1-Methyl-5-nitroimidazolium chloride

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The title salt, C4H6N3O2+·Cl−, exhibits multiple hydrogen-bonding interactions involving the nitroimidazolium cation and the chloride anion. Strong hydrogen bonds between the amine hydrogen atom and the chloride anion link the ionic moieties. Of note, with respect to H···Cl interactions, the central aromatic hydrogen atom displays a shorter interaction than the other aromatic hydrogen atom. Finally, interactions are observed between the nitro moiety and methyl H atoms. While no π–π stacking is observed, anion–π interactions are present. The crystal was refined as a two-component twin.

Structure description

The study of nitroimidazole-based compounds remains of interest due to their appearance on the World Health Organization’s list of essential drugs (Purgato & Barbui, 2012). Among the numerous functionalized derivatives of imidazoles, 5-nitroimidazoles have long been known to be effective antibiotics (Leiros et al., 2004). Recently, however, 5-nitroimidazole-based compounds have received renewed attention for the potential treatment of a slew of infectious diseases such as leishmaniasis and tuberculosis (Ang et al., 2017). A previous report by Bowden & Izadi (1998) analyzed the antibacterial activities of various derivatives of metronidazole, a compound bearing a 5-nitroimidazole core. In their work, several derivatives of metronidazole were chemically modified and studied with the intent of overcoming some of the disadvantages of 5-nitroimidazole-based pharmaceuticals (Bowden & Izadi, 1998). Furthermore, Miyamoto and coworkers reported the synthesis of a new class of nitroimidazole derivatives to combat drug-resistant strains of infections (Miyamoto et al., 2013). Hence, with the renewed interest in
these compounds, fundamental structural analysis of nitromidazoles is of importance to the advancement of drug development.

Herein we report the crystal structure of 1-methyl-5-nitromidazolium chloride (Fig. 1). While the overall crystalline forces are dominated by the Coulombic interactions between ion pairs, non-covalent interactions will still play a role in the formation of the crystal (Gavezzotti, 2010). The amine hydrogen atom, H3, exhibits the shortest hydrogen bond with the chloride anion with a distance of 2.160 (19) Å (Table 1). The 2-position of imidazolium cations is known to be relatively acidic (Noack et al., 2010). As such, the central aromatic hydrogen (H2) tends to form shorter interactions with anions when compared with the other aromatic H atoms on the heterocyclic cores (Dupont, 2004). This trend is observed within this structure as well with H2 displaying a shorter interaction with the anion (2.62 Å) than the other aromatic H atoms on the chloride anion (2.78 Å) (Table 1). hydrogen H4 (2.78 Å). As has been observed in related systems, the halide anions surround the cation in distinctive locations facilitating interactions with nearly all atoms of the heterocyclic core (Hunt et al., 2006; Sanchora et al., 2019; Matthews et al., 2015). For example, the chloride anion interacts with the methyl H atoms (H6A, H6B, and H6C) at distances of 3.14, 2.85, and 2.84 Å, respectively.

Nitro moieties are capable of exhibiting a diverse set of non-covalent interactions (Bauzá et al., 2019; Sikorski & Trzybiński, 2013). Within the title structure, both nitro O atoms (O1 and O2) participate in interactions with methyl H atoms H6A and H6B at distances of 2.56 and 2.90 Å, respectively. No short interactions with the aromatic H atoms are observed with the nitro group. The nitro moiety is nearly coplanar to the imidazole ring, with an N4—C5—C4—N3 torsion angle of 6.71 (10)°. As demonstrated by Bauzá et al., π-holes are present in nitroaromatics, forming an important set of potential interactions (Bauzá et al., 2015). For the title compound, the chloride anion is interacting with both faces of the π-hole of the nitro moiety at distances of 3.33 (10) and 3.37 (10) Å. The packing is shown in Fig. 2.

Synthesis and crystallization

The title compound is a hydrolysis product from the synthetic procedure described below, analogous to our previously reported synthesis of 2,3-dimethyl-1H-imidazol-3-ium chloride (Anderson et al., 2020).

In brief, 5-nitromidazole and trityl chloride were dissolved in separate 50 ml beakers with toluene. The reactants were then combined in a single-necked 100 ml round-bottom flask equipped with a magnetic stir bar and left to stir for 2 days at room temperature. The solvent was removed under vacuum leaving a white solid residue. This solid was washed twice with tetrahydrofuran and recovered via vacuum filtration. Crystals were grown at room temperature by vapor diffusion with acetonitrile as the solvent and tetrahydrofuran as the antisolvent. Colorless crystals of the hydrolyzed byproduct reported herein were observed within one week.

