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Conformational richness and multiple Z' in salt co-crystal of *N*-methylpiperidine betaine with *N*-methylpiperidine betaine hexafluorosilicate

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The co-crystal structure of *N*-methylpiperidine betaine with *N*-methylpiperidine betaine hexafluorosilicate represents an unusual case of a salt co-crystal with a high Z' value (3), unexpected conformational variability, and with nearly 50% of its contents disordered. The betaine units from the salt and co-crystal formers are paired into several homoconjugated dimers *via* very short, linear $O^{-}\cdots H^{+}\cdots O^{-}$ bridges. These hydrogen bonds are the dominating interactions in the co-crystal structure, in variance with the simple hexafluorosilicate salt, which has a structure governed by $COOH\cdots F$ hydrogen bonds. The SiF_6^{2-} anion in the co-crystal structure has only $C—H\cdots F$ interactions with the betaine units. The zwitterion:cation:anion stoichiometry is 3:3:1.5. Some of the betaine units display disorder, but each case is different. One of the SiF_6^{2-} anions is ordered while possessing exact crystallographic symmetry. The other one is disordered in a general position. In addition, there are three water molecules in the crystal structure. One is fully ordered, one has an H atom disordered in two positions and the third one occupies two alternative positions with unequal populations.

1. Introduction

The design of co-crystals has received much attention in recent years because of their potential applications as pharmaceutical agents. Salts of an ionizable active pharmaceutical ingredient (API) are generally preferred to the neutral compounds because of enhanced solubility, crystallinity and stability. Alternatively, API co-crystals can also be targeted to achieve the same effects (Vishweshwar *et al.*, 2006; Trask *et al.*, 2006; Li *et al.*, 2006; Variankaval *et al.*, 2006; Reddy *et al.*, 2006; Basavoju *et al.*, 2006; Bhatt *et al.*, 2005). A co-crystal is a multi-component system in which two or more components that are solids under ambient conditions co-exist in the same crystalline lattice (Almarsson & Zaworotko, 2004). The strategies employed in the design of co-crystals rely on the recognition of functional groups placed on different molecules that prefer to interact with each other rather than with themselves, and in most cases the constituents are uncharged neutral molecules (Aakeröy *et al.*, 2007; Braga *et al.*, 2007; Zaworotko, 2007; Sokolov *et al.*, 2006; Friščić *et al.*, 2006; Bis *et al.*, 2006; Ma & Coppens, 2003; Vishweshwar *et al.*, 2003). The first systematic method for designing co-crystals of a salt has been demonstrated by Childs and co-workers in the co-crystals of fluoxetine hydrochloride with benzoic, succinic and fumaric acids by making use of the underutilized hydrogen-bond acceptor ability of the chloride ion (Childs *et al.*, 2004). The strategy is effective in generating co-crystals of amine hydrochlorides with neutral organic acids. Herein we report the structure of a

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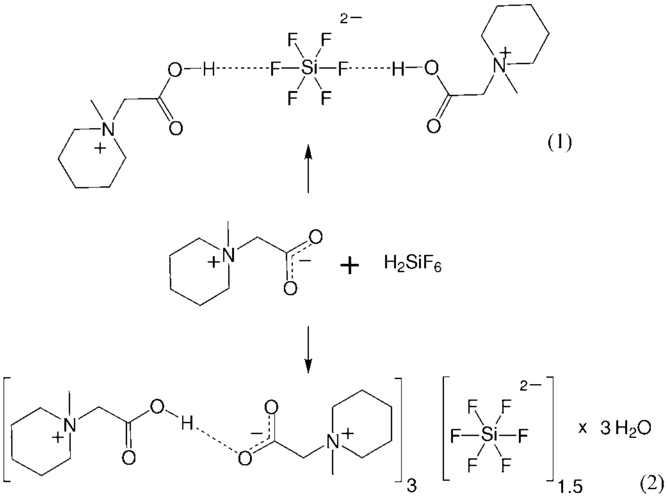
salt co-crystal (2) of *N*-methylpiperidine betaine (MPB, zwitterion) and *N*-methylpiperidine betaine hexafluorosilicate (see Scheme 1), the examination of which has interesting implications for novel strategies of salt co-crystal design.



Scheme 1

The present crystal structure is totally different from the previously reported $P2_1/c$ crystal structure of the *N*-methylpiperidine betaine hexafluorosilicate 2:1 salt (1) (see Scheme 1) reported by Szafran *et al.* (2001). Compound (1) has two ordered betaine cations and one ordered SiF_6^{2-} anion in the asymmetric unit ($Z' = 1$, $Z'' = 3$, Z'' corresponds to the total number of molecules of any type in the asymmetric unit; Steed, 2003). In (1) the carboxylic OH groups are involved in the formation of O—H···F hydrogen bonds (Desiraju & Steiner, 1999) to a common SiF_6^{2-} ion. Surprisingly, no O—H···O hydrogen bonds were observed in those crystals, despite the fact that O—H···O hydrogen bonds (especially assisted by electron resonance in carboxylic acid dimers, see Gilli *et al.*, 1989) would be expected to be stronger than O—H···F interactions. These observations prompted us to investigate the co-crystal-forming ability of MPB and (1). To our satisfaction, this is exactly what we found in the crystals obtained by mixing MPB with (1) in a 2:1 molar ratio in ethanol solution with subsequent solvent evaporation.

