The work reported in this thesis deals with the elucidation of crystal structure and structure activity relationships of eight compounds which are derivatives of 3-chloro-4-fluoro organofluorine compounds. Organofluorine compounds have been extensively studied in view of their wide ranging biological activities. Compounds like 5-fluorouracil, have found clinical applications in the chemotherapy of tumors. Introduction of fluorine in a variety of organic compounds like coumarins, styrenes and butadienes has been of great interest in the study of their packing modes and intermolecular interactions. Aromatic Schiff’s bases containing the azomethine group (C=N) have been extensively studied for their solid state conformations during the last three decades. 2-aryl 1,3-thiazolidin-4-ones which are obtained by the reaction of thiaglycollic acid with Schiff’s bases have been found to exhibit antibacterial, antiplatelet factor, antitubercular and antiviral activities. In view of the biological importance and structural interest of the compounds, it was thought of considerable interest to study the solid state conformations of fluorinated Schiff’s bases and the corresponding thiazolidinones.

The present thesis is divided into five chapters. The first chapter deals with an introduction to the theory and experimental techniques in X-ray crystallography.

The second chapter deals with the structural aspects and biological importance of aromatic Schiff’s bases, organofluorine compounds and substituted thiazolidin-4-ones, which are structurally related to the compounds under present investigation.
This chapter highlights the earlier reports on the crystal structure studies of schiff 's bases, organofluorine compounds, thiazolidinones and weak interactions.

The third chapter which is divided into six parts describes the crystal analysis of the fluorinated schiff 's bases carried out during the course of this work. Each part is further divided into four sections.

i) Introduction.

ii) Experimental.

iii) Structure solution and refinement.

iv) Results and discussion.

Chapter III part I deals with the crystal structure of N(benzylidene)-3-chloro-4-fluoroaniline, C_{13}H_{9}F N Cl. The title compound was synthesised by the reaction of 0.01M of 3-chloro-4-fluoroaniline dissolved in 30ml of absolute ethanol, 0.01M of benzaldehyde was added and this mixture was refluxed gently for one hour in the presence of 2-3 drops of glacial acetic acid. Afterwards the reaction mixture was cooled to room temperature, poured on crushed ice, the precipitate obtained was filtered, washed with ice cold water, dried in the air and finally recrystallised using ethanol. The parent benzylideneaniline was found to adopt a non-planar arrangement. Introduction of fluorine in a variety of aromatic compounds increases the molecular volume. It has been found to orient butadienes, styryl' coumarins for photodimerization and has been found not to accept hydrogen bonds. The crystals of
the compound belongs to monoclinic, P2₁/c having 4 molecules in the unit cell of dimension a= 5.787(1), b=7.533(1), c= 25.342 (2) Å and β=94.227 (8)°. The density measurement was made by flotation technique using potassium iodide solution.

The three dimensional intensity data was collected using CuKα radiation, at RSIC, I.I.T., Chennai, India for a crystal of size 0.2x0.1x0.1mm. The data corrected for lorentz and polarisation effects has 2457 unique reflections, of which 2082 with I ≥ 3 σ (I) were considered observed. The structure was solved by direct methods and refined by full-matrix least-squares refinement using SHELXL-97 (Sheldrick, 1997) Program. The final R-Value is 0.0349, R_w=0.1138. The entire molecule is planar and there are no deviations in the interplanar angles greater than 5°. The molecule adopts E-configuration i.e., the phenyl and 4-fluorophenyl moieties are on the opposite sides of the C-N bond.

Chapter III part II deals with the crystal structure of N [(4'-chloro) benzylidene]-3-chloro-4-fluoroniline, C₁₃ H₈ F N Cl₂. The crystals of the compound crystallises in monoclinic, space group P2₁/c having 4 molecules in the unit cell of dimensions a=3.878(4), b=12.210(5), c=24.528(6)Å, β=91.40(4)°. The density measurement was made by flotation technique using potassium iodide solution.

