Synopsis of the thesis

Entitled

Old Title: "Synthesis and study of novel heterocyclic compounds"

***Revised Title*: "Synthesis and study of mesogenic/biologically-active compounds"**

Submitted to

The Maharaja Sayajirao University of Baroda

For the degree of

Doctor of Philosophy

In

Applied Chemistry

Submitted by

Srujalkumar Anilkumar Sonera

under the supervision of

Prof. R.C.Tandel

Registration No. FOTE/1017 **Date: 27/12/2019**

APPLIED CHEMISTRY DEPARTMENT

FACULTY OF TECHNOLOGY & ENGINEERING

THE MAHARAJA SAYAJIRAO UNIVERSITY OF BARODAVADODARA-390001

Synopsis of the thesis

Entitled

"Synthesis and study of mesogenic/biologically-active compounds"

Submitted to

The Maharaja Sayajirao University of Baroda

For the degree of

Doctor of Philosophy

In

Applied Chemistry

Submitted by

Srujalkumar Anilkumar Sonera

under the supervision of

Prof. R.C.Tandel

Registration No. FOTE/1017 **Date: 27/12/2019**

APPLIED CHEMISTRY DEPARTMENT

FACULTY OF TECHNOLOGY & ENGINEERING

THE MAHARAJA SAYAJIRAO UNIVERSITY OF BARODAVADODARA-390001

Contents

Chapter I: Introduction

Chapter II: Synthesis, characterization and mesomorphic behavior of novel thiadiazole derivatives having azomethine linkages

Chapter III: Synthesis, characterization and study of nematogenic homologous series of coumarin derivatives containing azomethine-ester linkages

Chapter IV: Synthesis, characterization and study of unsymmetrical homologous series of nematogenic liquid crystal compounds possessing azomethine linkage

Chapter V: An efficient synthesis of some novel oxazolone derivatives showing cytotoxicity behavior

- **Optical textures captured in the Polarizing Optical Microscope (POM)**

References

- **Conferences/Symposiums/Seminars/Training/Poster & Oral Presentations**
- **List of Publications related to the Thesis**
- **Additional Publications non-related to the Thesis**

Chapter I: Introduction

Liquid crystals are recognized as the fourth state of matter. The primary distinctions between the common states of matter, liquid, gas, and solid are the kinds and levels of order that each phase contains. However these states of matter are not enough to describe the structures present in every system. Most substances change from being a solid (often crystalline, with great order) to an isotropic liquid (very disordered) when heated. On the other hand, some substances show transitional states that are more ordered than liquids but lack part of the order found in solids. Liquid crystals are these organized fluids. The difference between crystals and liquids is that the molecules in a crystal are ordered whereas in a liquid they are not. The order in a crystal is usually both positional and orientational, in that the molecules are constrained both to occupy specific sites in a lattice and to point their molecular axes in specific directions. The molecules in liquids, on the other hand, diffuse randomly throughout the sample container with the molecular axes tumbling wildly. Interestingly enough, many phases with more order than present in liquids but less order than typical of crystals also exist in nature. These phases are grouped together and called liquid crystals, since they share properties normally associated with both liquids and crystals. The discovery of liquid crystals is usually attributed to an Austrian botanist by the name of Friedrich Reinitzer. In 1888, he experimented with a substance Cholesteryl benzoate and noted that it had two melting points [1]. At 145.5 °C it melted from a solid to a cloudy liquid and at 178.5 °C it turned into a clear liquid. He also observed some unusual colour behaviour upon cooling; first a pale blue colour appeared as the clear liquid turned cloudy and second a bright blue violet colour was present as the cloudy liquid crystallized.

Liquid crystals have properties between those of conventional liquid and those of solid crystals. For instance, a liquid crystal shows fluidity like a liquid, but it also demonstrates optical anisotropy like a crystal.

The various liquid-crystal phases can be characterized by the type of ordering. Among them, there are mainly nematic, smectic, cholesteric, and discotic phases.

