl-3*H*-imidazo[4,5-*f*]quinolines, (I), are typical mutagens, while removal of the 2-amino group and substitution on the pyridine-fused ring promotes antimutagenic activity. It is, however, unclear whether the influence of the substituents reflects their effect on the charge distribution of the heterocyclic ring (and hence determines the orientation of the molecule in the DNA intercalation site) or results from interaction of the substituents with minor groove functionalities of DNA. Thus, detailed information on the three-dimensional and electronic structures of these heterocycles is useful for an analysis of structure–function relationships.

Though highly important, there have been only a few reports on these subjects. Of the electronic characteristics, only protonation, tautomerization and valence tautomerism of selected imidazo[4,5-*f*]quinolines have been studied using theoretical methods in the past few years (Ögretir & Kaniskan, 1993; Milata, 2001).

Similarly, as revealed by a search of the Cambridge Structural Database (CSD, Version of 2001; Allen & Kennard, 1993), only one crystal structure of the imidazo[4,5-*f*]quinoline family, namely 2-amino-3-methylimidazo[4,5-*f*]quinoline, (I) (Yokoyama *et al.*, 1980), has so far been reported. Consequently, the present crystal structure determination was undertaken in order to establish the precise molecular dimensions (bond lengths) of another derivative, the title compound, (II), which is a deamino isomerically methylated analogue of (I), as the chloride monohydrate.



(I) (II)

The asymmetric part of the unit cell of (II) consists of a protonated molecule of 1-methyl-1*H*-imidazo[4,5-*f*]quinoline, one Cl^- anion and one water molecule. A perspective view of the cation, along with the atom-numbering scheme, is shown in Fig. 1. The molecule as a whole (*i.e.* including the exocyclic methyl group) is planar within the limits of experimental error [r.m.s. deviation = 0.025 (4) Å].

As can be seen in Fig. 1, the first protonation has taken place at the pyridine N6 atom rather than at the imidazole N atom; this is in line with the theoretical calculations, which predicted the energy difference between the two protonated forms to be 8.7 kcal mol^{-1} (1 kcal mol^{-1} = 4.184 kJ mol^{-1}; Ögretir & Kaniskan, 1993).

As mentioned above, the main purpose of this work was to compare the molecular dimensions of the present derivative, (II), with its 2-amino analogue, (I), in order to shed more light on the relationship between the structure and (anti)mutagenic properties of compounds incorporating the imidazoquinoline heterocycle. This comparison has shown that the corresponding bond lengths in the two molecules are equal within experimental error, except for the C2—N3 bond distance, which is 0.035 (5) Å shorter in (II) than in (I), obviously due to

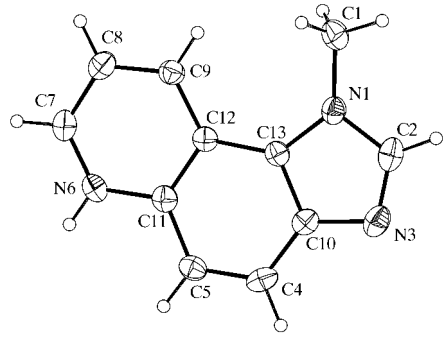


Figure 1
A view of the cation of (II) showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 35% probability level and H atoms are shown as small circles of arbitrary radii.

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conjugation of the lone pair electrons on the amine N atom with the adjacent double bond in (I). Thus, as judged from the distribution of bond lengths in molecules (I) and (II), the conjugation in (I) does not extend beyond the C=N double bond of the heterocyclic system. This means that the large difference in pharmacological properties between (I) and (II) lies in the interaction of the additional amino group with DNA functionalities, and not in the effect of the amino group on the π-electron distribution of the heterocyclic π system. These results will form the basis for subsequent quantum chemical calculations of the electronic structure and molecular modelling (docking) studies of DNA–ligand interactions.

The positive charge of the protonated molecule in (II) is neutralized by the Cl^- anion, which is involved in a hydrogen bond with N6$^+$—H [for N6—H$\cdots$Cl, N6—H 0.86 Å, H$\cdots$Cl 2.20 Å, N$\cdots$Cl 3.060 (4) Å and N—H$\cdots$Cl 177°]. The molecule of water of crystallization forms two rather weak hydrogen bonds to symmetrically related Cl^- ions. Apart from these hydrogen-bond interactions, there are no other contacts substantially shorter than van der Waals radii sums.