Refinement

For full experimental details including crystal data, data collection and structure refinement details, refer to Table 2. The structure emulates a double the volume orthorhombic C-centered cell and is twinned by this symmetry (180° rotation around the real space a axis or around the reciprocal direction [010]). Refinement with the transformation matrix 1 0 0, 0 −1 0, −1 0 −1 yielded a 0.555 (1) to 0.445 (1) twinning ratio.

Table 1

| Hydrogen-bond geometry (Å, °). | D—H · · · A | D—H | H · · · A | D—H · · · A |
|-----------------------------|-----------|------|---------|-----------|
| N3—H3···Cl1                 | 0.856 (19) | 2.160 (19) | 3.0141 (11) | 175.4 (15) |
| C4—H4···Cl1                 | 0.95      | 2.78  | 3.6161 (12) | 147       |
| C2—H2···Cl1                 | 0.95      | 2.62  | 3.4723 (12) | 150       |
| C6—H6B···Cl1a               | 0.98      | 2.85  | 3.7519 (13) | 154       |
| C6—H6C···Cl1a               | 0.98      | 2.84  | 3.6617 (13) | 142       |

Symmetry codes: (i) −x+1, −y+1, −z; (ii) x, −y+3, z+½; (iii) −x+1, y−½, z−½.
Table 2
Experimental details.

| Crystal data          | C₆H₆N₃O₂⁺·Cl⁻ |
|-----------------------|----------------|
| Chemical formula      |                |
| Mᵣ                   | 163.57         |
| Crystal system, space group | Monoclinic, P2₁/c |
| Temperature (K)       | 150            |
| a, b, c (Å)           | 6.3498 (5), 9.8991 (9), 11.5969 (10) |
| β (°)                 | 105.817 (3)    |
| V (Å³)                | 701.35 (10)    |
| Z                     | 4              |
| Radiation type        | Mo Kα          |
| μ (mm⁻¹)              | 0.49           |
| Crystal size (mm)     | 0.35 × 0.15 × 0.12 |

Data collection

| Diffractometer        | Bruker AXS D8 Quest diffractometer with PhotonII charge-integrating pixel array detector (CPAD) |
|-----------------------|--------------------------------------------------------------------------------------------------|
| Absorption correction | Multi-scan (SADABS; Krause et al., 2015)                                                          |
| Tmin, Tmax            | 0.659, 0.747                                                                                     |
| No. of measured, independent and observed | [I > 2σ(I)] reflections |
| R_{int}               | 0.037                                                                                           |
| (sin θ/λ)max (Å⁻¹)    | 0.771                                                                                           |
| Refinement            |                                                                                                 |
| R[F² > 2σ(F²)], wR(F²), S | 0.026, 0.072, 1.08                                       |
| No. of reflections    | 2681                                                                                           |
| No. of parameters     | 97                                                                                             |
| H-atom treatment      | H-atoms treated by a mixture of independent and constrained refinement                           |
| Δρ_{max}, Δρ_{min} (e Å⁻³) | 0.35, −0.24                                    |

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full crystallographic data

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Crystal data

\[\text{C}_4\text{H}_6\text{N}_3\text{O}_2^+ \cdot \text{Cl}^-\]  \(M_r = 163.57\)

Monoclinic, \(P2_1/c\)

\(a = 6.3498\) (5) Å

\(b = 9.8991\) (9) Å

\(c = 11.5969\) (10) Å

\(\beta = 105.817\) (3)°

\(V = 701.35\) (10) Å³

\(Z = 4\)

\(F(000) = 336\)

\(D_x = 1.549\) Mg m⁻³

Mo \(K\alpha\) radiation, \(\lambda = 0.71073\) Å

Cell parameters from 9893 reflections

\(\theta = 2.8–33.2°\)

\(\mu = 0.49\) mm⁻¹

\(T = 150\) K

Rod, colourless

0.35 × 0.15 × 0.12 mm

Data collection

Bruker AXS D8 Quest
diffractometer with PhotonII charge-integrating
pixel array detector (CPAD)

Detector resolution: 7.4074 pixels mm⁻¹

\(\omega\) and \(\phi\) scans

Absorption correction: multi-scan

(SADABS; Krause et al., 2015)

\(T_{\text{min}} = 0.659, T_{\text{max}} = 0.747\)

