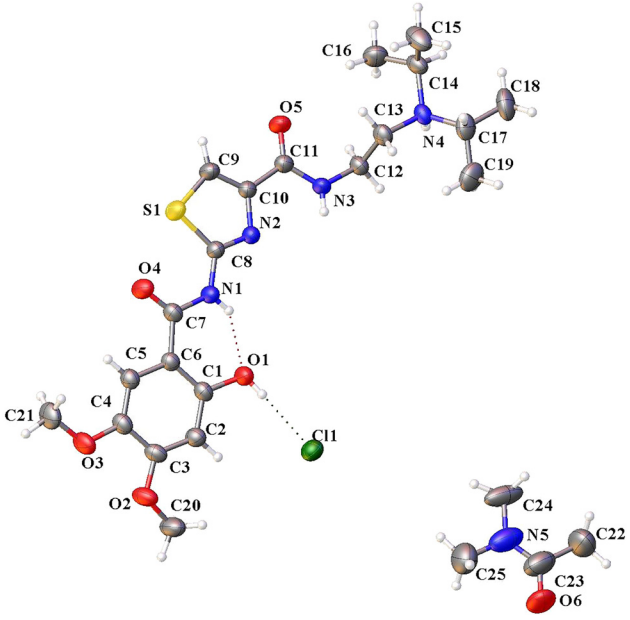
Yaqin Shan, Shuqiu Zhang and Guoshun Zhang*

Crystal structure of acotiamide hydrochloride dimethylacetamide solvate (1/1), $C_{25}H_{40}ClN_5O_6S$



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Abstract

$C_{25}H_{40}ClN_5O_6S$, triclinic, $P\bar{1}$ (no. 2), a = 7.9989(5) Å, b = 11.6765(8) Å, c = 16.2656(12) Å, α = 98.519(2)°, β = 96.748(2)°, γ = 99.796(2)°, V = 1446.57(17) Å^3, Z = 2, $R_{gt}(F)$ = 0.0556, $wR_{ref}(F^2)$ = 0.1537, T = 296(2) K.

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The asymmetric unit of the title molecular structure is shown in the figure. Table 1 contains the crystallographic data and the list of the atoms including atomic coordinates and displacement parameters can be found in the cif-file attached to this article.

***Corresponding author: Guoshun Zhang**, Department of Pharmacy, Shanxi Medical University, Taiyuan, Shanxi 030001, China, E-mail: zhangguoshunshun@126.com. https://orcid.org/0000-0001-8394-2594

Yaqin Shan and Shuqiu Zhang, Department of Pharmacy, Shanxi Medical University, Taiyuan, Shanxi 030001, China

Table 1: Data collection and handling.

Crystal:	Clear light colourless prism
Size:	0.17 × 0.07 × 0.02 mm
Wavelength:	Mo *K*α radiation (0.71073 Å)
μ:	0.25 mm^{-1}
Diffractometer, scan mode:	Bruker APEX-II, φ and ω scans
θ_{max}, completeness:	28.4°, 98 %
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	16708, 7182, 0.038
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\,\sigma\,(I_{obs})$, 4,292
$N(param)_{refined}$:	359
Programs:	Bruker,[1] SHELX,[2,3] Olex2[4]

1 Source of material

Acotiamide hydrochloride (AH; systematic name : *N*-(2-(2-(2-hydroxy-4,5-dimethoxybenzamido)thiazole-4-carboxamido) ethyl)-*N*-isopropylpropan-2-aminium chloride) was purchased from Anhui Dexinjia BioPharm Co., Ltd (Anhui, China). Dimethylacetamide (DMA) was of analytical grade and was provided from Sinopharm Chemical Reagent Company Ltd. (Shanghai, China). After completely dissolving AH (100 mg) in DMA (0.8 ml) at 313 K, the solution was filtered and cooled to room temperature. After five days, colourless prism crystals of acotiamide hydrochloride dimethylacetamide solvate (1AH-1DMA) was harvested.

2 Experimental details

A single crystal of 1AH-1DMA was selected via a microscope for single crystal X-ray diffraction experiments. Crystal data collection and structure refinement details are summarized in Table 1. H atoms bonded to N were determined by the experimental electron density map, and their isotropic displacement parameters and positions were refined freely. H atoms attached to C atoms were located in geometrically calculated positions and refined using a riding model with d(C–H) = 0.93 Å (aromatic ring-H), 0.96 Å (–CH), 0.97 Å (–CH_2) or 0.98 Å, (–CH_3). U_{iso}(H) = 1.2 U_{eq}(C) for CH and CH_2 or U_{iso}(H) = 1.5 U_{eq}(C) for CH_3 groups.

3 Comment

Acotiamide hydrochloride (AH) has been approved for treatment of functional dyspepsia due to the pharmacological

activities of improving gastric accommodation, promoting gastric motility and increasing gastric dilatation by antagonizing the M1 and M2 muscarinic receptors and inhibiting acetylcholinesterase.[5] The solid form of a drug is closely related to its physicochemical properties. Hence, the extensive investigations on solid-state forms of a drug are necessary.

Here, we successfully prepared the crystals of 1AH-1DMA through slow solvent evaporation. The complete set of X-ray diffraction data for the title compound was deposited to the Cambridge Crystallographic Data Center (CCDC entry no. 2456268). 1AH-1DMA crystallizes with one acotiamide cation, one chloride anion and one DMA molecule in the asymmetric unit. Intramolecular hydrogen bond with N1–H···O1 was generated to form a six ring-like structure. Intermolecular hydrogen bond with N3–H···O6 (1–*X*, 1–*Y*, 1–*Z*) was observed to stabilize DMA molecules. The hydrogen bond interactions with O1–H···Cl1 and N4–H···Cl1 (2–*X*, 2–*Y*, 1–*Z*) fixed the chloride anions. Cell parameters and molecular arrangements in 1AH-1DMA were similar to our previous reported solvate with 1AH-1DMSO–I.[6,7] Thus, the two solvates belonged to the isostructural type. The torsion angles for C6–C7–N1–C8, C10–C11–N3–C12 and N3–C12–C13–N4 in 1AH-1DMA were 173.3(3)°, 177.3(3)° and 178.59(19)°, respectively.

The Hirshfeld surface analysis for 1AH-1DMA was performed using Crystal Explorer 17.5[8] and its fingerprint plots were explored to obtain quantitatively various intermolecular interactions. It is obvious that the H···H interactions with 48.8 %, O···H interactions with 17.9 %, C···H interactions with 12.1 %, Cl···H interactions with 8.2 %, S···H interactions with 4.6 %, and N···H interactions with 4.2 % contributed significantly to the Hirshfeld surfaces.

Author contributions: All the authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.

Conflict of interest: The authors declare no conflicts of interest regarding this article.

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