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X-ray Structure Analysis Online

Crystal Structure of 4-Phenyl-piperazine-1-sulfonamide

Malika BERREDJEM,*, Radia BOUASLA,* Nour-Eddine AOUF,* and Carole BARBEY**†**

**LCOA, Bioorganique Chemistry Group, Sciences Faculty, Chemistry Départment, Badji Mokhar-Annaba University Box 12. Annaba-Algeria*

***Laboratoire CSPBAT, FRE 3043 CNRS, University of Paris 13, 74 rue Marcel Cachin, 93017 Bobigny Cedex, France*

The structure of 4-phenyl-piperazine-1-sulfonamide was determined by X-ray crystallography. The compound crystallized in a monoclinic system and was characterized as follows: $P2_1/c$, a = 24.1829(7), b = 9.5485(3), c = 9.7885(2)Å, β = 92.2337(16)˚, Z = 8, V = 2258.55(11)Å^3. The crystal structure was solved by direct methods and refined by full-matrix least-squares on F^2 to final values of $R1$ = 0.0427 for 3206 reflections [$I > 2\sigma(I)$] and $R1$ = 0.0739, $wR2$ = 0.1083 for all the 4589 unique reflections. The crystal structure consists of layers of polar regions that enclose a sulfonamide function linked by hydrogen bonds and hydrophobic regions with π-π stacking interactions.

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The introduction of sulfonamides into clinical medicine in the 1930s marked the beginning of microbial chemotherapy.[1] Sulfonamides, an important class of pharmaceutical compounds, actually exhibit a wide spectrum of biological activities including antibacterials, diuretics, hypoglycemics and HIV protease inhibitors.[2] The emerging resistance of microorganisms to some synthetic antimicrobial agents makes it necessary to continue the search for new antimicrobial substances. Therefore, numerous molecules containing sulfonamide structure have been created, such as the new modified sulfonamide title compound submitted to X-ray analysis.

The vast majority of sulfonamides are prepared from the reaction of a sulfonyl chloride with ammonia, or primary or secondary amines, or *via* related transformations.[3] More recently, a novel approach for the syntheses of alkyl and aryl sulfonamides has been reported by Shaabani *et al*.[4] In our previous works, we established that chlorosulfonyl isocyanate is a suitable reagent that allows the introduction of a sulfonamide moiety in bioactive molecules.[5] In this research 4-phenyl-piperazine-1-sulfonamide (Fig. 1) was prepared in two steps (carbamoylation-sulfamoylation) by the reaction of chlorosulfonyl isocyanate (1.62 g, 11.4 mmol) and dimethyl malate (1.84 g, 11.4 mmol) in anhydrous CH_2Cl_2 (20 mL). After 30 min, *N*-chlorosulfonylcarbamate was added to a solution of 4-phenyl-piperazine (1.47 g, 11.4 mmol) in the same solvent (20 mL) in the presence of triethylamine (1.1 equiv) at 0˚C. The resulting mixture was stirred for less than 2 h at room temperature. The reaction mixture was washed with 0.1 M HCl and water, and the organic layer was dried over anhydrous magnesium sulfate and concentrated in vacuum. The residue was purified by chromatography on silica gel (eluted with CH_2Cl_2) to give sulfonamide as a white solid in high yields (>80%). Single crystal suitable for X-ray structure analysis could be obtained by slow evaporation of a concentrated solution in ether at room temperature.

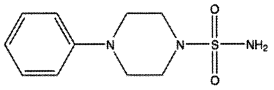


Fig. 1 Chemical diagram of the title compound.

The crystal and structure-refinement data are summarized in Table 1. An ORTEP plot of the molecule is given in Fig. 2.

All H atoms attached to C atoms were fixed geometrically and treated as riding with C–H = 0.93 Å (aromatic) or 0.97 Å (secondary CH_2 group) with U_{iso}(H) = 1.2 U_{eq}(C) or 1.5 U_{eq}(C),