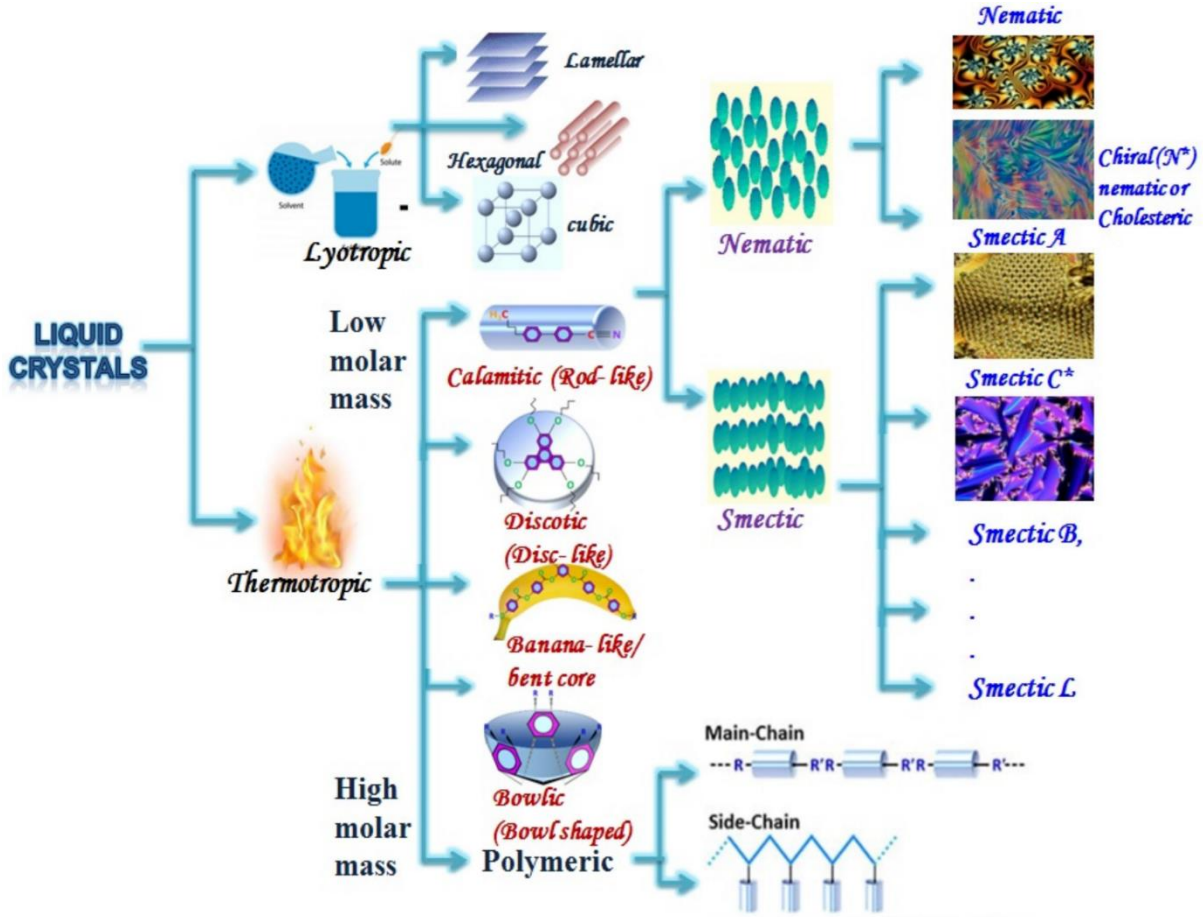


Figure 1. Classification of Liquid Crystals

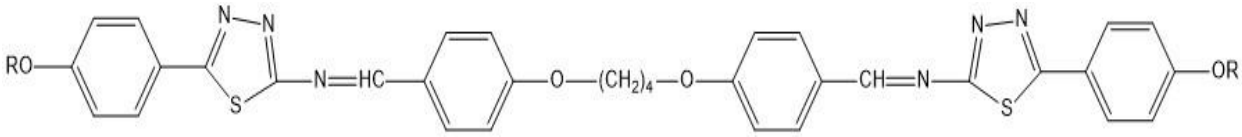
Due to their many important biological and medicinal applications, heterocyclic compounds have attracted a lot of research. Due to their vast synthetic investigation and functional utility, heterocyclic compounds are becoming the subject of growing amounts of research attention. They bridge the gap between biology and chemistry, where so much scientific discovery and application takes place, and are present in over 90% of innovative medications. Additionally, heterocycles are used in a variety of disciplines, such as biochemistry and medicinal chemistry. Heterocyclic compounds are mostly used in veterinary products, agrochemicals, and pharmaceuticals.

Chapter II: Synthesis, characterization and mesomorphic behavior of novel thiadiazole derivatives having azomethine linkages

Now a days, liquid crystalline materials have been widely grown and enhancement in this field is at a very fast rate due to their technical applications such as liquid crystal displays, organic light-emitting diodes, biosensors, and electro-optical devices [2,3]. From the literature, it was found that materials with azomethine moiety have been widely used and studied and used as linking groups for the enhancement of mesomorphic properties [4,5]. There is a continuous

