

The Crystal Structure of 2-Amino-5-methylpyridine Hydrochloride and Crystal Data for 2-Amino-5-methylpyridine Hydrobromide

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The crystal structure of 2-amino-5-methylpyridine hydrochloride has been solved using single-crystal X-ray diffraction techniques and refined to a conventional R index of 0.074 for 1277 counter-collected data with average net intensities greater than zero. The crystals are monoclinic, space group $P2_1/c$, with $a=7.144$ (8), $b=12.248$ (4), $c=8.845$ (4) Å, and $\beta=107.61$ (5)°. A comparison of this structure with that typical of hydrochloride salts of cytosine derivatives leads to the conclusion that C-H...O interactions in the cytosine salts not only are important in maintaining a coplanar array of molecules but also contribute appreciably to the overall stability of the crystals. Crystals of 2-amino-5-methylpyridine hydrobromide are isostructural with those of the hydrochloride salt and have cell dimensions $a=7.070$ (3), $b=12.684$ (5), $c=9.173$ (3) Å, and $\beta=109.41$ (3)°.

Introduction

A feature common to the crystal structures of all hydrochloride salts of cytosine derivatives that have so far been reported is the relationship of translationally equivalent cytosine rings and chloride ions, as shown in Fig. 1(a) (Sherfinski & Marsh, 1973). While this arrangement must be primarily dictated by the N-H...Cl hydrogen bonds, the C-H...O interactions may also be of importance. Characteristic values for the C...O and H...O distances are 3.2 and 2.6 Å; while this latter value is too large to suggest a true hydrogen bond, it may well represent sufficient electrostatic attraction to establish the coplanarity of adjacent rings. In order to gain some insight into the importance of these C-H...O interactions, we have investigated the crystal structure of the hydrochloride salt of 2-amino-5-methylpyridine [Fig. 1(b)], which bears strong resemblance to cytosine except for the replacement of the carbonyl grouping by the smaller, less functional methylidene (C-H) group.

Experimental

Approximately 0.5 g of practical-grade 2-amino-5-methylpyridine (hereafter, 2A5MP) was recrystallized from toluene, then from dilute hydrochloric acid. Clear needle-shaped crystals, elongated along **a**, were isolated. Preliminary diffraction photographs indicated the monoclinic space group $P2_1/c$ ($h0l$ absent for l odd, $0k0$ absent for k odd), and density measurements (by neutral buoyancy in a carbon tetrachloride/ethyl

acetate solution) indicated four molecules of the hydrochloride salt per cell. The crystal used for data collection was a small roughly cubic fragment, approximately 0.1 mm on an edge. Since the crystals appeared to interact with both epoxy and Duco cement, allowing neither to set firmly, the fragment was wedged into a hand-drawn soft glass capillary and mounted on a locally assembled, Syntex-automated E & A full-circle diffractometer, described by Samson & Hansen (1972). Unit-cell parameters obtained from a least-squares fit to the observed 2θ values for 13 reflections, as well as other pertinent data, are listed in Table 1.

Table 1. Crystal data

2A5MP.HCl	2A5MP.HBr
$C_6N_2H_7^+Cl^-$	$C_6N_2H_7^+Br^-$
Monoclinic	Monoclinic
Space group $P2_1/c$	Space group $P2_1/c$
$a=7.144$ (8) Å	$a=7.070$ (3) Å
$b=12.248$ (4)	$b=12.684$ (5)
$c=8.845$ (4)	$c=9.173$ (3)
$\beta=107.61$ (5)°	$\beta=109.41$ (3)°
$V=738$ Å ³	$V=776$ Å ³
F.W. 144.6	F.W. 189.1
$F(000)=304$	$F(000)=376$
$\mu=4.3$ cm ⁻¹ (Mo $K\alpha$)	$\mu=55.5$ cm ⁻¹ (Mo $K\alpha$)
$D_x=1.303$ (2) g cm ⁻³	$D_x=1.618$ (1) g cm ⁻³
$D_m=1.28$ (1)	$D_m=1.63$ (1)
$Z=4$	$Z=4$

