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The crystal structure of 1-[5-(2-fluorophenyl)-1-(pyridine-3-sulfonyl)-1H-pyrrol-3-yl]-N-methylmethanaminium 3-carboxyprop-2-enoate, $C_{21}H_{20}FN_3O_6S$

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Table 1: Data collection and handling.

Crystal:	Colorless block
Size:	0.22 × 0.20 × 0.18 mm
Wavelength:	Mo K α radiation (0.71073 Å)
μ :	0.20 mm ⁻¹
Diffractometer, scan mode:	Xcalibur, ω
$\theta_{\max}$, completeness:	25.3°, >99%
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	13924, 3987, 0.029
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2 \sigma(I_{\text{obs}})$, 3246
$N(\text{param})_{\text{refined}}$:	309
Programs:	CrysAlis ^{PRO} [1], SHELX [2, 3], Diamond [4]

Abstract

$C_{21}H_{20}FN_3O_6S$, monoclinic, $P2_1/n$ (no. 14), $a = 7.8502(4)$ Å, $b = 7.9892(4)$ Å, $c = 34.9707(19)$ Å, $\beta = 92.500(1)^\circ$, $V = 2191.2(2)$ Å³, $Z = 4$, $R_{\text{gt}}(F) = 0.0502$, $wR_{\text{ref}}(F^2) = 0.1361$, $T = 296(2)$ K.

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Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

Source of material

All chemicals, reagents and solvents are of analytical grade and are commercially available. Preparation of

[5-(2-fluorophenyl)-1-(pyridine-3-sulfonyl)-1H-pyrrol-3-yl]-N-methylmethanaminium 3-carboxyprop-2-enoate: 10.08 g (30.5 mmol) of 5-(2-fluorophenyl)-1-(pyridin-3-yl-sulfonyl)-1H-pyrrole-3-formaldehyde was dissolved in 150 ml methanol, and 4.7 g (45.8 mmol) of 30% methylamine methanol solution was slowly added at room temperature. 1.2 g (30.5 mmol) NaBH₄ was added under cooling with an ice bath for 3 h at room temperature, 1 N hydrochloric acid (about 30 ml) was added to adjust pH to 6–7. The methanol solvent was removed, 30 ml ethyl acetate was added, and then ammonia water (about 10 ml) was added to adjust pH to 12, stratification was carried out, 10 ml ethyl acetate was added to the water layer for stripping once. The organic layer was combined, washed with brine and dried with anhydrous sodium sulfate. Add 10 ml DMF, stir, add 3.543 g (30.5 mmol) fumaric acid, stir at 60 °C for 30 min, cool to room temperature, stir for 2 h, filter, wash the filter cake with 5 ml ethyl acetate: DMF = 1:2. Then wash with 2 ml ethyl acetate, dry to obtain about 8.87 g of a white solid, with a yield of 67.1%. ¹H NMR (600 MHz, DMSO) δ 10.420 (s, 2H), 8.885 (dd, $J = 4.8$, 1.3 Hz, 1H), 8.565 (d, $J = 2.3$ Hz, 1H), 7.888 (dt, $J = 8.3$, 1.8 Hz, 1H), 7.776 (s, 1H), 7.615 (dd, $J = 8.2$, 4.9 Hz, 1H), 7.528 (m, 1H), 7.240 (d, $J = 8.4$ Hz, 1H), 7.216 (d, $J = 6.6$ Hz, 1H), 7.103 (td, $J = 7.8$, 1.8 Hz, 1H), 6.508 (d, $J = 1.8$ Hz, 1H), 6.487 (s, 2H), 3.916 (s, 2H), 2.459 (s, 3H). Crystals were grown in methanol and water (7:3) at room temperature.