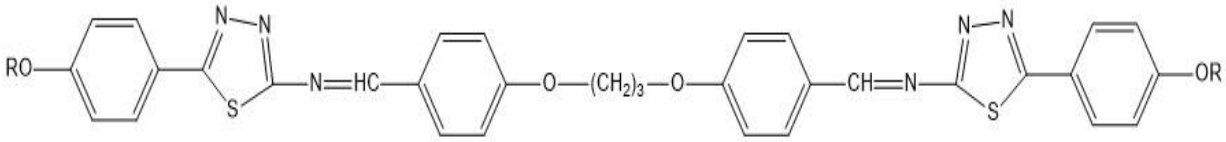
enhancement in the study of heterocyclic compounds containing phenyl derivatives and the addition of the heteroatoms strongly affects the mesomorphic behavior of the compounds. The presence of heteroatoms (O, N, and S) can increase the stability, polarity, polarizability, phase transition, and other properties of liquid crystal molecules. In the present chapter, we report the synthesis of two complete novel homologous series of compounds containing Schiff's Base and thiadiazole moiety incorporated in a molecule with an alkoxy group (n = 1-8, 10, 12, 14, 16) attached at both the terminal end of the molecule and studied the mesomorphic behavior of all the synthesized compounds. Their structure elucidation were assessed using FT-IR, ^{1}H-NMR and elemental analysis. The study of mesomorphic properties and the optical textures of all the synthesized compounds was carried out using the polarizing optical microscope in heating as well as cooling cycles. Determination of transition phase parameters such as phase transition temperature was confirmed with the help of instruments such as differential scanning calorimetry and polarizing optical microscope. The thermal stability of the prepared compounds was recorded using a thermogravimetric analysis. The structure-property relationship of all the synthesized compounds were carefully studied.

