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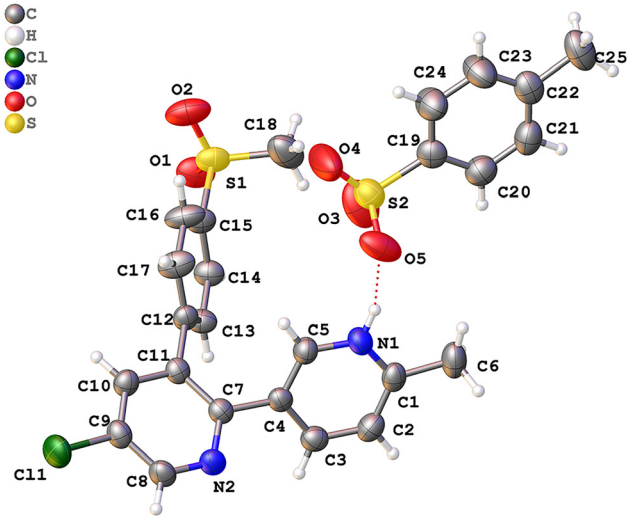
The crystal structure of 5-chloro-6′-methyl-3-(4-(methylsulfonyl)phenyl)-[2,3′-bipyridin]-1′-ium 4-methylbenzenesulfonate



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Abstract

$C_{18}H_{16}ClN_2O_2S{\cdot}C_7H_7O_3S$, monoclinic, $C2/c$ (no. 15), a = 36.911(9) Å, b = 9.931(2) Å, c = 14.795(3) Å, β = 112.32(3)°, V = 5017(2) Å^3, Z = 8, $R_{gt}(F)$ = 0.0500, $wR_{ref}(F^2)$ = 0.1447, T = 293 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:	Needle
Size:	0.30 × 0.30 × 0.30 mm
Wavelength:	Mo *K*α radiation (0.71073 Å)
μ:	0.36 mm^{-1}
Diffractometer, scan mode:	Bruker P4, ω
θ_{max}, completeness:	25.5°, >99 %
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	9199, 4617, 0.044
Criterion for I_{obs}, $N(hkl)_{gt}$:	I_{obs} > 2 σ(I_{obs}), 3253
$N(param)_{refined}$:	320
Programs:	Olex2 [1], SHELX [2, 3]

1 Source of material

In representative experiments, the etoricoxib (ETR; systematic name: 5-chloro-6′-methyl-3-(4-(methylsulfonyl)phenyl)-2,3′-bipyridine) was presented by Nanjing Zhengda Tianqing Pharmaceutical Co., Ltd. with no further purification. ETR (35.9 mg, 0.1 mmol) and *p*-toluenesulfonic acid (TsOH, 17.2 mg, 0.1 mmol) were mixed in 5.0 mL methanol, and the resulting mixture was stirred and dissolved at 60 °C to obtain a clear solution. Then the solution was filtered and placed in a sample vial, covered with membrane and punctured. Subsequently, the filtrate was set aside to allow slow evaporation at room temperature within one week.

2 Experimental details

Using Olex2 [1], the structure was solved and refined with the ShelXL refinement package. 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.

3 Comment

Etoricoxib, a relatively new selective cyclooxygenase-2(COX-2) nonsteroidal anti-inflammatory drug (NSAIDs), has been used in several clinical studies [4, 5]. While, the

