Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

5-[5-(4-Methoxyphenyl)-3-trifluoromethyl-1*H*-pyrazol-1-yl]-2-sulfamoylbenzyl propionate: a novel 1,5-diraylpyrazole class of COX-2 inhibitor

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Key indicators

Single-crystal X-ray study
T = 298 K
Mean σ(C–C) = 0.003 Å
R factor = 0.058
wR factor = 0.088
Data-to-parameter ratio = 11.9

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

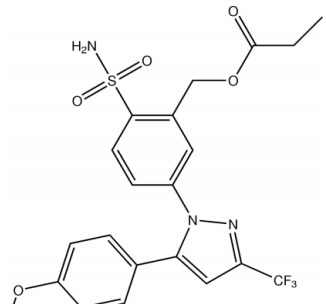
Received 1 October 2003
Accepted 9 October 2003
Online 23 October 2003

DRL publication No. 253-A.

The title compound, $C_{21}H_{20}F_3N_3O_5S$, has been made during our research program on COX-2 inhibitors. The molecules are held together by intermolecular hydrogen bonds involving the amide N atom with the unsubstituted N atom of the pyrazole ring and with an O atom of the sulfanamide group, across centers of symmetry.

Comment

With a view to identifying novel COX-2 inhibitors, we have carried out extensive chemical modification of celecoxib. The title compound, (I), emerged as one of the potent molecules from an SAR (structure–activity relationship) study. The molecular structure of (I) is shown in Fig. 1. The bond lengths and angles are normal (Allen *et al.*, 1987) and the five-membered ring is planar.



(I)

Weak intramolecular interactions, particularly C3—H1···O3, C6—H3···O1 and C7—H4···O2, influence the observed conformation of the molecule. In the crystal structure, the molecules are held together by hydrogen-bonding and C—H···O interactions. Both H atoms of the sulfonamide group are involved in intermolecular hydrogen bonds, connecting molecules across centers of symmetry. The N1—H20···N3^{ii} hydrogen bond results in the formation of hydrogen-bonded dimers (all symmetry codes in Table 1). These dimers are linked into a chain along the *a* axis by the hydrogen bond N1—H19···O1^{i}, which is supported by the weak interaction C20—H18···O1^{iv}. The weak interactions C12—H11···O4^{iii} and C18—H14···O2^{iii} connect molecules along the *bc* diagonal.

Experimental

The title compound was synthesized (Singh *et al.*, 2003) by chemoselective acylation of the intermediate 2-hydroxymethyl-4-[5-(4-methoxyphenyl)-3-trifluoromethyl-1*H*-1-pyrazolyl]-1-benzenesulfonamide (Lohray *et al.*, 2000). Crystals suitable for X-ray diffraction analysis were grown from methanol.

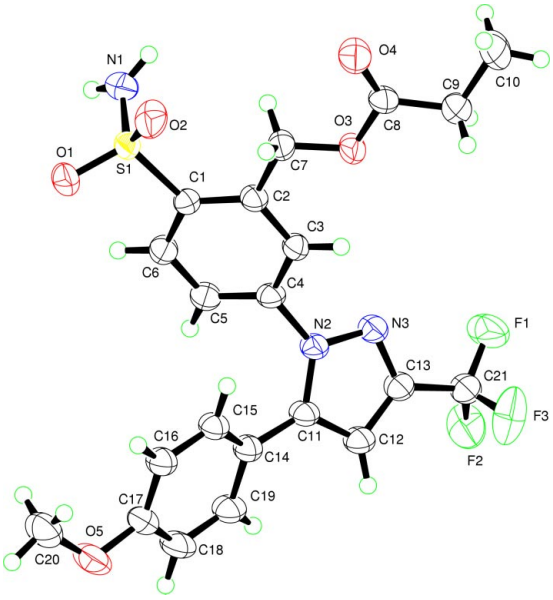


Figure 1
The structure of (I), showing 50% probability displacement ellipsoids and the atom-numbering scheme.

