Chapter 9

Summary

The main aim of crystal and molecular structure determination is to provide an insight for understanding the physical, chemical and biological properties of matter. The molecular structures of various therapeutically important compounds have been discussed in the previous chapters. This chapter summarizes the important results that can be derived from the structural studies of the various compounds.

9.1 Ethyl(4-[(diethylcarbamothioyl)sulfanyl]methyl)-2-oxo-2H-chromen-7-yl)carbamate (3a)

In the asymmetric unit of crystal, Ethyl(4-[(diethylcarbamothioyl)sulfanyl]methyl)-2-oxo-2H-chromen-7-yl)carbamate, C_{18}H_{22}N_{2}O_{4}S_{2}, the 2H-chromene ring system is essentially planar (r.m.s. deviation = 0.012 Å). The molecular conformation is stabilized by a C_{17}—H_{17}···O_{4} hydrogen bond. In the crystal, N_{7}—H_{7}···S_{2} and C_{25}—H_{25B}···O_{6} hydrogen bonds occur, the former enclosing an R_{2}^{2}(22) ring motif, and lead to the formation of a two-dimensional slab-like network lying parallel to (101). π—π interactions are observed between inversion-related aromatic rings [shortest centroid—centroid distance = 3.6300(11)Å]. The torsion angle of 79.44(15)° indicates that the diethyl carbamothioyl group substituted at C22 is oriented in + synclinal conformation with 2H Chromene ring1. The crystal packing shows stacking when viewed along a and b axes. The puckering analysis fails since the weighted average of the torsion angle is less than 5°.

9.2 2-Oxo-2-(2-oxo-2H-chromen-3-yl)ethylpyrrolidine-1-carbodithioate (3b)

The asymmetric unit of crystal, 2-Oxo-2-(2-oxo-2H-chromen-3-yl)ethylpyrrolidine-1-carbodithioate, C_{16}H_{15}NO_{3}S_{2}, contains two independent molecules in which the pyrrolidine rings adopt envelope conformations, with a methylene C atom as the flap. The dihedral angles between the near-planar 2Hchromene ring systems [maximum deviations = 0.0167 (20) and 0.0136 (19) Å] and the pyrrolidine rings (all atoms) are 83.83 (11)° and 82.43 (11)°. In the crystal, inversion dimmers linked by pairs of C_{9A}—H_{9A}···O_{5B} hydrogen bonds occur for one of the molecules. Further C_{15A}—
H15A⋯O5B links involving both molecules generate a three-dimensional network. The crystal packing is stabilized by π—π and C—H⋯π interactions between molecules. The crystal packing shows stacking when viewed along c axis. The torsion angles of 169.88(16)° & 175.02(14)° containing the atoms indicates that the ethylpyrrolidine carbodithioate group substituted at S1A and S1B lies in +anti-periplanar and +anti-periplanar conformation with the ring 2 & 6 respectively. The puckering analysis fails since the weighted average of the torsion angle is less than 5°.

9.3 6-bromo-2-oxo-2H-chromen-4-yl)methylmorpholine-4-carbodithioate (4a)

In the asymmetric unit of (6-bromo-2-oxo-2H-chromen-4-yl)methyl morpholine-4-carbodithioate, C15H14BrNO3S2, the 2H-chromene ring systems is nearly planar, with a maximum deviation of 0.0332(20) Å and the morpholine ring adopts a chair conformation. The dihedral angle between the 2H-chromene ring and the morpholine ring is 86.31(8)°. In the crystal structure, intermolecular C17—H17A⋯O5 & C17—H17B⋯S3 and intramolecular C19—H19A⋯S2 hydrogen bonds are observed. In the crystal, inversion related C19—H19B⋯S2 interactions generate an R22(10) ring pattern and link pair of independent molecules into dimers. In addition, π—π interactions between inversions related molecules are stabilized by crystal packing.

The torsion angles of -173.11(11)° indicated that the morpholyne carbodithioate group substituted at C17 lies in –anti-periplanar conformation with bromo substituted 2H- Chromene ring 1. The puckering analysis fails since the weighted average of the torsion angle is less than 5°.

9.4 (6-fluoro-2-oxo-2H-chromen-4-yl)methylpiperidine-1-carbodithioate (4b)

In the asymmetric unit of (6-fluoro-2-oxo-2H-chromen-4-yl)methylpiperidine-1-carbodithioate, C16H16FNO3S2, the 2H-chromene ring systems is nearly planar, with a maximum deviation of 0.0685(27) Å and the piperidine ring adopts a boat conformation. The dihedral angle between the 2H-chromene ring and the piperidine ring is 65.96 (12)°. In the crystal structure, intermolecular C12—H12⋯O5, C16—H16A⋯O5 & C8—H8⋯F3 and weak intramolecular C16—H16A⋯S2 hydrogen bonds are observed. In the crystal, inversion related C8—H8⋯F3 & C12—H12⋯O5
interactions generate an $R_2^2(8)$ ring pattern. In addition, $\pi-\pi$ interactions between molecules are stabilized by crystal packing.

