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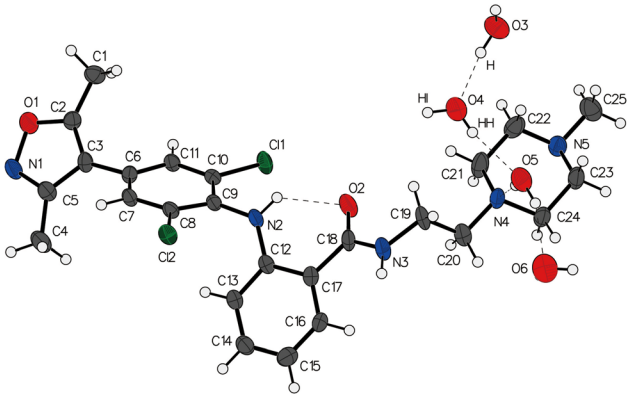
Crystal structure of 2-((2,6-dichloro-4-(3,5-dimethylisoxazol-4-yl)phenyl)amino)-*N*-(2-(4-methylpiperazin-1-yl)ethyl)benzamide hydrate, $C_{25}H_{37}Cl_2N_5O_6$



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Abstract

$C_{25}H_{37}Cl_2N_5O_6$, triclinic, $P\bar{1}$ (no. 2), a = 8.115(4) Å, b = 8.656(4) Å, c = 22.641(9) Å, α = 81.344(9)°, β = 80.173(9)°, γ = 65.833(8)°, V = 1423.9(10) Å^3, Z = 2, $R_{gt}(F)$ = 0.0652, $wR_{ref}(F^2)$ = 0.2010, T = 173 K.

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The molecular 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.

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Table 1: Data collection and handling.

Crystal:	Colourless needle
Size:	0.18 × 0.12 × 0.05 mm
Wavelength:	Mo *K*α radiation (0.71073 Å)
μ:	0.28 mm^{-1}
Diffractometer, scan mode:	Bruker APEX-II, φ and ω
θ_{max}, completeness:	27.5°, 99 %
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	12,547, 6361, 0.067
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\sigma(I_{obs})$, 3543
$N(param)_{refined}$:	358
Programs:	Bruker [1], SHELX [2, 3], Olex2 [4]

1 Source of materials

A mixture of 2-((2,6-dichloro-4-(3,5-dimethylisoxazol-4-yl)-phenyl)amino) benzoic acid (3.76 g, 10 mmol), pyrrolidine (1.57 g, 11 mmol), 2-(7-azabenzotriazol-1-yl)-*N*,*N*,*N*′,*N*′-tetramethyluronium hexafluorophosphate (HATU) (4.18 g, 11 mmol) and *N*,*N*-diisopropylethylamine (2.58 g, 20 mmol) was dissolved in *N*,*N*-dimethylformamide (25 mL). The mixture was stirred for 3 h at room temperature, until the TLC indicated the reaction was completed. The mixture was diluted with brine, and then extracted with ethyl acetate (3 × 30 mL). The organic phase was washed with brine (30 mL), dried with anhydrous sodium sulfate, and then concentrated under pressure. The title compound was separated by silica-gel column chromatography with ethyl dichloromethane-methanol (10 %) gradient solvent system. The target product was obtained as a white solid. Yield: 89.7 %.

2 Experimental details

The SHELXT [2] program was employed for the initial structure solution, followed by refinement using full-matrix least-squares procedures in SHELXL [3], within the OLEX2 program [4].