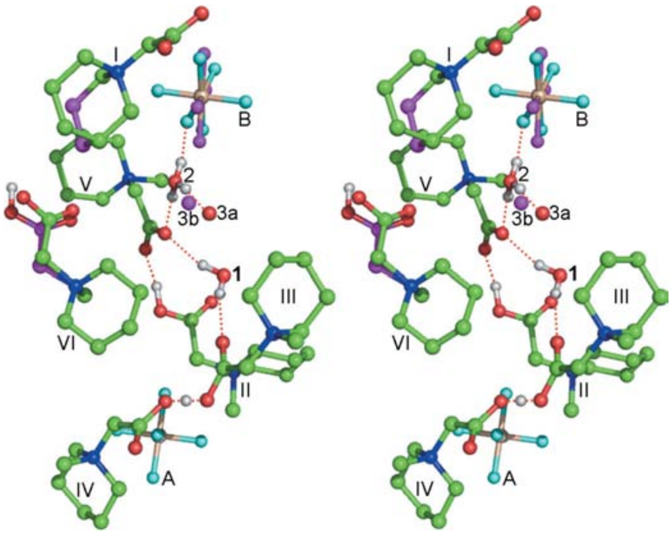


Figure 1
A stereo diagram showing the asymmetric unit of (2). The *N*-methylpiperidine betaine units are numbered (I)–(VI), the SiF_6^{2-} anions *A*–*B*, and the water molecules (1)–(3). The alternative components of the disordered moieties [betaine (I) and (VI)/anion *B*/water molecule (3)] are shown with magenta C/F/O atoms. Note that the disorder in betaines (I) and (VI) is correlated, *i.e.* the 'magenta' conformations should appear in both molecules simultaneously to minimize steric clashes.

Table 1
Experimental details.

Crystal data	
Chemical formula	$C_8H_{15}NO_2 \cdot C_8H_{16}NO_2 \cdot 0.5SiF_6 \cdot H_2O$
M_r	404.49
Cell setting, space group	Triclinic, $P\bar{1}$
Temperature (K)	100 (1)
a, b, c (Å)	11.554 (2), 12.621 (3), 22.763 (5)
α, β, γ (°)	83.87 (3), 84.81 (3), 63.86 (3)
V (Å^3)	2959.2 (10)
Z	6
D_x (Mg m^{-3})	1.362
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.15
Crystal form, colour	Prism, colourless
Crystal size (mm)	0.3 × 0.3 × 0.2
Data collection	
Diffractometer	KM4 CCD
Data collection method	Oscillation
Absorption correction	None
No. of measured, independent and observed reflections	27 619, 13 415, 8890
Criterion for observed reflections	$I > 2\sigma(I)$
$R_{\rm int}$	0.029
$\theta_{\rm max}$ (°)	27.5
Refinement	
Refinement on	F^2
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.056, 0.138, 1.05
No. of reflections	13 415
No. of parameters	847
H-atom treatment	Mixture of independent and constrained refinement
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.0636P)^2]$, where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\rm max}$	0.012
$\Delta\rho_{\rm max}$, $\Delta\rho_{\rm min}$ (e Å^{-3})	0.66, −0.39

Computer programs used: *CCD*, *CrysAlis* (Kuma Diffraction, 1999*b*), *SHELXS*97, *SHELXL*97, *SHELXTL* (Sheldrick, 2008), *PyMOL* (DeLano, 2002).

2. Materials and methods

2.1. Data collection, structure solution and refinement

The salt (1) was prepared according to a previously described procedure (Szafran *et al.*, 2001). Co-crystals of MPB with (1) were prepared by mixing 1 equiv each of MPB and *N*-methylpiperidine betaine hexafluorosilicate (1) in ethanol solution, followed by solvent evaporation under reduced pressure. Crystals of (2) suitable for single-crystal X-ray analysis were obtained by slow evaporation of an ethanol solution (m.p. 483–485 K).

A single crystal cut to the dimensions 0.2 × 0.3 × 0.3 mm was used for the X-ray measurements. The intensity data were

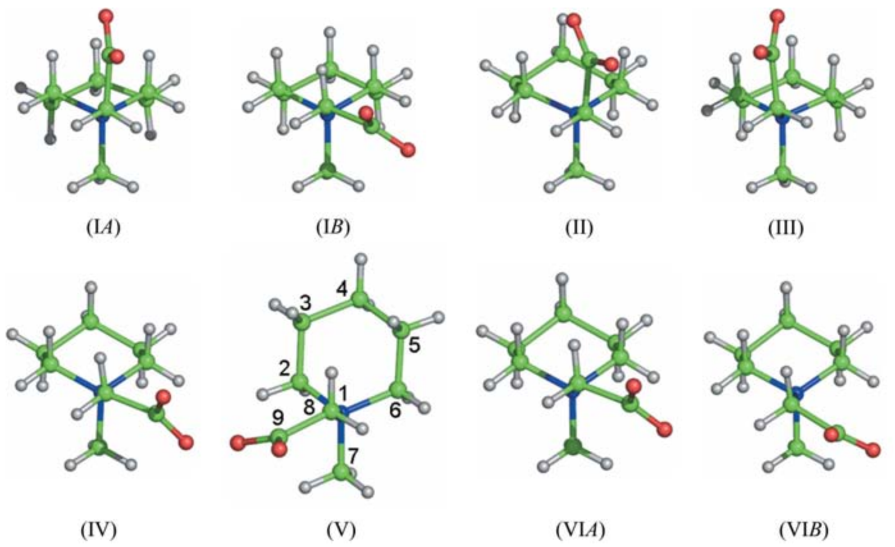


Figure 2
Eight distinct conformations of the *N*-methylpiperidine betaine moiety found in (2). The CH_2COOH/CH_2COO^- group occupies the equatorial position in all these conformers except in molecule (V), where it is axial. Molecules (I) and (VI) exist in two distinct conformations: (I*A*)/(I*B*) and (VI*A*)/(VI*B*), respectively. The numbering scheme of the N and C atoms is shown for molecule (V).

collected at 100 K using a KUMA CCD detector (Kuma Diffraction, 1999*a*) and graphite-monochromated Mo $K\alpha$ radiation generated from a sealed tube operated at 50 kV and 40 mA. 782 ω scans were collected in four orientations of the crystal. Each scan covered 0.75° rotation recorded in 22 s. The images were indexed, integrated and scaled using the *CrysAlis* data reduction package (Kuma Diffraction, 1999*b*). The final dataset consisted of 27 619 observations which were reduced to 13 415 unique data ($R_{\rm int}$ = 0.029, redundancy 2.06).