Series I



Where R = -$C_nH_{2n+1,}$ where n = 1-8, 10, 12, 14 & 16

Series II



Where R = -$C_nH_{2n+1,}$ where n = 1-8, 10, 12, 14 & 16

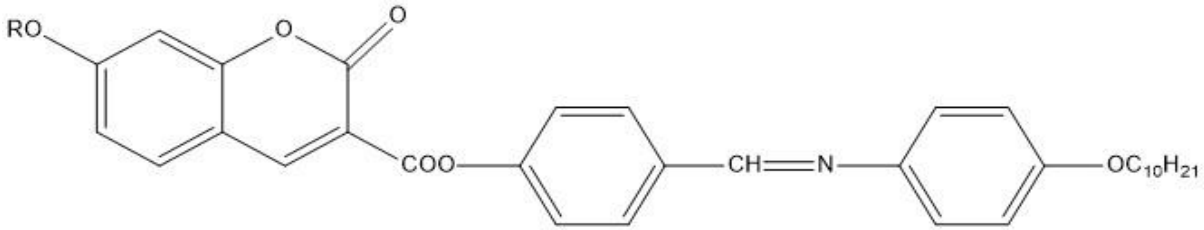
A polarizing optical microscope was used to observe the mesomorphic behavior of all the novel synthesized compounds, and the DSC traces of all novel synthesized compounds confirm the phase transition temperature obtained with POM. From the polarizing optical microscope and DSC analysis data of the novel synthesized compounds, it was observed that methoxy to n-propyloxy derivatives lack a smectic phase, they only exhibit pure nematic phase. The reason

behind this is in the lower homologs, the aromatic nuclei separation was observed at a minimum level and the cohesions occurring at the terminal position are at the strongest level and hence resulting in pure nematogens. As we ascend the series, the lateral cohesive forces increase with an increase in the terminal chain length, and the molecules are arranged in the layered structure before the commencement of the nematic phase. With the increase in the terminal chain length of the moiety, the smectic character appears and the moiety possesses both smectic as well as nematic phases.

Chapter III: Synthesis, characterization and study of nematogenic homologous series of coumarin derivatives containing azomethine-ester linkages

In recent years, enhancements in the research of coumarin derivatives have been found due to its wide range of applications in the field of organic light emitting diodes (OLEDs), light harvesting materials, chemosensors, photorefractive materials, non-linear optical materials and photo alignment of mesomorphic material possessing photochemical and photophysical properties [6-10]. Heteroatom incorporation (N, O, S, etc.) changes the polarity of the molecules, which can significantly alter the associated mesophases and their characteristics. The Coumarin molecule stands out among these heterocyclic units because it is polar and has a significant dipole moment (5.48 D) that is at an angle to the long molecular axis, which is typically a key component for the mesogenic and electronic properties of materials. Mesogenic coumarin derivatives have a broad range of potential uses, including in biological and display systems. In this chapter, we have report of the synthesis of a complete novel homologous series of compounds containing Schiff's Base and coumarin moiety incorporated in a molecule with an alkoxy groups (n = 1-10, 12, 14, 16) attached at one of the terminal ends and n-decyloxy at another terminal end of the molecule and studied the mesomorphic behavior of novel synthesized compounds. All the compounds were characterized using elemental analysis and spectroscopic techniques such as FT-IR, ^{1}H-NMR and ^{13}C-NMR. As the chain length of the terminal alkoxy group in a molecule increases, enhancement in the nematic phases was observed. The optical textures and the determination of phase transition temperatures was confirmed with the help of polarizing optical microscope and differential scanning calorimetry. The thermal behavior of all the synthesized compounds was assessed by thermogravimetric analysis. The effect of the alkoxy chain length as a terminal group of the molecule on the thermal stability and its transition mesomorphic phase change of the novel compounds were also studied. The photophysical properties have been carefully studied. All the synthesized

compounds were screened for their in-vitro antibacterial activity against *Escherichia Coli* and *Staphylococcus aureus* showing good to moderate activity compared to the used standard.