Intensities for all independent reflections out to $\sin^2 \theta/\lambda^2=0.32$ Å⁻² were measured by the $\theta-2\theta$ scan method, using graphite-monochromatized molybdenum radiation ($\lambda=0.71069$ Å) and a horizontal tube configuration. Scanning speed was variable, ranging from 0.5° min⁻¹ for the very weak reflections to 4° min⁻¹ for the very strong. Backgrounds were counted at the beginning and end of each scan, each for a period equal to one-half the scan time. The 258 reflec-

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tions with peak intensities greater than 50 counts per second were measured at least twice, and often three or four times; 291 other reflections were surveyed at least twice in order to confirm the reproducibility of the measurements. The total number of measurements was 2184. Three check reflections (340, 204, 161) were measured periodically; they showed 10–15% decreases in intensities during the month of data collection. The data were partitioned into several blocks, as a function of time, and an average correction factor was applied to each of these blocks. We estimate that the use of this step function rather than a smooth decay curve, and the ignoring of different decay rates in different regions of reciprocal space, could have caused errors in $F(\text{obs})$ amounting to no more than 2–3%.

Each reflection was assigned a variance $\sigma^2(I)$ based on counting statistics plus a term $(0.02s)^2$, where s is the scan count. The intensities and their variances were then corrected for Lorentz and polarization effects; absorption was ignored ($\mu r \leq 0.03$). Multiple observations were averaged, with the final weight taken as the sum of the weights of the individual observations. Of the 1493 reflections surveyed, 216 had net intensities less than zero.

Crystals of the hydrobromide salt were obtained by recrystallizing 2A5MP from dilute hydrobromic acid. Their morphology was similar to that of the 2A5MP.HCl crystals, and Weissenberg photographs indicated the two to be isostructural. Cell dimensions were obtained from the 2θ values of 19 reflections, measured on a modified General Electric XRD-5 quarter-circle diffractometer equipped with a molybdenum-target X-ray tube and a graphite monochromator; the density was measured by flotation in a carbon tetrachloride/dibromomethane solution. Crystal data are included in Table 1; no further work was carried out on these crystals.

The structure solution of 2A5MP.HCl was by the traditional Patterson–Fourier method, and refinement was by full-matrix least-squares calculations. Hydrogen atoms of the methyl group were located unambiguously from a difference map evaluated in their plane; others were initially assigned idealized coordinates. Atomic form factors for Cl^- were from

Cromer & Waber (1965); for C and N, from *International Tables for X-ray Crystallography* (1962); and for H, from Stewart, Davidson & Simpson (1965). Calculations were carried out on an IBM 370-155 computer under the CRYM system of crystallographic

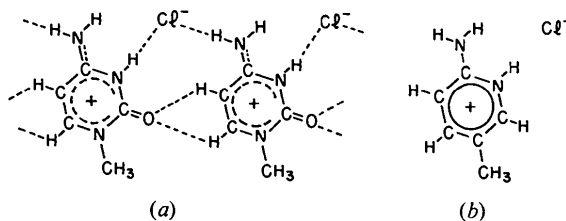


Fig. 1. (a) The translational arrangement of ions in crystals of 1-methylcytosine hydrochloride (Trus & Marsh, 1972). (b) 2-Amino-5-methylpyridine hydrochloride.

