CHAPTER 1

Introduction to Benzopyran Derivatives and their Applications

Coumarin(2H-chromen-2-one) is an oxygen containing and naturally occurring heterocyclic compound that is widespread in the plant kingdom, as well as in certain fungi and bacteria. It included in the benzopyran chemical class and coumarin itself is known for its natural fragrance characteristics. These applications cover wide range of uses, including the fragrance industry, cosmetics production and the incorporation of industrial additives.

What makes coumarins particularly attractive in drug research and development is their advantageous characteristics features of this compound, including its small molecular size, uncomplicated structure, excellent bioavailability, strong organic solvent solubility, minimal toxicity with few side effects, decreased susceptibility to drug resistance, wide-ranging applicability, and improved therapeutic outcomes across diverse diseases, have been documented. These qualities, combined with their multifaceted pharmacological effects including anticoagulant, antimicrobial, anti-inflammatory, neuroprotective, antidiabetic, anticonvulsant and anticancer properties, position them as promising lead compounds.

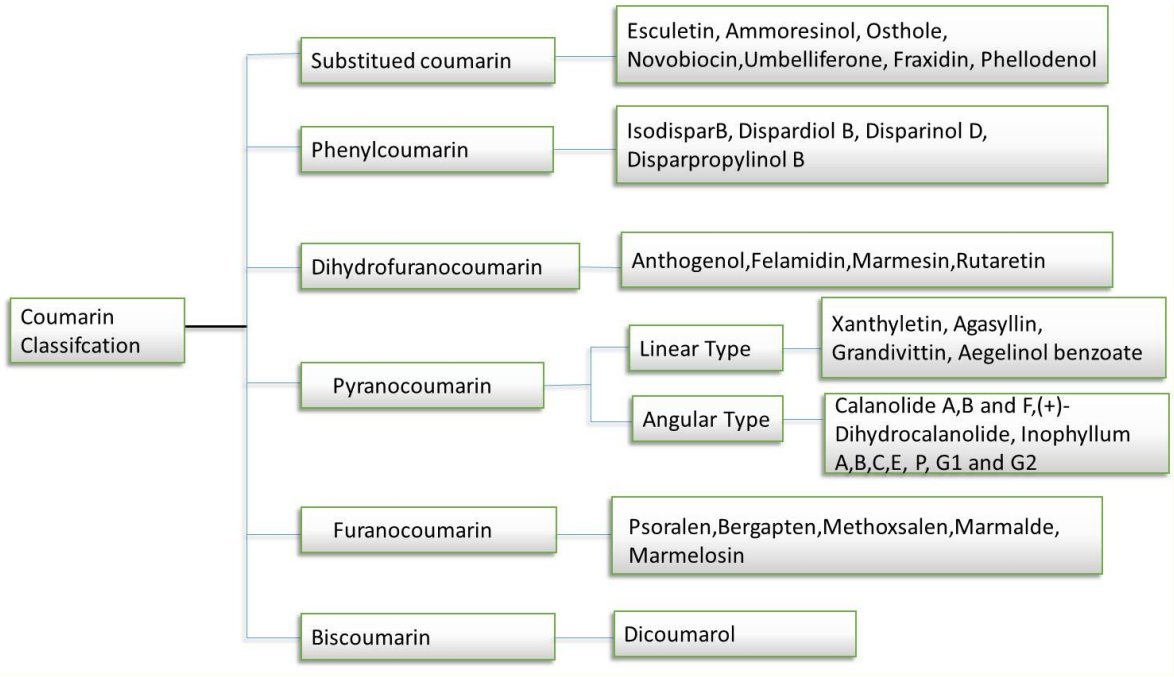


Figure-1: Classification of coumarin

Combining coumarin with various heterocyclic compounds featuring different heteroatoms like furan, pyridine, quinoline, pyrazole, benzothiazole, triazine, oxazole etc. leads to unpredictable activities within these heterocyclic rings, ultimately enhancing the physiochemical properties and biological effects of the coumarin moiety. Consequently, numerous coumarin-fused or coumarin linked/ attached heterocyclic compounds and their derivatives have been synthesized for their different biological applications.

