



Synthesis, crystal structure and Hirshfeld surface analysis of sulfamethoxazolium methylsulfate monohydrate

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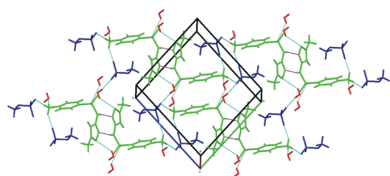
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The molecular salt sulfamethoxazolium {or 4-[(5-methyl-1,2-oxazol-3-yl)sulfamoyl]anilinium methyl sulfate monohydrate}, $C_{10}H_{12}N_3O_3S^+ \cdot CH_3O_4S^- \cdot H_2O$, was prepared by the reaction of sulfamethoxazole and H_2SO_4 in methanol and crystallized from methanol–ether–water. Protonation takes place at the nitrogen atom of the primary amino group. In the crystal, $N-H \cdots O$ hydrogen bonds (water and methylsulfate anion) and intermolecular $N-H \cdots N$ interactions involving the sulfonamide and isoxazole nitrogen atoms, link the components into a tri-dimensional network, additional cohesion being provided by face-to-face $\pi-\pi$ interactions between the phenyl rings of adjacent molecules. A Hirshfeld surface analysis was used to verify the contributions of the different intermolecular interactions, showing that the three most important contributions for the crystal packing are from $H \cdots O$ (54.1%), $H \cdots H$ (29.2%) and $H \cdots N$ (5.0%) interactions.

1. Chemical context

Sulfamethoxazole {SMX or 4-[(5-methylisoxazol-3-yl)amino-sulfonyl]aniline} is a widely employed sulfa drug that is effective against Gram-negative and Gram-positive bacteria, and active against some protozoans and fungi (Manyando *et al.*, 2013). Being structurally similar to *para*-aminobenzoic acid (PABA), it acts as a dihydrofolate reductase inhibitor (Cushion & Walzer, 2009); it also competitively inhibits the enzyme dihydropteroate synthase, preventing the biosynthesis of dihydropteroic acid, a precursor of folic acid that is required for bacterial growth (Khalil *et al.*, 2003).

SMX has both low solubility and permeability; therefore, it is a Class IV drug in the Biopharmaceutical Classification System (BCS). The poor solubility of SMX has elicited continuous interest in finding alternative forms of the drug with improved pharmacological profiles. As a result, several polymorphs (Price *et al.*, 2005), hydrates (Alsubaie *et al.*, 2018; Takasuka & Nakai, 2001), metal complexes (Habla *et al.*, 2021), co-crystals [including that with trimethoprim (Bettinetti & Giordano, 1988), with which it forms a useful pharmaceutical association], and salts (de Moura Oliveira *et al.*, 2019) of SMX have been reported. In connection with our research program on the characterization of new solid phases derived from poorly soluble active pharmaceutical ingredients, herein we report on the crystal structure and the supramolecular packing pattern of the acid methylsulfate monohydrate salt of SMX ($SMXHMeSO_4 \cdot H_2O$). Acid methylsulfate monohydrate



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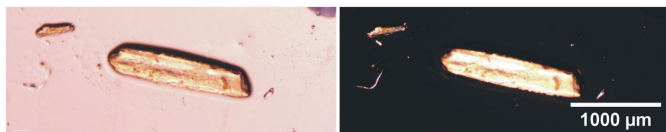
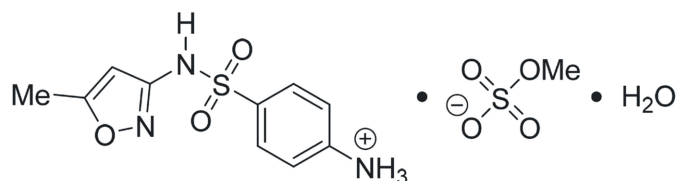


Figure 1
Microscopic view of a crystal of the title compound under white (left) and polarized (right) light.

salts of other active pharmaceutical ingredients have been reported (Gutiérrez *et al.*, 2020); among them is neostigmine methylsulfate, a cholinesterase inhibitor used in the treatment of myasthenia gravis and to reverse the effects of muscle relaxants (Papich, 2021) and pralidoxime methylsulfate, a widely agent used to treat organophosphate poisoning (Thompson *et al.*, 1987).



2. Structural commentary

The crystals of the title monohydrate salt $\text{SMXHMESo}_4 \cdot \text{H}_2\text{O}$, (I), appear as small white rods under white light that display birefringence under polarized light (Fig. 1) and have a melting point 374.5–375.5 K. The title compound crystallizes in the triclinic space group $P\bar{1}$ with one of each component (sulfamethoxazolium cation, methylsulfate anion, and water) in the asymmetric unit (Fig. 2).

