organic compounds

4-Aminopyridinium hydrogen succinate

Hoong-Kun Fun,^{a}* Jain John,^{b} Samuel Robinson Jebas^{a}‡ and T Balasubramanian^{b}

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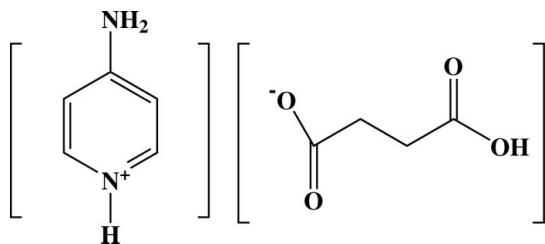Correspondence e-mail: hkfun@usm.my

In the title salt, $C_5H_7N_2{}^+ \cdot C_4H_5O_4{}^-$, the asymmetric unit comprises an aminopyridinium cation and a hydrogen succinate anion as protonation of the aromatic N atom of the 4-aminopyridine molecule has occurred. The crystal packing is stabilized by intermolecular O—H$\cdots$O and N—H$\cdots$O hydrogen bonds that lead to a two-dimensional array. Short C—H$\cdots$O contacts are also present.

Related literature

For the biological activity of 4-aminopyridine, see: Judge & Bever (2006); Schwid et al. (1997); Strupp et al. (2004). For the applications of succinic acid, see: Sauer et al. (2008); Song & Lee (2006); Zeikus et al. (1999). For related structures, see: Chao & Schempp (1977); Anderson et al. (2005); Bhattacharya et al. (1994); Karle et al. (2003); Gopalan et al. (2000); Leviel et al., (1981). For stability of the temperature controller, see: Cosier & Glazer (1986).

Experimental

Crystal data

$C_5H_7N_2{}^+ \cdot C_4H_5O_4{}^-$	$b = 22.2867$ (11) Å
$M_r = 212.21$	$c = 7.1112$ (4) Å
Monoclinic, $P2_1/c$	$\beta = 114.587$ (4)°
$a = 6.5443$ (3) Å	$V = 943.13$ (8) Å^3

$Z = 4$	$T = 100$ K
Mo $K\alpha$ radiation	$0.38 \times 0.14 \times 0.08$ mm
$\mu = 0.12$ mm^{-1}	

Data collection

Bruker SMART APEXII CCD area-detector diffractometer	7174 measured reflections
	2176 independent reflections
Absorption correction: multi-scan (*SADABS*; Bruker, 2005)	1483 reflections with $I > 2\sigma(I)$
$T_{min} = 0.956$, $T_{max} = 0.991$	$R_{int} = 0.066$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.062$	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.150$	
$S = 1.06$	
2176 reflections	$\Delta\rho_{max} = 0.44$ e Å^{-3}
148 parameters	$\Delta\rho_{min} = -0.46$ e Å^{-3}

Table 1
Hydrogen-bond geometry (Å, °).

D—H$\cdots A$	D—H	H$\cdots A$	$D\cdots A$	D—H$\cdots A$
O3—H1O3$\cdots$O2^i	1.09	1.40	2.482 (2)	176
N1—H1N1$\cdots$O3^{ii}	0.94 (3)	2.00 (3)	2.926 (3)	168 (3)
N2—H1N2$\cdots$O1^{iii}	0.90 (3)	2.59 (3)	3.115 (3)	118 (3)
N2—H1N2$\cdots$O2^{iii}	0.90 (3)	1.92 (3)	2.810 (3)	174 (3)
N1—H2N1$\cdots$O4	0.85 (3)	2.08 (3)	2.934 (3)	175 (2)
C1—H1A$\cdots$O4^{ii}	0.93	2.54	3.440 (3)	164
C2—H2A$\cdots$O1^{iii}	0.93	2.39	3.041 (3)	127
C3—H3A$\cdots$O1^{iv}	0.93	2.31	3.222 (3)	166

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

Data collection: *APEX2* (Bruker, 2005); cell refinement: *SAINT* (Bruker, 2005); data reduction: *SAINT*; program(s) used to solve structure: *SHELXTL* (Sheldrick, 2008); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL* and *PLATON* (Spek, 2009).