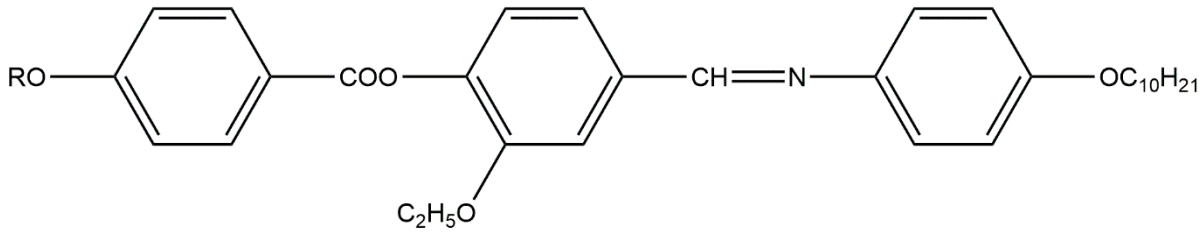


Where R = -$C_nH_{2n+1,}$ where n = 1-10, 12, 14 & 16

Mesomorphic properties of all the final compounds were examined under a polarizing optical microscope and their transition temperatures were compared with differential scanning calorimetry study. All the synthesized coumarin Schiff's-base derivatives possess enantiotropic nematic mesophases. The nematic mesophase persists till the last member of the series is investigated. In the homologous series, the presence of coumarin moiety results in high temperatures. To overcome that we have introduced an ester group in a moiety to attain low temperatures. It leads to a decrease in transition temperature while ascending the homologous series of the compound. Commencement of the nematic phase was observed in the prepared compounds due to the increase in the entropy of the molecules and the weak intermolecular forces of the alkoxy chain length. As we ascend the series, the terminal alkyl chains restrict the packing which may lead to exhibit the formation of nematogens.

Chapter IV: Synthesis, characterization and study of unsymmetrical homologous series of nematogenic liquid crystal compounds possessing azomethine linkage

In the present chapter, a novel homologous series of compounds with azomethine linkage has been synthesized. The structure of every proposed compound was elucidated using FT-IR, ^{1}H-NMR, ^{13}C-NMR, and elemental analysis. The mesomorphic behavior of all the prepared compounds was observed using a polarizing optical microscope. The transition temperatures and the phase transition enthalpy change data values were recorded using differential scanning calorimetry. By varying terminal alkoxy chain length (n = 1-10, 12, 14, 16) at one side, nematic phases were observed in heating and cooling cycles. The structure-property relationship to understand the effect of terminal alkyl chain length, lateral group substituent, and azomethine linkage on the mesomorphic properties was carefully studied. To assess the thermal stability of all prepared compounds, a thermogravimetry study was performed.

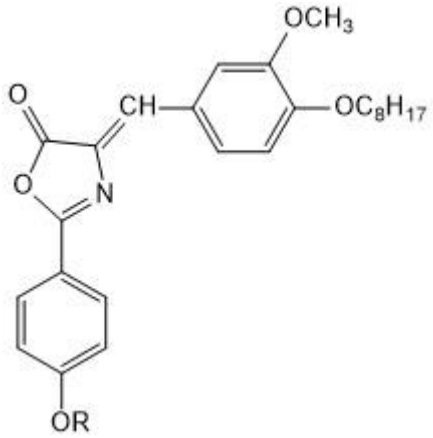


Where R = -C_nH_{2n+1}, n = 1-10, 12, 14 & 16

Chapter V: An efficient synthesis of some novel oxazolone derivatives showing cytotoxicity behaviour

