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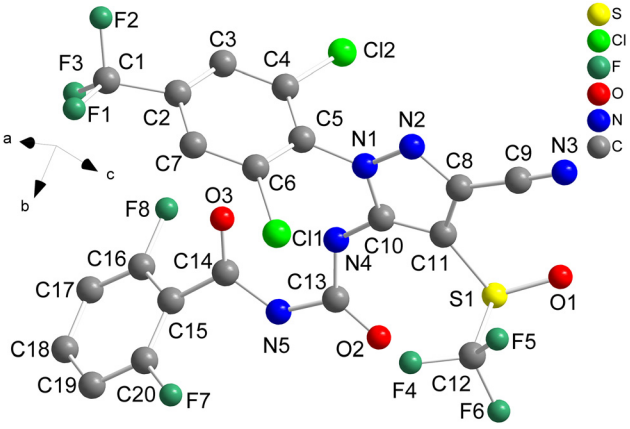
Crystal structure of *N*-((3-cyano-1-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4-(2,2,2-trifluoroacetyl)-1H-pyrazol-5-yl)carbamoyl)-2,6-difluorobenzamide, $C_{20}H_7Cl_2F_8N_5O_3S$



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Abstract

$C_{20}H_7Cl_2F_8N_5O_3S$, monoclinic, $P2_1/n$ (no. 14), a = 7.78993(14) Å, b = 11.8299(2) Å, c = 25.8640(5) Å, β = 93.1491(17)°, V = 2379.87(7) Å^3, Z = 4, $R_{gt}(F)$ = 0.0540, $wR_{ref}(F^2)$ = 0.1306, T = 100 K.

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The title crystal structure is shown in the figure. Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

1 Source of materials

2,6-Difluorobenzoyl isocyanate (0.1 mol, 18.3 g) was added to a three-neck flask and heated to 40 °C. Drop 5-amino-1-(2,6-dichloro-4-(trifluoromethyl)phenyl-4-((trifluoromethyl) sulfinyl)-1h–pyrazole-3-carbonitrile (0.1 mol, 43.7 g) of dichloroethane (100 g) solution with stirring at 40–45 °C. The suspension was stirred at 80 °C for 2 h and slowly cooled to 0 °C. Then the mixture was filtered and dried at 70–80 °C to get white powder. The white powder was dissolved in a mixed solution (ethyl acetate: *n*-heptane = 2:1, v/v) and then slowly volatilized at room temperature to obtain the single crystal.

Table 1: Data collection and handling.

Crystal:	Clear light colourless block
Size:	0.12 × 0.10 × 0.10 mm
Wavelength:	Cu *K*α radiation (1.54184 Å)
μ:	4.20 mm^{-1}
Diffractometer, scan mode:	Rigaku, Synergy, HyPix, φ and ω scans
θ_{max}, completeness:	71.1°, 100 %
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	11582, 4508, 0.030
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 4,223
$N(param)_{refined}$:	390
Programs:	Rigaku,[1] Olex2,[2] SHELX[3,4]

2 Experimental details

Absorption corrections were used by using multi-scan program.[1] The structure was solved with SHELX.[3,4] Hydrogen atoms were placed in their geometrically idealized positions. Hydrogen atoms were constrained to ride on their parent atoms.

3 Comment

Urea-based organic compounds are pivotal in the realm of drug discovery and development, owing to their distinct chemical architectures and broad spectrum of biological activities. Recent studies have shown that the classic drug phenobarbital, which contains a urea structure, has great potential to replace conventional benzodiazepine in the treatment of alcohol withdrawal syndrome (AWS).[5]