The structure was solved by direct methods using *SHELXS* (Sheldrick, 2008) and refined by least-squares minimization of $\Sigma[w(F_o^2 - F_c^2)^2]$ (Sheldrick, 2008) for all reflections with $2\theta \leq 55°$. Except for the H atoms of one molecule of water of hydration, which were not located, all atoms were included in the refinement, with anisotropic (non-H atoms) and isotropic (H atoms) displacement parameters. All H atoms were treated as riding atoms at calculated positions, except the H atoms of the carboxylic groups and two water molecules, whose coordinates were included in the refinement. When not fixed by symmetry, the coordinates of the H atoms of the carboxylic groups as well as of an ordered water molecule were refined freely, while for the second water molecule, where one of the H atoms is disordered over two positions, the three O—H distances were restrained. The H atoms for the third water molecule, whose O atom is disordered in two positions, could not be modeled. The refinement included all reflections and converged with wR_2 = 0.1383 [R = 0.0557 for $F \geq 4\sigma(F)$ data; Table 1[1]]. Molecular graphics were generated using *SHELXTL* (Sheldrick, 2008) and *PyMOL* (DeLano, 2002).

3. Results and discussion

The previously reported *N*-methylpiperidine betaine hexafluorosilicate salt (1) (Szafran *et al.*, 2001) has a 2:1 cation:anion stoichiometry, fully protonated betaine molecules and an ordered $P2_1/c$ crystal structure with two betaine cations and one SiF_6^{2-} anion in the asymmetric unit. The situation in the present crystal structure is very different. The symmetry of the present co-crystal is low ($P\bar{1}$) and the asymmetric unit is huge, comprising six betaine units, one-and-a-half of the SiF_6^{2-} anion and three water molecules (Z' = 3, Z'' = 10.5, Fig. 1). In terms of formal stoichiometry, in the present co-crystal (2), the zwitterion, cation and anion form a ratio of 3:3:1.5. Thus, the betaine molecules are hemiprotonated and form dimeric cations *via* very strong $O—H\cdots O^-$ hydrogen bonds. Some of the dimers are centrosymmetric, some are not. Some of the betaine units display disorder, but each case is different. One of the SiF_6^{2-} anions is ordered while possessing exact crystallographic symmetry. The other one is disordered in a general position. Of the three water molecules included in the asymmetric unit, one is fully ordered, one has an H atom disordered in two positions and the third one occupies two alternative positions with unequal populations.

3.1. The betaine moieties

3.1.1. Conformation. The six *N*-methylpiperidine betaine (MPB) molecules in the asymmetric unit are referred to as (I)–(VI) (Fig. 2). In all these molecules the piperidine ring assumes a chair conformation with the CH_2COOH/CH_2COO^- substituent occupying the equatorial position, except in molecule (V) where it is axial. Coexistence of equatorial and axial piperidine betaine moieties was also found in the previously reported 2:1 complex with hexafluorosilicic acid (Szafran *et al.*, 2001), and this rather unusual tendency of MPB to place the bulky carboxymethyl substituent in an axial orientation was confirmed in the 1:1 hydrochloride salt (Dega-Szafran *et al.*, 2003). The endocyclic bond angles of the piperidine rings are close to the tetrahedral value [107.3 (4)–113.9 (2)°, Table 2], and the average endocyclic torsion angle is 55.3 (4)° (Table 3). There are two different orientations of the CH_2COOH/CH_2COO^- substituent with respect to the piperidine ring. In the case of the major conformer of betaine (I), and in molecules (II) and (III) the disposition of this group around the N1—C8 exocyclic bond is staggered with C9 sitting between the C2 and C6 atoms of the piperidine ring (*gauche*–*gauche*). The carbonyl O2 atom accepts intramolecular $C—H\cdots O$ hydrogen bonds from the C2—H and C6—H donors in these cases (Table 4). In the minor conformation of (I), and in

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[1] Supplementary data for this paper are available from the IUCr electronic archives (Reference: RY5019). Services for accessing these data are described at the back of the journal.

Table 2
Bond lengths (Å) and angles (°) of the *N*-methylpiperidine betaine moieties represented by roman codes at the head of each column.

In cases of disorder [molecules (I) and (VI)], the values for both alternatives are listed (*A* – upper number, *B* – lower number).

