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Crystal Structures of Isomeric N-(2-chlorophenyl)-2,5-dimethoxybenzene-sulfonamide and N-(4-chlorophenyl)-2,5-dimethoxybenzenesulfonamide

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ABSTRACT

Crystal structures of two isomeric compounds of formula $C_{14}H_{14}NO_4SCl$, namely N-(2-chlorophenyl)-2,5-dimethoxybenzenesulfonamide (I) and N-(4-chlorophenyl)-2,5-dimethoxy-benzenesulfonamide (II) are described. Both the compounds crystallize in the triclinic crystal system and P-1 space group with the asymmetric unit of (I) consisting of one molecule, while, that of (II) containing two (Molecules A and B). The molecule of (I) is U shaped with the central $–C_{arm}$-S-N-C_{arm}- segment making a torsional angle of 75.5^o, while, the two symmetry independent molecules of (II) are V shaped with the central segments making torsions of -57.8(9)^o in Mol. A and -59.6(10)^o in Mol. B. The dihedral angle between the benzene rings is 84.73(7)^o in (I), and, 82.72(3) and 80.80(3)^o respectively in molecules A and B of (II). The supramolecular architecture exhibited by both is built by the common intermolecular interactions: N-H…O hydrogen bonds, C-H...O, C-H...π_{aryl} and π_{aryl}... π_{aryl} interactions. However, the role played by these interactions in supramolecular aggregation of molecules of (I) and (II) are different to some extent, and as a result, (I) consists of 2 dimensional (2D) sheets, while, (II) forms 1D zig-zag chains.

Keywords: Sulfonamides, Crystal structures, X-ray diffraction, N-H…O hydrogen bonds, C-H…O interactions, C-H...π, π…π interactions

INTRODUCTION

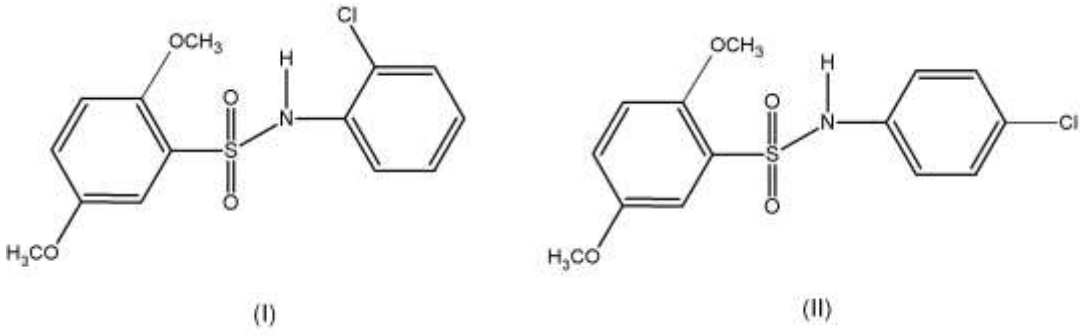
Sulfonamide drugs were the first among the chemotherapeutic agents to be used for the cure and prevention of bacterial infection in human beings [1]. They play a vital role as key constituent in a number of biologically active molecules. Till date, sulfonamides have been known to exhibit a wide variety of biological activities such as antibacterial [2], insecticidal [3], antifungal [4], antihepatitis [5], anti-inflammatory [6], antitumor [7], anticancer [8], anti-HIV [9] and antitubercular activities [10]. In recent years extensive research studies have been carried out on the synthesis and evaluation of pharmacological activities of molecules containing sulfonamide moiety for different activities, and have been reported to be important pharmacophores [11]. With these considerations in mind and based on our recent studies on the crystal structures of a few N-(aryl)-aryl sulfonamides [12-14], the crystal structures of two isomers N-(2-chlorophenyl)-2,5-dimethoxybenzenesulfonamide (I) and N-(4-chlorophenyl)-2,5-dimethoxy-benzenesulfonamide (II) are described here.

MATERIALS AND METHODS

All the reagents were purchased from Spectrochim Pvt. Ltd., India and were used without further purifications. Melting points of I and II were determined in open capillary tubes.

