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Synthesis and crystal structure of 5-(8-((3-carboxyazetidin-1-ium-1-yl)methyl)-7-hydroxy-4-oxo-4*H*-chromen-3-yl)-2-hydroxybenzenesulfonate monohydrate, $C_{20}H_{19}NO_{10}S$

Table 1: Data collection and handling.

Crystal:	Colorless plate
Size:	0.30 × 0.20 × 0.20 mm
Wavelength:	Cu K α radiation (1.54184 Å)
μ :	2.05 mm ⁻¹
Diffractometer, scan mode:	ROD, ω
$\theta_{\max}$, completeness:	75.8°, >99%
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	10313, 3921, 0.029
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2 \sigma(I_{\text{obs}})$, 3522
$N(\text{param})_{\text{refined}}$:	309
Programs:	CrysAlis ^{PRO} [1], Diamond [2], SHELX [3, 4]

Source of material

The title compound 5-(8-((3-carboxyazetidin-1-ium-1-yl)methyl)-7-hydroxy-4-oxo-4*H*-chromen-3-yl)-2-hydroxybenzenesulfonate was synthesized *via* a Mannich reaction. Formaldehyde (solution, 10 mL, 37%), water (10 mL), azetidine-3-carboxylic acid (1.52 g, 0.015 mol) and sodium 2-hydroxy-5-(7-hydroxy-4-oxo-4*H*-chromen-3-yl)benzenesulfonate (3.56 g, 0.01 mol) were added to ethanol (150 mL, 99.5%) and stirred for 24 h at 328 K. Then the mixture was filtered and the residue was collected. The residue was dried at 383 K. Sodium 5-(8-((3-carboxyazetidin-1-yl)methyl)-7-hydroxy-4-oxo-4*H*-chromen-3-yl)-2-hydroxybenzenesulfonate (2.93 g) was obtained. ¹H NMR (500 MHz, DMSO-*d*₆) δ : 8.34 (s, 1H, H9), 7.92 (d, J = 8.8 Hz, 1H, H3), 7.71 (d, J = 2.3 Hz, 1H, H11), 7.39 (dd, J = 8.4, 2.3 Hz, 1H, H15), 6.95 (d, J = 8.8 Hz, 1H, H2), 6.83 (d, J = 8.4 Hz, 1H, H14), 4.03 (s, 2H, H16A, H16B), 3.63 (t, J = 8.2 Hz, 2H, H17A, H19B), 3.51 (t, J = 7.4 Hz, 2H, H17B, H19A), 3.32–3.18 (m, 1H, H18). ¹³C NMR (125 MHz, DMSO-*d*₆) δ : 174.67 (C7), 173.98 (C20), 162.49 (C1), 155.42 (C5), 153.19 (C13), 152.81 (C9), 131.41 (C15), 130.60 (C12), 127.73 (C3), 126.06 (C11), 122.89 (C10), 122.28 (C8), 116.20 (C4), 116.17 (C14), 115.00 (C2), 108.51 (C6), 56.38 (C17, C19), 50.32 (C16), 33.41 (C18). A mixture of sodium salt described before (0.024 g),

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Abstract

$C_{20}H_{19}NO_{10}S$, triclinic, $P\bar{1}$ (no. 2), a = 8.3470(2) Å, b = 9.6701(2) Å, c = 12.9523(3) Å, α = 102.413(2)°, β = 103.199(2)°, γ = 97.753(2)°, V = 975.26(4) Å³, Z = 2, $R_{\text{gt}}(F)$ = 0.0439, $wR_{\text{ref}}(F^2)$ = 0.1244, T = 100(1) K.

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The asymmetric unit of the title structure is shown in the figure. Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

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Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²).