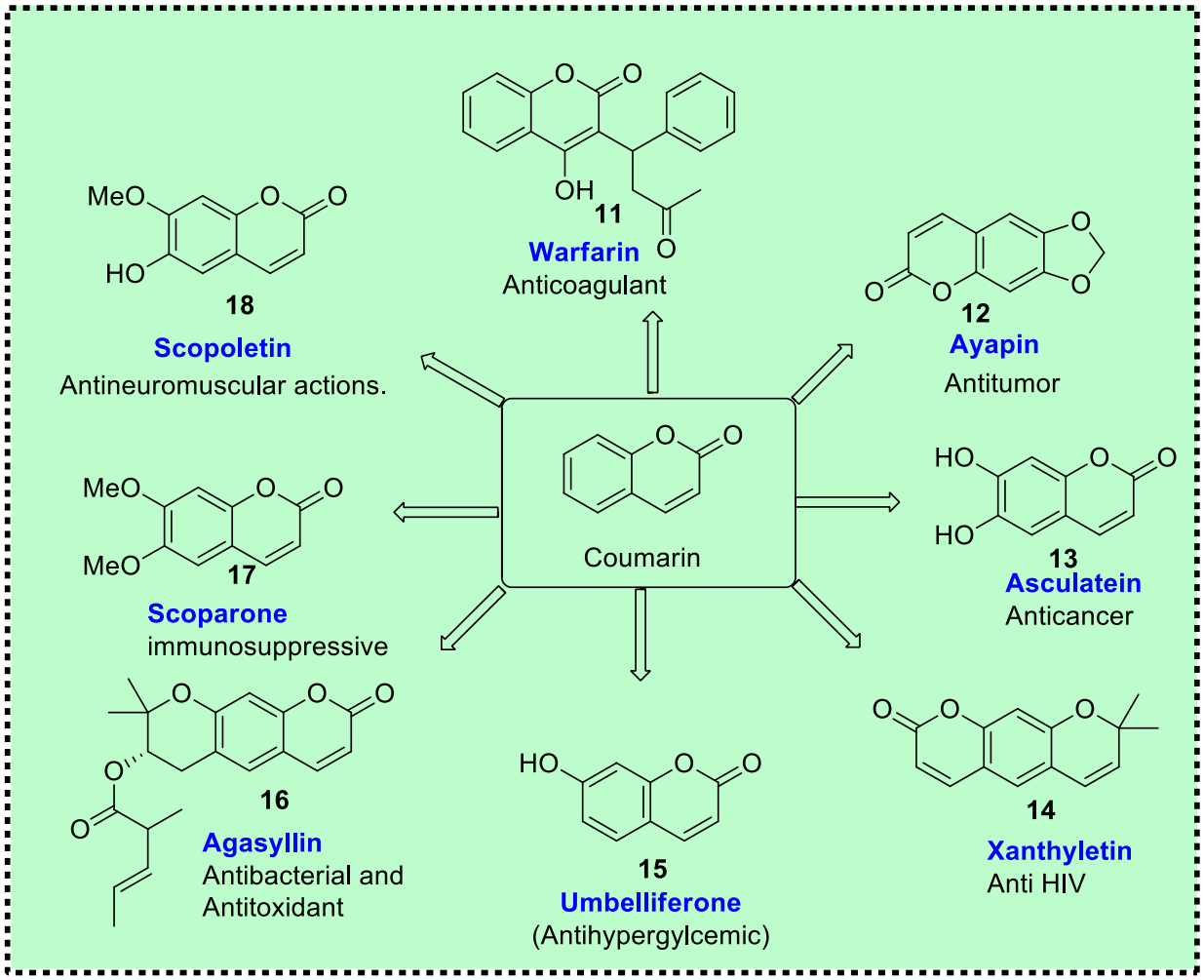


Figure-2: Examples of clinically used coumarin derivatives

Benzofuran is a heterocyclic compound consisting of a fused benzene and furan ring, and which imparts unique chemical properties to it. One of its most significant applications is in the pharmaceutical industry, where benzofuran derivatives serve as key structural motifs in the development of various bioactive compounds.

In heterocyclic chemistry pyrazolone derivatives have proven to be a remarkably diverse group of compounds, shows a wide array of biological activities. Pyrazolone is a heterocyclic organic compound characterized by a five-membered ring structure containing three carbon atoms and two nitrogen atoms, with a ketone functional group. This versatile chemical has found applications in diverse fields, including pharmaceuticals and medicinal field.