Synthesis

2-chloro/4-chloroaniline (10 mmol) and excess pyridine were dissolved in dichloromethane (20 ml) and a solution of 2,5-dimethoxybenzenesulfonyl chloride (13 mmol) in dichloromethane (20 ml) was added drop wise with vigorous stirring at 273 K. After 1 h, the reaction was quenched by addition of water and the oil thus obtained was washed with dilute HCl. The organic layer separated was evaporated to give the crude product, which was recrystallized from aqueous ethanol. I: Yield: 66%, M. pt. 443 K; II: Yield: 69%, M. pt. 456 K.



Structures of the two synthesized compounds

Preparation of crystals of I and II

Single crystals of both I and II suitable for single crystal X-ray studies were obtained from slow solvent evaporation technique at room temperature (27°C). Compounds (50 mg each) were dissolved in ethanol (15 ml) and to these clear solutions few drops of water was added. The solutions were slightly warmed and filtered. The solvent was allowed to evaporate at room temperature. Colourless prism-like crystals of both the compounds were obtained after few days.

X-ray crystallographic study

The X-ray intensity data were collected at a temperature of 296.1(5) K on a Bruker Proteum2 CCD diffractometer equipped with an X-ray generator operating at 45 kV and 10 mA, using Cu-Kα radiation of wavelength 1.54178 Å. Data were collected for 24 frames per set with different settings of φ (0^o and 90^o), keeping the scan width of 0.5^o, exposure time of 5 s, the sample-to-detector distance of 45.10 mm, and 2θ value at 46.6^o. Image processing and data reduction were done using SAINT-Plus and XPREP [15]. The structure was solved by direct methods using SHELXS-97 [16]. All the non-hydrogen atoms were revealed in the first-difference Fourier map itself and were refined anisotropically. All the hydrogen atoms were positioned geometrically. In I and II, the C-H atoms were positioned geometrically, with C-H=0.93-0.96 Å, and refined using a riding model with $U_{iso}(H)=1.2\text{-}1.5\ U_{eq}(C)$. The N-H hydrogen atoms in I was located in a difference map and was refined isotropically with the bond length restraint N-H = 0.86(4) Å, while in (II) it was positioned geometrically. A region of disordered electron density in (I), most probably disordered ethanol–water solvent molecules, was treated with the SQUEEZE routine in PLATON. The crystallographic data and refinement parameters for I and II are summarized in Table 1. All the geometrical calculations were carried out using the program PLATON [17] within the WinGX suite [18]. The molecular and packing diagrams were generated using the software MERCURY [19].

Table 1: Crystal data and structure refinements for I and II

Compound code	I	II
Empirical formula	$C_{14}H_{14}NO_4SCl$	$C_{14}H_{14}NO_4SCl$
Formula weight	327.79	327.79
Crystal system	Triclinic	triclinic
Space group	P-1	P-1
a/Å	8.532 (2)	10.5136 (8)
b/Å	10.432 (2)	11.0301 (8)
c/Å	11.092 (3)	13.6357 (10)
α/°	105.171 (17)	95.960 (3)
β/°	91.579 (19)	105.155 (3)
γ/°	106.522 (15)	98.704 (3)
Volume/$Å^3$	908.0 (4)	1491.57 (19)
Z	2	4
ρ_{calc} g/cm^3	1.1989	1.4596
μ/mm^{-1}	3.055	3.719
F(000)	342.4	684.8
Crystal size/mm^3	0.22 × 0.2 × 0.18	0.24 × 0.19 × 0.15
2θ range for data collection/°	12.96 to 129.36	6.8 to 128.86
Reflections collected	3875	12398
Independent reflections	2632 [R_{int}=0.0471, R_{sigma}=0.1026]	4599 [R_{int}=0.0563, R_{sigma}=0.0853]
Data/restraints/parameters	2632/1/197	4599/0/383
Goodness-of-fit on F^2	1.278	1.252
Final R indexes [I>=2σ (I)]	R_1=0.1339, wR_2=0.3160	R_1=0.1584, wR_2=0.4770
Final R indexes (All data)	R_1=0.1423, wR_2 =0.3280	R_1=0.2743, wR_2=0.5614
Largest diff. peak/hole/e $Å^{-3}$	1.21/-0.73	1.30/-1.20

RESULTS AND DISCUSSION

Molecular structures of I and II

The molecular structure of compounds I and II with thermal ellipsoids drawn at 30% probability is shown in Figure 1. In both the compounds, the bond lengths and angles are similar to those observed in the reported related structure [12] and, hence, are not discussed here.