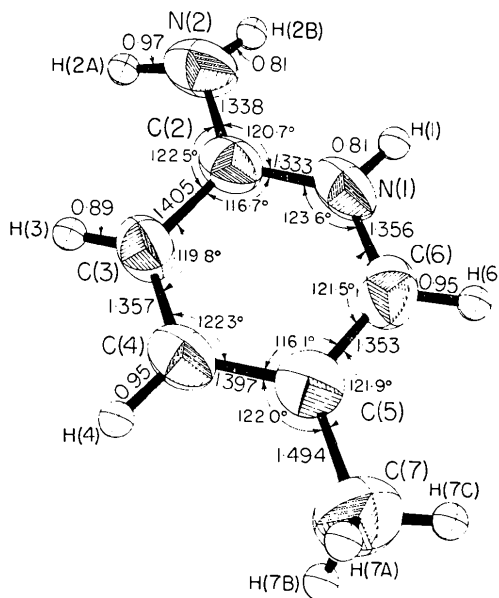


Fig. 2. Bond distances and angles. Estimated standard deviations are 0.007 Å and 0.4° for bonds involving only C and N atoms and 0.03 Å for bonds involving hydrogen atoms. Thermal ellipsoids for the carbon and nitrogen atoms are drawn at the 50% probability level (Johnson, 1965); hydrogen atoms are represented as spheres of arbitrary radius.

Table 2. Final atomic parameters and their e.s.d.'s (in parentheses)

Coordinates have been multiplied by 10^5 for Cl^- , by 10^4 for C and N, and by 10^3 for H; anisotropic temperature coefficients U_{ij} have been multiplied by 10^4 for Cl^- and 10^3 for C and N. The temperature factor is of the form

$$\exp[-2\pi^2(h^2a^{*2}U_{11} + \dots + 2k_1b^*c^*U_{23})].$$

	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
Cl^-	12017 (12)	35501 (6)	9592 (7)	1122 (7)	536 (4)	392 (3)	-3 (6)	147 (4)	-88 (4)
N(1)	2173 (4)	4799 (2)	4052 (3)	57 (2)	65 (2)	42 (1)	-16 (2)	20 (1)	-20 (1)
N(2)	745 (4)	6416 (3)	2888 (3)	72 (2)	83 (2)	39 (1)	-9 (2)	13 (1)	-1 (2)
C(2)	1656 (4)	5832 (2)	4179 (3)	49 (2)	58 (2)	45 (1)	-12 (2)	21 (1)	-6 (1)
C(3)	2168 (4)	6274 (3)	5717 (3)	60 (2)	52 (2)	45 (1)	1 (2)	12 (1)	-11 (1)
C(4)	3128 (5)	5648 (2)	6979 (3)	57 (2)	63 (2)	39 (1)	-5 (2)	10 (2)	-10 (1)
C(5)	3642 (4)	4564 (2)	6811 (3)	44 (2)	57 (2)	52 (2)	-4 (2)	15 (1)	-0 (1)
C(6)	3128 (5)	4170 (3)	5312 (3)	60 (2)	45 (2)	71 (2)	-8 (2)	30 (2)	-6 (2)
C(7)	4686 (7)	3876 (4)	8206 (5)	71 (3)	86 (3)	72 (2)	10 (3)	21 (2)	15 (2)

Table 2 (cont.)

	<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i> (Å ²)
H(1)	197 (4)	451 (2)	320 (3)	5.0 (0.7)
H(2A)	18 (5)	709 (3)	312 (4)	10.2 (1.3)
H(2B)	40 (4)	608 (2)	206 (3)	5.7 (0.8)
H(3)	175 (3)	695 (2)	581 (2)	3.2 (0.6)
H(4)	343 (3)	598 (2)	799 (3)	5.2 (0.6)
H(6)	343 (3)	344 (2)	511 (2)	3.7 (0.6)
H(7A)	594 (5)	407 (3)	874 (4)	7.1 (1.1)
H(7B)	400 (4)	389 (2)	893 (3)	5.8 (0.8)
H(7C)	484 (5)	316 (3)	791 (4)	7.6 (1.1)

programs. The quantity minimized in the least-squares calculations was $\sum w(F_o^2 - F_c^2)^2$, with weights *w* equal to $\sigma^{-2}(F_o^2)$.