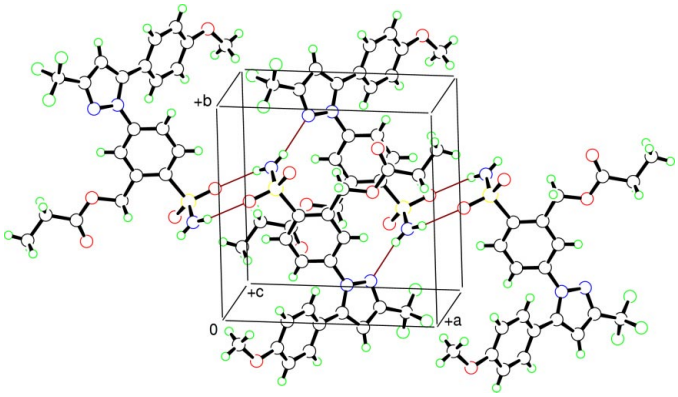


Figure 2
Packing of the molecules, viewed approximately down the *c* axis. Hydrogen bonds are indicated by thin lines.

Crystal data

$C_{21}H_{20}F_3N_3O_5S$
M_r = 483.46
Triclinic, $P\overline{1}$
a = 10.4490 (8) Å
b = 12.0126 (8) Å
c = 9.2196 (9) Å
α = 111.068 (6)°
β = 94.851 (7)°
γ = 86.328 (6)°
V = 1075.3 (2) Å^3
Z = 2
D_x = 1.493 Mg m^{-3}
Cu $K\alpha$ radiation
Cell parameters from 25 reflections
θ = 22.7–24.6°
μ = 1.94 mm^{-1}
T = 298.1 K
Block, colorless
0.50 × 0.50 × 0.40 mm

Data collection

Rigaku AFC-7*S* diffractometer
ω–2θ scans
Absorption correction: ψ scan (North *et al.*, 1968)
T_{min} = 0.346, T_{max} = 0.461
4902 measured reflections
3926 independent reflections
3801 reflections with $F^2 > 2\sigma(F^2)$
R_{int} = 0.051
θ_{max} = 68.0°
$h = -12 \rightarrow 12$
$k = -13 \rightarrow 14$
$l = -11 \rightarrow 4$
3 standard reflections
every 150 reflections
intensity decay: 2.6%

Refinement

Refinement on F
R = 0.058
wR = 0.088
S = 1.04
3854 reflections
325 parameters
H atoms treated by a mixture of independent and constrained refinement
Weighting by Chebychev polynomial with 3 parameters (Carruthers & Watkin, 1979): 232.809, 288.588, 57.8579
$(\Delta/\sigma)_{max}$ = 0.010
$\Delta\rho_{max}$ = 0.41 e Å^{-3}
$\Delta\rho_{min}$ = −0.35 e Å^{-3}
Extinction correction: Larson (1970) (equation 22)
Extinction coefficient: 416 (22)

Table 1
Hydrogen-bonding geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N1—H19···O1^{i}	0.85 (4)	2.25 (4)	3.057 (4)	159 (4)
N1—H20···N3^{ii}	0.85 (4)	2.26 (4)	3.103 (4)	169 (3)
C3—H1···O3	0.95	2.31	2.678 (3)	103
C6—H3···O1	0.95	2.47	2.852 (3)	104
C7—H4···O2	0.95	2.45	2.769 (3)	100
C12—H11···O4^{iii}	0.95	2.52	3.433 (4)	163
C18—H14···O2^{iii}	0.95	2.47	3.379 (3)	160
C20—H18···O1^{iv}	0.95	2.47	3.273 (3)	142

Symmetry codes: (i) $-x, 1-y, 1-z$; (ii) $1-x, 1-y, 1-z$; (iii) $x, y-1, z-1$; (iv) $-x, -y, 1-z$.

H atoms bonded to nitrogen were located in a difference map and were freely refined with individual U_{iso} values. Other H atoms were positioned geometrically and refined as riding, with C—H = 0.95 Å and U_{iso}(H) = 1.2U_{eq}(C).

Data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1994); cell refinement: *MSC/AFC Diffractometer Control Software*; data reduction: *CRYSTALS* (Watkin *et al.*, 1996); program(s) used to solve structure: *SIR*92 (Altomare *et al.*, 1993); program(s) used to refine structure: *CRYSTALS*; molecular graphics: *CrystalStructure* (Rigaku/MSC and Rigaku, 2003); software used to prepare material for publication: *CrystalStructure*.

The authors thank Dr A. Venkateswarlu and Dr K. Anji Reddy for their interest and encouragement in this work.

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