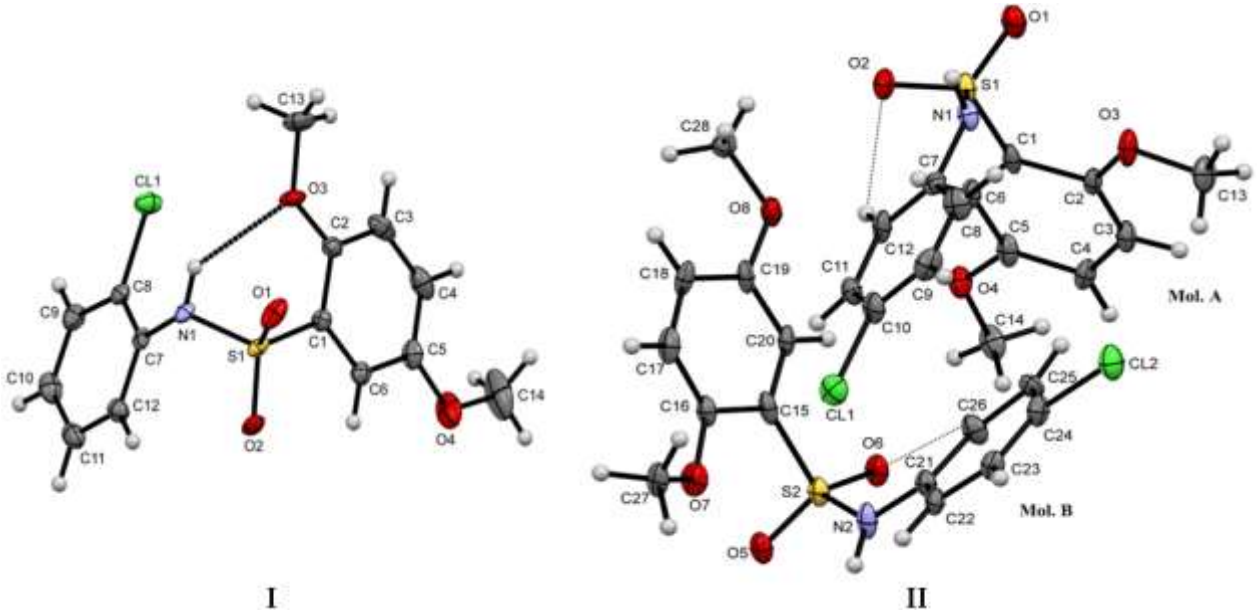


Figure 1: Molecular structure of I and II, showing thermal displacement ellipsoids drawn at the 30% probability level. Intra molecular hydrogen bonds are shown as thin lines

Both the compounds crystallize in the triclinic crystal system and P-1 space group with the asymmetric unit of (I) consisting of one molecule, while, that of (II) containing two (Molecules A and B). The molecule of (I) is U shaped with the central –C1-S1-N1-C7-segment making a torsional angle of 75.5^o, while, the two symmetry independent molecules of (II) are V shaped with the central segments making torsions of -57.8(9)^o in Molecules A and -59.6(10)^o in Molecules B. The dihedral angle between the benzene rings is 84.73(7)^o in (I), and, 82.72(3) & 80.80(3)^o respectively in molecules A and B of (II). The molecular conformation of I is stabilized by intramolecular N-H...$O_{o\text{-methoxy}}$ hydrogen bonds, while, that of molecules A & B of II by C-H... $O_{o\text{-methoxy}}$ interactions, closing into an S(6) loop in each case (Table 2) [20]. In the reported structure of N-(phenyl)-2,5-dimethoxybenzenesulfonamide [12], the L shaped molecular conformation is stabilized by C-H...$O_{sulfonyl}$ interactions and the two benzene rings are tilted with respect to one another with an angle of 89.17(9)^o. Thus, the nature and position of substituents on the aniline rings of these compounds have significant effect on the molecular conformations and on the nature of the intramolecular interactions stabilizing them.