The sulfamethoxazolium cation, which undergoes protonation at the primary amino nitrogen, is L-shaped. The C6–C5–S8–N11 torsion angle is 96.4 (2)°, while the dihe-

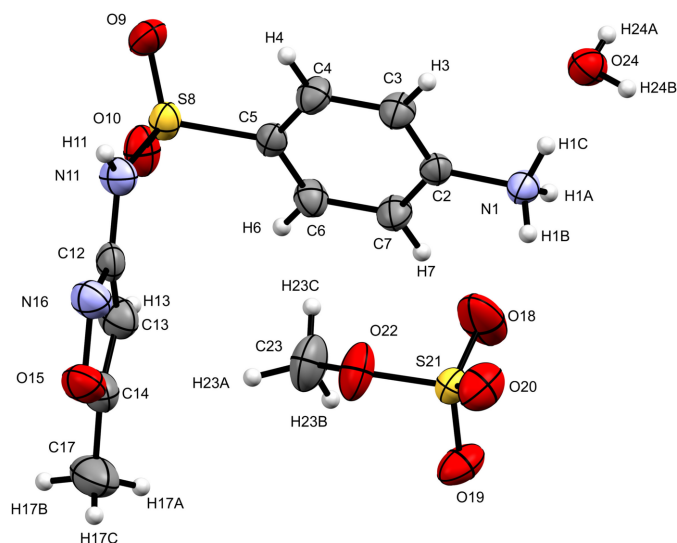


Figure 2
Crystal structure of title compound with the atom-labeling scheme (displacement ellipsoids are drawn at the 50% probability level).

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

$D-H \cdots A$	$D-H$	$H \cdots A$	$D \cdots A$	$D-H \cdots A$
C3–H3···O24	0.93	2.65	3.353 (3)	133
C4–H4···O24 ⁱ	0.93	2.54	3.469 (3)	177
C13–H13···O10	0.93	2.54	3.023 (3)	113
N1–H1A···O19 ⁱⁱ	0.89	1.91	2.800 (3)	175
N1–H1A···S21 ⁱⁱⁱ	0.89	2.94	3.774 (2)	156
N1–H1B···O18	0.89	1.95	2.761 (3)	152
N1–H1C···O24	0.89	1.89	2.772 (3)	170
N11–H11···N16 ⁱⁱⁱ	0.86	2.07	2.912 (3)	167
C23–H23B···O20 ^{iv}	0.96	2.65	3.506 (4)	149
O24–H24A···O10 ^v	0.76 (3)	2.54 (3)	3.140 (3)	137 (3)
O24–H24A···O15 ^{vi}	0.76 (3)	2.47 (3)	3.072 (3)	137 (3)
O24–H24B···O19 ^{vii}	0.81 (3)	2.03 (3)	2.821 (3)	163 (3)

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

dral angle between the planes formed by the aromatic rings is 88.83 (13)° and the S8–N11–C12–N16 torsion angle is 162.5 (2)°.

The nitrogen atom of the sulfonamide has sp^2 character, as a result of conjugation; the S8–N11–C12 angle is 125.09 (17)° and the N–H moiety is almost coplanar with the isoxazole ring, with the H11–N11–C12–N16 torsion angle being -17° . The cation and the anion in the asymmetric unit are linked by the N1–H1B···O18 hydrogen bond (Fig. 3 and Table 1). The methyl group of the anion occupies the hydrophobic pocket formed by the aromatic rings of the cation, with H23C located 2.96 Å from the centroid of the phenyl ring and H23A 2.81 Å from the centroid of the isoxazole ring. The N1–H1C···O24 hydrogen bond links the water molecule to the cation. Both sulfur atoms exhibit slightly distorted tetrahedral geometries; the O9–S8–O10 and O18–S21–O20 angles have values of 119.97 (12) and 115.06 (14)°, respectively, presenting the maximum deviations from the expected ones.

3. Supramolecular features

The salt structure is consolidated by a three-dimensional network of hydrogen bonds between the anions, cations, and water molecules, as well as by π – π interactions between aromatic rings (Fig. 3, Tables 1 and 2). Among the salient

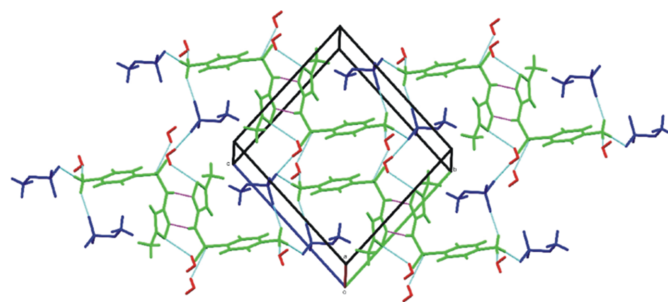


Figure 3
Crystal packing of the compound showing all the hydrogen-bonding interactions with an O atom as acceptor (cyan dashed lines) and the dimers formed by N–H···N interactions (magenta dashed lines).

Table 2

Selected details of π - π interactions (\AA , $^\circ$) for some sulfamethoxazolium salts.

Structures with centroid-centroid separations $< 6.0 \text{\AA}$ and $\alpha < 20.00^\circ$ according to *PLATON* (Spek, 2020). $Cg1$, $Cg2$, $Cg3$ and $Cg4$ are the centroids of the O15/N16/C12-C14, C2-C7, O15'/N16'/C12'-C14' and C2'-C7' rings, respectively. α is the dihedral angle between planes I and J ; ccd is the distance between ring centroids, ipd is the mean interplanar distance (distance from one plane to the neighboring centroid), slippage is distance between $Cg(I)$ and the perpendicular projection of $Cg(J)$ on ring I and sa is the mean slippage angle (angle subtended by the inter-centroid vector to the plane normal). For additional details, see Janiak (2000).