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{iso} [*] / <i>U</i> _{eq}
S1	0.32952 (6)	1.02505 (6)	0.27507 (4)	0.02944 (15)
O1	0.8547 (2)	0.31935 (17)	0.70992 (13)	0.0349 (4)
H1	0.812691	0.230914	0.686191	0.052 [*]
O2	0.7064 (2)	0.53247 (16)	0.27267 (12)	0.0345 (4)
O3	0.91535 (18)	0.74483 (15)	0.59367 (11)	0.0276 (3)
O4	0.54484 (19)	1.10244 (18)	0.13564 (13)	0.0350 (4)
H4	0.606955	1.120779	0.095664	0.052 [*]
O5	0.36072 (19)	1.18161 (17)	0.31074 (14)	0.0354 (4)
O6	0.27614 (19)	0.95781 (17)	0.35597 (13)	0.0336 (3)
O7	0.21524 (19)	0.96833 (18)	0.16621 (13)	0.0353 (4)
C1	0.8307 (3)	0.3832 (2)	0.62611 (17)	0.0298 (4)
C2	0.7558 (3)	0.3033 (2)	0.51718 (18)	0.0303 (4)
H2	0.720157	0.201624	0.501020	0.036 [*]
C3	0.7340 (3)	0.3724 (2)	0.43402 (18)	0.0296 (4)
H3	0.683211	0.318161	0.360512	0.035 [*]
C4	0.7866 (2)	0.5232 (2)	0.45705 (17)	0.0267 (4)
C5	0.8598 (2)	0.5986 (2)	0.56547 (17)	0.0266 (4)
C6	0.8830 (2)	0.5328 (2)	0.65227 (17)	0.0281 (4)
C7	0.7621 (3)	0.5994 (2)	0.37095 (17)	0.0279 (4)
C8	0.8017 (2)	0.7557 (2)	0.40900 (17)	0.0274 (4)
C9	0.8767 (3)	0.8169 (2)	0.51582 (17)	0.0280 (4)
H9	0.904785	0.919306	0.538307	0.034 [*]
C10	0.7430 (3)	0.8490 (2)	0.33547 (17)	0.0273 (4)
C11	0.5911 (3)	0.8909 (2)	0.33709 (17)	0.0283 (4)
H11	0.530742	0.861269	0.385058	0.034 [*]
C12	0.5252 (3)	0.9753 (2)	0.27009 (17)	0.0281 (4)
C13	0.6136 (3)	1.0209 (2)	0.19941 (17)	0.0288 (4)
C14	0.7673 (3)	0.9801 (2)	0.19900 (17)	0.0296 (4)
H14	0.829442	1.011125	0.152384	0.036 [*]
C15	0.8308 (3)	0.8950 (2)	0.26545 (18)	0.0291 (4)
H15	0.935378	0.867537	0.263397	0.035 [*]
C16	0.9590 (3)	0.6194 (3)	0.76862 (18)	0.0328 (5)
H16A ^a	1.044340	0.702711	0.771243	0.039 [*]
H16B ^a	1.014112	0.558952	0.813030	0.039 [*]
H16C ^b	1.071882	0.596747	0.791700	0.039 [*]
H16D ^b	0.976312	0.722136	0.767019	0.039 [*]
C17	0.8602 (3)	0.7436 (2)	0.93544 (18)	0.0337 (5)
H17A ^a	0.868785	0.849548	0.952386	0.040 [*]
H17B ^a	0.958451	0.717166	0.980506	0.040 [*]
H17C ^b	0.945466	0.769669	1.007065	0.040 [*]
H17D ^b	0.851131	0.828605	0.904998	0.040 [*]
C18	0.6900 (3)	0.6598 (3)	0.93670 (19)	0.0366 (5)
H18 ^c	0.599331	0.717743	0.934275	0.044 [*]
H18A ^d	0.612944	0.724971	0.914152	0.044 [*]
C19	0.6853 (3)	0.5632 (3)	0.82590 (19)	0.0351 (5)
H19A ^a	0.718724	0.469796	0.830475	0.042 [*]
H19B ^a	0.577189	0.548190	0.770036	0.042 [*]
H19C ^b	0.623800	0.594047	0.762558	0.042 [*]
H19D ^b	0.645980	0.459292	0.818317	0.042 [*]
O8 ^c	0.7990 (3)	0.4901 (2)	1.03187 (17)	0.0393 (5)
O9 ^c	0.6237 (2)	0.6199 (2)	1.09650 (15)	0.0320 (4)
H9A ^c	0.665273	0.600332	1.155863	0.048 [*]
N1 ^a	0.8202 (3)	0.6712 (2)	0.81336 (18)	0.0294 (5)
H1A ^a	0.768690	0.735728	0.770122	0.035 [*]
C20 ^c	0.7088 (3)	0.5797 (3)	1.0269 (2)	0.0292 (5)