	(I)	(II)	(III)	(IV)	(V)	(VI)
C9—O1	1.291 (3)	1.303 (3)	1.276 (2)	1.302 (3)	1.272 (3)	1.326 (6) 1.287 (6)
C9—O2	1.223 (3)	1.207 (3)	1.232 (3)	1.220 (3)	1.241 (3)	1.186 (9) 1.232 (9)
O1—H1	1.229 (3)	0.98 (4)	1.28 (4)	1.18 (4)	1.51 (3)	1.45 (6) 1.01 (6)
N1—C8	1.499 (3)	1.510 (3)	1.504 (3)	1.503 (3)	1.505 (3)	1.578 (10) 1.481 (11)
N1—C7	1.514 (3)	1.503 (3)	1.511 (3)	1.506 (3)	1.487 (3)	1.500 (3)
N1—C6	1.516 (3)	1.512 (3)	1.520 (3)	1.515 (3)	1.515 (3)	1.514 (3)
N1—C2	1.517 (3)	1.521 (3)	1.521 (3)	1.530 (3)	1.513 (3)	1.519 (3)
C2—C3	1.515 (3)	1.517 (3)	1.519 (3)	1.512 (3)	1.464 (5)	1.498 (3)
C3—C4	1.486 (4) 1.463 (4)	1.525 (3)	1.518 (4)	1.525 (3)	1.540 (4)	1.519 (3)
C4—C5	1.508 (4) 1.504 (5)	1.526 (3)	1.527 (3)	1.522 (3)	1.551 (5)	1.527 (4)
C5—C6	1.553 (4) 1.527 (4)	1.512 (3)	1.521 (3)	1.516 (3)	1.468 (5)	1.508 (4)
C8—C9	1.518 (3)	1.525 (3)	1.526 (3)	1.521 (3)	1.519 (3)	1.495 (11) 1.551 (12)
C7—N1—C8	106.23 (19)	106.09 (16)	105.94 (16)	110.62 (16)	108.8 (2)	118.1 (3) 101.4 (3)
C6—N1—C8	111.04 (19)	109.18 (16)	110.52 (17)	108.75 (16)	107.82 (18)	101.2 (3) 118.8 (3)
C6—N1—C7	109.3 (2)	110.32 (16)	109.71 (16)	112.61 (17)	108.0 (2)	111.67 (18)
C2—N1—C8	110.72 (19)	110.40 (16)	109.91 (15)	106.21 (16)	114.42 (19)	105.5 (4) 104.7 (4)
C2—N1—C7	109.0 (2)	109.15 (16)	109.99 (17)	109.27 (17)	108.9 (2)	110.03 (19)
C2—N1—C6	110.4 (2)	111.57 (16)	110.66 (16)	109.17 (16)	108.8 (2)	109.74 (18)
N1—C2—C3	112.6 (2)	112.73 (17)	112.05 (17)	112.50 (18)	113.9 (2)	112.61 (19)
C2—C3—C4	111.7 (3) 111.5 (4)	111.73 (18)	111.2 (2)	110.90 (19)	111.7 (3)	111.1 (2)
C3—C4—C5	112.3 (4) 107.3 (4)	109.96 (18)	110.9 (2)	109.84 (18)	107.4 (3)	108.2 (2)
C4—C5—C6	112.6 (4) 119.4 (4)	110.62 (19)	111.20 (19)	110.81 (19)	110.7 (3)	111.9 (2)
N1—C6—C5	107.0 (3) 104.5 (3)	113.10 (17)	112.21 (19)	113.15 (18)	113.4 (2)	112.64 (19)
N1—C8—C9	118.2 (2)	116.53 (18)	117.86 (17)	116.04 (18)	117.63 (18)	114.6 (7) 117.0 (7)
O1—C9—O2	125.5 (2)	125.7 (2)	125.4 (2)	124.9 (2)	125.4 (2)	122.8 (6) 128.1 (6)
O1—C9—C8	110.2 (2)	109.19 (19)	110.68 (18)	110.84 (19)	119.0 (2)	108.0 (5) 111.5 (6)
O2—C9—C8	124.3 (2)	125.1 (2)	123.93 (19)	124.3 (2)	115.5 (2)	129.1 (7) 120.3 (7)
C9—O1—H1	115.99 (17)	109 (2)	113.1 (15)	114.3 (16)	–	– 115 (3)

the betaine molecules (IV)–(VI), the orientation around the N1—C8 bond is also staggered, but the C9 substituent is *trans* with respect to one of the piperidine methylene groups (C2/C6) and *gauche* with respect to the methyl substituent (C7). The carbonyl O2 atom in these cases accepts intramolecular C—H···O hydrogen bonds from the C2—H/C6—H and C7—H donors. The N1—C8—C9—O1—O2 atoms in each betaine molecule are roughly coplanar, the mean deviations being 0.022–0.101 Å. This is equivalent to the carboxylate group being rotated 6–23° from the N1—C8—C9 plane (Table 3).

3.1.2. Disorder. In molecule (I) the piperidine ring and the methyl group are disordered in two positions with almost equal populations (55:45 occupancy), while in molecule (VI) the CH_2COOH/CH_2COO^- substituent is disordered in two conformations (50:50 occupancy). The betaine molecules (II)–(V) are ordered. The disorder in molecule (I) is quite unusual in that the smaller CH_2COOH/CH_2COO^- group is ordered, while the bulkier *N*-methylpiperidine moiety is disordered. In both conformers the methyl group occupies the axial position with different carboxylic/carboxylate rotamers (Figs. 2 and 3*a*). In betaine (VI) the situation is opposite: the *N*-methylpiperidine system has a single conformation, while the acetyl substituent has two alternative conformations (Fig. 2 and 3*d*). The equally populated alternative conformers are chemically different, one is protonated (*B*) while the other one is negatively charged (*A*). This requires the formation of two carboxyl···carboxylate dimers, one on each side of the inversion center. The *N*-methylpiperidine moiety of betaine (VI) seems, however, to be firmly locked in the crystal structure. The structural variability is achieved in an unusual fashion, by way of deformation of the covalent structure at the N1 atom. The two alternative C8 positions arise by splitting the ideal geometry by 19.6 (4)° (C8*A*—N1—C8*B*), symmetrically with respect to the C2—N1 bond. This results in approximately equal narrowing of the C2—N1—C8*A*/*B* angles and to very significant deformations of the remaining C—N1—C8*A*/*B* angles (increase/decrease by about 9°). The cause of this deformation, however, is not understood. It is possible, as suggested by Fig. 1, that the disorder of molecules (I) and (VI) is correlated.

3.1.3. The hemiprotonated betaine dimers. Formally, half of the betaine molecules are protonated with the acidic proton connecting them into $O-H\cdots O^-$ dimers. Betaines (I) and (VI) are paired into dimers with their own centrosymmetric copies. The dimerization scheme of the remaining molecules is (II)···(V) and (III)···(IV). In dimer (I)···(I′) the carboxylic H atom lies on the inversion center (Fig. 3*a*). The carboxylic H atom is bonded to O1 of molecule (II) in the (II)···(V) dimer, which involves betaine moieties with equatorial (II) and axial (V) CH_2COOH/CH_2COO^- substituents (Fig. 3*b*). The H atom is placed close to the center of the O···O distance within the (III)···(IV) hydrogen-bonded pair, with rather similar

Table 3
Torsion angles (°) of the *N*-methylpiperidine betaine moieties represented by roman codes at the head of each column.