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4-Aminopyridinium hydrogen succinate

Hoong-Kun Fun, Jain John, Samuel Robinson Jebas and T Balasubramanian

S1. Comment

4-Aminopyridine (Fampridine) is used clinically in Lambert-Eaton myasthenic syndrome and multiple sclerosis because by blocking potassium channels it prolongs action potentials thereby increasing transmitter release at the neuromuscular junction (Judge & Bever, (2006); Schwid *et al.*, 1997; Strupp *et al.*, 2004). The structure of 4-aminopyridine has been reported (Chao & Schempp, 1977) as has a redetermination (Anderson *et al.*, 2005). Succinic acid is a dicarboxylic acid and is a precursor for many chemicals of industrial importance (Zeikus *et al.*, 1999; Song & Lee, 2006). Succinic acid derivatives are mostly being used in chemicals, food and pharmaceuticals (Sauer *et al.*, 2008). The crystal structure of succinic acid has also been reported (Gopalan *et al.*, 2000; Leviel *et al.*, 1981). As an extension of our systematic study of hydrogen bonding patterns of 4-aminopyridine with carboxylic acids, the title compound (I) has been synthesized and the crystal structure determined.

The asymmetric unit of (I) (Fig. 1) contains a 4-aminopyridinium cation and a succinic acetate anion, indicating that proton transfer occurred during the co-crystallisation experiment. Protonation leads to the widening of C2–N2–C3 angle in the pyridine ring to 120.7 (2)°, compared to 115.25 (13)° in 4-aminopyridine (Anderson *et al.*, 2005). This type of protonation has been observed in various 4-aminopyridine acid complexes (Bhattacharya *et al.*, 1994; Karle *et al.*, 2003). Otherwise, the bond lengths and bond angles in 4-aminopyridinium cation are comparable to the values reported earlier for 4-aminopyridine (Chao & Schempp, 1977; Anderson *et al.*, 2005). The 4-aminopyridine ring is essentially planar with the maximum deviation from planarity being -0.011 (3) Å for atom C5. The bond lengths and bond angles of the succinic acetate are found to have normal values (Gopalan *et al.*, 2000; Leviel *et al.*, 1981).
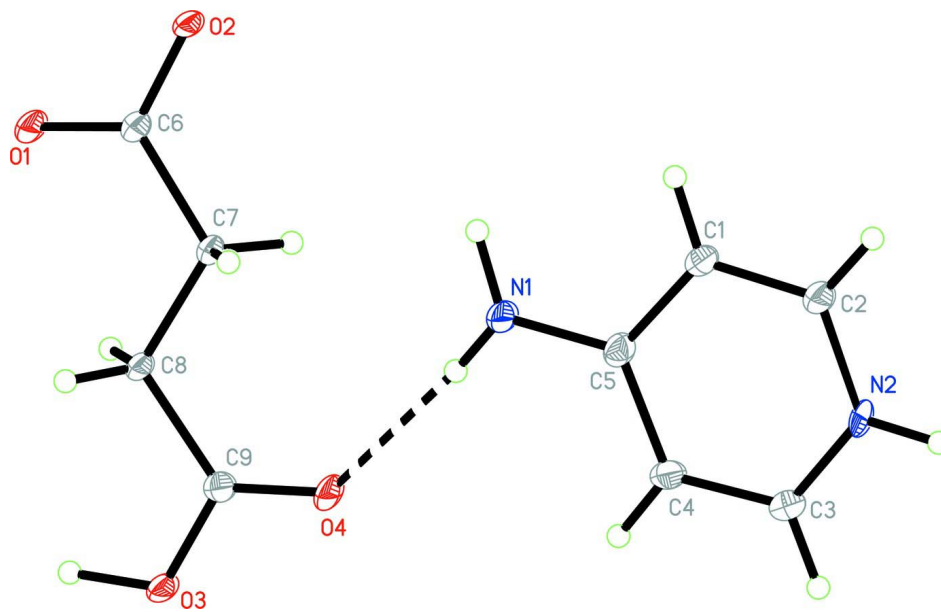
The crystal packing is consolidated by O—H···O and N—H···O intermolecular hydrogen bonds (Table 1) supported by C—H···O contacts. An intramolecular N—H···O hydrogen bond stabilises the conformation of the molecule. The molecules aggregate to form a 2-D array parallel to the *ab*-plane (Fig. 2).

