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N-(3-Phenoxy-4-pyridinio)methane-sulfonamidate

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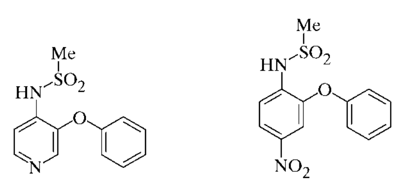
The title compound, $C_{12}H_{12}N_2O_3S$, is a strict pyridine analogue of nimesulide, a selective inhibitor of cyclooxygenase-2. The structure is characterized by a pyridinium ring with a deprotonated sulfonamide group. An intermolecular charge-assisted hydrogen bond between these two groups is observed within the crystal packing, linking the molecules into an infinite chain running along the *b*-axis direction.

Comment

N-(3-Phenoxy-4-pyridyl)methanesulfonamide, also known as FJ1, (I), a strict pyridine analogue of nimesulide, (II), has been structurally studied to compare it with nimesulide, which is a selective inhibitor of cyclooxygenase-2 (COX-2) (Dupont, Pirotte *et al.*, 1995), and to try to understand its unexpected inactivity towards the cyclooxygenases (Julémont, 2001).



(I) (II)

The molecular structure of the zwitterionic form of (I) is shown in Fig. 1. The pyridine group appears as a pyridinium nucleus and the sulfonamide group is deprotonated. Bond lengths and angles (Table 1), in particular C11—N10—C9 [120.6 (1)°, greater than in the pyridine ring, between 116 and 118°] and C13—N14 [1.354 (2) Å], agree with a zwitterionic structure where N14 is deprotonated and N10 protonated. Such a structure was also observed in a pyridylsulfonylcyanoguanidine compound, where the main bond lengths and angles are comparable (Dupont, Masereel *et al.*, 1995).

A geometry optimization by an *ab initio* 6-31g* method at the B3LYP level using *GAUSSIAN*98 (Frisch *et al.*, 1998) was performed on the zwitterionic form of (I), (*a*), and the neutral form, (*b*). The results are as follows: form (*a*) C—N—C 120.54° and C—N 1.313 Å; form (*b*) C—N—C 116.96° and C—N 1.401 Å. After optimization, the bond lengths and angles of form (*a*) are the closest to those in the crystal structure. In nimesulide, where the sulfonamide group is not deprotonated, the C13—N14 bond length is longer [1.409 (4) Å] than that in (I) [1.354 (2) Å] because of the weaker delocalization.

Unlike nimesulide, (I) does not show any strong intramolecular hydrogen bonds. The crystal cohesion comes principally from van der Waals interactions and an intermolecular charge-assisted (Giacovazzo *et al.*, 1992) and strongly directional N10—H10···N14 hydrogen bond (Table 2).

In the Cambridge Structural Database (CSD; Version 5.21; Allen & Kennard, 1993), 31 structures possess a pyridinium group and intermolecular hydrogen bonds are observed. Strongly directional hydrogen bonds are found in only nine structures; the others have weaker hydrogen bonds and less directionality. The acceptor changes from structure to structure and is either neutral or charged: $–COO^-$, –CO, –OH, $–PO_3H^-$, $–N^-$ or –N (pyridine group).

The crystal packing of (I) also involves four C—H···O interactions (Fig. 2) that may be classified as weak donor–

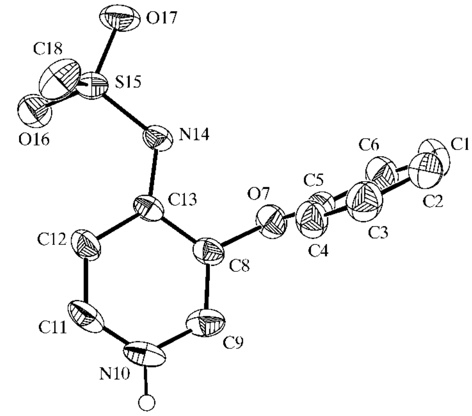


Figure 1
A view of the molecular structure of (I) with the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms have been omitted, except for N10—H.

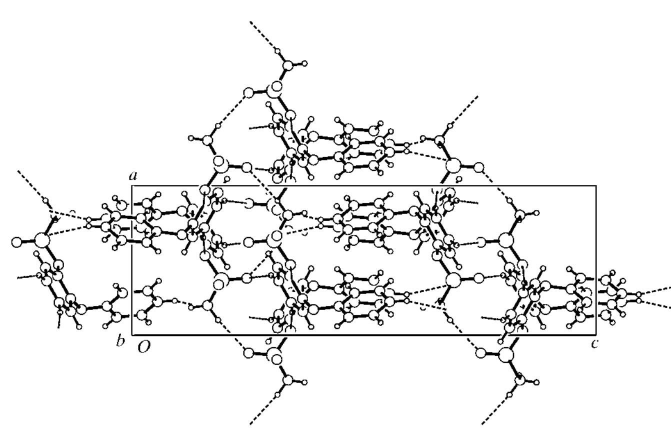


Figure 2
A packing diagram of (I), illustrating the hydrogen-bonding network.

