Abstract

This thesis encompasses the doctoral work carried out during 2004–2007. The crystal and molecular structure analyses of 1,2,4-Triazole and 1-Benzhydryl piperazine derivatives are detailed here. The text of this thesis is spread over four chapters; a brief description of each chapter is presented here.

Chapter 1. Materials and X-ray techniques

This chapter gives a brief general introduction on heterocycles and their biological importance. This is followed by the history of X-ray crystallography, the basic concepts of diffraction of X-rays by crystals, the methods of determining the unit cell parameters and the space groups, instrumentation and practical aspects of collecting and processing the intensity data, direct methods for structure determination and also the refinement procedure. This chapter also provides the information about the working principle of the DIPLabo Image Plate diffractometer which was used to collect the data. The conformational parameters viz., torsion angles, dihedral angles and the ring conformations of the five and six-membered rings have been discussed. This chapter also briefly discusses about the hydrogen bonds and their role in biological activities.

Chapter 2. 1,2,4-Triazole derivatives

The second chapter has a brief introduction to the importance and the application of triazole derivatives. This chapter also provides information about the method employed for data collection and the different softwares used to arrive at the crystal structure. Also it gives a detailed description about the crystal and molecular structure of one triazole derivative and two triazolothiadiazole derivatives viz.,
Abstract

2-(4-Methyl-2'-biphenyl)-4-amino-1,2,4-triazole-3-thiol

The compound, \( C_{15}H_{14}N_4S \), crystallizes in the primitive monoclinic crystal system under the space group \( P2_1/c \) with cell parameters \( a = 11.2730(3) \text{ Å}, b = 17.2450(15) \text{ Å}, c = 7.4130(10) \text{ Å}, \beta = 97.742(5)^\circ \) and \( Z = 4 \). The structure was solved by direct methods and refined to \( R_1 = 0.0612 \). The title compound exhibits strong tautomerism. The 1,2,4-triazole and the phenyl rings are independently planar. The structure exhibits an intermolecular hydrogen bond of the type \( \text{N-H} \cdots \text{S} \). The molecules are interlinked by this hydrogen bond to form a linear polymeric chain.

3-paratolyl-6-(4'methyl-biphenyl-2-yl)-1,2,4-triazolo[3,4-b][1,3,4]thiadiazole

The compound, \( C_{23}H_{18}N_4S \), crystallizes in the Monoclinic crystal class in the space group \( P2_1/c \) with cell parameters \( a = 10.378(2) \text{ Å}, b = 5.9050(4) \text{ Å}, c = 25.026(3) \text{ Å}, \beta = 127.981(3)^\circ \) and \( Z = 4 \). The structure was solved by direct methods and refined to \( R_1 = 0.0925 \). The 1,2,4-triazolothiadiazole ring is planar. The presence of the methylphenyl ring in the third position of the triazole ring leads to the elongation of \( N1-N2 \) bond length to 1.399(5) Å. The C-N bond lengths in the five membered triazole ring system are longer than a typical C=N bond, but shorter than the C-N bond, indicating electron delocalization in the ring. The thiadiazole moiety displays differences in the pairs of bonds due to the fused 1,2,4-triazole ring and the two different groups attached to either side of the triazolothiadiazole system. No classic hydrogen bonds are observed in the structure.

3-(4-Chlorophenyl)-6-(4'methylbiphenyl-2-yl)-1,2,4-triazolo[3,4-b][1,3,4]thiadiazole

The compound, \( C_{22}H_{15}ClN_4S \), crystallizes in the triclinic crystal class in the space group \( P\overline{1} \) with cell parameters \( a = 8.9750(5) \text{ Å}, b = 9.5530(10) \text{ Å}, c = 11.2670(12) \text{ Å}, \alpha = 85.248(2)^\circ, \beta = 87.089(7)^\circ, \gamma = 84.025(6)^\circ \) and \( Z = 2 \). The structure was solved by direct methods and refined to \( R_1 = 0.0472 \). The 1,2,4-triazolothiadiazole ring is planar. The dihedral angle between the fused triazolothiadiazole ring and the chlorophenyl indicates that they are almost coplanar. The C-N bond
lengths in the five membered triazole ring system are longer than a typical C=N bond but shorter than the C–N bond, indicating electron delocalization in the ring. The thiadiazole moiety displays differences in the pairs of bonds due to the fused 1,2,4-triazole ring and the two different groups attached to either side of the triazolothiadiazole system. The structure exhibits an intermolecular hydrogen bond of the type C–H⋯N. The molecules form hydrogen bonded dimers.

