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X-ray and DFT studies of the structure, vibrational and NMR spectra of 2-amino-pyridine betaine hydrochloride

M. Szafran*, I. Kowalczyk, J. Koput, A. Katrusiak

Faculty of Chemistry, Adam Mickiewicz University, Ul. Grunwaldzka 6, 60-780 Poznań, Poland

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Abstract

The effect of hydrogen bonding, inter- and intramolecular electrostatic interactions on the conformation of 2-amino-pyridine betaine hydrochloride (1-carboxymethyl-2-amino-pyridinium chloride), 2-NH_2PBH$\cdots$Cl(c), in the crystal and its isolated molecules has been studied by X-ray diffraction, FT-IR, Raman, ^{1}H and ^{13}C NMR spectroscopies, and by DFT calculations. In the crystal, the Cl^- anion is connected with protonated betaine via hydrogen bond, O–H$\cdots Cl^- = 2.975(2)$ Å, two N(12)–H$\cdots Cl^-$ hydrogen bonds and two N(1) H$\cdots Cl^-$ intermolecular electrostatic interactions. Two minima are located in the potential energy surface at the B3LYP/6-31G(d,p) level, 2-NH_2PBH$\cdots$Cl(t) and 2-NH_2PB$\cdots$HCl(c), with the latter being 20,7 kcal/mol higher in energy. The optimized bond lengths and angles of 2-NH_2PBH$\cdots$Cl(t) at B3LYP level of theory are in good agreement with X-ray data, except for the conformation of the COOH group, which is *cis* (*syn*) in the crystal and *trans* (*anti*) in the single molecule. The probable assignments for the anharmonic experimental solid state vibrational spectra of 2-NH_2PBH$\cdots$Cl(c) and 2-ND_2PBD$\cdots$Cl(c) based on the calculated B3LYP/6-31G(d,p) harmonic frequencies have been made. ^{1}H and ^{13}C NMR screening constants for both single molecules have been calculated in the GIAO/B3LYP/6-31G(d,p) approach. Linear correlation between the calculated and experimental ^{1}H chemical shifts holds only for *cis* conformer. The lack of such a correlation for *trans* conformer indicates that it is absent in D_2O solution.

1. Introduction

Betaines are zwitterionic compounds containing a carboxylate group and a quaternary ammonium group. The chemistry of betaines has become a subject of particular interest due to their applications in biological research, especially in regard to their important roles in amino acid synthesis as methyl transfer agents [1]. Betaines containing a hydrophobic chain in the range of 8–20 carbon atoms show unique properties characteristic of amphoteric surfactants and their current industrial application is in toiletries and personal care products [2]. Several betaines and their 1:1 and 2:1 complexes with various acids have been structurally characterized *via* single-crystal X-ray analysis [3,4]. Many of these complexes display interesting physical properties, exhibiting phase transitions with ferroelectric, antiferroelectric and ferroelastic behaviour as well as phases with commensurate and incommensurate superstructures [5]. Betaines have a variety of uses in medicine, pharmacy, biology and other scientific fields [2].

From the structural point of view, quaternary ammonium and pyridinium halides containing COOH group can be considered as bifunctional compounds. The cohesion forces in the crystals of these compounds are dominated by COO$\cdots X^-$ hydrogen bonds, electrostatic $N^+\cdots X^-$ and $N^+\cdots$O interactions and C–H$\cdots X^-$ contacts [6,7]. The electrostatic contacts depend on the number of methylene groups in tether connecting the positively charged nitrogen atom with COO^- or COOH groups, counter anions, and also on additional substituents.

Several substitute pyridine betaine compounds, including 3-carboxy-1-(carboxymethyl)pyridinium inner salt [8], 1-(carboxymethyl)-4-(dimethylamino)-pyridinium inner salt dihydrate [9], 1-(carboxymethyl)-2-(amino)-pyridinium hydrate inner salt [10], 3-(2-bromo-pyridinium)-propionic

* Corresponding author. Tel.: +48 61 8291320; fax: +48 61 8658008.
E-mail address: szafran@main.amu.edu.pl (M. Szafran).

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acid bromide [11], 3-(2-hydroxymethyl-pyridinium)-propionic acid bromide and 3-(2-hydroxyethyl-pyridinium)-propionic acid bromide [12], 4-dimethylpyridinium-1-squarate [13] have been analyzed by X-ray diffraction.

In this paper the effect of NH_2 group in position 2 of the pyridine ring on the structure, conformation and hydrogen bonding of 2-NH_2PBH·Cl is analyzed by X-ray diffraction, FTIR, Raman, ^{1}H and ^{13}C NMR spectroscopies, and DFT calculations.

2. Experimental

2.1. Synthesis

2-Amino-pyridine betaine (2-amino-*N*-carboxymethyl-pyridinium inner salt) monohydrate (2-NH_2PB.H_2O) was prepared by the method reported in [14]. To a solution of aqueous 2-aminopyridine (9.41 g) sodium chloroacetate (11.6 g) in methanol:water (1:5) was added. The solution was warmed in a water-bath for 4 h at 75 °C. The resulting pink solid was dried under vacuum reduced pressure. The crude product was recrystallized from a mixture of iso-propanol:water (1:1), m.p. 280–282 °C. The anhydrous complex 2-NH_2PB was obtained by dehydratation of monohydrate in vacuum at 80° over P_2O_5 for 10 h, which slowly converts to monohydrate when left in an open cell.