12789 measured reflections

2681 independent reflections

2556 reflections with \(I > 2\sigma(I)\)

\(R_{\text{int}} = 0.037\)

\(\theta_{\text{max}} = 33.3°, \theta_{\text{min}} = 2.8°\)

\(h = -8→9\)

\(k = -15→14\)

\(l = -16→17\)

Refinement

Refinement on \(F^2\)

Least-squares matrix: full

\(R[F^2 > 2\sigma(F^2)] = 0.026\)

\(wR(F^2) = 0.072\)

\(S = 1.08\)

2681 reflections

97 parameters

0 restraints

Primary atom site location: structure-invariant
direct methods

Secondary atom site location: difference Fourier map

Hydrogen site location: mixed

H atoms treated by a mixture of independent and constrained refinement

\(w = 1/[\sigma^2(F^2) + (0.039P)^2 + 0.1001P]\)

where \(P = (F^2 + 2F^2)/3\)

\((\Delta/\sigma)_{\text{max}} = 0.001\)

\(\Delta\rho_{\text{max}} = 0.35\) e Å⁻³

\(\Delta\rho_{\text{min}} = -0.24\) e Å⁻³

Special details

Geometry. All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

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IUCrData (2022). 7, x220878
**Refinement.** Refined as a two-component twin. H atoms attached to carbon atoms were positioned geometrically and constrained to ride on their parent atoms. C—H bond distances were constrained to 0.95 Å for aromatic C—H moieties with $U_{	ext{iso}}(H) = 1.2 \times U_{	ext{eq}}(C)$, and to 0.98 Å for CH₃ moieties with $U_{	ext{iso}}(H) = 1.5 \times U_{	ext{eq}}(C)$. The N—H proton on N3 was located as residual electron density and allowed to refine freely.

**Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters ($\overline{\text{Å}}^2$)**

|         | x         | y         | z         | $U_{\text{iso}}*/U_{\text{eq}}$ |
|---------|-----------|-----------|-----------|-------------------------------|
| Cl1     | 0.75167 (5) | 0.72586 (3) | 0.07499 (2) | 0.02027 (7) |
| O1      | −0.1250 (2)  | 0.37864 (11) | 0.13424 (9)  | 0.0313 (2)   |
| O2      | −0.14844 (16) | 0.45993 (11) | 0.30478 (8)  | 0.02609 (19) |
| N3      | 0.42357 (17) | 0.61303 (11) | 0.19454 (9)  | 0.02019 (19) |
| H3      | 0.512 (3)    | 0.6439 (18)  | 0.1567 (14)  | 0.019 (4)*   |
| N1      | 0.25774 (17) | 0.58619 (10) | 0.33532 (8)  | 0.01734 (17) |
| N4      | −0.05494 (18) | 0.44564 (10) | 0.22517 (8)  | 0.01998 (18) |
| C5      | 0.14730 (19) | 0.51334 (11) | 0.23575 (9)  | 0.01723 (18) |
| C4      | 0.2514 (2)   | 0.53027 (13) | 0.14779 (10) | 0.0202 (2)   |
| H4      | 0.211185     | 0.491815    | 0.069785    | 0.024*       |
| C2      | 0.4252 (2)   | 0.64545 (12) | 0.30717 (10) | 0.0202 (2)   |
| H2      | 0.530167     | 0.702184    | 0.358999    | 0.024*       |
| C6      | 0.2176 (2)   | 0.59302 (13) | 0.45524 (10) | 0.0224 (2)   |
| H6A     | 0.081178     | 0.642222    | 0.449455    | 0.034*       |
| H6B     | 0.339456     | 0.640052    | 0.510943    | 0.034*       |
| H6C     | 0.205596     | 0.501290    | 0.484604    | 0.034*       |