Chapter 3. 1-Benzhydrylpiperazine derivatives

This chapter encompasses a brief introduction to 1-Benzhydrylpiperazine derivatives and their applications in various fields. This chapter also has information about the crystal and molecular structures of nine benzhydryl piperazine derivatives viz.,

1-Benzhydrylpiperazine

This molecule, C_{17}H_{20}N_{2}, crystallizes in the primitive monoclinic lattice in the space group P2_1/c with cell parameters a = 10.1710(8) Å, b = 9.5990(5) Å, c = 15.5260(13) Å, β = 107.861(2)° and Z = 4. The structure was solved by direct methods and the residuals finally converged to R_1 = 0.0580. The piperazine ring in the structure is in the chair conformation. The bond N4–C7 lies in the equatorial plane of the piperazine ring. The sum of the bond angles around the piperazine N atoms indicate that they are sp^3 hybridized. The dihedral angle between the least-squares plane of the piperazine ring and the two phenyl rings [C8–C13] and [C14–C19] are 86.39(12)° and 65.01(12)° respectively. The dihedral angle between the two phenyl rings bridged by the carbon atom is 81.14(13)°.

1-Benzhydryl-4-(4-chloro-2-fluoro-benzenesulfonyl)-piperazine

The compound, C_{23}H_{22}ClFN_{2}O_{2}S, crystallizes in the monoclinic crystal class in the space group P2_1/c with cell parameters a = 9.6180(7) Å, b = 12.9670(10) Å, c = 19.4020(12) Å, β = 114.716(3)° and Z = 4. The structure was solved by direct methods and the residuals converged to R_1 = 0.0440. A study of torsion angles, asymmetric parameters and least-squares plane calculation reveals that the piperazine ring in the structure is in a chair conformation. The substituents on both the nitrogens of
the piperazine ring are in the equatorial position. The sulfonyl O atoms O9 and O8 are oriented in +synclinal and -synclinal conformations respectively. The geometry around the S atom is distorted tetrahedral. The sum of the bond angles around the piperazine N atoms indicate that they adopt a pyramidal geometry and are $sp^3$ hybridized. The steric hindrance caused by the bulky sulfonyl group is more than the steric effects caused by the diphenylmethyl rings which are attached on either side of the piperazine ring. No classic hydrogen bonds are found in the structure.

**1-Benzhydryl-4-(3,5-dimethyl-isoxazole-4-sulfonyl)-piperazine**

The compound, C$_{22}$H$_{25}$N$_3$O$_3$S, crystallizes in the triclinic crystal class in the space group $P1$ with cell parameters $a = 9.2600(7)$ Å, $b = 9.5450(5)$ Å, $c = 12.2490(9)$ Å, $\alpha = 76.836(5)^\circ$, $\beta = 82.444(2)^\circ$, $\gamma = 86.054(5)^\circ$ and $Z = 2$. The structure was solved by direct methods and the residuals converged to $R_1 = 0.0465$. The piperazine ring in the structure is in a chair conformation. The bonds N1–S7 and N4–C17 are in the equatorial plane of the piperazine ring. The sum of the bond angles around the atoms N1 and N4 indicate that these atoms are $sp^3$ hybridized and they adopt a pyramidal geometry. The geometry around the S atom is distorted tetrahedral. The sulfonyl O atoms O8 and O9 are oriented in +synclinal and -synclinal conformations respectively. The steric hindrance caused by the bulky sulfonyl group is more than the steric effects caused by the diphenylmethyl rings which are attached on either side of the piperazine ring. This is evident from the bond angle values of $112.3(2)^\circ$ and $109.4(2)^\circ$ for C6–N1–C2 and C3–N4–C5 respectively. No classic hydrogen bonds are found in the structure.