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

Atom	x	y	z	U _{iso} */U _{eq}
F1A ^a	0.0874 (6)	−0.1222 (6)	0.12937 (14)	0.0684 (17)
F1B ^b	−0.1513 (4)	0.2482 (4)	0.21207 (9)	0.0730 (12)
C1	−0.0984 (4)	0.0956 (4)	0.20479 (9)	0.0522 (7)
H1 ^a	−0.1327	0.2033	0.2109	0.063*
C2	−0.1182 (4)	−0.0301 (5)	0.23108 (10)	0.0667 (9)
H2	−0.1632	−0.0071	0.2547	0.080*
C3	−0.0709 (4)	−0.1886 (5)	0.22208 (11)	0.0694 (10)
H3	−0.0837	−0.2743	0.2397	0.083*
C4	−0.0041 (4)	−0.2238 (4)	0.18700 (11)	0.0649 (9)
H4	0.0265	−0.3327	0.1808	0.078*
C5	0.0164 (4)	−0.0955 (4)	0.16141 (9)	0.0501 (7)
H5 ^b	0.0623	−0.1188	0.1379	0.060*
C6	−0.0296 (3)	0.0681 (3)	0.16969 (8)	0.0401 (6)
C7	−0.0062 (3)	0.2029 (3)	0.14155 (7)	0.0375 (6)
C8	−0.0934 (3)	0.2358 (3)	0.10806 (8)	0.0427 (6)
H8	−0.1891	0.1780	0.0986	0.051*
C9	−0.0153 (3)	0.3728 (3)	0.08967 (7)	0.0382 (6)
C10	0.1214 (3)	0.4203 (3)	0.11206 (7)	0.0395 (6)
H10	0.1973	0.5056	0.1067	0.047*
C11	0.3870 (3)	0.1348 (3)	0.17531 (7)	0.0329 (5)
C12	0.3723 (3)	0.0148 (3)	0.20328 (7)	0.0423 (6)
H12	0.3117	0.0356	0.2250	0.051*
C13	0.4506 (4)	−0.1366 (4)	0.19783 (9)	0.0500 (7)
H13	0.4448	−0.2212	0.2160	0.060*
C14	0.5377 (4)	−0.1608 (4)	0.16506 (9)	0.0522 (7)
H14	0.5875	−0.2649	0.1615	0.063*
C15	0.4795 (3)	0.1017 (3)	0.14341 (8)	0.0434 (6)
H15	0.4890	0.1849	0.1250	0.052*
C16	−0.0695 (3)	0.4493 (3)	0.05203 (7)	0.0428 (6)
H16A	−0.0869	0.3612	0.0332	0.051*
H16B	0.0207	0.5215	0.0436	0.051*
C17	−0.2140 (4)	0.6948 (4)	0.07991 (10)	0.0656 (9)
H17A	−0.1875	0.6577	0.1056	0.098*
H17B	−0.3197	0.7554	0.0792	0.098*
H17C	−0.1246	0.7666	0.0717	0.098*
C18	0.3860 (3)	1.3032 (3)	0.04141 (7)	0.0371 (6)
C19	0.3044 (4)	1.1353 (4)	0.03467 (9)	0.0521 (7)
H19	0.1954	1.1310	0.0232	0.063*
C20	0.3786 (4)	0.9975 (4)	0.04408 (9)	0.0518 (7)
H20	0.4849	1.0030	0.0568	0.062*
C21	0.3038 (4)	0.8278 (4)	0.03573 (9)	0.0543 (7)
N1	0.1284 (3)	0.3191 (3)	0.14459 (6)	0.0372 (5)
N2	−0.2299 (3)	0.5488 (3)	0.05427 (6)	0.0393 (5)
H1N	−0.316 (3)	0.481 (3)	0.0606 (8)	0.047*
H2N	−0.256 (3)	0.584 (3)	0.0306 (6)	0.047*
N3	0.5555 (3)	−0.0451 (3)	0.13799 (7)	0.0532 (6)
O1	0.2070 (3)	0.3366 (3)	0.21468 (5)	0.0558 (5)
O2	0.3938 (3)	0.4586 (2)	0.16699 (6)	0.0564 (5)
O3	0.3126 (2)	1.4208 (2)	0.02315 (5)	0.0409 (4)
O4	0.5120 (2)	1.3194 (2)	0.06391 (5)	0.0479 (5)
O5	0.1548 (3)	0.8072 (3)	0.02459 (9)	0.0834 (8)
O6	0.4121 (3)	0.7116 (3)	0.04125 (8)	0.0721 (7)
H1O	0.368 (5)	0.613 (3)	0.0348 (11)	0.087*
S1	0.28475 (8)	0.32843 (8)	0.178744 (18)	0.03953 (19)

^aOccupancy: 0.410(5), ^bOccupancy: 0.590(5).

Experimental details

Hydrogen atoms were placed in their geometrically idealized positions and constrained to ride on their parent atoms. The fluoro substituent is disordered over two positions (Table 2).

Comment

1-[5-(2-Fluorophenyl)-1-(pyridine-3-sulfonyl)-1*H*-pyrrol-3-yl]-*N*-methylmethanaminium 3-carboxyprop-2-enoate (Vonoprazan fumarate) is a novel proton pump inhibitor (PPI), potassium competitive acid blocker (P-CAB) by competitive inhibition of proton pump (H⁺, K⁺-ATPase) and in the function of K⁺ is a reversible antagonist [5–7]. Different from traditional PPIs, the effect of Vonoprazan fumarate is independent of proton pump activation conditions. P-CABs can significantly reduce the occurrence of nocturnal acid breakthrough [8–10]. The structure of the title compound was elucidated by spectroscopic methods (NMR) and X-ray diffraction. All bond lengths and angles in the crystal structure are within the normal range [11]. Intermolecular hydrogen bonds are found through the chain structure of the anions (fumarate) oxygen atoms [O6⋯O3: 2.523(2) Å].

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

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

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