Cancer is characterized by uncontrolled cell proliferation, disrupting normal processes due to the failure of old cells to undergo programmed cell death. Common types include lung, cervical, breast, and prostate cancer, with breast cancer being the leading cause of death among women. Treatments like surgery, chemotherapy, and radiotherapy can harm healthy cells, and the global cancer burden continues to rise.

Apart from their biological and industrial applications comarin derivatives have found applications in various fields, including, laser dyes, nonlinear optical materials, photosensitive materials. and exhibit luminescence due their electron-rich conjugated π-π systems materials. Within the coumarin compounds, studied characteristics such as colour characteristic, luminescence, mesogenic behavior, and showed gel formation in both water and organic solvents. These attributes have garnered significant interest as they are seen as potential candidates for the development of next-generation materials, owing to their responsive nature, ecological suitability, and energy-efficient processing methods.

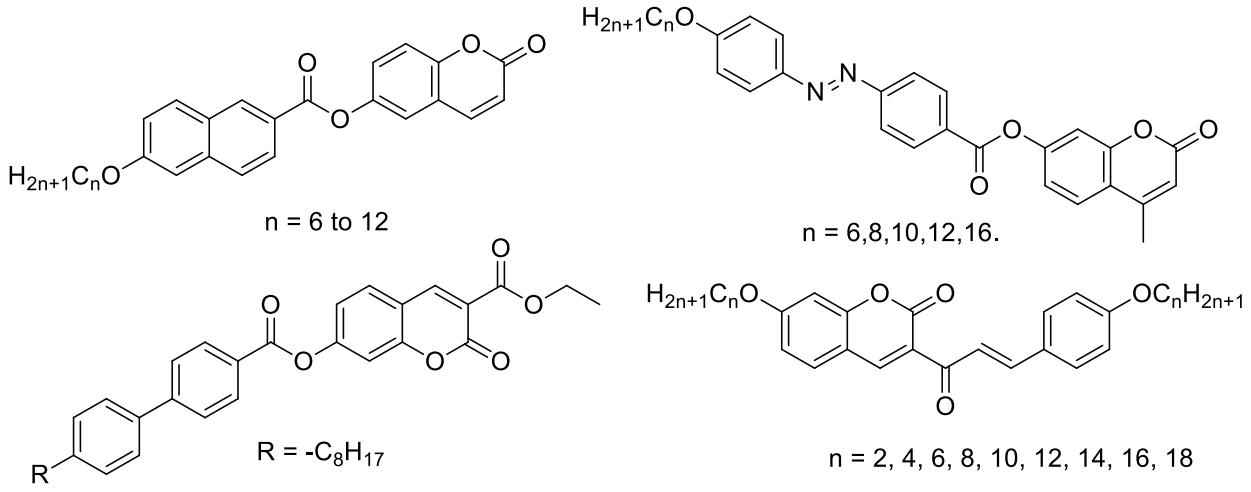


Figure-3: Chromene-2-one derivatives with liquid crystalline properties

CHAPTER 2

Design, Synthesis and Anticancer Activity of Amide Derivatives of Substituted 3-Methyl-benzofuran-2-carboxylic acid

Chapter 2 divided into 3 series, in which synthesis of intermediate 3-methyl-6-propoxybenzofuran-2-carboxylic acid was carried out and then various amide derivatives was synthesized by reaction with different phenyl sulphonyl piperazines, substituted phenyl hydrazides and phenyl hyrazines. All the synthesized compounds were characterized by different spectral techniques such as ^{1}H-NMR, ^{13}C-NMR, IR, ESI-MS and CHN analysis.

Compounds were screened for their anticancer activity by using MTT assay in two cell lines, lungs cancer (A549) and breast cancer (MCF7) cell lines. Compound **2b** showed excellent activity against A549 cell line with IC_{50} value 0.858 µM[a] and compound **1d** showed excellent activity against MCF7 cell line with IC_{50} value 2.07 µM[a]. Compound **1d** and **2b** studied further for LDH assay, Ethidium bromide assay, Trypan blue, DCFH-DA Assay, In-silico based ADME and Toxicity study and DFT study.