In cases of disorder [molecules (I) and (VI)], the values for both alternatives are listed (*A* – upper number, *B* – lower number).

	(I)	(II)	(III)	(IV)	(V)	(VI)
C7—N1—C2—C3	−61.7 (3)	−71.9 (2)	−66.9 (2)	−69.2 (2)	−170.6 (3)	69.4 (2)
C8—N1—C2—C3	−178.2 (2)	171.84 (17)	176.84 (19)	171.44 (17)	67.4 (3)	−162.2 (3) 177.6 (3)
C6—N1—C2—C3	58.4 (3)	50.3 (2)	54.5 (2)	54.3 (2)	−53.2 (3)	−53.9 (2)
N1—C2—C3—C4	−52.9 (4) 59.2 (4)	−53.4 (2)	−55.9 (3)	−57.0 (2)	56.8 (4)	58.4 (3)
C2—C3—C4—C5	50.5 (5) −51.2 (5)	56.4 (2)	55.8 (3)	56.9 (2)	−56.5 (5)	−58.0 (3)
C3—C4—C5—C6	−54.7 (6) 55.1 (7)	−57.3 (2)	−55.3 (3)	−56.3 (2)	57.3 (5)	56.9 (3)
C4—C5—C6—N1	57.9 (5) −57.4 (5)	55.9 (2)	54.9 (3)	56.5 (2)	−58.7 (4)	−55.6 (3)
C7—N1—C6—C5	61.1 (3) −64.7 (3)	69.6 (2)	67.5 (2)	67.4 (2)	172.3 (3)	−70.0 (3)
C8—N1—C6—C5	178.0 (3) 175.4 (3)	−174.20 (18)	−176.05 (18)	−169.64 (17)	−70.2 (3)	163.4 (4) 172.6 (5)
C2—N1—C6—C5	−58.8 (3) 56.1 (3)	−51.9 (2)	−54.1 (2)	−54.2 (2)	54.3 (3)	52.3 (2)
C7—N1—C8—C9	−177.4 (2)	177.07 (18)	−175.09 (18)	68.7 (2)	−57.9 (3)	−62.3 (6) −64.5 (5)
C6—N1—C8—C9	63.9 (3)	58.2 (2)	66.1 (2)	−55.5 (2)	−174.7 (2)	59.9 (6) 58.2 (6)
C2—N1—C8—C9	−59.2 (3)	−64.8 (2)	−56.3 (2)	−172.87 (18)	64.1 (3)	174.3 (5) −178.9 (4)
N1—C8—C9—O2	−5.5 (4)	21.0 (3)	−9.4 (3)	−22.9 (3)	159.8 (2)	10.1 (10) 6.2 (8)
N1—C8—C9—O1	175.3 (2)	−161.02 (18)	171.37 (18)	158.65 (18)	−23.4 (3)	−168.4 (5) −172.1 (4)

O1$\cdots$H distances (1.18/1.28 Å; Fig. 3*c*). This dimer closely mimics the symmetric dimer (I)$\cdots$(I′) despite the fact that the interacting betaine molecules contain different CH$_2$COOH/CH$_2$COO$^-$ rotamers. In dimer (VI)$\cdots$(VI′), the link involves two equally populated acetyl$\cdots$acetate conformers (Fig. 3*d*).

The COO$\cdots$H$\cdots$OOC atoms in the betaine dimer (I)$\cdots$(I′) lie in one plane with the O2 atoms being *transoidal* across the O1$\cdots$H$\cdots$O1′ hydrogen bond by virtue of symmetry. The COO planes of the individual betaines in the (II)$\cdots$(V) dimer form an angle of 86°. This nearly perpendicular arrangement is achieved primarily by a rotation about the hydrogen bond O$\cdots$O axis, the pseudotorsion O—O$\cdots$(H)$\cdots$O—O angle being −93°. The COO/COO interplanar angle in the (III)$\cdots$(IV) pair is 22° and it is again the effect of a pseudotorsional deformation about the hydrogen-bond axis (−160°). The disposition of the hydrogen-bonded alternatives of the COO group of molecule (VI) (*A* and *B*) is nearly identical as in (III)$\cdots$(IV), the corresponding angles being 23 and −160°.

3.1.4. The short O$\cdots$H$\cdots$O hydrogen bonds. With one acidic proton shared by the two COO$^-$ groups within the betaine dimers, the homoconjugated (—COO$^-\cdots$H$^+\cdots{}^-$OOC–) bridge has a formal unit of negative charge. The O$\cdots$O distances between the hydrogen-bonded COO groups range from 2.452 (5) to 2.479 (3) Å with the O$\cdots$H$\cdots$O angles nearly linear [171 (3)–180.0°; Table 4]. These parameters define the O$\cdots$O hydrogen bonds connecting the betaine units as very strong. Among those O$\cdots$O distances, three are nearly identical and correspond to the coplanar arrangements of the hydrogen-bonded COO groups. The dimer with perpendicular COO groups (II)$\cdots$(V) has the O$\cdots$O distance slightly longer and the most pronounced O—H/O$\cdots$H difference. In spite of the strong character of the O$\cdots$O hydrogen bonds, the location of the proton clearly defines the donor and acceptor groups. The only exception is the centrosymmetric (I)$\cdots$(I′) dimer, but here the centrosymmetric position of the proton may be a crystallographic artifact. This is supported by the values of the refined isotropic displacement parameters of the acidic H atoms, which are 0.15 (3), 0.08 (1), 0.08 (1) and 0.05 (2) Å^2 for the dimers (I)$\cdots$(I′), (II)$\cdots$(V), (III)$\cdots$(IV) and (VI)$\cdots$(VI′), respectively. The geometries of all the COO groups are generally consistent with the hydrogen-bonding schemes. In each hydrogen-bonded pair, the two C9—O1 distances are in good agreement with their donor/acceptor character, *i.e.* show larger differences when the proton is shifted further away from the center. The only exception is found in the disordered (VI)$\cdots$(VI′) dimer where the C9—O1 distance of the donor is shorter than that of the acceptor.