Refcode	$Cg(I)\cdots Cg(J)$	α	ccd	ipd	slippage	sa
(I)	$Cg1\cdots Cg1^i$	0.02 (14)	4.8490 (16)	3.5028 (10)	3.353	43.7
	$Cg2\cdots Cg2^{ii}$	0.03 (11)	5.8838 (16)	3.0064 (10)	5.058	59.3
	$Cg2\cdots Cg2^{iii}$	0.03 (11)	4.3764 (14)	3.5674 (10)	2.535	35.4
CIDDAY	$Cg2\cdots Cg2^{iv}$	0	3.8532	3.5757	1.436	21.9
TUJPEV	$Cg2\cdots Cg2^v$	0	5.9284	3.3032	4.923	56.1
GAGLAS	$Cg1\cdots Cg1^{vi}$	17	5.4016	3.4095	4.190	50.9
RISZAV	$Cg1\cdots Cg2^{vii}$	0	4.2924	3.8496	1.899	26.3
	$Cg1\cdots Cg1^{viii}$	17	4.7430	3.8184	2.813	36.4
	$Cg1\cdots Cg1^{ix}$	17	4.7430	2.9750	3.694	51.2
	$Cg1\cdots Cg1^x$	0	4.4550	3.2790	3.016	42.6
GOGLEW	$Cg2\cdots Cg2^{xi}$	0	5.5620	3.0159	4.673	57.2
	$Cg1/Cg3^{xii}$	0	3.8495	3.3844	1.834	28.5
	$Cg1\cdots Cg3^{xiii}$	0	3.9641	3.2582	2.258	34.7
	$Cg2\cdots Cg2^{iii}$	0	5.3927	3.0874	4.421	55.1
	$Cg4\cdots Cg4^{xiv}$	0	5.3927	3.0831	4.424	55.1
AWARIC	$Cg1\cdots Cg1^{xv}$	0	4.3792	4.1868	1.283	17.0
	$Cg2\cdots Cg2^{xvi}$	0	4.1198	3.4480	2.255	33.2

Symmetry codes: (i) $2 - x, 1 - y, -z$; (ii) $-1 + x, y, z$; (iii) $1 - x, 1 - y, 1 - z$; (iv) $1 - x, 2 - y, 1 - z$; (v) $1 - x, 2 - y, 1 - z$; (vi) $1 - x, y, \frac{1}{2} - z$; (vii) $1 - x, -y, -z$; (viii) $\frac{1}{2} - x, -y, -\frac{1}{2} + z$; (ix) $\frac{1}{2} - x, -y, \frac{1}{2} + z$; (x) $1 - x, -y, 2 - z$; (xi) $x, y, -1 + z$; (xii) $1 - x, \frac{1}{2} + y, 1 - z$; (xiii) $1 - x, \frac{1}{2} + y, 2 - z$; (xiv) $1 - x, y, z$; (xv) $2 - x, -y, -z$; (xvi) $1 - x, -y, -1 - z$.

features, each water molecule establishes hydrogen bonds with $SMXH^+$ units, acting through O24 as an acceptor with H1C (protonated primary amino group, x, y, z) and through H24A as a donor with both, O10 (sulfonamide, $-x + 1, -y + 1, -z + 1$) and O15 (isoxazole, $x - 1, y, z + 1$) in a bifurcated interaction. An additional hydrogen bond relates H24B with O19 of the methylsulfate anion ($-x, -y, -z + 1$).

Each methylsulfate anion establishes four interactions; two of them are hydrogen bonds $O18\cdots H1B$ (x, y, z) and $O19\cdots H1A$ ($-x + 1, -y, -z + 1$) with slightly different lengths (1.944 and 1.913 \AA , respectively), that bridge a pair of adjacent SMX molecules through their protonated amino moieties, while the third hydrogen bond is an interaction with a water molecule ($O19\cdots H24B$). The fourth is a C-H \cdots O intermolecular interaction between H23B and O20 of a neighboring methylsulfate anion ($x + 1, y, z$), which results in a chain of methylsulfate anions running along the a -axis direction.

In addition, the $SMXH^+$ units are also directly connected through pairs of $N11-H11\cdots N16$ hydrogen bonds ($-x + 1, -y + 1, -z$), which involve the isoxazole nitrogen atom (N16) and the sulfonamide N-H moiety (N11-H11).

The structure also features face-to-face π - π interactions between the phenyl rings of adjacent molecules, which adopt an antiparallel arrangement, in parallel planes. In one of them ($1 - x, 1 - y, 1 - z$), the planes are 3.5674 (10) \AA apart (Table 2), and the stacked aromatic rings are slipped by 2.535 \AA . This aromatic ring displacement (slippage) is the

distance between the perpendicular projection of the centroid of one ring on the other and the centroid of the latter. In addition, the mean slippage angle (sa, the angle subtended by the inter-centroid vector to the plane normal) is 35.4° , whereas the distance between centroids is 4.3764 (14) \AA . Face-to-face π - π interactions are also observed between the isoxazole rings ($2 - x, 1 - y, -z$), which are also arranged in an antiparallel fashion. The interplanar distance is 3.5028 (10) \AA while the intercentroid distance is 4.8490 (16) \AA , resulting in a slippage angle of 43.7° and a slippage of 3.353 \AA . Considering the geometrical requirements for interactions between aromatic rings (Hunter & Sanders, 1990), the parameters of both slipped packings correspond to attractive interactions.

The π - π interactions between aromatic rings play an important role in controlling the packing or assembly of molecules. Usually, they take the form of an offset or slipped stacking, where the rings are parallel displaced a certain distance (slippage, aromatic ring displacement). These interactions between aromatic rings of adjacent molecules seem to be one of the characteristic features of the sulfamethoxazolium derivatives, being found in several congeners of the title compound (Table 2).