Final refinement included coordinates of all atoms, anisotropic temperature parameters for the Cl, C, and N atoms, isotropic temperature parameters for the H atoms, and a scale factor; in the last cycle, the largest parameter shift was 0.36σ . The final *R* index, based on *F*, was 0.074 for 1277 reflections with net intensities greater than zero, and a more respectable 0.047 for the 882 reflections with intensities greater than 2 e.s.d.'s above background; the goodness-of-fit, $\sum w(F_o^2 - F_c^2)^2 / (n-p)$, was 1.47 for *n*=1493 reflections (including those with negative intensities) and *p*=118 parameters. Final values for the atomic parameters are given in Table 2.*

* A list of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 30792 (11 pp., 1 microfiche). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

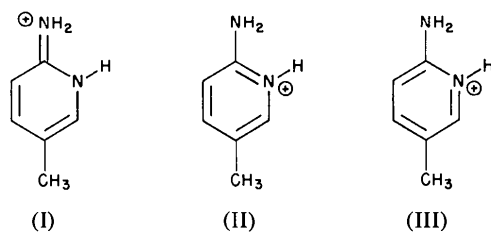
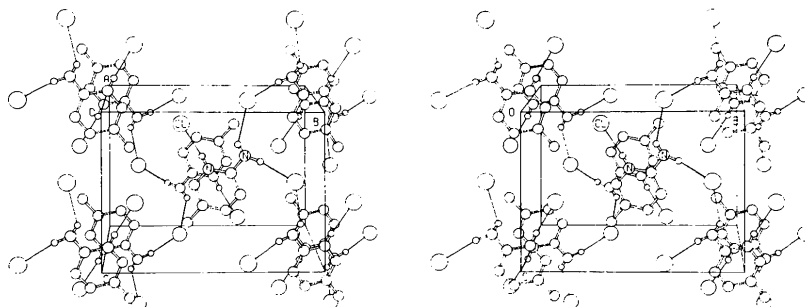


Fig. 3. Contributing resonance structures.

Fig. 4. A stereoscopic view of the structure, as seen along the *a** direction (Johnson, 1965).

Discussion

Bond distances and angles are given in Fig. 2 and Table 3. The presence of the amino group has resulted in relatively large asymmetry in the six-membered pyridine ring, the resonance form (I) shown in Fig. 3 obviously being a large contributor. In addition, the C(2)–N(1) and C(6)–N(1) distances suggest that form (II) is more important than (III). The enlargements of the C(2)–N(1)–C(6) angle and, more surprisingly, of the C(3)–C(4)–C(5) angle, which were noted by Rérat (1962) in crystals of pyridine hydrochloride, are confirmed here.

Table 3. Distances (Å) and angles (°) involving the hydrogen atoms

Estimated standard deviations are 0.03 Å and 1.5–2.0°.			
C(7)—H(7A)	0.91	H(4)—C(4)—C(3)	117
C(7)—H(7B)	0.92	H(4)—C(4)—C(5)	121
C(7)—H(7C)	0.93	H(7A)—C(7)—H(7B)	106
H(1)—N(1)—C(2)	122	H(7A)—C(7)—H(7C)	102
H(1)—N(1)—C(6)	115	H(7B)—C(7)—H(7C)	110
H(2A)—N(2)—C(2)	114	H(7A)—C(7)—C(5)	117
H(2A)—N(2)—H(2B)	126	H(7B)—C(7)—C(5)	109
H(2B)—N(2)—C(2)	116	H(7C)—C(7)—C(5)	112
H(3)—C(3)—C(2)	117	H(6)—C(6)—C(5)	121
H(3)—C(3)—C(4)	123	H(6)—C(6)—N(1)	118

Details of the mean plane of the cation are given in Table 4. The nitrogen atom N(2) of the amino group is slightly pyramidal, due principally to the out-of-plane displacement of H(2A) in a direction so as to improve the linearity of the N–H...Cl hydrogen bond. The methyl group has an eclipsed conformation, H(7C) lying essentially in the plane of the ring. The H(6)...H(7C) distance is a comfortable 2.40 Å.