The torsion angles of 175.7(2)$^\circ$ containing the atoms N6-C17-S1-C16 indicated that the piperidine carbodithioate group substituted at C16 lies in $+\text{anti-periplanar}$ conformation with fluoro substituted 2H-Chromene ring 1 (C9-C8-C7-O4-C11-C10). The puckering analysis fails since the weighted average of the torsion angle is less than 5$^\circ$.

9.5 (7-methyl-2-oxo-2H-chromen-4-yl)methylpiperidine-1-carbodithioate (4c).

The asymmetric unit of crystal, (7-methyl-2-oxo-2H-chromen-4-yl)methylpiperidine-1-carbodithioate, $C_{17}H_{19}NO_2S_2$. The 2H-chromene ring system is essentially planar, with a maximum deviation of 0.037(2) Å and the piperidine ring adopts a chair conformation. The dihedral angle between the 2H-chromene ring and the piperidine ring is 32.81(15)$^\circ$. In addition, intermolecular C13—H13⋯O4 and weak C16—H16B⋯S2 hydrogen bonds link the components into chains along [001]. The crystal structure also features C—H⋯π and π—π interactions further stabilize the crystal packing. The torsion angles of 176.5(2)$^\circ$ indicated that the piperidine carbodithioate group substituted at C16 lies in $+\text{anti-periplanar}$ conformation with methyl substituted 2H-Chromene ring 1. The puckering analysis fails since the weighted average of the torsion angle is less than 5$^\circ$.

9.6 4'-(5-(benzylthio)-2H-tetrazol-2-yl) methyl} biphenyl-2-carbonitrile (5a)

The asymmetric unit of the structure of 4'-(5-(benzylthio)-2H-tetrazol-2-yl)methyl]biphenyl-2-carbonitrile, $C_{22}H_{17}N_5S$ contains two independent molecules A & B are shown in Figure and exhibits a short intramolecular S1A⋯N4B contact of 3.345 (18)Å. The dihedral angle between the tetrazilidine ring and the benzene rings are for A molecules 78.98 (16)$^\circ$, 70.53 (16)$^\circ$, 68.16 (17)$^\circ$ & for B molecules 71.65 (17)$^\circ$, 62.84 (16)$^\circ$ & 51.29 (19)$^\circ$ respectively. The crystal structure is further stabilized by other intermolecular C22A—H22A⋯N6A hydrogen bonds, $\pi-\pi$ and C—H⋯π interactions. The packing of the molecules form a stacking when viewed down a axis. The torsion angle of 2.7(3)$^\circ$ substituted at C13A indicates that the
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tetrazilidine ring 1 is oriented in \( \text{+syn-periplanar} \) conformation with the benzene ring 2 for the molecule A and the torsion angle of \(-57.8(3)^\circ\) substituted at C15B indicates that the tetrazilidine ring 6 is oriented in \(-\text{syn-clinal}\) conformation with the benzene ring 7 for the independent molecule B.

**9.7 1-(4-bromobenzyl)-5-(1-phenyl-4,5-dihydro-1\(H\)-pyrazol-3-yl)-2,5-dihydro-1\(H\)-tetrazole (5b)**

In the asymmetric unit of the structure of 1-(4-bromobenzyl)-5-(1-phenyl-4,5-dihydro-1\(H\)-pyrazol-3-yl)-2,5-dihydro-1\(H\)-tetrazole, \( \text{C}_{17}\text{H}_{13}\text{BrN}_6 \), the dihedral angle between the tetrazole ring and the pyrazole & two terminal benzene rings of the molecules are \(4.2(2)^\circ\), \(69.30(19)^\circ\) & \(4.78(19)^\circ\) respectively. The crystal structure is further stabilized by other intermolecular C8—H8⋯N5 and intramolecular C14—H14B⋯N6 hydrogen bonds.

The torsion angles of \(-3.5(5)^\circ\) & \(176.4(3)^\circ\) respectively substituted at C15 & C19 indicates that the pyrazole ring 2 is in \(-\text{syn periplanar}\) conformation with the tetrazole ring 1 and \(+\text{-anti-periplanar}\) conformation with the benzene ring 4. The puckering analysis fails since the weighted average of the torsion angle is less than \(5^\circ\).