The formation of antiparallel π -stacking interactions in these compounds may contribute to the cohesion of the crystal, considering that the phenyl ring has an electron-poor region at the sulfonamide side, opposite to a more electron-rich zone on the protonated amino region. In addition, the positively charged atom contributes to the attractive π - σ interaction due to the induced σ polarization.

4. Hirshfeld surface analysis

The three-dimensional Hirshfeld surface (McKinnon *et al.*, 2007) with a d_{norm} (normalized contact distance) plot (Fig. 4) and two-dimensional fingerprint plots (Spackman & McKinnon, 2002) were generated with *Crystal Explorer 17.5* (Spackman *et al.*, 2021). This analysis was carried out to verify the presence of intermolecular interactions and hydrogen bonds in the crystal structure and assess the contributions

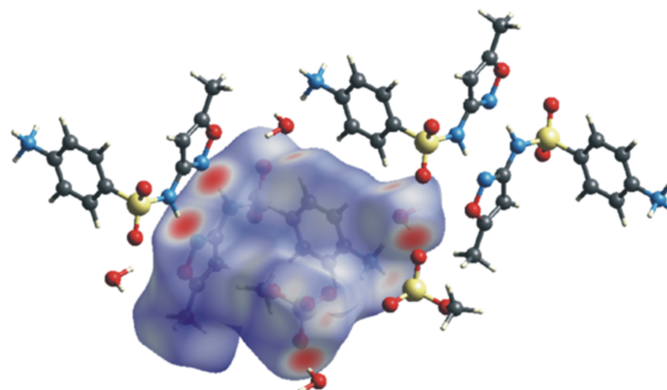


Figure 4
View of the three-dimensional Hirshfeld surface of the title molecule plotted over d_{norm} .

from the different intermolecular interactions in the title compound.

The Hirshfeld surface was plotted over the range -0.6318 (red) to $+1.4441$ (blue) a.u. The red spots on the top left of the surface indicate the sites of the $N11-H11 \cdots N16$ interactions ($-x+1, -y+1, -z$) between the sulfonamide N-H moiety and the nitrogen atom of the isoxazole, while at the top right, the place of the $O \cdots H$ interaction between the sulfonamide and the isoxazole with water can be observed.

A $C4-H4 \cdots O24$ (x, y, z) interaction site with water is also visible on top. In addition, the sites of interaction of H_2O with oxygen atoms of the neighbouring methylsulfate anion $O24-H24B \cdots O19$ ($-x, -y, -z+1$) are shown on the top right and the same interaction can be observed at the bottom right. The 2D fingerprint plots (Fig. 5) revealed that the greatest contributions to the total intermolecular interactions (Fig. 5A) are from $H \cdots O/O \cdots H$ contacts (54.1%), which appear in the middle of the scattered points of the 2D fingerprint plot, along with two symmetrical broad wings (Fig. 5B), followed by $H \cdots H$ contacts observed in the middle of the scattered points in the plot (29.2%, Fig. 5C), and $H \cdots N/N \cdots H$ contacts (5.0%, Fig. 5D), which result from the interactions between the sulfonamide N-H moiety and the nitrogen atom of the isoxazole to form a dimer, and are present as sharp symmetrical spikes at diagonal axes.

The proportions of these contributions are the expected ones due to the significant hydrogen content, which is present in the three components of the salt, and the fact that many of them are attached to heteroatoms. These interactions suggest that hydrogen bonding plays a major role in the crystal packing. The contributions to the Hirshfeld surface from other interatomic interactions include $H \cdots C/C \cdots H$, which are displayed as bump symmetrical spikes at diagonal axes (5.0%, Fig. 5E), $C \cdots O/O \cdots C$ (2.6%) and $C \cdots N/N \cdots C$ contacts (1.0%, Fig. 5F). In comparison, $N \cdots O/O \cdots N$ (1.1%), $C \cdots S/$

Table 3
Experimental details.

Crystal data	
Chemical formula	$C_{10}H_{12}N_3O_3S^+ \cdot CH_3O_4S^- \cdot H_2O$
M_r	383.39
Crystal system, space group	Triclinic, $P\bar{1}$
Temperature (K)	298
a, b, c (Å)	5.8838 (8), 11.6532 (15), 12.3276 (16)
α, β, γ (°)	84.722 (6), 78.442 (5), 81.940 (5)
V (Å ³)	818.14 (19)
Z	2
Radiation type	Mo $K\alpha$
μ (mm ⁻¹)	0.37
Crystal size (mm)	1.00 × 0.35 × 0.12
Data collection	
Diffractometer	Bruker D8 Quest ECO
Absorption correction	Multi-scan (SADABS; Krause <i>et al.</i> , 2015)
T_{min}, T_{max}	0.854, 0.956
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	18938, 3318, 2716
R_{int}	0.047
$(\sin \theta/\lambda)_{max}$ (Å ⁻¹)	0.625
Refinement	
$R[F^2 > 2\sigma(F^2)], wR(F^2), S$	0.043, 0.100, 1.06
No. of reflections	3318
No. of parameters	226
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}, \Delta\rho_{min}$ (e Å ⁻³)	0.33, -0.32

Computer programs: APEX4 and SAINT (Bruker, 2019), SHELXS97 (Sheldrick, 2008), SHELXL2019/I (Sheldrick, 2015), POV-RAY (Cason, 2004), Mercury (Macrae *et al.*, 2020), PLATON (Spek, 2020), publCIF (Westrip, 2010) and WinGX (Farrugia, 2012).