**1-Benzhydryl-4-phenylmethane sulfonyl piperazine**

The compound, C$_{24}$H$_{26}$N$_2$O$_2$S, crystallizes in the orthorhombic crystal class in the space group $Pbca$ with cell parameters $a = 11.1240(10)$ Å, $b = 9.4940(15)$ Å, $c = 40.239(4)$ Å and $Z = 8$. The structure was solved by direct methods and the residuals finally converged to $R_1 = 0.0561$. The structure reveals that the piperazine ring is in a chair conformation. This has been conformed by the least-squares plane calculations and the intra-ring torsion angles for the atom sequence N1/C2/C3/N4/C5/C6. The conformation of the attachment of the diphenylmethyl and the sulfonyl groups to the piperazine ring are well described by the torsion angles i.e.
they adopt -antiperiplanar and +antiperiplanar conformations with respect to one another. The sum of the bond angles around the piperazine N atoms indicate that they are \(sp^3\) hybridized and adopt a pyramidal geometry. The steric hindrance caused by the bulky sulfonyl group is more than the steric effects caused by the diphenylmethane ring which are attached on either side of the piperazine ring. This is evident from the bond angle values of 111.5(3)° and 108.7(3)° for C6-N1-C2 and C3-N4-C5 respectively. The angular disposition of the bonds about the S atom shows significant deviation from that of a regular tetrahedron. The sulfonyl O atoms are oriented in -synclinal and +synclinal conformations respectively. The structure exhibits intermolecular hydrogen bonds of the type C-H-•O. These hydrogen bonds link the molecules to form a polymeric chain like structure.

\* 1-Benzhydryl-4-methane sulfonyl piperazine

The compound, \(C_{18}H_{22}N_2O_2S\), crystallizes in the monoclinic crystal class in the space group \(P2_1/c\) with cell parameters \(a = 9.5820(4)\ \text{Å}, b = 16.8150(12)\ \text{Å}, c = 13.5280(8)\ \text{Å}, \beta = 127.270(5)°\) and \(Z = 4\). The structure was solved by direct methods and refined to \(R_1 = 0.0395\). The study of torsion angles, asymmetric parameters and the least-squares plane calculations reveal that the piperazine ring in the structure is in a chair conformation. The bonds N1-S7 and N4-C11 connecting the sulfonyl and the diphenylmethyl groups to the Cremer and Pople plane of the piperazine ring are in the equatorial plane. The sum of the bond angles around the piperazine N atoms indicate that they are \(sp^3\) hybridized and adopt a pyramidal geometry. The sulfonyl O atoms are oriented in +synclinal and -synclinal conformations respectively. The bond angle for C6-N1-C2 = 111.7(2)° is significantly larger than that for C3-N4-C5 = 107.9(2)°. The difference seems to result from the steric effects of the sulfonic group attached to the piperazine N atom. The conformation of the attachment of the diphenylmethyl and the sulfonyl groups to the piperazine ring is well described by the torsion angle values of 169.4(2)° and -176.4(2)° for S7-N1-C6-C5 and C11-N4-C3-C2 respectively, i.e., they adopt +antiperiplanar and -antiperiplanar conformations with respect to one another. The geometry around the S atom is distorted tetrahedral. No classic hydrogen bonds were found in the structure.
**1-[bis-(4-fluorophenyl)-methyl]-4-methane sulfonyl piperazine**

The compound, C₁₈H₂₀F₂N₂O₂S, crystallizes in the monoclinic crystal class in the space group \( P\overline{2}_1/c \) with cell parameters \( a = 9.9050(6) \ \text{Å}, b = 16.9070(15) \ \text{Å}, c = 13.4720(9) \ \text{Å}, \beta = 127.764(5)^\circ \) and \( Z = 4 \). The structure was solved by direct methods and refined to \( R_1 = 0.0409 \). The piperazine ring in the structure adopts almost a perfect chair conformation. The bonds N₁-S₇ and N₄-C₁₁ are in the equatorial plane of the piperazine ring. The sum of the bond angles around the piperazine N atoms indicate that they are \( sp^3 \) hybridized and adopt a pyramidal geometry. The sulfonyl O atoms O₉ and O₈ adopt -synclinal and +synclinal conformations respectively. The steric hindrance caused by the bulky sulfonyl group is more than the steric effects caused by the dimethylphenyl ring which are attached on either side of the piperazine ring. This is evident from the bond angle values of 111.9(2)^° and 107.6(2)^° for C₆-N₁-C₂ and C₃-N₄-C₅ respectively. The geometry around the S atom is distorted from regular tetrahedron. The structure exhibits a weak intermolecular hydrogen bond of the type C-H⋯F. The molecules form hydrogen bonded dimers.