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

	x	*y*	*z*	U_{iso}*/U_{eq}
Cl1	0.69034 (13)	0.63675 (8)	0.73260 (4)	0.0499 (3)
Cl2	0.24050 (11)	0.37725 (8)	0.62286 (3)	0.0443 (2)
S1	0.04661 (8)	0.64347 (5)	0.80877 (2)	0.02156 (17)
F4	0.3240 (3)	0.77674 (18)	0.82028 (9)	0.0490 (6)
F5	0.2931 (3)	0.66252 (19)	0.88237 (8)	0.0462 (5)
F6	0.1264 (3)	0.8039 (2)	0.87404 (12)	0.0710 (9)
F7	0.3911 (3)	1.04613 (16)	0.63247 (7)	0.0373 (4)
F8	0.1436 (3)	0.80823 (16)	0.50333 (8)	0.0482 (6)
O1	−0.0107 (3)	0.56185 (17)	0.84797 (8)	0.0297 (5)
O2	0.1018 (3)	0.81029 (19)	0.73317 (8)	0.0372 (6)
O3	0.3245 (3)	0.73556 (18)	0.59696 (8)	0.0351 (5)
N1	0.3704 (3)	0.50706 (19)	0.71503 (9)	0.0243 (5)
N2	0.3853 (3)	0.42874 (19)	0.75328 (9)	0.0268 (5)
N3	0.2520 (4)	0.3464 (2)	0.87025 (10)	0.0400 (7)
N4	0.2365 (3)	0.6745 (2)	0.68766 (9)	0.0279 (5)
H4	0.2681 (3)	0.6580 (2)	0.65640 (9)	0.0334 (7)*
N5	0.1874 (3)	0.8514 (2)	0.65244 (9)	0.0291 (6)
H5	0.1453 (3)	0.9200 (2)	0.65527 (9)	0.0349 (7)*
C2	0.6821 (4)	0.5164 (3)	0.58868 (13)	0.0355 (8)
C3	0.5320 (4)	0.4549 (3)	0.58467 (12)	0.0332 (7)
H3	0.4988 (4)	0.4163 (3)	0.55351 (12)	0.0399 (8)*
C4	0.4301 (4)	0.4503 (2)	0.62700 (11)	0.0260 (6)
C5	0.4800 (4)	0.5059 (2)	0.67268 (11)	0.0236 (6)
C6	0.6333 (4)	0.5660 (2)	0.67617 (12)	0.0303 (7)
C7	0.7354 (4)	0.5717 (3)	0.63410 (15)	0.0387 (8)
H7	0.8403 (4)	0.6128 (3)	0.63629 (15)	0.0464 (10)*
C8	0.2802 (4)	0.4667 (2)	0.78822 (11)	0.0248 (6)
C9	0.2632 (4)	0.4010 (2)	0.83436 (11)	0.0291 (7)
C10	0.2590 (4)	0.5924 (2)	0.72492 (11)	0.0247 (6)
C11	0.1975 (4)	0.5695 (2)	0.77282 (11)	0.0232 (6)
C12	0.2102 (4)	0.7278 (2)	0.84775 (13)	0.0295 (7)
C13	0.1693 (4)	0.7797 (2)	0.69484 (12)	0.0282 (6)
C14	0.2634 (4)	0.8275 (2)	0.60674 (11)	0.0274 (6)
C15	0.2676 (4)	0.9231 (2)	0.56947 (11)	0.0256 (6)
C16	0.2114 (5)	0.9091 (3)	0.51785 (12)	0.0317 (7)
C17	0.2169 (5)	0.9941 (3)	0.48153 (12)	0.0356 (8)
H17	0.1745 (5)	0.9823 (3)	0.44682 (12)	0.0427 (9)*
C18	0.2861 (5)	1.0974 (3)	0.49707 (12)	0.0359 (8)
H18	0.2937 (5)	1.1565 (3)	0.47242 (12)	0.0431 (9)*
C19	0.3441 (5)	1.1159 (3)	0.54774 (13)	0.0350 (7)
H19	0.3914 (5)	1.1869 (3)	0.55818 (13)	0.0420 (9)*
C20	0.3320 (4)	1.0292 (3)	0.58280 (11)	0.0283 (6)
F1	0.9688 (12)	0.5866 (11)	0.5652 (4)	0.060 (3)[a]
F2	0.8555 (18)	0.4413 (8)	0.5299 (5)	0.063 (3)[a]
F3	0.754 (4)	0.603 (2)	0.5115 (11)	0.045 (4)[a]
C1	0.820 (3)	0.5394 (17)	0.5507 (8)	0.047 (3)[a]
F1A	0.7452 (6)	0.4406 (3)	0.50546 (15)	0.0542 (13)
F2A	0.9496 (5)	0.5117 (6)	0.55385 (17)	0.0751 (17)
F3A	0.7586 (17)	0.6199 (8)	0.5166 (4)	0.0453 (18)
C1A	0.7835 (9)	0.5205 (6)	0.5401 (3)	0.0383 (14)

[a]Occupancy: 0.289 (8).

Glimepiride containing sulfonylurea structure is the third generation of long-acting anti-diabetic drugs, the main mechanism of its hypoglycemic effect is to stimulate the secretion of insulin by islet bet which is very important in the treatment of diabetes.[6] Levastinib, a versatile anticancer drug containing urea structure, is often used in clinical studies in combination with other medicines and has shown excellent results.[7] In this paper, a new compound was synthesized by referring to the phenylpyrazole structure of the analgesic celecoxib and the structure of the drug urea described above.[8]

The title molecule in the crystal structure is a flexible molecule and each title molecule contains two phenyl rings, one pyrazole ring and one urea group. Intermolecular and intramolecular connectivity are achieved through hydrogen bonds. First hydrogen bond is N4–H4···O3, the distance of N4–H4 bond is 0.88 Å, the distance of H4···O3 bond is 1.86 Å, the angle of N4–H4···O3 is 138°, its an intramolecular hydrogen bond.[9] Second hydrogen bond is N5–H5···F7, the distance of N5–H5 bond is 0.88 Å, the distance of H5···F7 bond is 2.52 Å, the angle of N5–H5···F7 is 104°, its an intramolecular hydrogen bond.[10] Third hydrogen bond is N4–H5···O1, the distance of N4–H5 bond is 0.95 Å, the distance of H5···O1 bond is 1.98 Å, the angle of N4–H5···O1 is 168°.

In addition, there are two intermolecular C–F···π interactions and one intramolecular C–O···π interaction among the aromatic rings from neighboring molecules. The first C–F···π interaction is C12–F4···Cg^i (C2–C7; symmetry code *i*: 1 − *x*, 1/2 + *y*, 3/2 − *z*), the shortest distance between *F* and center of Cg^i is 3.118(3) Å.[11] The second C–F···π interaction is C12–F6···Cg^i, the shortest distance between F and center of Cg^i is 3.346(3) Å. The first C–O···π interaction is C14–O3···Cg^{ii} (C2–C7; symmetry code *i*: *x*, *y*, *z*), the shortest distance between *F* and center of Cg^{ii} is 3.414(3) Å.[12] All geometric parameters are in the expected ranges.[13]

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