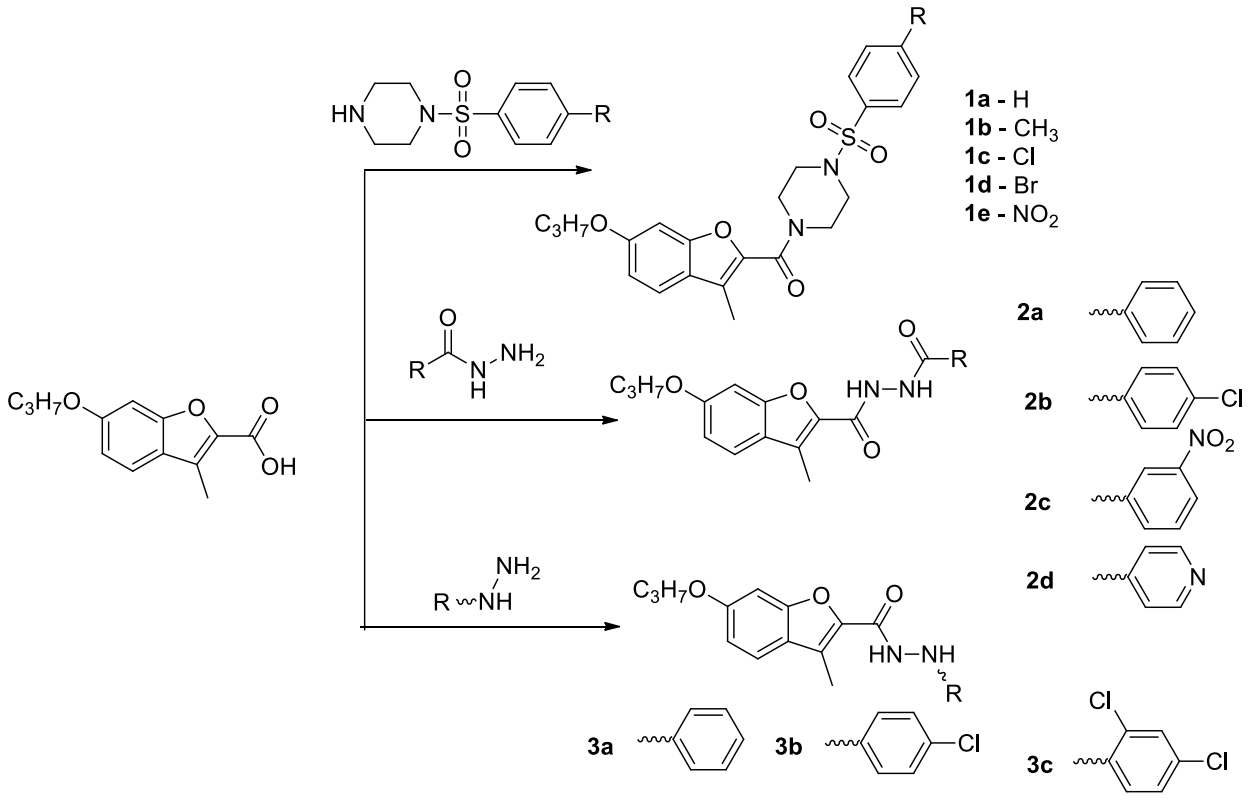


Figure-1: Amide derivatives of substituted 3-methyl-benzofuran-2-carboxylic acid

CHAPTER 3

3a: Synthesis of Pyrazolone Derivatives of Coumarin as Anticancer agents

Chapter 3a deals with two series in first series synthesis of pyrazolone derivatives of 7-amino-4-methyl-2H-chromen-2-one carried out and in second series pyrazolone derivatives of 6-amino-2H-chromen-2-one was carried out. All the intermediates and final compounds were characterized by different spectral techniques such as ^{1}H-NMR, ^{13}C-NMR, IR, ESI-MS and CHN analysis.Compounds were screened for their anticancer activity by using MTT assay in two cell lines, lungs cancer (A549) and breast cancer (MCF7) cell lines. Compound **9c** showed excellent activity against A549 cell line with IC_{50} value 1.22 μM[a] and compound **10b** showed excellent activity against MCF7 cell line with IC_{50} value 1.66 μM[a]. Compound **9c** and **10b** studied further for DCFH-DA Assay, and DFT study.