Crystal structures of I and II

The crystal structure of I features a strong N1-H1...O1 hydrogen bonds between the molecules resulting in the formation of an inversion related $R_2^2(8)$ [20] dimer. The molecules of the adjacent $R_2^2(8)$ dimers are linked to one another via C12-H12...O2 intermolecular interactions to form another dimer with graph-set notation $R_2^2(12)$ [20] (Figure 2 and Table 2). The alternating $R_2^2(8)$ and $R_2^2(12)$ dimers produce double C(10) chains [20] running along a axis as shown in Figure 2. The molecules of the neighbouring double chains are interconnected via C10-H10...π_1 interactions (Table 2), π_1 being the centroid of the benzene sulfonyl ring (C1-C6), to form a 2D zig-zag sheet along the ab-plane (Figure 3). The 2D sheet thus obtained is stabilized by π_2...π_2 interactions, π_2 being the centroid of the aniline ring (C7-C12), with centroid-centroid distance = 3.8624(1) Å; interplanar distance=3.3267(1) Å; slippage=1.962(1) Å.

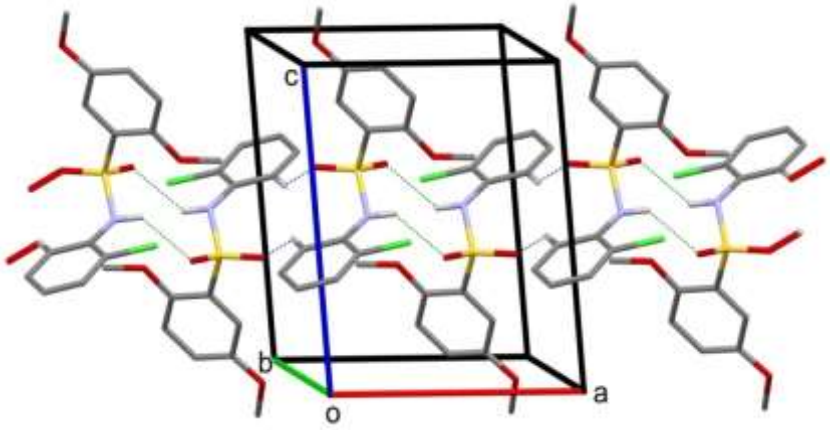


Figure 2: A view of the crystal packing of (I) displaying the C(10) double chains running along a axis