S2. Experimental

Equimolar quantities of 4-aminopyridine (0.094 g, 1 mmol) and succinic acid (0.118 g, 1 mmol) were dissolved in ethanol (10 ml) and water (10 ml), respectively. The aqueous solution of succinic acid was added drop wise to the solution of 4-aminopyridine and stirred well for 4 h. The solution is refluxed at 343°K for 6 h. Colourless crystals were harvested after one month of solvent evaporation.

S3. Refinement

The N-bound H atoms were located from the Fourier map and are allowed to refine freely (N-H = 0.85 - 0.94 (3) Å). The O-bound H atom was located from the Fourier map and fixed in that position, with O—H = 1.09 Å, and allowed to refine with $U_{iso}(H) = 1.2U_{eq}(O)$. All other H atoms were placed in calculated positions, with C—H = 0.93 — 0.97 Å, and refined using a riding model with $U_{iso}(H) = 1.2U_{eq}(C)$.

Figure 1

The molecular structure of (I), showing 50% probability displacement ellipsoids and the atom numbering scheme. The dashed line indicates hydrogen bonding.

Figure 2

A 2-D supramolecular layer in (I), viewed along the *c* axis. Dashed lines indicate the hydrogen bonding.

4-Aminopyridinium hydrogen succinate

Crystal data

$C_5H_7N_2{}^+ \cdot C_4H_5O_4{}^-$	$F(000) = 448$
$M_r = 212.21$	$D_x = 1.494$ Mg m^{-3}
Monoclinic, $P2_1/c$	Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Hall symbol: -P 2ybc	Cell parameters from 1804 reflections
$a = 6.5443$ (3) Å	$\theta = 3.4$–30.1°
$b = 22.2867$ (11) Å	$\mu = 0.12$ mm^{-1}
$c = 7.1112$ (4) Å	$T = 100$ K
$\beta = 114.587$ (4)°	Plate, colourless
$V = 943.13$ (8) Å^3	$0.38 \times 0.14 \times 0.08$ mm
$Z = 4$	

Data collection

Bruker SMART APEXII CCD area-detector diffractometer	7174 measured reflections
Radiation source: fine-focus sealed tube	2176 independent reflections
Graphite monochromator	1483 reflections with $I > 2\sigma(I)$
φ and ω scans	$R_{int} = 0.066$
Absorption correction: multi-scan (*SADABS*; Bruker, 2005)	$\theta_{max} = 27.5°$, $\theta_{min} = 3.3°$
$T_{min} = 0.956$, $T_{max} = 0.991$	$h = -8 \rightarrow 8$
	$k = -28 \rightarrow 28$
	$l = -9 \rightarrow 8$

Refinement

Refinement on F^2	Secondary atom site location: difference Fourier map
Least-squares matrix: full	Hydrogen site location: inferred from neighbouring sites
$R[F^2 > 2\sigma(F^2)] = 0.062$	
$wR(F^2) = 0.150$	H atoms treated by a mixture of independent and constrained refinement
$S = 1.06$	$w = 1/[\sigma^2(F_o^2) + (0.0786P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
2176 reflections	
148 parameters	$(\Delta/\sigma)_{max} = 0.001$
0 restraints	$\Delta\rho_{max} = 0.44$ e Å^{-3}
Primary atom site location: structure-invariant direct methods	$\Delta\rho_{min} = -0.46$ e Å^{-3}

Special details

Experimental. The crystal was placed in the cold stream of an Oxford Cyrosystems Cobra open-flow nitrogen cryostat (Cosier & Glazer, 1986) operating at 100.0 (1) K.