3.2. The SiF$_6^{2-}$ anions

One of the octahedral SiF$_6^{2-}$ ions (*A*) is ordered, while the other one (*B*) is disordered (Fig. 4). The ordered SiF$_6^{2-}$ ion occupies the special position at the inversion center. The Si—F bond lengths of this anion range from 1.6808 (14) to 1.6951 (13) Å with F—Si—F angles of 89.44 (7)–90.56 (7) and 180.0°. The second SiF$_6^{2-}$ ion is in a general position and is rotationally disordered along the F21—Si2—F26 axis. Two sets of equatorial F atoms with 0.50:0.50 occupancy are roughly perpendicular to the axial bonds that connect the three ordered atoms. The Si—F bond lengths and F—Si—F angles are, respectively, 1.620 (3)–1.740 (4) Å and 82.75 (19)–96.74 (19), 173.4 (3)–179.34 (9)°. While the geometrical parameters, especially the Si—F distances, of the hexafluorosilicate ion may have appreciable spread, it is obvious that the geometry of the SiF$_6^{2-}$ (*B*) anion is affected by disorder. The Si—F distances and the F—Si—F angles of the SiF$_6^{2-}$ ion in the 2:1 salt of MPB are 1.6699 (7)–1.7181 (7) Å and 89.19 (4)–90.97 (4), 178.70 (4)–179.29 (4)°, respectively (Szafran *et al.*, 2001). The mean geometries of 38 ordered SiF$_6^{2-}$ entries with an *R* factor $\leq$ 0.075 found in the Cambridge Structural

Table 4
Geometry of the hydrogen bonds (Å and °) observed in (2) (Spek, 1990).

The C—H distances are normalized in the cases where the H atoms were generated at calculated positions in the refinement (Desiraju & Steiner, 1999).

D—H···*A*	*D*—H	H—*A*	*D*···*A*	*D*—H···*A*
O—H···O$^-$ in betaine dimers				
O11—H11···O11^{i}	1.229 (3)	1.229 (3)	2.458 (3)	180.0
O21—H21···O51	0.98 (4)	1.51 (3)	2.479 (3)	171 (3)
O41—H41···O31	1.18 (4)	1.28 (4)	2.458 (3)	175 (2)
O61*B*—H61···O61*A*^{ii}†	1.01 (6)	1.45 (6)	2.452 (5)	176 (7)
O$_{water}$—H···O/F				
O1—H1*A*···O32^{iii}	0.79 (5)	2.08 (5)	2.851 (3)	166 (5)
O1—H1*B*···O52	0.91 (5)	1.95 (5)	2.841 (3)	166 (4)
O2—H2*A*···O52	0.83 (4)	1.90 (3)	2.726 (3)	173 (3)
O2—H2*B*···O3*A*†	0.84 (5)	1.59 (5)	2.401 (6)	162 (7)
O2—H2*C*···F24*A*†	0.82 (2)	1.71 (2)	2.526 (4)	172 (4)
C—H···O intra				
C12—H12*B*···O12	1.08	2.35	3.066 (4)	122
C16—H16*B*···O12	1.08	2.39	3.075 (4)	120
C22—H22*B*···O22	1.08	2.21	2.991 (3)	127
C26—H26*A*···O22	1.08	2.43	3.143 (3)	123
C32—H32*B*···O32	1.08	2.28	3.033 (3)	125
C36—H36*B*···O32	1.08	2.34	3.077 (3)	124
C46—H46*A*···O42	1.08	2.41	3.079 (3)	118
C47—H47*A*···O42	1.08	2.31	3.013 (3)	121
C52—H52*B*···O51	1.08	2.19	2.944 (4)	125
C57—H57*C*···O51	1.08	2.43	3.094 (4)	118
C66—H66*A*···O62*A*†	1.08	2.30	2.970 (9)	118
C67—H67*A*···O62*A*†	1.08	2.50	3.163 (8)	119
C66—H66*A*···O62*B*†	1.08	2.47	3.098 (10)	116
C67—H67*A*···O62*B*†	1.08	2.08	2.823 (8)	123
C—H···O inter				
C23—H23*B*···O31^{iv}	1.08	2.47	3.549 (3)	175
C26—H26*B*···O32^{iii}	1.08	2.34	3.348 (3)	154
C28—H28*A*···O41^{iii}	1.08	2.41	3.444 (3)	159
C37—H37*B*···O21^{v}	1.08	2.40	3.407 (3)	155
C44—H44*A*···O22	1.08	2.46	3.437 (3)	150
C45—H45*A*···O1	1.08	2.33	3.296 (4)	148
C55—H55*A*···O11^{vi}	1.08	2.38	3.410 (4)	158
C66—H66*B*···O12^{vii}	1.08	2.29	3.293 (3)	153
C68*A*—H66*B*···O12^{vii}	1.08	2.34	3.326 (11)	150
C35—H35*B*···O3*A*^{viii}†	1.08	2.21	3.094 (7)	137
C54—H54*A*···O61*A*^{ii}†	1.08	2.36	3.103 (6)	124
C58—H58*A*···O62*A*†	1.08	2.15	3.141 (8)	150
C—H···F inter				
C17—H17*C*···F26	1.08	2.23	3.267 (3)	159
C28—H28*B*···F12^{ix}	1.08	2.21	3.262 (3)	163
C32—H32*A*···F12^{viii}	1.08	2.19	3.124 (3)	143
C38—H38*B*···F13^{ix}	1.08	2.13	3.138 (3)	154
C42—H42*B*···F13^{x}	1.08	2.27	3.278 (3)	155
C42—H42*A*···F26	1.08	2.26	3.251 (4)	152
C48—H48*A*···F21	1.08	2.19	3.206 (3)	155
C48—H48*B*···F11^{x}	1.08	2.16	3.140 (3)	150
C56—H56*A*···F26	1.08	2.05	3.099 (4)	163
C18—H18*B*···F23*A*†	1.08	2.18	3.215 (7)	160
C36—H36*A*···F22*A*^{v}†	1.08	2.15	3.176 (6)	156
C36—H36*A*···F22*B*^{v}†	1.08	2.30	3.244 (5)	145
C38—H38*A*···F22*B*^{v}†	1.08	2.31	3.276 (5)	147
C57—H57*A*···F25*A*†	1.08	2.12	3.143 (7)	157
C58—H58*B*···F25*B*†	1.08	2.11	3.114 (5)	154
C62—H62*B*···F23*A*^{iii}†	1.08	2.20	3.187 (9)	150
C67—H67*B*···F23*B*^{iii}†	1.08	2.33	3.276 (8)	145
C68*B*—H68*D*···F23*A*^{iii}†	1.08	2.11	3.129 (13)	155
C68*B*—H68*D*···F23*B*^{iii}†	1.08	1.98	3.026 (13)	160

