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# Nafimidone hemihydrate hemihydrochloride

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**Key indicators**

Single-crystal X-ray study
*T* = 294 K
Mean σ(C–C) = 0.005 Å
Disorder in main residue
*R* factor = 0.052
*wR* factor = 0.162
Data-to-parameter ratio = 9.6

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



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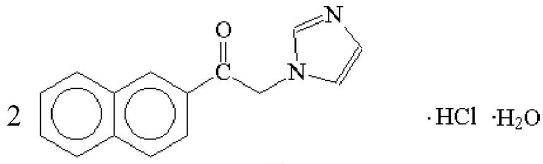
In the crystal structure of the title compound, 2-(1*H*-imidazol-1-yl)-1-(2-naphthyl)ethanone hemihydrate hemihydrochloride, $2C_{15}H_{13}N_2O_2\cdot H_2O\cdot HCl$ or $C_{30}H_{25}N_4O_4^+\cdot Cl^-\cdot H_2O$, there are two independent molecules of nafimidone in the asymmetric unit. The imidazole and the naphthalene rings in both molecules are planar. The water molecule is hydrogen bonded to $Cl^-$ ions. The protonation occurs at the unsubstituted N atom in both molecules, with 50% occupancy, linking the molecules together by hydrogen bonding. A network of weak non-standard hydrogen bonds exists in the crystal structure.

## Comment

Crystals of nafimidone hemihydrate hemihydrochloride, (I), different from the preceding paper (nafimidone monohydrate; Hempel *et al.*, 2005), were obtained during crystallization trials and the structure was determined to investigate conformational properties in the different crystal form and the environment of the molecule.




(I)

The molecular structure of (I) is shown in Fig. 1. Bond distances and angles are consistent with normal values. As in nafimidone monohydrate, both nafimidone molecules (*A* and *B*) in the asymmetric unit of this crystal form adopt extended conformations. The naphthalene and imidazole rings are planar and the angle between the planes is 62.54 (10) and 80.94 (10)° in molecules *A* and *B*, respectively [77.05 (11)° in nafimidone monohydrate]. The three atoms of the alkylene bridge show less coplanarity with the naphthalene moiety than in the nafimidone monohydrate structure, with the largest deviation for atom C17 of 0.352 (5) and 0.375 (5) Å for molecules *A* and *B*, respectively. The sums of the angles around N11 are both 360°, indicating $sp^2$ hybridization.

In this crystal form, molecules *A* and *B* are hydrogen bonded to each other by the protonated and non-protonated N13 atoms. Protonation occurs in 50% of the *A* molecules and 50% of the *B* molecules; refinement of atom H13 occupancies gave 46 and 50% for *A* and *B*, respectively; thus, they were fixed at 50:50. In the case of nafimidone monohydrate, dimers were held together by water molecules; in this structure, the water molecules are hydrogen bonded to the $Cl^-$ anions, forming rings around crystallographic inversion centres. Weak non-standard hydrogen bonds of types C—H···O and C—

H···Cl$^-$ (Steiner, 1997) and van der Waals interactions also contribute to the crystal packing (Table 1 and Fig. 2). The shortest intermolecular distances between naphthalene ring atoms are in the range 3.47 (3)–3.58 (3) Å, but the rings are not parallel and so do not produce significant $\pi$–$\pi$ stacking.

## Experimental

Crystals suitable for data collection were obtained from 95% ethanol by slow evaporation of a nafimidone hydrochloride solution over a two-week period. The crystals were colorless needles.

*Crystal data*

$C_{30}H_{25}N_4O_2^+\cdot Cl^-\cdot H_2O$
$M_r$ = 527.01
Triclinic, $P\overline{1}$
$a$ = 9.171 (3) Å
$b$ = 9.428 (2) Å
$c$ = 16.783 (2) Å
$\alpha$ = 77.19 (1)°
$\beta$ = 75.44 (1)°
$\gamma$ = 75.11 (1)°
$V$ = 1338.1 (6) Å$^3$
$Z$ = 2
$D_x$ = 1.308 Mg m$^{-3}$
Cu $K\alpha$ radiation
Cell parameters from 32 reflections
$\theta$ = 31–52°
$\mu$ = 1.58 mm$^{-1}$
$T$ = 294 (2) K
Needle, colorless
0.51 × 0.13 × 0.08 mm

*Data collection*

Picker FACS-1 four-circle diffractometer
$\omega/2\theta$ scans
Absorption correction: $\psi$ scan (North *et al.*, 1968)
$T_{min}$ = 0.785, $T_{max}$ = 0.885
3600 measured reflections
3348 independent reflections
2773 reflections with $I > 2\sigma(I)$
$R_{int}$ = 0.021
$\theta_{max}$ = 55.0°
$h = -9 \rightarrow 9$
$k = -10 \rightarrow 0$
$l = -17 \rightarrow 17$
3 standard reflections
every 100 reflections
intensity decay: 0.6%