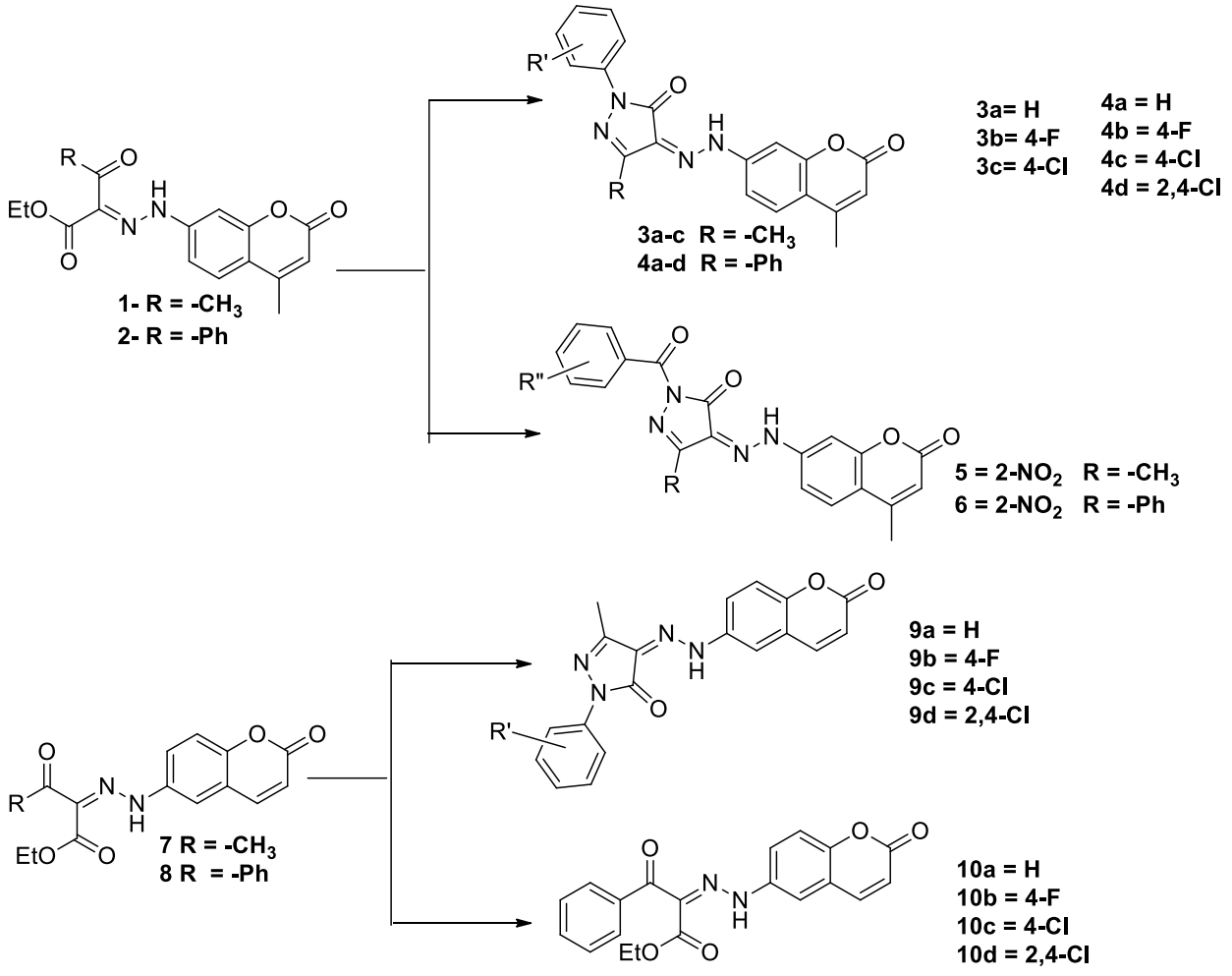


Figure-1: Pyrazolone derivatives of 7-amino 4-methyl coumarin and 6-aminocoumarin

Chapter-3b:

Design and Synthesis of Piperazine Derivatives of Coumarin as Anticancer Agents

In this chapter firstly we synthesized 6-bromoacetamide coumarin Further bromo group of 6-bromoacetamide coumarin was replaced by different phenyl sulphonyl piperazines and phenyl piperazines using base in DMF to give desired 6-substituted aminocoumarin based acetamide derivatives. All the intermediates and final compounds were characterized by different spectral techniques such as ^{1}H-NMR, ^{13}C-NMR, IR, ESI-MS and CHN analysis.