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strong acceptor hydrogen bonds (Desiraju & Steiner, 1999). Indeed, the H$\cdots$*A* lengths are between 2 and 3 Å, the *D*$\cdots$*A* lengths between 3 and 4 Å and the *D*—H$\cdots$*A* angles between 90 and 180° (Table 2). The two rings and the sulfone of (I) are involved in these hydrogen bonds. One is an intramolecular hydrogen bond (C12—H12$\cdots$O16), which should partly contribute to the molecular conformation of the sulfonamide group of (I).

In conclusion, (I) appears structurally different from nimesulide, with its zwitterionic form and its interactions within the crystal packing. Consequently, binding of (I) onto the COX-2 enzyme will also be different. The positive charge on the pyridine group would lead to unfavourable interaction. The loss of the intramolecular hydrogen bond in (I) induces a different position of the phenoxy group with regard to nimesulide.

Experimental

Slow evaporation of a solution of (I) in methanol gave colourless crystals suitable for X-ray analysis.

Crystal data

$C_{12}H_{12}N_2O_3S$	Cu $K\alpha$ radiation
$M_r = 264.30$	Cell parameters from 25 reflections
Orthorhombic, *Pbca*	$\theta = 30$–$40°$
$a = 8.059$ (1) Å	$\mu = 2.42$ mm^{-1}
$b = 12.116$ (1) Å	$T = 293$ (2) K
$c = 24.744$ (2) Å	Needle, colourless
$V = 2416.1$ (4) Å^3	$0.64 \times 0.31 \times 0.19$ mm
$Z = 8$	
$D_x = 1.453$ Mg m^{-3}	

Data collection

Enraf–Nonius CAD-4 diffractometer	$R_{int} = 0.011$
$\theta/2\theta$ scans	$\theta_{max} = 71.9°$
Absorption correction: analytical (North *et al.*, 1968)	$h = -9 \rightarrow 9$
$T_{min} = 0.306$, $T_{max} = 0.656$	$k = 0 \rightarrow 14$
4729 measured reflections	$l = 0 \rightarrow 30$
2366 independent reflections	3 standard reflections every 200 reflections
2257 reflections with $I > 2\sigma(I)$	intensity decay: 3%

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0635P)^2 + 0.4886P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)] = 0.032$	$(\Delta/\sigma)_{max} = 0.001$
$wR(F^2) = 0.096$	$\Delta\rho_{max} = 0.24$ e Å^{-3}
$S = 1.07$	$\Delta\rho_{min} = -0.31$ e Å^{-3}
2366 reflections	Extinction correction: *SHELXL*97
212 parameters	Extinction coefficient: 0.0029 (2)
All H-atom parameters refined	

All H atoms were refined; C—H distances are in the range 0.89 (2)–1.03 (3).

Data collection: *CAD*-4 *Software* (Enraf–Nonius, 1989); cell refinement: *CAD*-4 *Software*; data reduction: *HELENA* (Spek, 1997); program(s) used to solve structure: *SIR*97 (Altomare *et al.*, 1999); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 1990); software used to prepare material for publication: *SHELXL*97.

Table 1
Selected geometric parameters (Å, °).

C8—C9	1.363 (2)	C11—C12	1.366 (2)
C8—C13	1.418 (2)	C12—C13	1.418 (2)
C9—N10	1.343 (2)	C13—N14	1.354 (2)
N10—C11	1.338 (2)	N14—S15	1.6094 (11)
C11—N10—C9	120.6 (1)		

Table 2
Hydrogen-bonding geometry (Å, °).

D—H$\cdots$*A*	*D*—H	H$\cdots$*A*	*D*$\cdots$*A*	*D*—H$\cdots$*A*
N10—H10$\cdots$N14^{i}	0.93 (2)	1.96 (2)	2.878 (2)	172 (2)
C2—H2$\cdots$O17^{ii}	0.94 (2)	2.54 (2)	3.453 (2)	163 (2)
C11—H11$\cdots$O16^{iii}	0.90 (2)	2.35 (2)	3.195 (2)	156 (1)
C12—H12$\cdots$O16	0.89 (2)	2.51 (2)	3.011 (2)	116 (1)
C18—H18*A*$\cdots$O16^{iv}	0.98 (2)	2.43 (2)	3.398 (2)	171 (2)

Symmetry codes: (i) $\frac{3}{2}-x, y-\frac{1}{2}, z$; (ii) $x-\frac{1}{2}, \frac{1}{2}-y, -z$; (iii) $2-x, y-\frac{1}{2}, \frac{1}{2}-z$; (iv) $\frac{1}{2}+x, y, \frac{1}{2}-z$.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1503). Services for accessing these data are described at the back of the journal.

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