2-NH_2PBH·Cl was prepared by mixing equivalents (4 g) of 2-NH_2PB·H_2O in water with concentrated HCl (36%) (2.5 g) in methanol. The solvent was evaporated under reduced pressure and the residue was dried over P_4O_{10} and then recrystallized from anhydrous methanol. M.p. 230–233 °C. Analysis exp. and (calc): %C 44.52 (44.58); %H 4.79 (4.81); %N 14.82 (14.85). Deuterated samples were obtained by dissolving the complexes in D_2O (twice), evaporating to dryness and recrystallization from a CH_3OD.

2.2. Instrumentation

The X-ray diffraction measurements were carried out using a KUMA-4 CCD diffractometer. The structure was solved by direct methods with SHELXS-97 [15] and refined by the full-matrix least squares method on F^2 data using SHELXS-97 [16]. The crystal data and details concerning the data collection and structure refinement are given in Table 1. Atomic coordinates and equivalent displacement parameters are listed in Table 2 and geometrical parameters in Tables 3–5. The parameters in the CIF form are available as Electronic Supplementary Publication No. CCDC 242846 from Cambridge Crystallographic Data-base Centre.

All NMR spectra were recorded on a Varian Gemini 300 VT spectrometer, operating at 300.07 and 75.4614 Hz for ^{1}H and ^{13}C, respectively. Typical conditions for the proton

Table 1
Crystal data and structure refinement for 2-amino-pyridine betaine hydrochloride, 2-NH_2PBH···Cl

Empirical formula	$C_7H_9ClN_2O_2$
Formula weight	188.61
Temperature (K)	100(2)
Wavelength (Å)	0.71073
Crystal system	Orthorhombic
Space group	$P2_12_12_1$
Unit cell dimensions	
a (Å)	8.6613(4)
b (Å)	8.9178(4)
c (Å)	11.0160(5)
β (deg)	90
Volume (Å^3)	850.87(9)
Z	4
Calculated density (g/cm^3)	1.472
Absorption coefficient (mm^{-1})	0.408
F(000)	392
Crystal size (mm)	0.3×0.3×0.15
θ range for data collection (deg)	2.94–29.65
Index range	$-11\leq h\leq 11$
	$-8\leq k\leq 12$
	$-14\leq l\leq 14$
Reflections collected/unique	6125/2143
R(int)	0.0525
Completeness to refinement method	θ=29.65 91.9%
Refinement method	Full-matrix least squares on F^2
Data/restraints/parameters	2143/0/119
Goodness-of-fit on F^2	1.274
Final R indices [$I>2\sigma(I)$]	$R1$=0.0380, $wR2$=0.1006
R indices (all data)	$R1$=0.0411, $wR2$=0.1129
Absolute structure parameter	−0.01(7)
Extinction coefficient	0.109(12)
Largest diff. peak and hole (e Å^{-3})	0.791 and −0.602

Table 2
Atomic coordinates and equivalent isotropic displacement parameters for the 2-amino-pyridine betaine hydrochloride, 2-NH_2PBH·Cl. U(eq) defined as one third of the trace of the ortogonalized U_{ij} tensor

	x	y	z	U(eq)
Cl(21)	−0.0741(1)	0.6021(1)	0.5825(1)	0.016(1)
N(1)	0.5002(2)	0.9196(2)	0.8127(2)	0.012(1)
C(77)	0.6315(2)	0.8574(2)	0.7668(2)	0.013(1)
N(12)	0.6427(2)	0.8255(2)	0.6492(2)	0.016(1)
C(9)	0.7546(3)	0.8280(2)	0.8484(2)	0.016(1)
C(10)	0.7396(3)	0.8614(2)	0.9684(2)	0.018(1)
C(8)	0.6011(3)	0.9235(2)	1.0128(2)	0.017(1)
C(6)	0.4856(3)	0.9518(2)	0.9338(2)	0.014(1)
C(2)	0.3676(2)	0.9496(2)	0.7335(2)	0.013(1)
C(3)	0.2753(2)	0.8094(2)	0.7107(2)	0.013(1)
O(4)	0.1504(2)	0.8416(2)	0.6477(1)	0.018(1)
O(5)	0.3106(2)	0.6861(2)	0.7483(2)	0.018(1)
H(16)	0.7410(60)	0.7510(40)	0.6280(40)	0.076(12)
H(17)	0.5620(40)	0.8530(30)	0.5900(30)	0.027(8)
H(14)	0.8458	0.7858	0.8199	0.019
H(15)	0.8211	0.8431	1.0213	0.021
H(13)	0.5895	0.9445	1.0949	0.021
H(11)	0.3943	0.9940	0.9621	0.017
H(18)	0.4039	0.9896	0.6568	0.015
H(19)	0.3019	1.0245	0.7711	0.015
H(20)	0.1099	0.7714	0.6418	0.052(12)