Table 2: (continued)

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{iso} [*] / <i>U</i> _{eq}
O8A ^d	0.7696 (12)	0.5924 (11)	1.0976 (9)	0.0393 (5)
H8A ^d	0.733365	0.553297	1.141914	0.059 [*]
O9A ^d	0.5176 (11)	0.6564 (10)	1.0654 (7)	0.0320 (4)
N1A ^b	0.8817 (10)	0.6091 (9)	0.8531 (7)	0.0294 (5)
H1AA ^b	0.934801	0.544207	0.895186	0.035 [*]
C20A ^d	0.6481 (14)	0.6395 (15)	1.0394 (10)	0.0292 (5)
O10	0.7320 (2)	1.19437 (18)	0.01927 (13)	0.0365 (4)
H10A	0.734750	1.144244	−0.044482	0.055 [*]
H10B	0.724942	1.280205	0.010318	0.055 [*]

^aOccupancy: 0.805(4), ^bOccupancy: 0.195(4), ^cOccupancy: 0.833(2),^dOccupancy: 0.167(2).

ammonium iron(II) sulfate hexahydrate (0.039 g), concentrated nitric acid (50 µL) and water (10 mL) was sealed in a 20 mL vial and sonicated for 5 min. Then the mixture was heated at 363 K for 30 min. Colorless plate-shaped crystals of the title compound were obtained. **IR spectra** (potassium bromide pellet) were recorded on a Nicolet 6700. **IR** (ν/cm^{−1}): 3382, 3021, 2635, 1703, 1632, 1570, 1510, 1445, 1417, 1351, 1290, 1230, 1201, 1170, 1094, 1080, 1049, 1024, 916, 898, 845, 837, 814, 798, 780, 737, 727, 650, 639, 627, 557, 540, 496.

Experimental details

Carbon-bound H atoms were placed in calculated positions and were included in the refinement in the riding model approximation, with *U*_{iso}(H) set to 1.2 *U*_{eq}(C). The oxygen-bound and nitrogen-bound H atoms were located on a difference Fourier map. The carboxylic acid group and N1 atoms were disordered.

Comment

Azetidine-3-carboxylic acids are a kind of strained four-membered heterocyclic amino acid. In the past decade, azetidine-3-carboxylic acid has become an important pharmaceutical intermediate for the preparation of various medicines [5–8]. Our previous investigations showed that sodium 2-hydroxy-5-(7-hydroxy-4-oxo-4*H*-chromen-3-yl) benzenesulfonate reacts with amino acids by Mannich reaction [9–13]. The reaction takes place without a catalyst. As a continuation, we synthesized the anazetidine-3-carboxylic acid derivative, sodium 5-(8-((3-carboxyazetidin-1-yl) methyl)-7-hydroxy-4-oxo-4*H*-chromen-3-yl)-2-hydroxy-benzenesulfonate. In this paper, the title compound

was obtained by reaction of the aforementioned sodium salt. Studies of the pharmacological activities of the title compound are in progress. The title compound contains one zwitterion and one water molecule in the asymmetric unit (cf. the figure). The bond distances and bond angles are in normal ranges [9–13]. The dihedral angle between planar rings B (C10–C15) and C (C7–C9/O3/C5/C4) is 85.89° . The nitrogen atom N1 is protonated. There exist various O–H...O and N–H...O hydrogen bonds. A two dimensional layer along the *bc* plane is formed by intermolecular hydrogen bonds. There are $\pi\cdots\pi$ stacking interactions between C1–C6 phenyl rings from adjacent layers. The centroid-centroid distance is $3.6746(13)$ Å. Together with the $\pi\cdots\pi$ stacking interactions a three-dimensional network is obtained.

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