Experimental

A stirred solution of 9-chloro-1-methyl-1*H*-imidazo[4,5-*f*]quinoline (0.35 g, 1.5 mmol), prepared previously (Milata, 2001), and solid NaOH (0.15 g) was hydrogenated at 120 kPa on Raney nickel until the theoretical amount of hydrogen (60 ml) was consumed. The catalyst was filtered off, and the filtrate was neutralized with 10% HCl and purified by column chromatography (silica gel, chloroform–methanol 10:1). Crystallization from ethanol–water (2:1) afforded the title compound, (II) (yield 40%, m.p. 601–603 K).

Crystal data

$C_{11}H_{10}N_3^+\cdot Cl^-\cdot H_2O$
M_r = 237.69
Triclinic, $P\overline{1}$
a = 7.544 (5) Å
b = 9.084 (6) Å
c = 9.152 (8) Å
α = 72.65 (6)°
β = 66.61 (5)°
γ = 76.96 (7)°
V = 545.3 (7) Å^3
Z = 2
D_x = 1.448 Mg m^{-3}
D_m = 1.45 (1) Mg m^{-3}
D_m measured by flotation in bromoform–*c*-hexane
Mo $K\alpha$ radiation
Cell parameters from 15 reflections
θ = 8–22°
μ = 0.33 mm^{-1}
T = 293 (2) K
Prism, colourless
0.35 × 0.30 × 0.20 mm

Data collection

Syntex $P2_1$ diffractometer
$\theta/2\theta$ scans
2511 measured reflections
2511 independent reflections
1197 reflections with $I > 2\sigma(I)$
θ_{max} = 27.6°
$h = 0 \rightarrow 9$
$k = -11 \rightarrow 11$
$l = -10 \rightarrow 11$
2 standard reflections
every 98 reflections
intensity decay: 2%

Refinement

Refinement on F^2
$R(F)$ = 0.070
$wR(F^2)$ = 0.201
S = 0.92
2511 reflections
146 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.1128P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.002
$\Delta\rho_{max}$ = 0.34 e Å^{-3}
$\Delta\rho_{min}$ = −0.44 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

N1—C2	1.355 (5)	N6—C7	1.307 (5)
N1—C13	1.378 (5)	N6—C11	1.367 (5)
N1—C1	1.441 (5)	C7—C8	1.377 (6)
C2—N3	1.302 (6)	C8—C9	1.358 (6)
N3—C10	1.367 (5)	C9—C12	1.400 (5)
C4—C5	1.351 (6)	C10—C13	1.387 (5)
C4—C10	1.399 (6)	C11—C12	1.404 (5)
C5—C11	1.405 (5)	C12—C13	1.411 (5)
C2—N1—C13	105.6 (4)	N3—C10—C4	128.8 (4)
C2—N1—C1	125.1 (4)	C13—C10—C4	120.3 (4)
C13—N1—C1	129.3 (3)	N6—C11—C12	117.5 (4)
N3—C2—N1	114.4 (4)	N6—C11—C5	119.5 (4)
C2—N3—C10	104.0 (3)	C12—C11—C5	123.0 (4)
C5—C4—C10	119.3 (4)	C9—C12—C11	118.6 (4)
C4—C5—C11	120.3 (4)	C9—C12—C13	126.8 (4)
C7—N6—C11	123.2 (4)	C11—C12—C13	114.6 (3)
N6—C7—C8	121.1 (4)	N1—C13—C10	105.0 (3)
C9—C8—C7	118.7 (4)	N1—C13—C12	132.5 (4)
C8—C9—C12	120.8 (4)	C10—C13—C12	122.5 (4)
N3—C10—C13	110.9 (4)		

Although all the H atoms were seen in a difference Fourier map, they were refined with fixed geometry (C—H = 0.93–0.96 Å and N—H = 0.86 Å), riding on their carrier atoms, with U_{iso}(H) set to 1.2 (1.5 for the methyl H atoms) times U_{eq} of the parent atom, except for the water H atoms, the coordinates of which were kept fixed at their experimentally found values, with U_{iso}(H) equal to 1.2U_{eq} of the O*W* atom.

Data collection: *Syntex Software* (Syntex, 1973); cell refinement: *Syntex Software*; data reduction: *XP*21 (Pavelčík, 1987); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1990); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*II (Johnson, 1976); software used to prepare material for publication: *SHELXL*97.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1549). Services for accessing these data are described at the back of the journal.

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