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

Atom	x	y	z	U_{iso}*/U_{eq}
C1	0.2267 (5)	0.1911 (4)	0.68834 (19)	0.0335 (9)
C2	0.2241 (5)	0.0190 (4)	0.69663 (17)	0.0277 (8)
C3	0.2422 (5)	−0.0965 (4)	0.65821 (16)	0.0255 (8)
C4	0.2218 (6)	−0.3958 (5)	0.6819 (2)	0.0423 (11)
C5	0.2246 (5)	−0.2340 (4)	0.69660 (17)	0.0314 (9)
C6	0.2714 (5)	−0.0807 (4)	0.59140 (16)	0.0236 (8)
C7	0.4049 (5)	−0.2104 (4)	0.56055 (16)	0.0252 (8)
C8	0.4295 (5)	−0.1983 (4)	0.49845 (16)	0.0240 (8)
C9	0.3158 (5)	−0.0610 (4)	0.46343 (15)	0.0233 (8)
C10	0.1884 (5)	0.0723 (4)	0.49577 (16)	0.0226 (8)
C11	0.1651 (5)	0.0664 (4)	0.55827 (16)	0.0248 (8)
C12	0.3072 (4)	−0.1664 (4)	0.36895 (16)	0.0233 (8)
C13	0.2783 (5)	−0.3089 (4)	0.39809 (17)	0.0271 (8)
C14	0.2629 (5)	−0.4253 (5)	0.36652 (19)	0.0327 (9)
C15	0.2782 (6)	−0.4041 (5)	0.3045 (2)	0.0392 (10)
C16	0.3011 (6)	−0.2609 (5)	0.27477 (18)	0.0334 (9)
C17	0.3131 (5)	−0.1394 (4)	0.30578 (16)	0.0257 (8)
C18	0.3189 (5)	0.0237 (4)	0.27291 (16)	0.0292 (9)
C19	0.3863 (5)	0.1719 (5)	0.17742 (18)	0.0350 (10)
C20	0.2186 (6)	0.2555 (5)	0.14340 (18)	0.0357 (10)
C21	0.1123 (7)	0.5418 (5)	0.16926 (18)	0.0454 (11)
C22	0.0787 (6)	0.7234 (5)	0.1473 (2)	0.0430 (11)
C23	0.0328 (6)	0.6803 (5)	0.05183 (18)	0.0387 (10)
C24	0.0688 (6)	0.4953 (4)	0.07252 (18)	0.0373 (10)
C25	−0.0860 (6)	0.9651 (5)	0.0821 (2)	0.0463 (11)
Cl1	0.05030 (13)	0.25476 (10)	0.45630 (4)	0.0340 (3)
Cl2	0.61309 (12)	−0.36043 (10)	0.46347 (4)	0.0298 (2)
H	0.618570	0.658869	0.143450	0.055*
HA	0.715241	0.766987	0.129489	0.055*
HB	0.348281	0.034573	0.379750	0.034*
HC	0.431636	−0.078185	0.198393	0.039*
HD	0.078225	0.161089	0.578234	0.030*
HE	0.481066	−0.309303	0.582355	0.030*
HF	0.308793	−0.245095	0.232101	0.040*
HG	0.269124	−0.325938	0.440770	0.032*
HH	0.656574	0.385797	0.111920	0.102*
HI	0.715134	0.353972	0.169830	0.102*
HJ	0.241591	−0.520320	0.387457	0.039*
HK	0.497752	0.142093	0.148136	0.042*
HL	0.387910	0.253884	0.203240	0.042*
HM	0.234313	0.188489	0.109556	0.043*
HN	0.109640	0.255475	0.170805	0.043*
HO	0.148443	0.690318	0.033794	0.046*
HP	−0.050975	0.721082	0.020568	0.046*
HQ	0.102562	0.276792	0.686468	0.050*
HR	0.302944	0.202749	0.650809	0.050*
HS	0.276510	0.207710	0.722278	0.050*
HT	−0.047950	0.484368	0.088116	0.045*
HU	0.124875	0.425970	0.037827	0.045*
HV	0.273191	−0.486829	0.282394	0.047*
HW	0.196223	0.502625	0.200430	0.054*
HX	−0.004020	0.534232	0.187957	0.054*
H0AA	−0.162658	1.001257	0.049409	0.069*
HY	0.028535	0.978792	0.067579	0.069*
HZ	−0.149651	1.034933	0.115720	0.069*
H1AA	0.028113	0.794505	0.181654	0.052*
H2AA	0.195335	0.731931	0.129594	0.052*
H3AA	0.339564	−0.462592	0.660192	0.063*
H4AA	0.125317	−0.369220	0.656554	0.063*
H5AA	0.198854	−0.461564	0.719156	0.063*
N1	0.2009 (5)	−0.2055 (4)	0.75334 (14)	0.0369 (8)
N2	0.3271 (4)	−0.0511 (3)	0.40063 (13)	0.0283 (7)
N3	0.3863 (4)	0.0193 (4)	0.21460 (14)	0.0327 (8)
N4	0.1909 (4)	0.4304 (4)	0.12006 (13)	0.0298 (7)
N5	−0.0475 (4)	0.7861 (4)	0.10239 (14)	0.0329 (8)
O1	0.2023 (4)	−0.0436 (3)	0.75422 (12)	0.0416 (7)
O2	0.2588 (4)	0.1560 (3)	0.29803 (12)	0.0409 (7)
O3	0.6078 (4)	0.7639 (3)	0.13587 (15)	0.0461 (8)
O4	0.6582 (7)	0.4326 (4)	0.1431 (2)	0.0850 (14)
O5	0.5212 (4)	0.3765 (4)	0.04784 (13)	0.0429 (7)
H5A	0.532098	0.320348	0.017641	0.052*
H5B	0.414799	0.397558	0.068571	0.052*
O6	0.5522 (6)	0.1276 (5)	−0.02736 (19)	0.0807 (12)
H6A	0.437943	0.149220	−0.006993	0.097*
H6B	0.543859	0.168144	−0.062273	0.097*

3 Comment

Benzamide is a type of aromatic amide containing a carboxylic acid group, commonly used for synthesizing a variety of compounds. Halogen-substituted derivatives of benzamide exhibit notable properties such as antipsychotic, anticancer, and antiemetic effects, and show potential for treating human tumors [5]. There are numerous similar structures reported in literature [6–9]. This article reports the comprehensive single crystal structure of a newly identified benzamide compound.

In the molecular structure of the titled organic compound, the piperazine hexagonal ring adopts a chair conformation, while the five-membered ring of isoxazolidine exhibits almost planar characteristics with the atoms lying in the same plane. The dihedral angle of C2–C3–C5–O1 is only 1.0(3)°, indicating minimal torsion. The two benzene rings in the molecule are non-coplanar and display evident torsion. All bond lengths, bond angles, and dihedral angles in the molecule fall within reasonable ranges, resembling similar structures reported in the literature [10–15].

Within the molecule, a hydrogen bond (N2–HB···O2) is formed, with a bond angle of 127.3(3)° and a bond length of 2.075(3) Å, which also contributes to the relatively small dihedral angle (27.3(4)°) of N2–C12–C18–O2. Water molecules in the crystal structure are stabilized by hydrogen bonding

interactions with hydrogen atoms in the organic compound, as well as with other water molecules.

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

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