Symmetry codes: (i) $1-x, -y, 1-z$; (ii) $2-x, 1-y, 1-z$; (iii) $x, 1+y, z$; (iv) $1-x, 1-y, -z$; (v) $-1+x, -1+y, z$; (vi) $2-x, -y, 1-z$; (vii) $1-x, 1-y, 1-z$; (viii) $x, -1+y, z$; (ix) $1+x, y, z$; (x) $1+x, -1+y, z$. † Contacts involving disordered atoms.

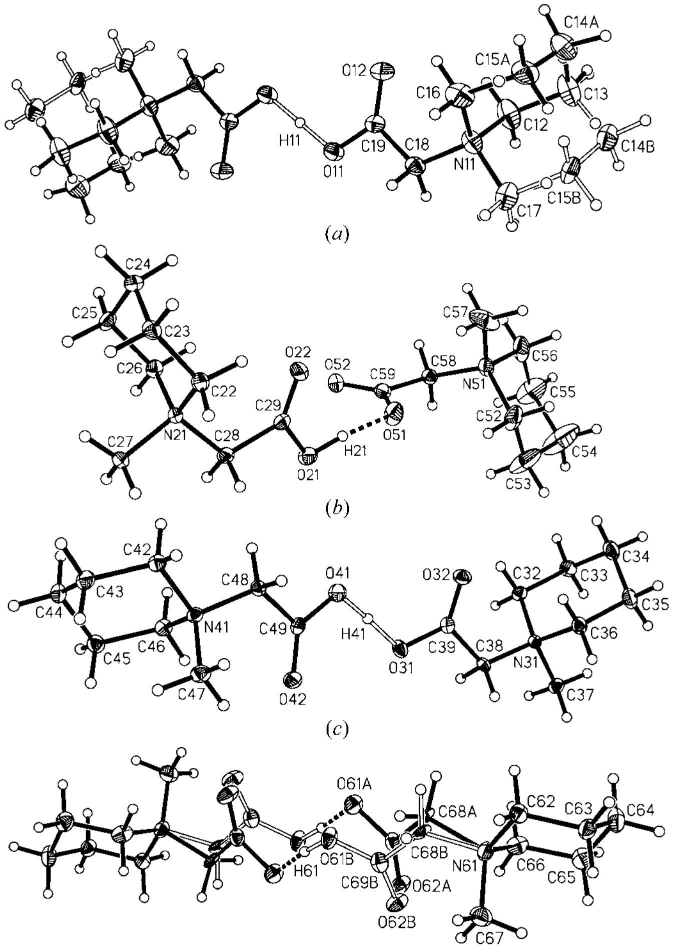

Figure 3
ORTEP plots of the hydrogen-bonded dimers of the hemiprotonated *N*-methylpiperidine betaine molecules with atom numbering and with displacement ellipsoids of non-H atoms drawn at the 50% probability level: (*a*) (I)···(I′); (*b*) (II)···(V); (*c*) (III)···(IV); (*d*) (VI)···(VI′). The betaine molecules in the hydrogen-bonded pairs (I)···(I′) and (VI)···(VI′) are inversion-related while they are symmetry-independent in (*b*) and (*c*). The labels *A*/*B* denote the two alternatives, which are drawn with heavy/open lines. In the dimers (I)···(I′) and (III)···(IV), where the acidic proton is located centrally or nearly centrally in the O···H···O hydrogen bonds, both H···O components are shown with open lines.

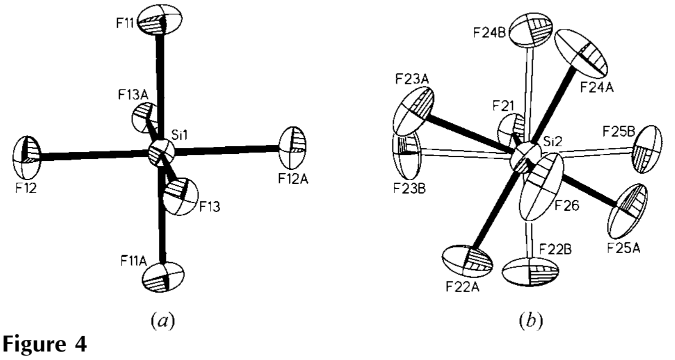

Figure 4
The (*a*) centrosymmetric and (*b*) general-position hexafluorosilicate anions. The general-position anion is viewed along the F26—Si2—F21 axis, around which it is disordered. The two sets of equatorial Si—F bonds are drawn with full and open lines representing the major (*A*) and minor (*B*) sets, respectively. The atomic displacement ellipsoids are at the 50% probability level.

Database (CSD Version 5.23; Allen, 2002) are 1.677 (20) Å and 90.0 (12), 179.1 (11)°.