$S \cdots C$ (0.1%), and $H \cdots S/S \cdots H$ (0.1%) contacts represent additional, minor participations.

5. Database survey

A simple search in the Cambridge Structural Database (CSD, accessed via WebCSD on September 19, 2024; Groom *et al.*, 2016) with the keyword 'sulfamethoxazole' gave 73 hits, of which only six involved the sulfamethoxazolium ion, and included the following salts: chloride (SIMJEE, Subashini *et al.*, 2007), bromide (GAGLAS, de Moura Oliveira *et al.*, 2019), nitrate (GOGLEW, de Moura Oliveira *et al.*, 2019), pentaiodide monohydrate (CIDDAY, de Moura Oliveira *et al.*, 2019), 3,5-dinitrosalicylate (TUJPEV, Malathy *et al.*, 2015), and the metallic complex *catena*-[bis(sulfamethoxazolium)(μ_2 -chloridotrichloridocadmium(II) monohydrate)] (RISZAV, Subashini *et al.*, 2008). A more in-depth search of the database, using the keyword 'sulfamethoxazolium' uncovered the metallic complex trichloro-[4-[(5-methyl-1,2-oxazol-3-yl)sulfamoyl]anilinium]zinc (AWARIC, Habila *et al.*, 2021) as the seventh member of this family of compounds.

In all cases, the structure of the protonated form of SMX is L-shaped, displaying dihedral angles between the mean planes of the phenyl ring and the isoxazole unit of 58° (SIMJEE), 75° (GAGLAS), 87° (GOGLEW), 87° (CIDDAY), 82° (TUJPEV), 88.3° (RISZAV) and 89.2° (AWARIC). The simple halide salts (chloride and bromide) displayed the

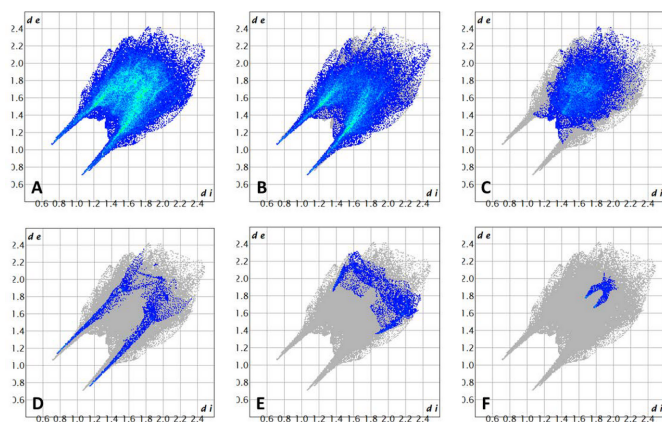


Figure 5

Two-dimensional fingerprint plots for the title molecule showing (A) all interactions, and those delineated into (B) $H \cdots O/O \cdots H$ interactions, (C) $H \cdots H$ interactions, (D) $H \cdots N/N \cdots H$ interactions (E) $H \cdots C/C \cdots H$ interactions, and (F) $C \cdots N/N \cdots C$ interactions. The d_i and d_e values are the closest internal and external distances (in Å) from given points on the Hirshfeld surface.

smallest values for the dihedral angle between the planes containing the isoxazole and anilinium rings. The S8–N11–C12–N16 torsion angles of the compounds presented the following values: -57.2 (4) $^\circ$ (SIMJEE), -25.3 (4) $^\circ$ (GAGLAS), -26.38 (1) $^\circ$ (CIDDAY), -152.4 (4)/ 151.5 (4) $^\circ$ (GOGLEW), -164.3 (2) $^\circ$ (AWARIC), 164.49 (14) $^\circ$ (TUIPEV) and 158.6 (3) $^\circ$ (RISZAV). Accordingly, salts in this series could be grouped in two sets; on one side the halides, with a small torsion angle, measuring less than 60° , and the remaining compounds including SMXHMeSO₄·H₂O on the other, with large torsions, where the angles are above 150° . This suggests that the isoxazole ring in these compounds adopts two main orientations.

6. Synthesis and crystallization

A sample of sulfamethoxazole (250 mg, 0.99 mmol) was dissolved in methanol (25 mL) at room temperature and treated with a methanolic solution of H₂SO₄ (0.507 M, 1.95 mL, 0.99 mmol). After stirring for 30 min, the solution was allowed to concentrate to 12 mL (3 days) at room temperature, when Et₂O (54 mL) containing water (0.1%, 0.054 mL, 3 mmol) was added. The system was left to stand at room temperature and crystals (15 mg) were collected after 6 d.

7. Refinement

Table 3 summarizes crystal data, data collection, and structure refinement details. The H atoms were positioned geometrically and refined using a riding model: O–H = 0.82 Å, N–H = 0.86–0.89 Å, and C–H = 0.93–0.96 Å with $U_{\text{iso}}(\text{H}) = 1.5U_{\text{eq}}(\text{C,O,N})$ for methyl and ammonium H atoms and $1.2U_{\text{eq}}(\text{C,N})$ for aromatic and other H atoms. Water H atoms were found in difference-Fourier maps and refined independently.