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

Refinement. Refinement of F^2 against ALL reflections. The weighted R-factor wR and goodness of fit S are based on F^2, conventional R-factors R are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > \sigma(F^2)$ is used only for calculating R-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F, and R- factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	y	z	$U_{iso}*/U_{eq}$
O1	−0.1281 (3)	0.19522 (7)	0.2994 (3)	0.0174 (4)
O2	−0.4204 (3)	0.24560 (7)	0.2995 (3)	0.0153 (4)

O3	0.4285 (3)	0.34855 (7)	0.2828 (3)	0.0176 (4)
O4	0.1374 (3)	0.40250 (7)	0.2633 (3)	0.0189 (4)
N1	−0.2764 (4)	0.44695 (9)	0.2808 (3)	0.0171 (5)
N2	−0.4551 (3)	0.62442 (9)	0.2152 (3)	0.0151 (5)
C1	−0.5396 (4)	0.52400 (10)	0.2605 (4)	0.0151 (5)
H1A	−0.6369	0.4962	0.2769	0.018*
C2	−0.5929 (4)	0.58295 (10)	0.2401 (4)	0.0155 (5)
H2A	−0.7272	0.5953	0.2432	0.019*
C3	−0.2614 (4)	0.60783 (10)	0.2064 (4)	0.0156 (5)
H3A	−0.1701	0.6368	0.1864	0.019*
C4	−0.1974 (4)	0.54940 (10)	0.2261 (4)	0.0159 (5)
H4A	−0.0632	0.5387	0.2195	0.019*
C5	−0.3347 (4)	0.50458 (10)	0.2570 (4)	0.0132 (5)
C6	−0.2223 (4)	0.24291 (10)	0.3003 (4)	0.0124 (5)
C7	−0.1087 (4)	0.30270 (9)	0.3032 (4)	0.0119 (5)
H7A	−0.2001	0.3251	0.1798	0.014*
H7B	−0.1002	0.3257	0.4220	0.014*
C8	0.1262 (4)	0.29562 (10)	0.3127 (4)	0.0124 (5)
H8A	0.2230	0.2786	0.4458	0.015*
H8B	0.1206	0.2674	0.2067	0.015*
C9	0.2288 (4)	0.35388 (10)	0.2832 (4)	0.0136 (5)
H1O3	0.4901	0.3032	0.2838	0.016*
H1N1	−0.378 (4)	0.4190 (13)	0.292 (4)	0.020 (7)*
H1N2	−0.490 (5)	0.6636 (14)	0.204 (4)	0.027 (8)*
H2N1	−0.155 (5)	0.4361 (11)	0.273 (4)	0.013 (6)*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0163 (9)	0.0058 (8)	0.0317 (11)	−0.0004 (6)	0.0114 (8)	−0.0008 (7)
O2	0.0120 (8)	0.0061 (8)	0.0294 (11)	−0.0011 (6)	0.0102 (8)	0.0000 (6)
O3	0.0139 (9)	0.0067 (8)	0.0366 (12)	0.0003 (6)	0.0149 (8)	0.0014 (7)
O4	0.0182 (9)	0.0057 (8)	0.0358 (12)	0.0021 (6)	0.0141 (8)	0.0021 (7)
N1	0.0141 (10)	0.0079 (10)	0.0326 (14)	0.0014 (8)	0.0131 (10)	0.0008 (8)
N2	0.0170 (11)	0.0035 (10)	0.0235 (13)	0.0024 (7)	0.0071 (9)	0.0001 (8)
C1	0.0144 (12)	0.0104 (12)	0.0225 (15)	−0.0008 (8)	0.0096 (11)	0.0020 (9)
C2	0.0142 (12)	0.0092 (12)	0.0240 (15)	0.0000 (8)	0.0089 (11)	0.0002 (9)
C3	0.0139 (12)	0.0131 (12)	0.0204 (14)	−0.0026 (9)	0.0076 (11)	0.0010 (10)
C4	0.0125 (12)	0.0111 (12)	0.0255 (15)	−0.0021 (8)	0.0093 (11)	−0.0014 (9)
C5	0.0147 (11)	0.0092 (11)	0.0137 (13)	−0.0011 (8)	0.0038 (10)	−0.0012 (9)
C6	0.0128 (11)	0.0082 (11)	0.0162 (14)	−0.0009 (8)	0.0060 (10)	0.0000 (9)
C7	0.0117 (11)	0.0067 (11)	0.0175 (14)	0.0002 (8)	0.0063 (10)	0.0005 (9)
C8	0.0115 (11)	0.0063 (11)	0.0205 (14)	−0.0005 (8)	0.0076 (10)	0.0004 (9)
C9	0.0122 (11)	0.0107 (12)	0.0195 (14)	−0.0002 (8)	0.0081 (11)	−0.0001 (9)