There are heterocyclic compounds in both natural and man-made forms. It also has a variety of biological functions and is vital to human survival. Azlactone (Oxazolone), which falls under the general category of heterocyclic compounds, is one of the five-membered heterocyclic compounds with a variety of therapeutic uses. New medicinal compounds have been discovered using a variety of techniques. Oxazolone moieties were synthesized using such techniques. Oxazolone was a versatile compound that demonstrated a variety of biological actions and was extremely beneficial in both research and industrial applications. The molecule contained numerous reactive sites that facilitate a variety of applications in the fields of chemistry, biology, and material science. The 4-arylidene-2-phenyl-5(4H)-oxazolone, a significant family of five-membered heterocyclic moiety with nitrogen and oxygen as heteroatoms in its structure, was created and first reported in 1893 by Friedrich Gustav Carl Emil Erlenmeyer. According to published research, Oxazolone's C-2 and C-4 locations are important for a number of biological functions. Other chemical compounds, such as N-substituted pyrroles, amino acids, -acyl-amino alcohols, thiamine, amides, peptides, and other heterocyclic precursors, were also synthesized using oxazolones as an intermediary. Heterocyclic compounds with hetero atoms of nitrogen, sulfur, and oxygen in five and six-membered ring structures are crucial. The five-membered heterocyclic molecule oxazolone comes in two isomeric forms depending on where the double bond is located and one isomeric form depending on where the carbonyl group is located. In this chapter, we report the synthesis of new model compounds that comprises oxazolone derivatives by using two different schemes. The oxazolone moiety has served as a crucial structural component for a number of physiologically active molecules during the past few decades, including both natural and manufactured drugs. An investigation into novel oxazolone compounds was done utilizing barley and moong seeds to demonstrate action like seed germination. According to Scheme 1, 4-n-alkoxybenzoyl glycine and 3-methoxy-4-n-octyloxybenzaldehyde were used to prepare 3-

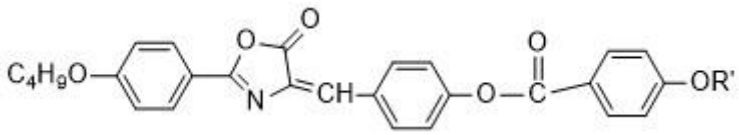
methoxy-4-octyloxybenzylidene)-2-(4-alkoxyphenyl)oxazol-5-one. Another synthesis pathway, shown in Scheme 2, was used to prepare several novel oxazolone (azlactone) derivatives. Their characterization data, including FT-IR, ^{1}H-NMR, and elemental Analysis, confirmed the final product. The TLC method has been used to verify the purity of the produced compounds.



,

Where R = -C_nH_{2n+1}, where n = 6, 8, 10, 12 & 14

(a)



Where R = -C_nH_{2n+1}, where n = 1, 8, 14 & 16

(b)

(a) indicates Scheme 1 compounds, (b) indicates Scheme 2 compounds.

The melting point of all the novel synthesized compounds (Scheme 1 & 2) was taken on polarizing optical microscope. From the polarizing optical microscopic study of all the novel synthesized compounds of Scheme 1, it was observed that none of the compounds exhibit mesomorphic behavior (liquid crystalline property) due to the hydrogen bonding of amide linkage. In the new class of synthesized compounds containing an oxazolone ring (Scheme 1), the methoxy group is present at a lateral position in the ring which hinders the liquid crystalline property. All the novel synthesized compounds (Scheme 1) possess nonlinearity in their molecular structure hence decreasing the mesomorphic nature of the compound. In Scheme 2, a new class of compounds was synthesized containing an oxazolone ring by using p-

hydroxybenzoic acid as a starting material. For the longer chain length compounds (Scheme 2), the separation of aromatic nuclear is at maximum and its terminal cohesions are strongest. Hence, it decreases the planarity of the molecule and increases the breadth of the molecule rendering the compounds to be non-mesogenic.

Biological Activity

Seed Infusion Technique (Cytotoxicity)

Using organic solvents like acetone or dichloromethane, bioactive compounds are directly absorbed into seeds in this process. By allowing the bioactive compounds dissolved in the organic solvents to permeate into the seed tissues, these solvents make the seed coverings permeable. This technique involves soaking barley and moong seeds for one to four hours in a solvent (acetone or dichloromethane) that contains the required solute. The targeted bioactive molecule was absorbed into the seed during these hours. After the infusion procedure, the seeds are taken out of the specific solution and put on a petri dish with filter paper that has been moistened with water to aid in germination. The seeds are kept at a temperature of 25 to 30 °C, and the germination process was seen.