**1-Benzhydryl-4-benzenesulfonyl-piperazine**

The compound, C₂₃H₂₄N₂O₂S, crystallizes in the monoclinic crystal class in the space group \( P\overline{2}_1/c \) with cell parameters \( a = 13.2390(10) \ \text{Å}, b = 9.1960(7) \ \text{Å}, c = 18.5810(16) \ \text{Å}, \beta = 110.873(3)^\circ \) and \( Z = 4 \). The structure was solved by direct methods and the residuals finally converged to \( R_1 = 0.0603 \). The piperazine ring in the structure is in a chair conformation. This has been confirmed by the study of torsion angles, asymmetric parameters and the least-squares plane calculations for the atom sequence N₁/C₂/C₃/N₄/C₅/C₆. The substituents on the piperazine ring are in the equatorial position of the Cremer and Pople plane of the piperazine ring as indicated by the angles 85.93(15)^° and 73.00(19)^° for the bonds N₁-S₇ and N₄-C₁₆ respectively. Thus the molecule has an extended conformation. The bond angle C₆-N₁-C₂ = 111.5(2)^° is significantly larger than C₃-N₄-C₅ = 108.2(2)^°. This difference in angle results from the steric hindrance caused by the sulfonic group attached to the piperazine N atom. The sulfonyl O atoms O₈ and O₉ are oriented in -synclinal and +synclinal conformations respectively. The geometry around the S atom is distorted...
tetrahedral. The structure exhibits an intermolecular hydrogen bond of the type C-H···O. The molecules form hydrogen bonded dimers.

1-Benzhydryl-4-(toluene-4-sulfonyl)-piperazine

The compound, C24H26N2O2S, crystallizes in the monoclinic crystal class under the space group \(P2_1/c\) with cell parameters \(a = 13.5800(10) \text{ Å}, b = 8.9630(7) \text{ Å}, c = 18.9040(10) \text{ Å}, \beta = 106.851(3)\degree\) and \(Z = 4\). The structure was solved by direct methods and the residuals converged to \(R_1 = 0.0468\). The structure revealed that the piperazine ring is in a chair conformation with the substituents on the nitrogens lying in the equatorial plane. The bond angle around \(C_2-N_1-C_6 = 111.0(2)\degree\) differs significantly from \(C_3-N_4-C_5 = 108.0(2)\degree\) in the piperazine ring. This is because the steric hindrance caused by the bulky sulfonyl group is much greater than the steric effect caused by the diphenylmethyl group. The angular dispositions of the bonds about the sulfonyl S atom deviate significantly from that of a regular tetrahedron. The sulfonyl atoms O8 and O9 are oriented in +antiperiplanar and +synclinal conformations. No classic hydrogen bonds were observed in the structure.

1-Benzhydryl-4-(5-nitro-benzenesulfonyl)-piperazine

The compound, C23H23N3O4S, crystallizes in the monoclinic crystal class in the space group \(C2/c\) with cell parameters \(a = 13.1120(9) \text{ Å}, b = 21.4990(9) \text{ Å}, c = 16.6550(10) \text{ Å}, \beta = 111.352(2)\degree\) and \(Z = 8\). The structure was solved by direct methods and refined to \(R_1 = 0.0433\). A study of the torsion angles, asymmetric parameters and least-squares plane calculations reveals that the piperazine ring in the structure is in the chair conformation. The conformation of the attachment of the diphenylmethyl and the sulfonyl groups to the piperazine ring are well described by the torsion angle values of 175.73(18)° and –168.72(17)° for C19-N4-C3-C2 and S7-N1-C6-C5 respectively, i.e., they adopt +antiperiplanar and -antiperiplanar conformations with respect to one another. The bonds N1–S7 and N4–C19 lie in the equatorial plane of the piperazine ring. The nitro group is twisted out of the plane of the adjacent aryl ring. This twisted conformation may be ascribed to the occurrence of the C–H–O hydrogen bonds in the structure. The bond angle \(C_6-N_1-C_2 = 112.1(2)\degree\) is significantly larger than \(C_3-N_4-C_5 = 107.8(2)\degree\). This difference in angle results from the steric hindrance caused by the sulfonic group attached.
to the piperazine N atom. The sulfonyl atoms O8 and O9 are oriented in +synclinal and -synperiplanar conformations respectively. The angular disposition of the bonds about the S atom shows significant deviation from that of a regular tetrahedron. The structure exhibits an intermolecular hydrogen bond of the type C–H⋯O. The molecules form hydrogen bonded dimers.

Chapter 4. Summary

This chapter summarizes the results of the structure elucidated earlier. The molecular structures of similar compounds of 1,2,4-Triazoles and 1-Benzhydryl piperazines are compared. The effects of various substituents on the parent molecule are brought out.