Compounds were screened for their anticancer activity by using MTT assay in two cell lines, lungs cancer (A549) and breast cancer (MCF7) cell lines. Compound **10c** showed excellent activity against A549 cell line with IC_{50} value 0.4 μM[a] and MCF7 cell line with IC_{50} value 0.51 μM[a].

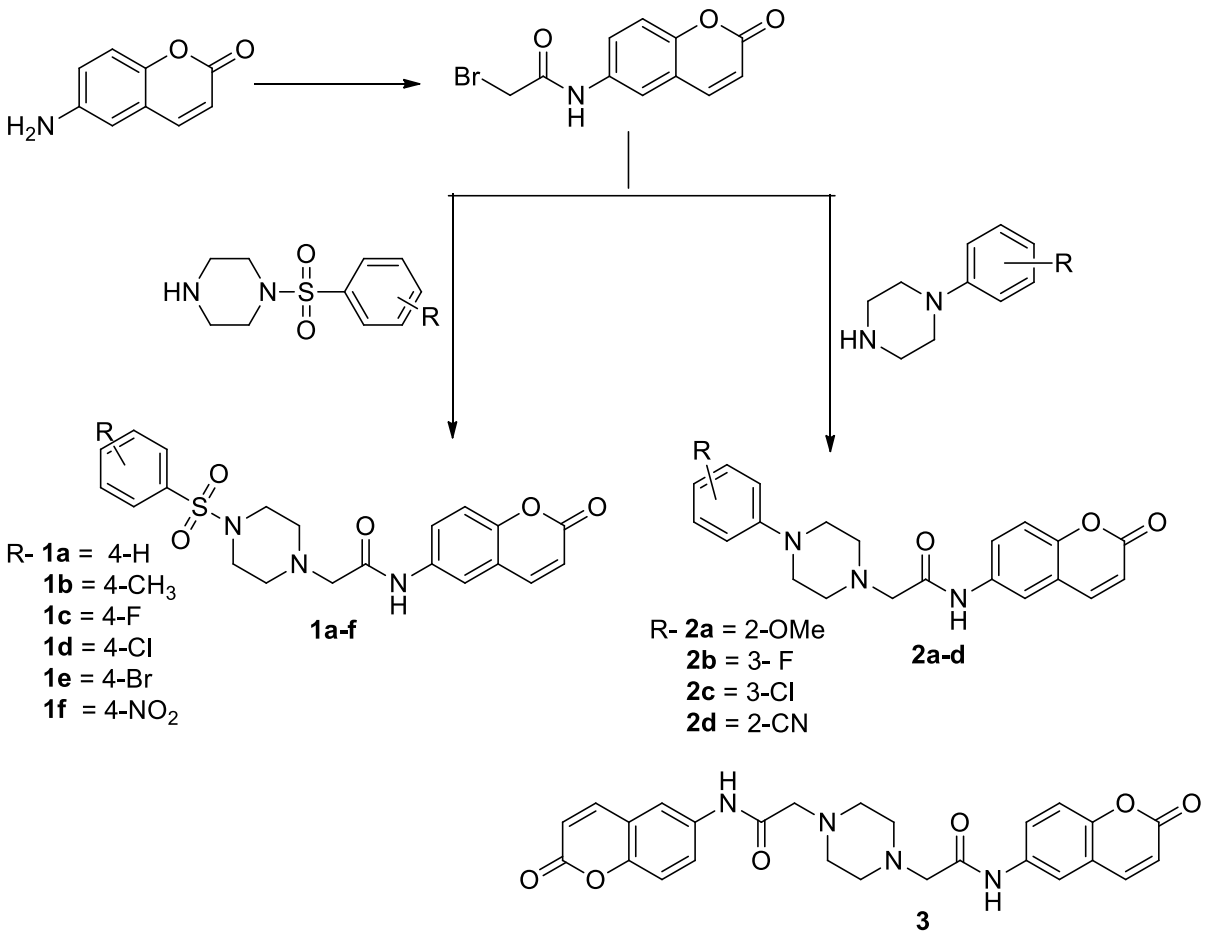


Figure-1: Piperazine derivatives of 6-aminocoumarin

CHAPTER 4

Design of Unsymmetric Coumarin Chalcone Derivatives with Tunable Self-Assembling Behavior