The three dimensional intensity data were measured on Enraf-nonius CAD4 diffractometer with CuKα radiation, at ISU, I.I.Sc., Bangalore, India for a crystal of
size 0.3 x 0.2 x 0.1mm. The data corrected for Lorentz and polarisation effects has 1657 unique reflections of which 1493 with $1 \geq 3.0 \sigma (I)$ were considered observed. The structure was solved by direct methods and refined by full-matrix least-squares method using SHELXL-93 (Sheldrick, 1993) Program. The refinement was continued till the final R-value is 0.0547.

The two planar phenyl rings make a dihedral angle of 10.70(3)$^\circ$. The atoms Cl(2) and F attached to one of the phenyl rings have deviations -0.008(11) and 0.19(11)$\text{Å}$ respectively. Cl(1) attached to the other phenyl ring has a deviation of -0.028(10)$\text{Å}$. The molecules are packed in layers parallel to (101) plane, and form C-H . . . F bonds.

Chapter III part III deals with the crystal structure of N[(4'-nitro)benzylidene]-3-chloro-4-fluoroaniline, $C_{13}H_{18}F_2N_2O_2Cl$. The compound belongs to a class of organic compounds benzylidene anilines which is found to adopt a non-planar arrangement in the solid state. Introduction of groups like chloro, nitro and dichloro in this class revealed many interesting features like polymorphism, nature of twist of the benzene rings and their thermal sensitivity. They have been synthesised as possible anti-inflammatory agents. The crystals of the compound belongs to monoclinic, $P2_1/c$, with 4 molecules in the unit cell of dimensions $a=3.816(2)$, $b=12.669(2)$, $c=24.677(5)$ Å and $\beta=91.34(3)^\circ$. 

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The three dimensional intensity data was collected at ISU, I.I.Sc., Bangalore, India using Moka radiation for a crystal of size 0.2x0.2x0.2mm. The data corrected for Lorentz and Polarisation effects has 2111 unique reflections of which 1344 with $I \geq 2.5\sigma(I)$ were considered observed. The structure was solved by direct methods using NRCVAX-Crystal structure solution program and the structure thus obtained was refined by full-matrix least-squares methods using SHELXL-97 (Sheldrick, 1997) program. The refinement was continued till the final value of $R=0.053$. The molecular packing of the non-planar molecules are held by Van der waals interaction.

Chapter III part IV deals with the crystal structure of N[(4'-dimethylamino)benzylidene]-3-chloro-4-fluoroaniline, C$_{15}$H$_{14}$F$_{2}$N$_{2}$Cl. This compound belongs to class benzylidene anilines. Introduction of fluoro substitutent in a variety of organic compounds has been found to increase crystal densities and enhance the reactivity in solid state photochemical dimerization. 3-chloro-4-fluoroaniline moiety has been found to be the pharmacophore in a variety of biologically active organofluorine compounds. The title compound was synthesised as a possible anti-inflammatory agent. The crystal of the compound belong to triclinic, $\overline{1}$, having 2 molecules in the unit cell of dimensions $a=9.721(3)$, $b=11.447$ (3) and $c=6.745$ (2)$\AA$, $\alpha=103.28(2)$, $\beta=102.94(2)$ and $\gamma=72.07(2)^{\circ}$.

The three dimensional intensity data was collected on Rigaku auto four circled 7S (AFC7S) diffractometer with Moka radiation at Department of Physics,
Manasagangothri, University of Mysore, Mysore, India. The data corrected for Lorentz and polarisation effects has 2003 unique reflections of which 1975 with $I \geq 4.0\sigma(I)$ were considered observed. The structure was solved by direct methods using SHELXS-86 (Sheldrick, 1986) program and the structure thus obtained was refined using SHELXL-93 (Sheldrick, 1993) program by a full-matrix least-squares method. A sigma weighting scheme was applied and the refinement was continued till final value of $R=0.047$. The molecular packing of the non-planar molecules are held by Van der waals interactions.