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Synthesis, crystal structure and Hirshfeld surface analysis of sulfamethoxazolium methylsulfate monohydrate

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Computing details

4-[(5-Methyl-1,2-oxazol-3-yl)sulfamoyl]anilinium methyl sulfate monohydrate

Crystal data

$C_{10}H_{12}N_3O_3S^+ \cdot CH_3O_4S^- \cdot H_2O$

$M_r = 383.39$

Triclinic, $P\bar{1}$

$a = 5.8838$ (8) Å

$b = 11.6532$ (15) Å

$c = 12.3276$ (16) Å

$\alpha = 84.722$ (6)°

$\beta = 78.442$ (5)°

$\gamma = 81.940$ (5)°

$V = 818.14$ (19) Å³

$Z = 2$

$F(000) = 400$

$D_x = 1.556$ Mg m⁻³

Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å

Cell parameters from 1942 reflections

$\theta = 2.3$ – 26.2 °

$\mu = 0.37$ mm⁻¹

$T = 298$ K

Needle, colourless

$1.00 \times 0.35 \times 0.12$ mm

Data collection

Bruker D8 Quest ECO

diffractometer

Radiation source: Sealed tube

ω scan

Absorption correction: multi-scan
(SADABS; Krause *et al.*, 2015)

$T_{\min} = 0.854$, $T_{\max} = 0.956$

18938 measured reflections

3318 independent reflections

2716 reflections with $I > 2\sigma(I)$

$R_{\text{int}} = 0.047$

$\theta_{\max} = 26.4$ °, $\theta_{\min} = 3.4$ °

$h = -7 \rightarrow 7$

$k = -14 \rightarrow 14$

$l = -15 \rightarrow 15$

Refinement

Refinement on F^2

Least-squares matrix: full

$R[F^2 > 2\sigma(F^2)] = 0.043$

$wR(F^2) = 0.100$

$S = 1.06$

3318 reflections

226 parameters

0 restraints

Hydrogen site location: mixed

H atoms treated by a mixture of independent
and constrained refinement

$w = 1/[\sigma^2(F_o^2) + (0.0142P)^2 + 1.0486P]$

where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{\max} < 0.001$

$\Delta\rho_{\max} = 0.33$ e Å⁻³

$\Delta\rho_{\min} = -0.32$ e Å⁻³

Special details

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

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

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
C3	0.3075 (4)	0.3673 (2)	0.4655 (2)	0.0359 (5)
H3	0.152494	0.384591	0.500421	0.043*
C4	0.4132 (4)	0.4451 (2)	0.3856 (2)	0.0375 (5)
H4	0.330192	0.515477	0.366393	0.045*
C6	0.7715 (4)	0.3127 (2)	0.3633 (2)	0.0368 (5)
H6	0.926915	0.295236	0.329032	0.044*
C7	0.6653 (4)	0.2354 (2)	0.4430 (2)	0.0367 (5)
H7	0.748077	0.165273	0.462965	0.044*
C13	0.9869 (5)	0.3140 (2)	0.0578 (2)	0.0475 (6)
H13	1.096502	0.312564	0.102944	0.057*
N1	0.3214 (3)	0.18050 (16)	0.57383 (16)	0.0334 (4)
H1A	0.418354	0.149870	0.618726	0.050*
H1B	0.284132	0.124328	0.538887	0.050*
H1C	0.192294	0.216536	0.613491	0.050*
C2	0.4356 (4)	0.26394 (19)	0.49225 (18)	0.0293 (5)
C5	0.6438 (4)	0.41640 (19)	0.33507 (18)	0.0301 (5)
S8	0.77327 (11)	0.51495 (5)	0.23174 (5)	0.03585 (16)
O9	0.6651 (4)	0.63011 (15)	0.25416 (15)	0.0480 (5)
O10	1.0205 (3)	0.48770 (17)	0.21978 (15)	0.0489 (5)
N11	0.6972 (4)	0.48975 (18)	0.11723 (16)	0.0389 (5)
H11	0.595794	0.540280	0.092239	0.047*
C12	0.7835 (4)	0.3928 (2)	0.05656 (18)	0.0357 (5)
C14	0.9881 (5)	0.2412 (2)	−0.0204 (2)	0.0488 (7)
O15	0.7978 (4)	0.27161 (17)	−0.06734 (15)	0.0530 (5)
N16	0.6641 (4)	0.36926 (19)	−0.01609 (18)	0.0452 (5)
C17	1.1508 (7)	0.1406 (3)	−0.0656 (3)	0.0721 (10)
H17A	1.196861	0.090255	−0.005591	0.108*
H17B	1.286665	0.167607	−0.112248	0.108*
H17C	1.074268	0.098765	−0.108343	0.108*
O18	0.2313 (5)	0.0622 (2)	0.40614 (18)	0.0788 (8)
O19	0.3568 (3)	−0.09508 (15)	0.28979 (18)	0.0516 (5)
O20	−0.0403 (3)	−0.00330 (17)	0.30985 (18)	0.0548 (5)
S21	0.19689 (10)	0.01013 (5)	0.31111 (5)	0.03422 (16)
O22	0.2620 (4)	0.09783 (18)	0.20879 (18)	0.0594 (6)
C23	0.4913 (6)	0.1348 (3)	0.1905 (3)	0.0656 (9)
H23A	0.538503	0.158159	0.113494	0.098*
H23B	0.600925	0.071669	0.211404	0.098*
H23C	0.487101	0.199088	0.234604	0.098*
O24	−0.1063 (3)	0.28881 (17)	0.67780 (16)	0.0431 (4)