In this chapter unsymmetric Coumarin chalcone derivatives were designed with various alkoxy chain at both terminal end of the molecule. All the compounds **1a-e** and **2a-e** were synthesized and fully characterized by different spectral techniques such as ^{1}H-NMR, ^{13}C-NMR, IR, ESI-MS and elemental analysis. Compounds **1a-e** and **2a-e** were analysed using POM for mesophase identification and optical textures. Further, all the compounds were analysed using DSC to calculate thermograms in heating and cooling scan. In this particular series, types of mesophases were also confirmed from the powder X-ray diffraction. Further, compounds were studied for DFT calculations to obtain the various geometrical parameters, which can be used further to correlate the observed mesomorphic properties and estimated theoretical simulations.

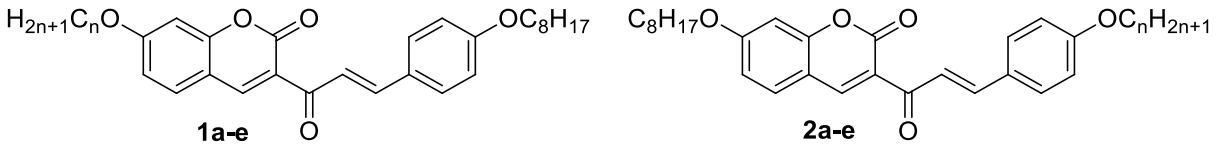


Figure-1: Chromen 2-one chalcone derivatives studied for mesogenic property

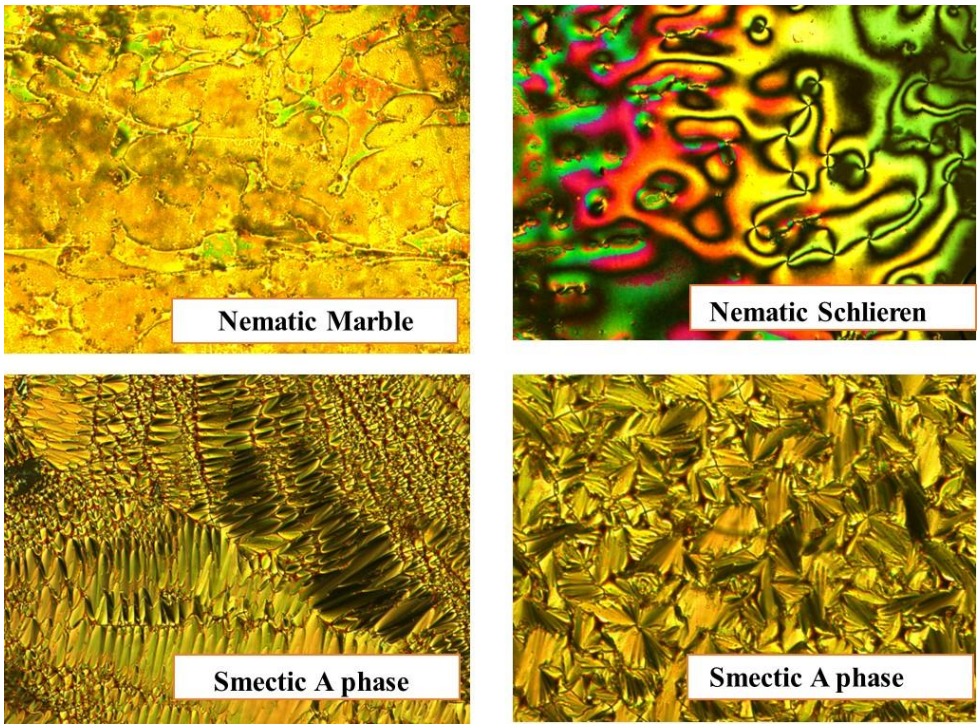
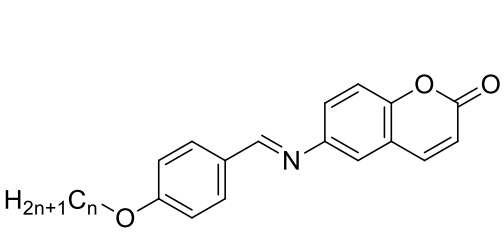