Chapter III part V deals with the crystal structure of N[(2'-hydroxy)benzylidene]-3-chloro-4-fluoroaniline, C$_{13}$H$_9$FNOCl. The compound belongs to the family of fluorine substituted benzylidene anilines. These compounds have been studied as useful models in the development of the principles of crystal engineering. The title compound crystallises in monoclinic, space group P2$_1$/n with 4 molecules per unit cell of dimensions $a=3.879(1)$, $b=10.809(2)$, $c=26.262(7)$Å, $\beta=94.17(1)^{\circ}$. The crystal density was measured by flotation technique.

The three dimensional intensity data was collected at RSIC, I.I.T., Chennai, India using CuK$_\alpha$ radiation for crystal of size 0.2x0.2x0.1mm. The data corrected for Lorentz and polarisation effects has 2080 unique reflections of which 1909 with $I \geq 4\sigma(I)$ were considered observed. The structure was solved by direct methods and refined by full-matrix least-squares methods using SHELXL-97 (Sheldrick, 1997)
program. The molecule is planar on the whole and molecules are held by some C-H...F and O-H...N hydrogen bonds.

Chapter III part VI deals with the crystal structure of N[(3',4',5'-trimethoxy) benzildene]-3-chloro-4-fluoroaniline, C₁₆H₁₅FNO₃Cl. The title compound was screened for anti-inflammatory activity. Furthermore, the 3',4',5'-trimethoxy phenyl moiety is present in the clinically useful drug trimethoprim. It has also been found that the thiosemicarbazone from the above said aldehyde exists as its monohydrate in the non-planar triclinic form. The title compound crystallises in monoclinic, P2₁/n with 4 molecules in the unit cell of dimensions a=7.086(4), b=8.328(1), c=26.139(9) Å and β=91.29(4)°. The density measurement was done by flotation technique.

The three dimensional X-ray intensity data were collected on Rigaku auto four circled 7S (AFC7S) diffractometer at Department of Physics, Manasagangotri, University of Mysore, Mysore, India using MoKα radiation for a crystal of 0.3x0.2x0.1mm. The data corrected for Lorentz and polarisation effects, has 2154 unique reflections of which 2144 with I ≥ 4.0σ(I) were considered observed. The structure was solved by direct methods using SHELXS-86 (Sheldrick, 1986) and refined by a full-matrix least-squares method using SHELXL-93 (Sheldrick, 1993) Program with isotropic thermal parameters for H-atom and anisotropic thermal parameters for non H-atoms. A sigma weighting scheme was applied and the
refinement was continued till final value of $R=0.049$. The molecule on the whole is non-planar and the crystal structure is stabilised by Van der waals interactions.

Chapter IV describes the structure analysis of the tricyclic thiazolidinones. This chapter deals with the crystal structure of 2-phenyl-3N[(3'-chloro-4'-fluoro)phenyl]-4-thiazolidinone, $C_{15}$ $H_{11}$ $F$ $O$ $S$ $Cl$. The title compound belongs to the family of thiazolidinones inhibits carrageenan rat paw edema volume by 32.3% compared to the relaxant standard drug ibuprofen which reduced the edema by 47.7% and is a anti-inflammatory agent. The substituted thiazolidine exhibits various biological properties like anti-fungal, anti-tubercular, anti-viral and myorelaxant properties. Substituents at position 5 have emerged as a new class of platelet factor antagonists etc. The compound crystallises in triclinic system, space group $P\overline{1}$ with 2 molecules in the unit cell of dimensions $a=6.019(1)$, $b=10.256(1)$, $c=11.549(3)\AA$ and $\alpha=75.50(1)$, $\beta=78.47(2)$ and $\gamma=76.08(1)^0$. The density measurement was done by flotation technique.

The three dimensional intensity data was collected using Cu$\alpha$ radiation for a crystal of size $0.2x.2x.15mm$ at RSIC, I.I.T., Chennai, India. The data corrected for Lorentz and polarisation effects has 2516 unique reflections of which 2423 with $I \geq 4\sigma(I)$ were considered observed. The structure was solved by direct methods and refined by full-matrix least-squares method using SHELXL-97 (Sheldrick, 1997) program. The refinement was continued till the final value of $R=0.0413$. The
carbonyl oxygen attached to C9 is almost eclipsed with a dihedral angle of 10.3 (3)°. The two benzene rings are cis to C-N bond and are in gauche arrangement with C1-N-C7-C1’ torsion angle of 55° and the thiazolidinone ring is non-planar as indicated by the torsion angle C8-S-C7-N of -28.3(2)°.