H24A	-0.102 (5)	0.317 (3)	0.730 (3)	0.052*
H24B	-0.199 (5)	0.242 (3)	0.696 (2)	0.052*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C3	0.0297 (11)	0.0353 (12)	0.0408 (13)	-0.0011 (9)	-0.0058 (10)	0.0009 (10)
C4	0.0379 (13)	0.0318 (12)	0.0416 (13)	-0.0005 (10)	-0.0101 (11)	0.0037 (10)
C6	0.0303 (12)	0.0414 (13)	0.0354 (12)	-0.0026 (10)	-0.0007 (10)	0.0000 (10)
C7	0.0348 (12)	0.0320 (12)	0.0390 (13)	0.0026 (10)	-0.0031 (10)	0.0021 (10)
C13	0.0503 (16)	0.0525 (16)	0.0381 (14)	0.0032 (13)	-0.0121 (12)	-0.0013 (12)
N1	0.0324 (10)	0.0298 (10)	0.0361 (10)	-0.0043 (8)	-0.0029 (8)	0.0005 (8)
C2	0.0331 (11)	0.0284 (11)	0.0277 (11)	-0.0075 (9)	-0.0062 (9)	-0.0021 (8)
C5	0.0359 (12)	0.0309 (11)	0.0262 (11)	-0.0089 (9)	-0.0101 (9)	-0.0003 (9)
S8	0.0424 (3)	0.0375 (3)	0.0309 (3)	-0.0151 (3)	-0.0095 (2)	0.0020 (2)
O9	0.0693 (13)	0.0306 (9)	0.0461 (10)	-0.0144 (8)	-0.0106 (9)	-0.0014 (8)
O10	0.0410 (10)	0.0654 (12)	0.0441 (10)	-0.0233 (9)	-0.0105 (8)	0.0070 (9)
N11	0.0472 (12)	0.0394 (11)	0.0315 (10)	-0.0008 (9)	-0.0142 (9)	-0.0012 (8)
C12	0.0431 (13)	0.0385 (13)	0.0244 (11)	-0.0097 (10)	-0.0045 (10)	0.0059 (9)
C14	0.0604 (17)	0.0471 (15)	0.0342 (13)	-0.0007 (13)	-0.0039 (12)	0.0015 (11)
O15	0.0699 (13)	0.0505 (11)	0.0399 (10)	-0.0009 (10)	-0.0138 (9)	-0.0115 (9)
N16	0.0529 (13)	0.0470 (13)	0.0366 (11)	-0.0016 (10)	-0.0116 (10)	-0.0070 (10)
C17	0.087 (3)	0.063 (2)	0.0548 (19)	0.0158 (18)	-0.0010 (17)	-0.0110 (16)
O18	0.0975 (18)	0.1011 (19)	0.0486 (12)	-0.0523 (15)	-0.0010 (12)	-0.0284 (12)
O19	0.0400 (10)	0.0333 (9)	0.0801 (14)	0.0002 (8)	-0.0135 (10)	0.0011 (9)
O20	0.0323 (10)	0.0514 (11)	0.0801 (15)	-0.0074 (8)	-0.0105 (9)	0.0018 (10)
S21	0.0355 (3)	0.0317 (3)	0.0360 (3)	-0.0073 (2)	-0.0072 (2)	0.0005 (2)
O22	0.0530 (12)	0.0613 (13)	0.0628 (13)	-0.0149 (10)	-0.0189 (10)	0.0302 (10)
C23	0.0603 (19)	0.066 (2)	0.069 (2)	-0.0264 (16)	-0.0070 (16)	0.0193 (16)
O24	0.0424 (10)	0.0425 (11)	0.0451 (11)	-0.0108 (8)	-0.0041 (9)	-0.0080 (8)

Geometric parameters (Å, °)

C3—C2	1.378 (3)	S8—N11	1.626 (2)
C3—C4	1.388 (3)	N11—C12	1.391 (3)
C3—H3	0.9300	N11—H11	0.8600
C4—C5	1.384 (3)	C12—N16	1.312 (3)
C4—H4	0.9300	C14—O15	1.351 (3)
C6—C5	1.385 (3)	C14—C17	1.481 (4)
C6—C7	1.385 (3)	O15—N16	1.412 (3)
C6—H6	0.9300	C17—H17A	0.9600
C7—C2	1.374 (3)	C17—H17B	0.9600
C7—H7	0.9300	C17—H17C	0.9600
C13—C14	1.340 (4)	O18—S21	1.429 (2)
C13—C12	1.405 (4)	O19—S21	1.4472 (18)
C13—H13	0.9300	O20—S21	1.4291 (18)
N1—C2	1.463 (3)	S21—O22	1.5689 (19)
N1—H1A	0.8900	O22—C23	1.442 (3)

