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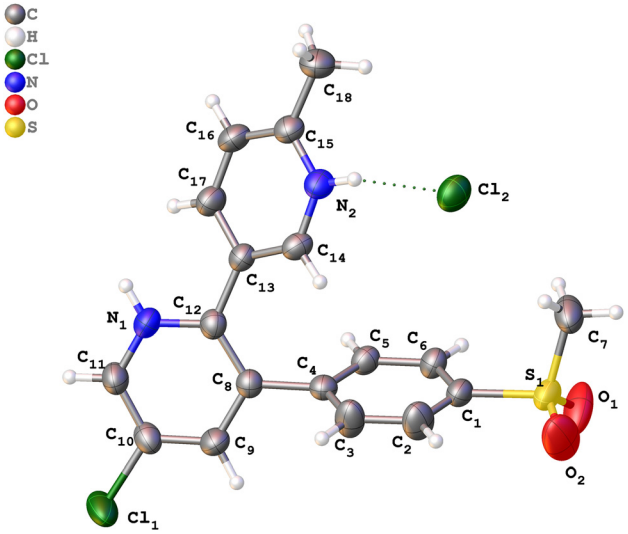
The salt crystal structure of etoricoxib hydrochloride, $C_{18}H_{16}Cl_2N_2O_2S$



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Abstract

$C_{18}H_{16}Cl_2N_2O_2S$, monoclinic, $P2_1/c$ (no. 14), a = 10.915(2) Å, b = 11.801(2) Å, c = 14.059(3) Å, β = 90.10(3)°, V = 1810.9(6) Å^3, Z = 4, $R_{gt}(F)$ = 0.0585, $wR_{ref}(F^2)$ = 0.1532, T = 293(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.

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Table 1: Data collection and handling.

Crystal:	Colourless block
Size:	0.20 × 0.20 × 0.10 mm
Wavelength:	MoKα radiation (0.71073 Å)
μ:	0.49 mm^{-1}
Diffractometer, scan mode: ω	Nonius CAD4,
θ_{max}, completeness:	25.4°, >99 %
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	3510, 3327, 0.033
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\sigma(I_{obs})$, 2,220
$N(param)_{refined}$:	228
Programs:	Olex2[1,2], SHELX[3,4]

1 Source of material

1.1 Experimental details

Single-crystal diffraction data were collected on a Nonius CAD4 with a MoKα X-ray source (λ = 0.71073 Å). The crystal structures were solved by using Olex2.[1,2] The model was solved with the ShelXT[3] structure solution program and further refinement with the ShelXL[4] refinement package. Hydrogen atoms on carbon atoms were placed in their geometrically idealized positions. All carbon bound hydrogen atoms were positioned geometrically. The H atoms were placed in idealized positions and treated as riding on their parent atoms, with the d(C–H) = 0.96 Å (methyl) and d(C–H) = 0.93 Å (aromatic). And U_{iso}(H) = 1.2 times U_{iso}(C) and U_{iso}(H) = 1.5 times U_{iso}(O), respectively.

2 Comment

Etoricoxib is a specific inhibitor of cyclooxygenase-2, employed for the management of osteoarthritis, rheumatoid arthritis, and acute gout attacks.[1] In accordance with the Biopharmaceutics Classification System (BCS), ETR falls under Class II drugs, characterized by low bioavailability.[5] Its poor aqueous solubility, coupled with a pronounced pH-dependency, poses constraints on its clinical utilization. Etoricoxib is an intriguing molecule, devoid of traditional hydrogen bond donors, yet featuring potent electronegativity from its pyridine nitrogen and sulfonyl oxygen atoms. To