**Atomic displacement parameters ($\overline{\text{Å}}^2$)**

|         | $U_{11}$ | $U_{22}$ | $U_{33}$ | $U_{12}$ | $U_{13}$ | $U_{23}$ |
|---------|---------|---------|---------|---------|---------|---------|
| Cl1     | 0.02085 (12) | 0.01942 (11) | 0.02158 (11) | −0.00029 (9) | 0.00752 (10) | 0.00269 (9) |
| O1      | 0.0386 (6)  | 0.0293 (5)  | 0.0243 (4)  | −0.0130 (4)  | 0.0060 (4)  | −0.0054 (3)  |
| O2      | 0.0224 (4)  | 0.0351 (5)  | 0.0225 (4)  | −0.0009 (4)  | 0.0090 (3)  | 0.0033 (3)   |
| N3      | 0.0207 (4)  | 0.0232 (5)  | 0.0186 (4)  | 0.0012 (4)   | 0.0086 (4)  | 0.0026 (3)   |
| N1      | 0.0206 (4)  | 0.0166 (4)  | 0.0161 (4)  | −0.0004 (3)  | 0.0071 (3)  | −0.0011 (3)  |
| N4      | 0.0217 (4)  | 0.0195 (4)  | 0.0182 (4)  | −0.0011 (4)  | 0.0045 (3)  | 0.0033 (3)   |
| C5      | 0.0194 (5)  | 0.0169 (4)  | 0.0152 (4)  | 0.0010 (4)   | 0.0044 (4)  | 0.0010 (3)   |
| C4      | 0.0223 (5)  | 0.0229 (5)  | 0.0160 (4)  | 0.0016 (4)   | 0.0060 (4)  | 0.0014 (4)   |
| C2      | 0.0214 (5)  | 0.0200 (5)  | 0.0199 (5)  | −0.0011 (4)  | 0.0068 (4)  | −0.0001 (4)  |
| C6      | 0.0306 (6)  | 0.0232 (5)  | 0.0162 (4)  | −0.0047 (4)  | 0.0110 (4)  | −0.0038 (4)  |

**Geometric parameters (Å, °)**

|          | O1—N4   | 1.2223 (14) | N4—C5   | 1.4239 (16) |
|----------|---------|-------------|---------|-------------|
| O2—N4    | 1.2343 (13) | C5—C4      | 1.3687 (16)  |
| N3—H3    | 0.856 (19)  | C4—H4      | 0.9500   |
| N3—C4    | 1.3553 (16) | C2—H2      | 0.9500   |
| N3—C2    | 1.3423 (15) | C6—H6A     | 0.9800   |
| N1—C5    | 1.3797 (14) | C6—H6B     | 0.9800   |
| N1—C2    | 1.3307 (16) | C6—H6C     | 0.9800   |
N1—C6 1.4822 (14)

C4—N3—H3 125.4 (11) N3—C4—C5 106.06 (10)
C2—N3—H3 125.5 (11) N3—C2—H2 125.1
C2—N1—C6 129.12 (10) N1—C2—N3 109.79 (11)
C2—N1—C6 124.29 (10) N1—C2—H2 125.1
O1—N4—O2 124.85 (12) N1—C6—H6A 109.5
O1—N4—N3 115.92 (10) N1—C6—H6B 109.5
O2—N4—N3 119.21 (10) N1—C6—H6C 109.5
N1—C5—N4 123.97 (10) H6A—C6—H6B 109.5
C4—C5—N1 108.73 (10) H6A—C6—H6C 109.5
C4—C5—N4 126.94 (10) H6B—C6—H6C 109.5

O1—N4—N3—C2 −175.66 (11) C4—N3—C2—N1 −0.17 (14)
O1—N4—N3—C4 11.97 (18) C2—N3—C4—C5 0.12 (14)
O2—N4—N3—C2 5.77 (16) C2—N1—C5—N4 −173.64 (11)
O2—N4—N3—C4 −166.59 (12) C2—N1—C5—C4 −0.08 (13)
N1—C5—C4—N3 −0.02 (13) C6—N1—C5—N4 10.81 (18)
N4—C5—C4—N3 173.29 (11) C6—N1—C5—C4 −175.63 (11)
C5—N1—C2—C3 0.15 (13) C6—N1—C2—N3 175.98 (10)

Hydrogen-bond geometry (Å, °)

| D—H···A | D—H | H···A | D···A | D—H···A |
|---------|-----|------|-------|---------|
| N3—H3···Cl1 | 0.856 (19) | 2.160 (19) | 3.0141 (11) | 175.4 (15) |
| C4—H4···Cl1i | 0.95 | 2.78 | 3.6161 (12) | 147 |
| C2—H2···Cl1ii | 0.95 | 2.62 | 3.4723 (12) | 150 |
| C6—H6B···Cl1iii | 0.98 | 2.85 | 3.7519 (13) | 154 |
| C6—H6C···Cl1iiii | 0.98 | 2.84 | 3.6617 (13) | 142 |

Symmetry codes: (i) −x+1, −y+1, −z; (ii) x, −y+3/2, z+1/2; (iii) −x+1, y−1/2, −z+1/2.