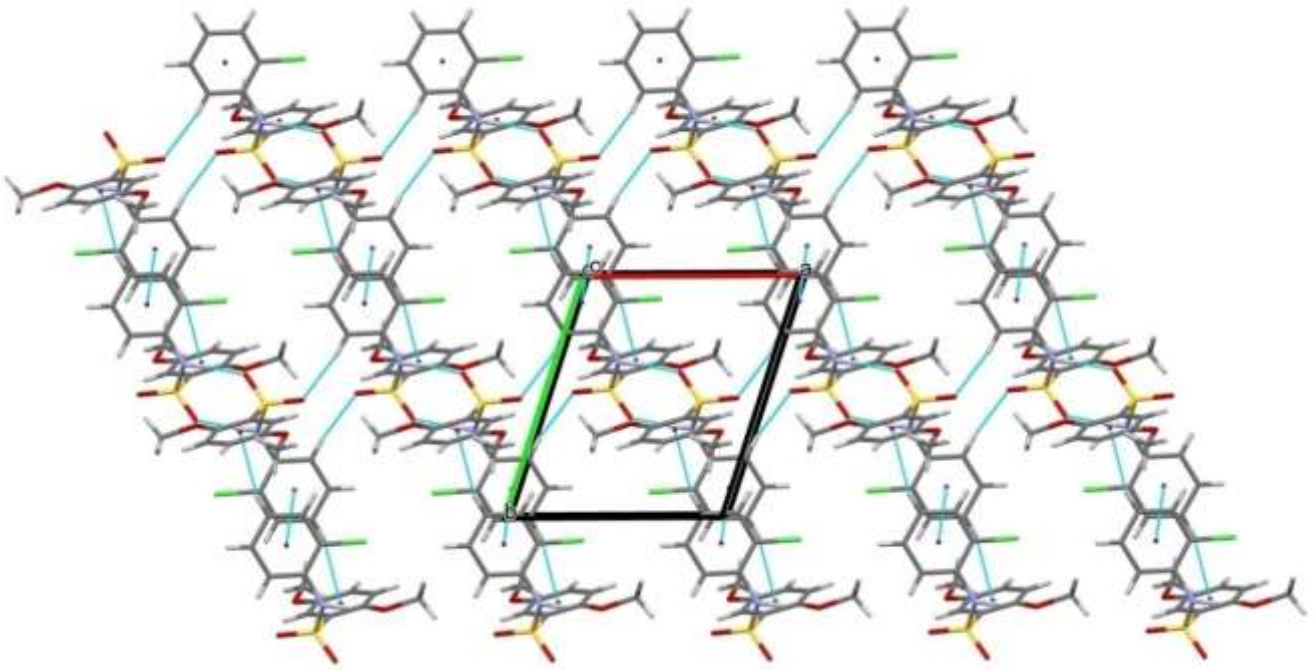


Figure 3: Crystal packing of (I) when viewed down the c axis displaying the 2D sheets formed parallel to the ab-plane

In the crystal structure of II, N2-H2...O5 hydrogen bonds between the B molecules result in the formation of $R_2^2(8)$ dimers. Each molecule of this dimeric motif is connected to the A molecule via C6-H6...O8 intermolecular interactions to form a discrete tetrameric unit (Table 2 and Figure 4). The tetramer is further stabilized by C11-H11...π_1 and C25-H25... π_2 interactions between the A and B molecules, π_1 and π_2 being the centroids of the sulfonyl benzene rings (C15-C20) and (C1-C6), respectively. Further, the A molecules of the adjacent tetramers are interconnected by π_2...π_2 interactions with centroid-centroid distance = 3.9226(1) Å; interplanar distance=3.4330(1) Å; slippage=1.898(1) Å. The result is a one dimensional zig-zag supramolecular architecture as displayed in Figure 5.

Table 2: Geometric parameters for hydrogen bonds and other intermolecular contacts (Å, °) operating in the crystal structures of I and II

I					II				
D-H…A	**D-H**	**H…A**	**D…A**	**D-H…A**	**D-H…A**	**D-H**	**H…A**	**D…A**	**D-H…A**
N1-H1…O3$^{\#}$	0.87	2.33	2.9762	131	C12-H12…O2$^{\#}$	0.93	2.50	3.1138	124
N1-H1…O1^{i}	0.87	2.33	2.9977	133	C26-H26…O6$^{\#}$	0.93	2.40	3.0721	129
C12-H12…O2^{ii}	0.93	2.58	3.4079	148	N2-H2…O5^{i}	0.86	2.21	2.9648	147
C10-H10…π_1^{iii}	0.93	2.77	3.6712	164	C6-H6...O8	0.93	2.52	3.3356	147
π_2... π_2^{iii}	-	-	3.8624	-	C11-H11…π_1	0.93	2.87	3.6753	145
					C25-H25…π_2	0.93	3.00	3.7776	142
					π_2... π_2^{ii}	-	-	3.9226	-
#: Intra; i: 1-x,1-y,1-z; ii: -x,1-y,1-z; iii: -x,-y,1-z					#: Intra; i: 2-x,1-y,-z; ii: 1-x,1-y,1-z				