**9.8 2-methyl-3-[2-(1\(H\)-1,2,4-triazol-1-yl)ethyl]-4\(H\)-pyrido[1,2-a]pyrimidin- 4-one (6)**

In the asymmetric unit of (2-methyl-3-[2-(4\(H\)-1,2,4-triazol-4-yl)ethyl]-4\(H\)-pyrido [1,2-a] pyrimidin-4-one), \( \text{C}_{13}\text{H}_{15}\text{N}_5\text{O} \), the 4\(H\)-pyrido[1,2-a]pyrimidine ring is almost planar with a maximum deviation of \(0.0102(20)^\AA\). This ring forms a dihedral angle of \(47.88(16)^\circ\) with the 1,2,4-triazole ring. In the crystal structure of the molecules are linked into planes parallel to the ab-plane by intermolecular C8—H8⋯N5 hydrogen bonds. Furthermore, the crystal structure packing also exhibits C10—H10B⋯\(\pi\)Cg(1) and C15—H15B⋯Cg(1) and \(\pi—\pi\) interactions, with distance of \(3.4927(19)^\AA\) between the centroids of 4\(H\)-pyrido[1,2-a] pyrimidine ring of molecules. The crystal packing shows stacking when viewed along a and b axes.
The torsion angles of -96.1(2)° substituted at N2 indicates that the ethyl group is oriented in -anticlinal conformation with the 1,2,4-triazole ring 1. The puckering analysis fails since the weighted average of the torsion angle is less than 5°.

9.9 6-chloro-5-(2-chloroethyl)-3-isopropyldiene-1,3-dihydro-2H-indol-2-one (7)

In the asymmetric unit of 6-chloro-5-(2-chloroethyl)-3-isopropyldiene-1,3-dihydro-2H-indol-2-one, C13H13Cl2NO, the indoline ring system is nearly planar, with a maximum deviation of 0.0615(30)Å. In the crystal structure, intramolecular N4—H4···O3 and C6—H6B···C12 hydrogen bonds is observed. In the crystal, inversion related N4—H4···O3 interactions generate an R22(8) ring pattern and link pairs of independent molecules into dimers. In addition, the crystal packing is stabilized by π—π interactions between inversions related molecules. The crystal packing is further stabilized by π—π interactions. The overall crystal packing components generate a three-dimensional network.

The crystal packing shows stacking when viewed along a, b and c axis. The torsion angles of 173.9(3)° & -179.8(3)° respectively substituted at C15 indicates that the methyl groups are in +anti-periplanar and -anti-periplanar conformation with the indoline ring system. The puckering analysis fails since the weighted average of the torsion angle is less than 5°.

9.10 1,1',1''',1''''-(oxydimethanetriyl)tetrakis(4-fluorobenzene) (8)

In the molecular unit of 1,1′,1″,1‴-(oxydimethanetriyl)tetrakis (4-fluorobenzene), C26H18F4O2, the dihedral angles between each pair of benzene rings are 80.55 (8)° [(C6–C11) 1 and (C13–C18) 2] and 79.11 (7)° [(C20–C25) 3 and (C26–C31) 4] respectively. The crystal packing is stabilized by C7—H7···π Cg(4) interactions and shows stacking when viewed along c axis.

The torsion angles of -46.67(15)° & 50.75(16)° respectively substituted at C19 indicates that the benzene ring 4 and benzene ring 3 are in –synclinal conformation with each other. The puckering analysis fails since the weighted average of the torsion angle is less than 5°.
9.2 Compounds with Medicinal Significance

All the compounds studied in this thesis show a wide spectrum of biological activities.

The various substituted Chromene molecules (compounds 3a, 3b, 4a, 4b & 4c) reported with diverse structural features and versatile biological properties such as anti-inflammatory [1], antioxidant [2], vasorelaxant [3], cytotoxic [4], anti-HIV [5], antitubercular [6] and antimicrobial [6]. They also exhibit a variety of valuable biological effects, including antibacterial activity [7], antifungal activity [8], anticancer activity [9].

The tetrazole substituents (compounds 5a & 5b) shows remarkable pharmacological activities like antipsychotic, antimalarial, anticonvulsant, antiarrhythmic, antimicrobial, antioxidant and cytotoxic activities [10].

The triazole substituents (compound 6) belong to a class of exceptionally active compounds possessing a wide spectrum of biological properties, including anti-inflammatory [11], anti-fungal [12], anti-viral [13], analgesic, anti-convulsant [14], anti-parasitic [15], anti-depressant and anti-cancer [16] activities.

The derivatives of the indole (compound 7) shows biological activities like antimicrobial, antiviral, antitubercular, anti-inflammatory, anticancer, antidiabetic, antioxidant, antidepressant, anticonvulsant activities [17].

The tetrakis derivative (compound 8) shows anti-plasmodial and anti-trypanosomal action [18], anti-depressant and anti-parkinsonian [19,20], anti-histaminic [21] and anti-spasmodic [22] activities.
9.3 Reference