N1—H1B	0.8900	C23—H23A	0.9600
N1—H1C	0.8900	C23—H23B	0.9600
C5—S8	1.763 (2)	C23—H23C	0.9600
S8—O10	1.4253 (19)	O24—H24A	0.76 (3)
S8—O9	1.4285 (19)	O24—H24B	0.81 (3)
C2—C3—C4	119.0 (2)	N11—S8—C5	106.22 (10)
C2—C3—H3	120.5	C12—N11—S8	125.09 (17)
C4—C3—H3	120.5	C12—N11—H11	117.5
C5—C4—C3	119.0 (2)	S8—N11—H11	117.5
C5—C4—H4	120.5	N16—C12—N11	117.4 (2)
C3—C4—H4	120.5	N16—C12—C13	112.3 (2)
C5—C6—C7	119.3 (2)	N11—C12—C13	130.3 (2)
C5—C6—H6	120.4	C13—C14—O15	109.8 (2)
C7—C6—H6	120.4	C13—C14—C17	134.3 (3)
C2—C7—C6	118.9 (2)	O15—C14—C17	115.9 (3)
C2—C7—H7	120.5	C14—O15—N16	108.66 (19)
C6—C7—H7	120.5	C12—N16—O15	104.5 (2)
C14—C13—C12	104.7 (2)	C14—C17—H17A	109.5
C14—C13—H13	127.6	C14—C17—H17B	109.5
C12—C13—H13	127.6	H17A—C17—H17B	109.5
C2—N1—H1A	109.5	C14—C17—H17C	109.5
C2—N1—H1B	109.5	H17A—C17—H17C	109.5
H1A—N1—H1B	109.5	H17B—C17—H17C	109.5
C2—N1—H1C	109.5	O18—S21—O20	115.06 (14)
H1A—N1—H1C	109.5	O18—S21—O19	111.33 (15)
H1B—N1—H1C	109.5	O20—S21—O19	113.41 (11)
C7—C2—C3	122.3 (2)	O18—S21—O22	106.60 (14)
C7—C2—N1	118.9 (2)	O20—S21—O22	103.29 (12)
C3—C2—N1	118.9 (2)	O19—S21—O22	106.17 (12)
C4—C5—C6	121.5 (2)	C23—O22—S21	117.03 (18)
C4—C5—S8	118.33 (17)	O22—C23—H23A	109.5
C6—C5—S8	120.15 (18)	O22—C23—H23B	109.5
O10—S8—O9	119.97 (12)	H23A—C23—H23B	109.5
O10—S8—N11	108.68 (11)	O22—C23—H23C	109.5
O9—S8—N11	104.56 (11)	H23A—C23—H23C	109.5
O10—S8—C5	107.58 (11)	H23B—C23—H23C	109.5
O9—S8—C5	109.04 (11)	H24A—O24—H24B	106 (3)
C2—C3—C4—C5	0.2 (4)	O9—S8—N11—C12	172.3 (2)
C5—C6—C7—C2	-0.1 (4)	C5—S8—N11—C12	-72.5 (2)
C6—C7—C2—C3	-0.4 (4)	S8—N11—C12—N16	162.55 (18)
C6—C7—C2—N1	178.0 (2)	S8—N11—C12—C13	-19.1 (4)
C4—C3—C2—C7	0.4 (4)	C14—C13—C12—N16	1.1 (3)
C4—C3—C2—N1	-178.0 (2)	C14—C13—C12—N11	-177.3 (2)
C3—C4—C5—C6	-0.7 (4)	C12—C13—C14—O15	-0.4 (3)
C3—C4—C5—S8	178.67 (18)	C12—C13—C14—C17	178.0 (3)
C7—C6—C5—C4	0.7 (4)	C13—C14—O15—N16	-0.4 (3)

C7—C6—C5—S8	-178.69 (18)	C17—C14—O15—N16	-179.2 (2)
C4—C5—S8—O10	160.72 (18)	N11—C12—N16—O15	177.28 (19)
C6—C5—S8—O10	-19.9 (2)	C13—C12—N16—O15	-1.4 (3)
C4—C5—S8—O9	29.1 (2)	C14—O15—N16—C12	1.1 (3)
C6—C5—S8—O9	-151.45 (19)	O18—S21—O22—C23	55.1 (3)
C4—C5—S8—N11	-83.0 (2)	O20—S21—O22—C23	176.7 (2)
C6—C5—S8—N11	96.4 (2)	O19—S21—O22—C23	-63.7 (3)
O10—S8—N11—C12	43.0 (2)		

Hydrogen-bond geometry (Å, °)

<i>D</i> —H \cdots <i>A</i>	<i>D</i> —H	H \cdots <i>A</i>	<i>D</i> \cdots <i>A</i>	<i>D</i> —H \cdots <i>A</i>
C3—H3 \cdots O24	0.93	2.65	3.353 (3)	133
C4—H4 \cdots O24 ⁱ	0.93	2.54	3.469 (3)	177
C13—H13 \cdots O10	0.93	2.54	3.023 (3)	113
N1—H1A \cdots O19 ⁱⁱ	0.89	1.91	2.800 (3)	175
N1—H1A \cdots S21 ⁱⁱ	0.89	2.94	3.774 (2)	156
N1—H1B \cdots O18	0.89	1.95	2.761 (3)	152
N1—H1C \cdots O24	0.89	1.89	2.772 (3)	170
N11—H11 \cdots N16 ⁱⁱⁱ	0.86	2.07	2.912 (3)	167
C23—H23B \cdots O20 ^{iv}	0.96	2.65	3.506 (4)	149
O24—H24A \cdots O10 ^v	0.76 (3)	2.54 (3)	3.140 (3)	137 (3)
O24—H24A \cdots O15 ^{vi}	0.76 (3)	2.47 (3)	3.072 (3)	137 (3)
O24—H24B \cdots O19 ^{vii}	0.81 (3)	2.03 (3)	2.821 (3)	163 (3)

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