The last chapter i.e. Chapter V will be dealing with the effect of substituents observed in the fluorinated schiff’s bases especially at position 4. However effect of the introduction of fluorine is also highlighted by comparison with the structurally related schiff’s bases from the literature. This chapter deals with the crystal structure of 2-(3'-nitrophenyl)-3N[(3-chloro-4-fluoro)phenyl]-4-thiazolidinone, C_{15} H_{10} F N_{2} O_{3} S Cl. The title compound belongs to the family of thiazolidinones inhibits carrageenan rat paw edema volume by 36.7% compared to the standard drug ibuprofen which reduced the edema by 47.7% and is a anti-fungal, anti-tubercular, anti-viral and myorelaxant properties. The compound crystallises in orthorhombic space group P2_{1}2_{1}2_{1} with 4 molecules in the unit cell of dimensions a=7.4305, b=12.0071, c=16.4810Å. The density measurement was done by flotation technique.

The three dimensional intensity data was collected using Mokα radiation for a crystal of size 0.15x0.15x0.1 mm at RSIC, I.I.T., Chennai, India. The data corrected for Lorentz and polarisation effects has 1503 unique reflections of which 1503 with I ≥ 3.0 σ (I) were considered observed. The structure was solved by direct methods and
refined by full-matrix least-squares method using SHELXL-97 (Sheldrick, 1997) program. The refinement was continued till the final value of R=0.0531. The thiazolidinone ring exhibits a slightly twisted conformation.

Based on the work reported in this thesis following papers have been published or under publication.

1. Crystal and molecular structure of N-benzylidene-3-chloro-4-fluoroaniline.
   Arjuna Gowda, K.V., Kokila, M.K., Puttaraja, Kulkarni, M.V and Shivaparakash, N.C.,

2. Crystal and molecular structure of N(p-chlorobenzylidene)-3-chloro-4-fluoroaniline.

3. Crystal and molecular structure of N(p-nitrobenzylidene)-3-chloro-4-fluoroaniline.
   K.V. Arjuna Gowda, M.K. Kokila, Puttaraja, M.V. Kulkarni and N.C Shiva prakash.

   K.V. Arjuna Gowda, M.K. Kokila, Puttaraja, M.V.Kulkarni, J.Shashidhara Prasad
   and N.C Shivaparakash,

5. Crystal and molecular structure of N[(2'-hydroxy)benzylidene]-3-chloro-4-fluoroaniline.
   Arjuna Gowda, K.V., Kokila, M.K., Puttaraja, Kulkarni, M.V and Shivaparakash, N.C.
   (Communicated to Acta cryst.C ).  

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6. Crystal and molecular structure of N[(3',4',5'-trimethoxy)benzylidene]-3-chloro-4-fluoroaniline.
K.V. Arjuna Gowda, M.K. Kokila, Puttaraja, M.V. Kulkarni, J. Shashidhara Prasad and N.C. Shivaprakash,
(Accepted in Indian J. of Chemistry.)

7. Crystal and molecular structure of 2-Phenyl-3N[(3''-chloro-4''-fluoro)phenyl]-4-Thiazolidinone.
Arjuna Gowda, K.V., Kokila, M.K., Puttaraja, Kulkarni, M.V and Shivaprakash, N.C.
(Communicated to Indian J. of Physics).

8. Crystal and molecular structure of 2-[(3'-nitrophenyl)-3N[(3''-chloro-4''-fluoro)phenyl]-4-Thiazolidinone.
Arjuna Gowda, K.V., Kokila, M.K., Puttaraja, Kulkarni, M.V and Shivaprakash, N.C.
(Communicated to Acta cryst.C).