The arrangement of molecules is shown in Fig. 4. This arrangement is quite different from that typical of cytosine derivatives (e.g. 1-methylcytosine hydrochloride: Trus & Marsh, 1972); while all three acidic protons participate in N–H...Cl hydrogen bonds, the planar, repeating array [Fig. 1(a)] is not present. In comparing the structure of 2A5MP.HCl with that of methylcytosine.HCl, one notes that the three N...Cl hydrogen bonds in 2A5MP.HCl (Table 5) are shorter by an average of about 0.04 Å, and the stacking inter-

Table 4. *The least-squares plane of the cation*

The plane was passed through the six ring atoms indicated with an asterisk, all weighted equally. It has direction cosines 0.948, 0.305 and -0.373 relative to the crystal axes a , b and c ; the origin-to-plane distance is 1.924 Å.

Deviations of atoms from the plane (Å)

N(1)*	0.003	H(1)	0.04
C(2)*	-0.003	H(2A)	-0.19
C(3)*	0.002	H(2B)	-0.06
C(4)*	0.000	H(3)	-0.06
C(5)*	-0.001	H(4)	-0.01
C(6)*	0.001	H(6)	0.00
N(2)	0.025	H(7A)	0.74
C(7)	-0.012	H(7B)	-0.71
		H(7C)	-0.07

Cl	-0.100 Å [H bonded to N-H(1)]
Cl(a)†	-0.877 [H bonded to N-H(2A)]
Cl(b)†	-0.011 [H bonded to N-H(2B)]

† (a) at $(-x, \frac{1}{2} + y, \frac{1}{2} - z)$; (b) at $(-x, 1 - y, -z)$.

actions (see Fig. 5) are somewhat stronger. Surprisingly, then, the volume per formula unit of 2A5MP.HCl is greater than that of methylcytosine.HCl, indicating a lower packing efficiency. In addition, 2A5MP.HCl melts at 190–190.5°C whereas methylcytosine.HCl begins to turn brown and decompose only at 270°C. We thus have the conflicting observations of methylcytosine hydrochloride forming more stable crystals while exhibiting weaker hydrogen bonding and stacking interactions. The obvious difference in the two structures is the array of C-H...O interactions in methylcytosine.HCl. Accordingly, we believe that these interactions not only stabilize the specific arrangement of ions shown in Fig. 1(a), but also contribute quite appreciably to the stability of the crystal structure.

Table 5. *Details of the hydrogen bonds D-H...A*

D	H	A	D...A	H...A	D-H...A
N(1)	H(1)	Cl	3.025 Å	2.22 Å	173°
N(2)	H(2A)	Cl(a)*	3.265	2.31	171
N(2)	H(2B)	Cl(b)*	3.263	2.61	139

* (a) at $-x, \frac{1}{2} + y, \frac{1}{2} - z$; (b) at $-x, 1 - y, -z$.

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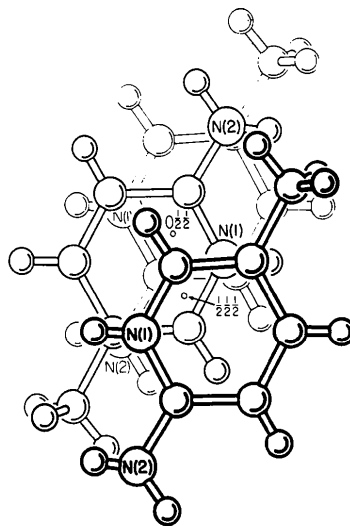


Fig. 5. The stacking of 2A5MP cations. Shortest distances between molecules related by the center of symmetry at $\frac{1}{2}, \frac{1}{2}, \frac{1}{2}$ are N(1)...C(5), 3.39 and N(1)...C(6), 3.47 Å; between molecules related by the center at $0, \frac{1}{2}, \frac{1}{2}$, N(1)...C(3), 3.43 and N(2)...C(5), 3.44 Å.

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