3.3. The water molecules

There are three water molecules in the asymmetric unit, whose presence in the crystal was not expected. One of the water molecules (1) is fully ordered, another one (2) has one of the H atoms disordered in two positions (50:50 occupancy), while in the case of the third water molecule (3) the O atom is disordered in two positions (59:41 occupancy). The extent of disorder of these water molecules is consistent with the number and character of their hydrogen-bonding partners (see below).

3.4. Crystal packing

The asymmetric unit of (2) is shown in Fig. 1. The hydrogen-bonded betaine dimers (II)···(V) and (III)···(IV) are cross-linked by O—H···O hydrogen bonds involving the O—H donors of the ordered water molecule (1) and the carbonyl acceptors of the betaine molecules (III) and (V) (Table 4). The disordered H atom of the second water molecule (2) is alternately involved in hydrogen-bond links to the major component of the third water (3*a*) and to one of the F atoms of the disordered SiF_6^{2-} ion, while the ordered H atom of the second water molecule (2) is hydrogen-bonded to the carbonyl O atom of molecule (V). A layer of various betaine dimers and $SiF_6{}^{2-}$ units parallel to the crystallographic ($\bar{1}$13) plane is shown in Fig. 5. All the dimeric cations and the SiF_6^{2-} anions are interconnected by a profusion of C—H···O/O$^-$ and C—H···F hydrogen bonds (Desiraju & Steiner, 1999; Table 4). It is interesting to note that each component is disordered and has multiple copies in the crystal structure. The effect of factors such as packing complexities, interaction frustration, better interactions, equi-energetic conformations, structural modulations, pseudo-symmetry and crystallization kinetics including the crystallization of metastable or fossil forms among others are suggested to be responsible for high Z' structures (Anderson *et al.*, 2006; Anderson & Steed, 2007; Desiraju, 2007). In contrast to the O—H···F interactions dominating the crystal lattice formation in the salt (1) (2:1 salt), the driving force for the co-crystal formation of (2) is the O—H···O$^-$ hydrogen bonds. From these two structures it is evident that the outcome, salt or co-crystal, depends on which type of interactions become dominant. A similar situation has been reported in another study, where modulation of hydrogen-bonding capacity *via* protonation and deprotonation of carboxylic groups in organometallic compounds was shown to lead to a variety of hydrogen-bonding networks in the crystals (Braga *et al.*, 2000).

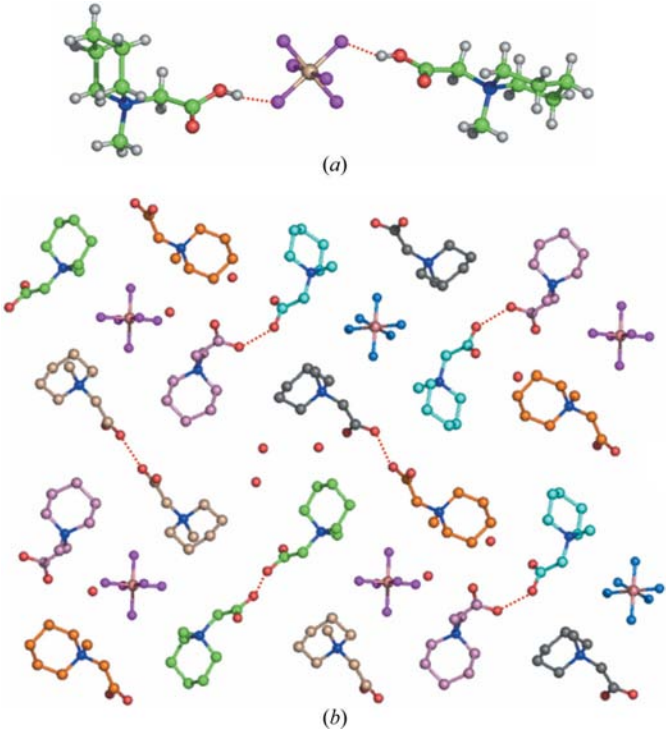

Figure 5
(*a*) Hydrogen-bonding interactions in (1) (salt; Szafran *et al.*, 2001). (*b*) A layer of various betaine dimers, SiF_6^{2-} anions and water molecules parallel to the crystallographic ($\bar{1}$13) plane in (2) (co-crystal; this work). Molecules (I)–(VI) are shown with wheat, cyan, gray, orange, pink and green C atoms, respectively, while the ordered (*A*) and the disordered (*B*) SiF_6^{2-} anions are shown with blue and magenta F atoms, respectively. To simplify the figure, for the disordered moieties [(I), (VI), $SiF_6(B)$, water, (3)], only one alternative is shown (the major one in case of unequal occupancies).

4. Conclusions

The co-crystal structure of *N*-methylpiperidine betaine and *N*-methylpiperidine betaine hexafluorosilicate exhibits several interesting features:

(1) It is an example of a rationally designed salt co-crystal, in which both the co-crystal former and the salt former are derived from the same chemical source.

(2) It has high Z' and Z'' values ($Z' = 3$, $Z'' = 10.5$).

(3) It contains a large disordered component (~50%) resulting in the occurrence of multiple (eight) conformers of the betaine unit, one of which has the bulky $—CH_2COO^-$ group in the axial position.

(4) In spite of the disorder and conformational variability, all the betaine units are paired into hemiprotonated cations with very short intermolecular O···O hydrogen bonds; these hydrogen bonds are the strongest interactions governing the organization of the crystal structure.

(5) In this salt co-crystal, there are no direct O—H···F interactions between the betaine and SiF_6^{2-} components; instead, there is a profusion of C—H···F hydrogen bonds.

In a more general aspect, this study underlies the notion that co-crystals of salts can be designed by utilizing differences in cation···anion and cation/anion···co-crystal hydrogen-bonding strengths. In addition, this study is a prompt to re-examine the known structures of hemisalts in the present context to arrive at a more robust set of rules that govern salt co-crystal formation. Currently, we are investigating co-crystal forming abilities of other betaines and betaine salts with carboxylic acids.

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