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

Atom	x	y	z	U_{iso}*/U_{eq}
C1	0.68970 (8)	0.0244 (3)	0.6246 (2)	0.0440 (7)
C2	0.66503 (9)	−0.0844 (3)	0.6133 (2)	0.0480 (8)
H2	0.67475 (9)	−0.1716 (3)	0.6173 (2)	0.0576 (9)*
C3	0.62602 (9)	−0.0639 (3)	0.5961 (2)	0.0441 (7)
H3	0.60966 (9)	−0.1375 (3)	0.5899 (2)	0.0529 (9)*
C4	0.61087 (8)	0.0661 (3)	0.58801 (19)	0.0367 (6)
C5	0.63652 (8)	0.1708 (3)	0.6003 (2)	0.0427 (7)
H5	0.62754 (8)	0.2589 (3)	0.5961 (2)	0.0513 (8)*
C6	0.73222 (9)	0.0148 (4)	0.6433 (3)	0.0626 (10)
H6a	0.73541 (9)	−0.013 (2)	0.5845 (6)	0.0938 (15)*
H6b	0.74431 (17)	0.1011 (7)	0.6634 (18)	0.0938 (15)*
H6c	0.74434 (17)	−0.0500 (19)	0.6939 (13)	0.0938 (15)*
C7	0.57008 (8)	0.0947 (3)	0.57652 (19)	0.0366 (6)
C8	0.52353 (9)	0.0537 (3)	0.6402 (2)	0.0451 (7)
H8	0.51452 (9)	0.0032 (3)	0.6804 (2)	0.0541 (9)*
C9	0.50082 (8)	0.1583 (3)	0.5871 (2)	0.0429 (7)
C10	0.51190 (8)	0.2278 (3)	0.52118 (19)	0.0411 (7)
H10	0.49608 (8)	0.2955 (3)	0.48255 (19)	0.0493 (8)*
C11	0.54706 (8)	0.1949 (3)	0.51371 (19)	0.0368 (6)
C12	0.55882 (8)	0.2596 (3)	0.43744 (19)	0.0381 (6)
C13	0.56581 (9)	0.1792 (3)	0.3691 (2)	0.0426 (7)
H13	0.56338 (9)	0.0863 (3)	0.3718 (2)	0.0511 (8)*
C14	0.57628 (9)	0.2349 (3)	0.2972 (2)	0.0434 (7)
H14	0.58034 (9)	0.1803 (3)	0.2509 (2)	0.0520 (8)*
C15	0.58068 (9)	0.3733 (3)	0.2949 (2)	0.0421 (7)
C16	0.57376 (12)	0.4542 (3)	0.3616 (2)	0.0602 (9)
H16	0.57674 (12)	0.5470 (3)	0.3593 (2)	0.0722 (11)*
C17	0.56237 (11)	0.3986 (3)	0.4323 (2)	0.0548 (9)
H17	0.55708 (11)	0.4541 (3)	0.4764 (2)	0.0658 (10)*
C18	0.64601 (11)	0.4175 (5)	0.2509 (3)	0.0770 (12)
H18a	0.65154 (11)	0.3230 (5)	0.261 (2)	0.1155 (18)*
H18b	0.65666 (17)	0.451 (3)	0.2055 (10)	0.1155 (18)*
H18c	0.65766 (15)	0.464 (2)	0.3120 (11)	0.1155 (18)*
C19	0.75381 (9)	0.5189 (3)	0.5957 (2)	0.0490 (8)
C20	0.78265 (10)	0.4261 (4)	0.6016 (2)	0.0573 (9)
H20	0.77680 (10)	0.3347 (4)	0.5938 (2)	0.0688 (11)*
C21	0.81984 (10)	0.4702 (4)	0.6189 (3)	0.0609 (9)
H21	0.83900 (10)	0.4072 (4)	0.6226 (3)	0.0731 (11)*
C22	0.82989 (10)	0.6041 (4)	0.6309 (2)	0.0563 (9)
C23	0.80113 (11)	0.6940 (4)	0.6250 (3)	0.0724 (11)
H23	0.80716 (11)	0.7852 (4)	0.6330 (3)	0.0868 (13)*
C24	0.76322 (11)	0.6529 (4)	0.6074 (3)	0.0689 (10)
H24	0.74414 (11)	0.7163 (4)	0.6036 (3)	0.0827 (13)*
C25	0.87037 (10)	0.6521 (5)	0.6459 (3)	0.0764 (12)
H25a	0.88805 (19)	0.5769 (7)	0.662 (2)	0.1146 (18)*
H25b	0.8701 (2)	0.693 (3)	0.5869 (8)	0.1146 (18)*
H25c	0.8789 (4)	0.717 (2)	0.6980 (15)	0.1146 (18)*
Cl02	0.45825 (2)	0.19849 (10)	0.60421 (7)	0.0605 (3)
N1	0.67431 (7)	0.1475 (3)	0.61843 (18)	0.0459 (6)
H1	0.68960 (7)	0.2156 (3)	0.62654 (18)	0.0550 (8)*
N2	0.55773 (7)	0.0226 (3)	0.63597 (17)	0.0431 (6)
O1	0.57901 (8)	0.3620 (3)	0.11824 (15)	0.0639 (7)
O2	0.58822 (9)	0.5838 (3)	0.19742 (19)	0.0782 (8)
O3	0.69416 (8)	0.3843 (4)	0.48241 (18)	0.0933 (10)
O4	0.68228 (9)	0.5867 (3)	0.5588 (3)	0.1136 (13)
O5	0.70588 (8)	0.3882 (3)	0.65132 (17)	0.0768 (8)
S1	0.59589 (3)	0.44228 (8)	0.20461 (6)	0.0510 (3)
S2	0.70493 (3)	0.46650 (10)	0.56784 (7)	0.0570 (3)

poor aqueous solubility of etoricoxib has been limited its use in pharmaceutical preparations and clinical trials. Salt formation is one of the most commonly used methods to improve the solubility of insoluble drugs without influencing pharmacological activities of APIs [6], and five solid forms including ETR–succinic acid, ETR–glutaric acid, ETR–adipic acid, ETR–suberic acid, ETR–caprolactam and ETR– phthalic acid have been reported [7–9]. To explore more solid forms of ETR into a drug candidate, in this paper, one more ETRH^+ salt is described.

X-ray diffraction analysis shows the expected crystal structure of the ETRH^+ salt with 4-methylbenzenesulfonate as counteranion. As observed in the crystal, the connection between anion and cation was formed due to the strong hydrogen bonding network which involves the H atom of the pyridinyl moiety as donor and the O5 atom. The hydrogen bonding interaction strengthens the stability of the solid form. And there are no specific interactions formed by the Cl atoms. In general, all bond lengths and angles are in the expected ranges [9].

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