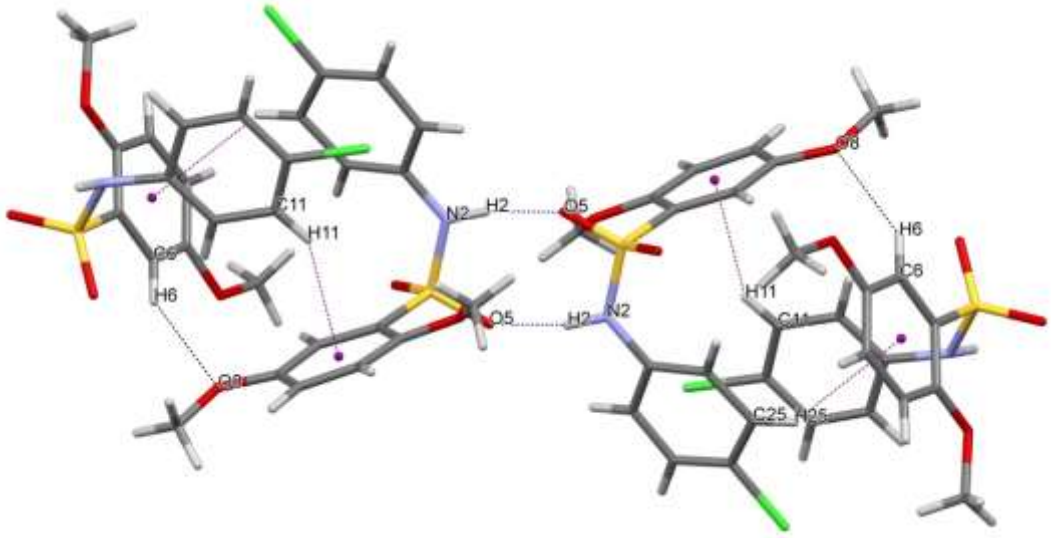


Figure 4: A view of the crystal packing of (II), displaying the formation of a discrete tetrameric unit via N-H...O hydrogen bonds and C-H...O interactions

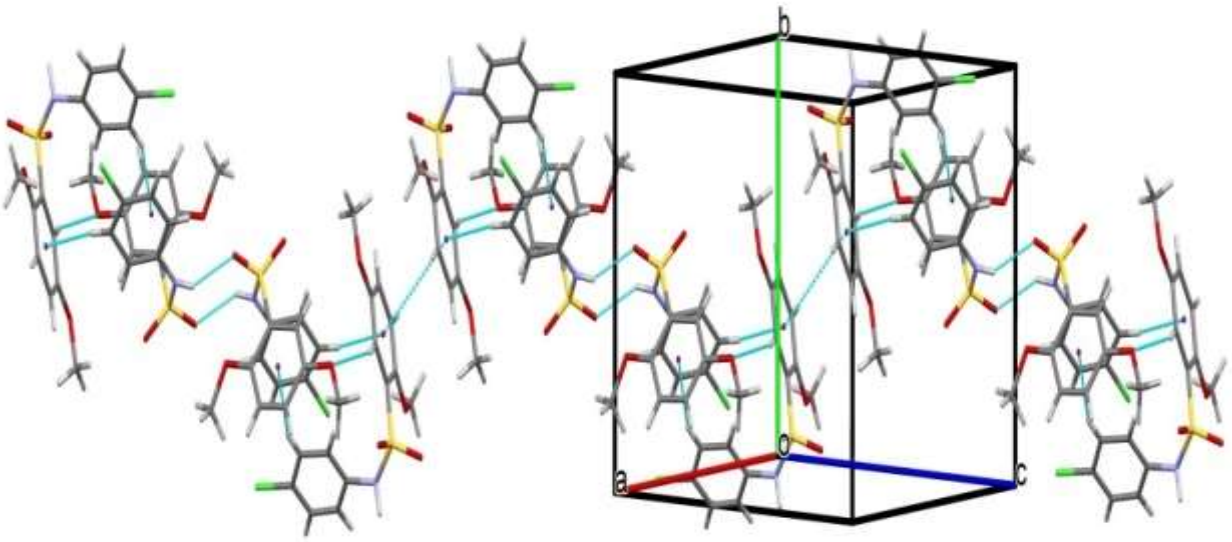


Figure 5: One dimensional zig-zag chains observed in (II)

CONCLUSION

Crystal structures of N-(2-chlorophenyl)-2,5-dimethoxybenzenesulfonamide (I) and N-(4-chlorophenyl)-2,5-dimethoxybenzenesulfonamide (II) are described. The asymmetric unit of (I) consists of one molecule, while, that of (II) contains two. The molecular conformations of both (I) and (II) are stabilized by N-H...O intramolecular hydrogen bonds. The supramolecular architecture exhibited by both is built by the common intermolecular interactions: N-H…O hydrogen bonds, C-H...O, C-H...π_{aryl} and π_{aryl}...π_{aryl} interactions. However, the role played by these interactions in supramolecular aggregation of molecules of (I) and (II) are different to some extent, and as a result, (I) consists of 2 dimensional (2D) sheets, while, (II) forms 1D zig-zag chains.

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