Table 1 Crystal, experimental and refinement data

Chemical formula: $C_{10}H_{15}N_3O_2S$
Formula weight = 241.31 g mol^{-1}
T = 293(2)K
Crystal system: monoclinic
Space group: $P21/c$, Z = 8
Cell dimensions: a = 24.1829(7)Å, b = 9.5485(3)Å, c = 9.7885(2)Å, β = 92.2337(16)˚
V = 2258.55(11)Å^3
D_x = 1.419 g cm^{-3}
Radiation: Mo K_α (λ = 0.71073 Å)
Crystal size = 0.3 × 0.1 × 0.1 mm^3
θ range for data collection: 2.3˚ to 26.4˚
Reflections collected/unique/with [$I > 2\sigma(I)$]: 20269/4589/3206
Data/restraints/parameters: 4589/6/302
Goodness of fit on F^2: 1.020
Final R indices [$I > 2\sigma(I)$]: $R1$ = 0.0427, $wR2$ = 0.0952
R indices (all data): $R1$ = 0.0739, $wR2$ = 0.1083
$(\Delta/\sigma)_{max}$: 0.005
$(\Delta\rho)_{max}$: 0.186 e.Å^{-3} $(\Delta\rho)_{min}$: –0.298 e.Å^{-3}
Measurement: Enraf-Nonius CAD4
Programs system: WinGX Package[6]: SHELXS–97[7], Structure determination: SHELXS-97[7]
Refinement method: Full-matrix least-squares (SHELXL-97[7])
CCDC deposition number: 726198

† To whom correspondence should be addressed.
E-mail: carole.barbey@smbh.univ-paris13.fr

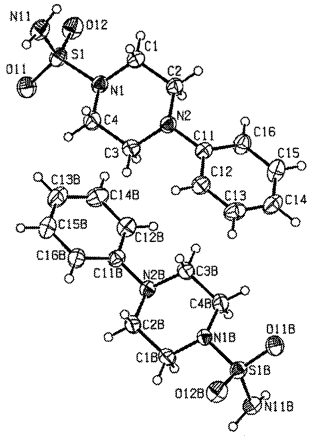


Fig. 2 ORTEP structure of the 4-phenyl-piperazine-1-sulfonamide, showing 40% probability ellipsoids.

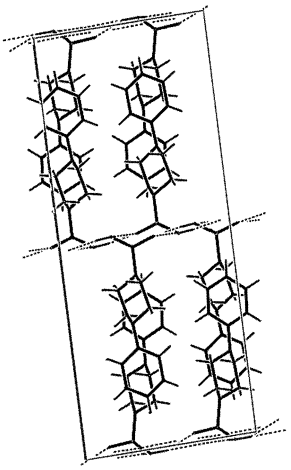


Fig. 3 Molecular packing viewed down the *b*-axis, showing an alternate stacking of hydrophilic and hydrophobic layers along the *a* direction. H-bonds implying sulfonamide functions are represented as dashed lines (PLUTO diagram from PLATON[9]).

Table 2 Hydrogen-bonds geometry (Å and °)

D-H···A	D-H	H···A	D···A	DHA
N(11)-H(11A)...O(12A)$^{(i)}$	0.897	2.321	3.170	157.70
N(11)-H(11A)...O(11A)$^{(ii)}$	0.897	2.621	3.138	117.53
N(11)-H(11B)...O(12A)$^{(iii)}$	0.894	2.350	3.210	161.30
N(11B)-H(11C)...O(11B)$^{(iv)}$	0.902	2.230	3.092	159.91
N(11B)-H(11D)...O(11B)$^{(v)}$	0.899	2.509	3.348	155.52
N(11B)-H(11D)...O(12B)$^{(vi)}$	0.899	2.515	3.130	126.07

Symmetry transformations used to generate equivalent atoms:
(i) $-x+1, -y-1, -z+1$; (ii) $-x+1, y-1/2, -z+3/2$; (iii) $x, -y-1/2, z+1/2$; (iv) $-x, y+1/2, -z+3/2$; (v) $-x, -y, -z+1$; (vi) $x, -y+1/2, z-1/2$.

respectively. H atoms of amino group were located in a difference Fourier map and included in subsequent refinement restraints (N–H = 0.90(1)Å and H···H = 1.66(2)Å with U_{iso}(H) = 1.2 U_{eq}(N). In the last stage of refinement, they were treated as riding on their parent N atom.

The asymmetric unit of the title compound is built up from 2 molecules oriented face to face in an antiparallel manner (Fig. 2). The piperazine ring has a chair conformation, the most stable chemical conformation, with bond angles of around 109°. The crystal structure consists of hydrophilic layers that enclose a sulfonamide function and hydrophobic layers made of a phenyl-piperazine structure. These layers are stacking along the *a* direction (Fig. 3). In this crystal packing, the molecules are linked *via* weak intermolecular N–H···O=S hydrogen bonds, forming an infinite intermolecular hydrogen-bond network present along the *b* and *c* directions (Table 2). This study revealed that the π-π stacking interaction between nearby phenyl ring is an T-shaped edge-to-face arrangement[8] with a distance of 5.504 Å between the ring centers. These edge-to-face interactions play an essential role in the cohesion of the crystal.

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