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

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
C1	0.2797 (3)	0.4196 (3)	0.5263 (3)	0.0412 (9)
C2	0.3957 (4)	0.3872 (4)	0.5548 (3)	0.0577 (11)
H2A	0.432971	0.422219	0.606539	0.069*
C3	0.4562 (4)	0.3023 (4)	0.5056 (3)	0.0564 (11)
H3	0.535068	0.281639	0.523770	0.068*
C4	0.4010 (3)	0.2483 (3)	0.4306 (2)	0.0353 (8)
C5	0.2858 (3)	0.2823 (3)	0.4023 (2)	0.0379 (8)
H5	0.248467	0.247017	0.350696	0.045*
C6	0.2251 (3)	0.3679 (3)	0.4494 (3)	0.0402 (8)
H6	0.147675	0.390555	0.429345	0.048*
C7	0.0893 (4)	0.4580 (4)	0.6547 (3)	0.0700 (14)
H7A	0.044050	0.512065	0.691562	0.105*
H7B	0.127611	0.404170	0.696456	0.105*
H7C	0.034656	0.419075	0.612252	0.105*
C8	0.4649 (3)	0.1545 (3)	0.3784 (2)	0.0358 (8)
C9	0.5669 (3)	0.1809 (3)	0.3237 (3)	0.0438 (9)
H9	0.597259	0.254547	0.322226	0.053*
C10	0.6221 (3)	0.0967 (3)	0.2718 (3)	0.0430 (9)
C11	0.5792 (3)	−0.0126 (3)	0.2768 (3)	0.0468 (10)
H11	0.618598	−0.068697	0.241834	0.056*
C12	0.4261 (3)	0.0411 (3)	0.3799 (2)	0.0363 (8)
C13	0.3186 (3)	−0.0022 (3)	0.4339 (2)	0.0360 (8)
C14	0.2762 (3)	0.0436 (3)	0.5180 (2)	0.0383 (8)
H14	0.314408	0.107376	0.543205	0.046*
C15	0.1215 (3)	−0.0962 (3)	0.5344 (3)	0.0414 (9)
C16	0.1598 (4)	−0.1437 (3)	0.4502 (3)	0.0468 (9)
H16	0.120262	−0.207787	0.426789	0.056*
C17	0.2558 (3)	−0.0976 (3)	0.4002 (3)	0.0460 (9)
H17	0.279525	−0.130426	0.342979	0.055*
C18	0.0198 (4)	−0.1403 (3)	0.5945 (3)	0.0580 (11)
H18A	0.052597	−0.189730	0.642447	0.087*
H18B	−0.036943	−0.181525	0.555413	0.087*
H18C	−0.021674	−0.078065	0.624364	0.087*
Cl1	0.74754 (11)	0.12534 (10)	0.19970 (9)	0.0747 (4)
Cl2	0.09593 (10)	0.16098 (9)	0.70782 (7)	0.0562 (3)
N1	0.4834 (3)	−0.0407 (2)	0.3299 (2)	0.0444 (8)
N2	0.1807 (3)	−0.0026 (2)	0.5640 (2)	0.0415 (7)
H2	0.155975	0.029646	0.615321	0.050*
O1	0.1395 (4)	0.5983 (3)	0.5223 (2)	0.0870 (12)
O2	0.2851 (3)	0.5788 (3)	0.6535 (3)	0.1014 (14)
S1	0.20075 (10)	0.52766 (8)	0.58930 (7)	0.0506 (3)

date, several solid forms, including polymorphs, solvates, cocrystals and salts, have been reported.[6–11] To explore more solid forms of ETR into a drug candidate, in this paper, a new hydrochloride salt has been explored.

ETR–Bz crystallized in monoclinic, $P2_1/c$ space group, with four asymmetric units in a unit cell (Z = 4). Each asymmetric unit contains one ETR^+ cation and one Cl^- anion (Z' = 1). As expected, intermolecular proton transfer occurs from the chloride, forming charge-assisted hydrogen bond, N_2–H_2···Cl_2 (2.127 Å, 158.8°). The intermolecular hydrogen bonding interactions reinforce the robustness and stability of the solid state. The torsion angle [C4–C8–C12–C13] of the pyridine ring of ETR is −0.905°. In general, all bond lengths and angles are in the expected ranges in both molecules.

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

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

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