*Refinement*

Refinement on $F^2$
$R[F^2 > 2\sigma(F^2)]$ = 0.053
$wR(F^2)$ = 0.162
$S$ = 1.18
3348 reflections
349 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0929P)^2 + 0.2986P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.63 e Å$^{-3}$
$\Delta\rho_{min}$ = −0.21 e Å$^{-3}$
Extinction correction: *SHELXL97*
Extinction coefficient: 0.0064 (10)

**Table 1**
Hydrogen-bonding geometry (Å, °).

| $D$—H···$A$ | $D$—H | H···$A$ | $D$···$A$ | $D$—H···$A$ |
|---|---|---|---|---|
| O—H1$W$···Cl | 1.165 (18) | 1.992 (15) | 3.154 (3) | 175 (3) |
| O—H2$W$···Cl$^{i}$ | 1.06 (5) | 2.41 (6) | 3.399 (3) | 154.9 (16) |
| N13$A$—*H13$A$···N13$B$ | 0.86 | 1.83 | 2.686 (4) | 177 |
| N13$B$—*H13$B$···N13$A$ | 0.86 | 1.83 | 2.686 (4) | 171 |
| C5$A$—H5$A$···O18$B^{ii}$ | 0.93 | 2.59 | 3.439 (4) | 153 |
| C12$B$—H12$B$···Cl$^{iii}$ | 0.93 | 2.72 | 3.618 (3) | 164 |
| C14$B$—H14$B$···O | 0.93 | 2.57 | 3.376 (4) | 146 |
| C15$A$—H15$A$···O18$B^{iv}$ | 0.93 | 2.56 | 3.333 (4) | 141 |
| C17$A$—H17$B$···Cl | 0.97 | 2.80 | 3.594 (3) | 140 |
| C17$B$—H17$D$···O18$A^{v}$ | 0.97 | 2.43 | 3.349 (4) | 159 |
| C17$B$—H17$C$···Cl$^{v}$ | 0.97 | 2.76 | 3.666 (3) | 155 |

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

All the H atoms, except for those of the solvent water molecule, were placed in calculated positions (C—H = 0.93–0.97 Å) and refined in a riding-model approximation with separate group isotropic displacement parameters for aromatic and methylene H atoms. The

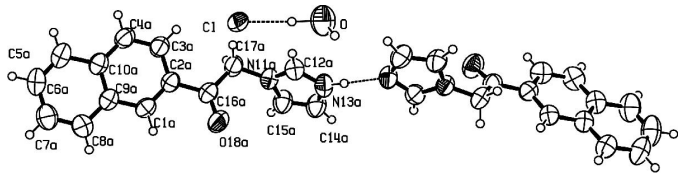



**Figure 1**
The molecular structure of nafimidone hemihydrate hemihydrochloride, showing 50% probability displacement ellipsoids. H atoms are drawn as small circles of arbitrary radii. For clarity, only one N13 atom in the pair of hydrogen-bonded molecules is shown to have an H atom. The atom numbering of the second molecule follows the same scheme as that of the first, which is shown.

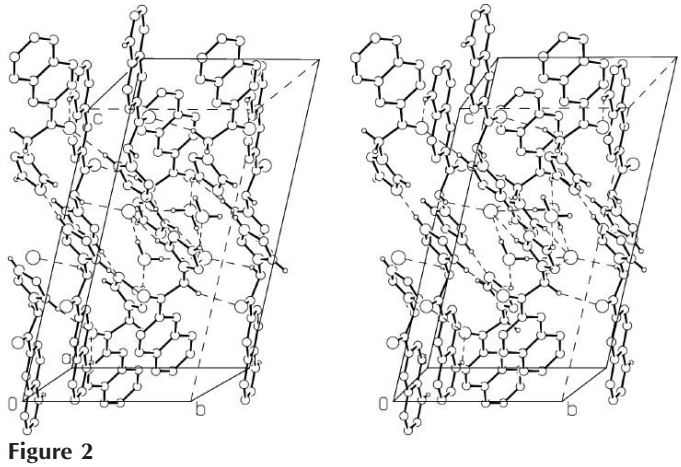



**Figure 2**
Stereoscopic diagram of the molecular packing and hydrogen-bonding scheme. Atoms are drawn as circles of arbitrary radii and hydrogen bonds are indicated by dashed lines between atoms.

difference map showed an H-atom position roughly between two N13 atoms in different molecules; however, its positional parameters would not refine satisfactorily. Therefore, half-occupancy H atoms were placed in calculated positions for each N atom and refined using the riding-model approximation. The H atoms of the water molecule were found in a difference map and refined. The geometrical parameters for the water molecule are: O—H1$W$ = 1.17 (2) Å, O—H2$W$ = 1.06 (5) Å and H1$W$—O—H2$W$ 120 (2)°.

Data collection: *Picker Operating Manual* (Picker, 1967); cell refinement: *Picker Operating Manual*; data reduction: *DATRDN* (Stewart, 1976); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997); software used to prepare material for publication: *SHELXL97*.

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