Figure-2: POM images of compound **1a** and **2d**

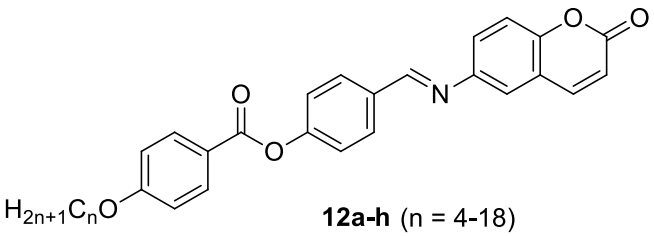
Chapter-5

Studies in Synthesis of 6-Aminocoumarin Schiff Base Derivatives as Mesogens and their DFT Approach

This chapter contains two series, in first series, 6-amino coumarin Schiff base derivatives **1a-g** were synthesized with varies alkoxy chain (n = 6-18) and studied for their mesomorphic properties. In another series of Schiff base derivatives **2a-h** (n = 4-18) additional ester linkage was introduced at aldehyde end and were studied for their mesomorphic behavior. These new imine derivatives **1a-g** and **2a-h** were characterized by ^{1}H-NMR, ^{13}C-NMR, IR, ESI-MS and elemental analysis. Compounds **1a-g** and **2a-h** were analysed using POM for mesophase identification and optical textures. Further, all the compounds were analysed using DSC to calculate thermograms in heating and cooling scan. In this particular series, types of mesophases were also confirmed from the powder X-ray diffraction. Further, compounds were studied for DFT calculations.



10a-g (n = 6-18)



12a-h (n = 4-18)

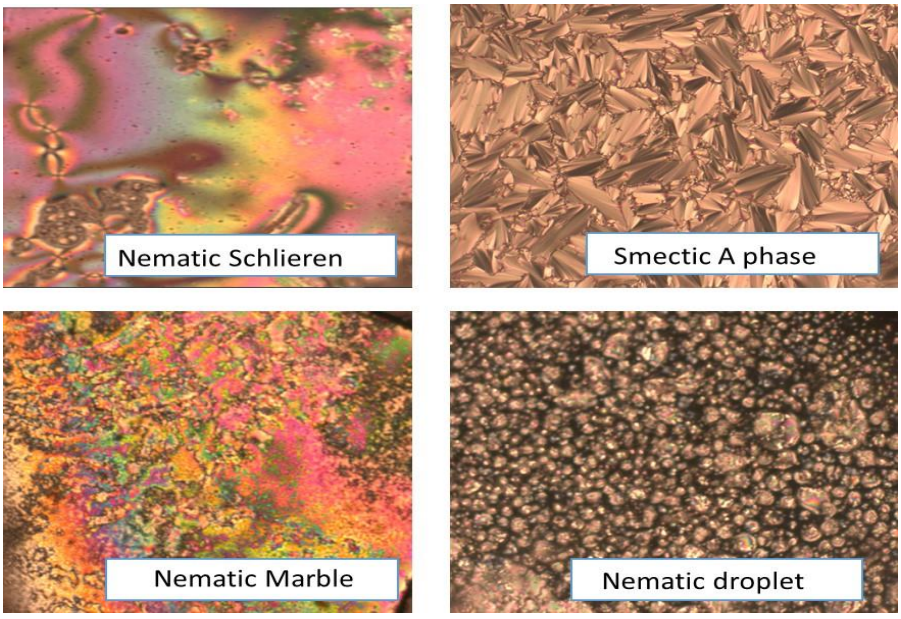


Figure-1: POM images of compounds **1b** (on cooling), **1d** (on heating) and **2d** (on heating and cooling)**.**