Geometric parameters (Å, º)

O1—C6	1.230 (3)	C1—H1A	0.9300
O2—C6	1.295 (3)	C2—H2A	0.9300
O3—C9	1.313 (3)	C3—C4	1.357 (3)
O3—H1O3	1.0871	C3—H3A	0.9300
O4—C9	1.217 (3)	C4—C5	1.420 (3)
N1—C5	1.331 (3)	C4—H4A	0.9300
N1—H1N1	0.94 (3)	C6—C7	1.522 (3)
N1—H2N1	0.86 (3)	C7—C8	1.519 (3)
N2—C3	1.347 (3)	C7—H7A	0.9700
N2—C2	1.354 (3)	C7—H7B	0.9700
N2—H1N2	0.90 (3)	C8—C9	1.516 (3)
C1—C2	1.352 (3)	C8—H8A	0.9700
C1—C5	1.419 (3)	C8—H8B	0.9700
C9—O3—H1O3	116.8	N1—C5—C4	122.1 (2)
C5—N1—H1N1	118.3 (16)	C1—C5—C4	116.8 (2)
C5—N1—H2N1	119.4 (17)	O1—C6—O2	122.88 (19)
H1N1—N1—H2N1	122 (2)	O1—C6—C7	120.88 (19)
C3—N2—C2	120.7 (2)	O2—C6—C7	116.24 (18)
C3—N2—H1N2	118.4 (17)	C8—C7—C6	112.93 (18)
C2—N2—H1N2	120.9 (17)	C8—C7—H7A	109.0
C2—C1—C5	119.9 (2)	C6—C7—H7A	109.0
C2—C1—H1A	120.1	C8—C7—H7B	109.0
C5—C1—H1A	120.1	C6—C7—H7B	109.0
C1—C2—N2	121.4 (2)	H7A—C7—H7B	107.8
C1—C2—H2A	119.3	C9—C8—C7	113.79 (18)
N2—C2—H2A	119.3	C9—C8—H8A	108.8
N2—C3—C4	121.0 (2)	C7—C8—H8A	108.8
N2—C3—H3A	119.5	C9—C8—H8B	108.8
C4—C3—H3A	119.5	C7—C8—H8B	108.8
C3—C4—C5	120.2 (2)	H8A—C8—H8B	107.7
C3—C4—H4A	119.9	O4—C9—O3	121.5 (2)
C5—C4—H4A	119.9	O4—C9—C8	123.62 (19)
N1—C5—C1	121.0 (2)	O3—C9—C8	114.91 (18)
C5—C1—C2—N2	0.3 (4)	C3—C4—C5—C1	1.5 (4)
C3—N2—C2—C1	1.2 (4)	O1—C6—C7—C8	−2.1 (3)
C2—N2—C3—C4	−1.3 (4)	O2—C6—C7—C8	177.7 (2)
N2—C3—C4—C5	−0.1 (4)	C6—C7—C8—C9	171.3 (2)
C2—C1—C5—N1	178.7 (2)	C7—C8—C9—O4	3.3 (3)
C2—C1—C5—C4	−1.6 (4)	C7—C8—C9—O3	−177.5 (2)
C3—C4—C5—N1	−178.8 (2)		

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O3—H1*O3*···O2ⁱ	1.09	1.40	2.482 (2)	176
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