Scheme 1 Compound codes were attributed as follows:

CO = control, A = Hexa-1, B = Octyl-2, C = Decyl-3, D = Dodecyl-4, E = Nitro-6

Scheme 2 Compound codes were attributed as follows:

A = methyl', B = Octyl-2', C = tetradecyl-3', D = Hexadecyl-4'

Figure 2 Photograph showing the effect of the compounds on Barley seed germination on Scheme-1 compounds

Figure 3 Photograph showing the effect of the compounds on Moong seed germination Scheme-1 compounds.

Optical Textures captured in the Polarizing Optical Microscope

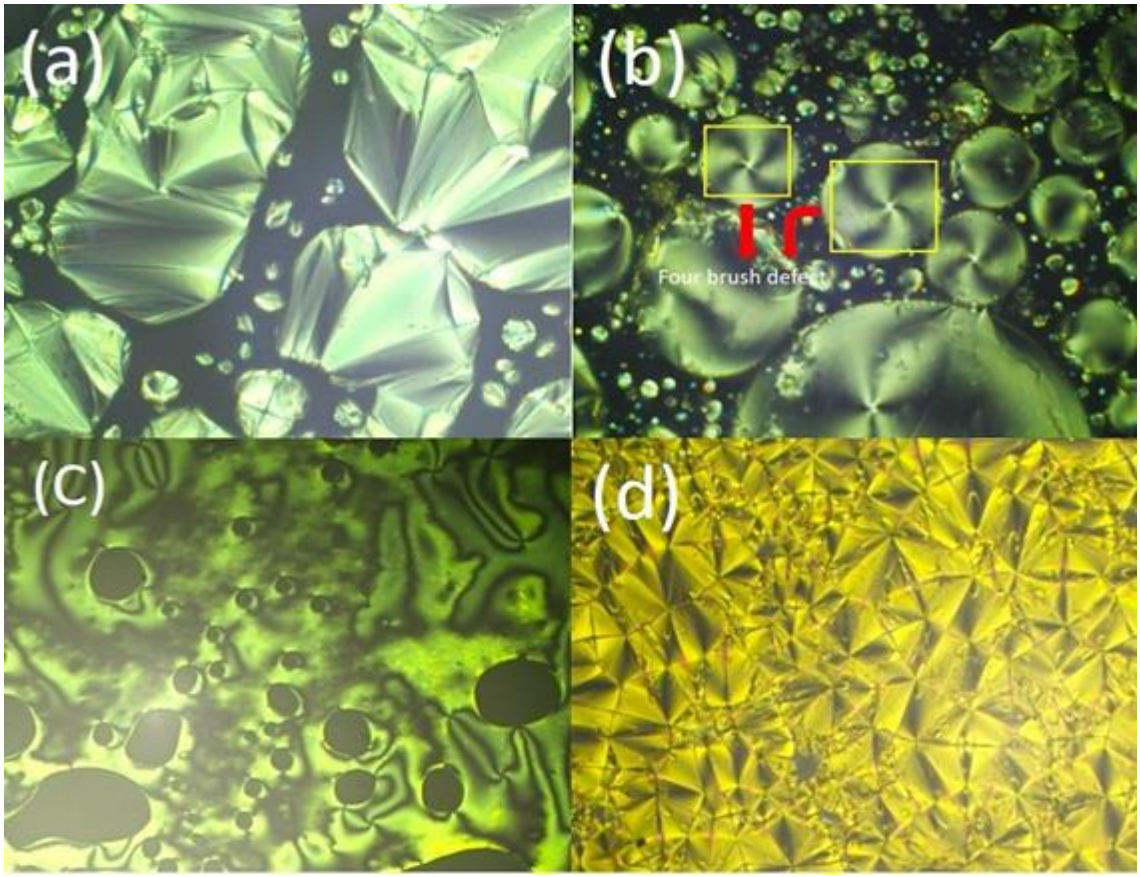


Figure 4. Fan shaped texture of smectic phase and typical marble texture of nematic phase in heating and cooling cycles. (a) & (d) Smectic A textures, (b) & (c) Nematic textures

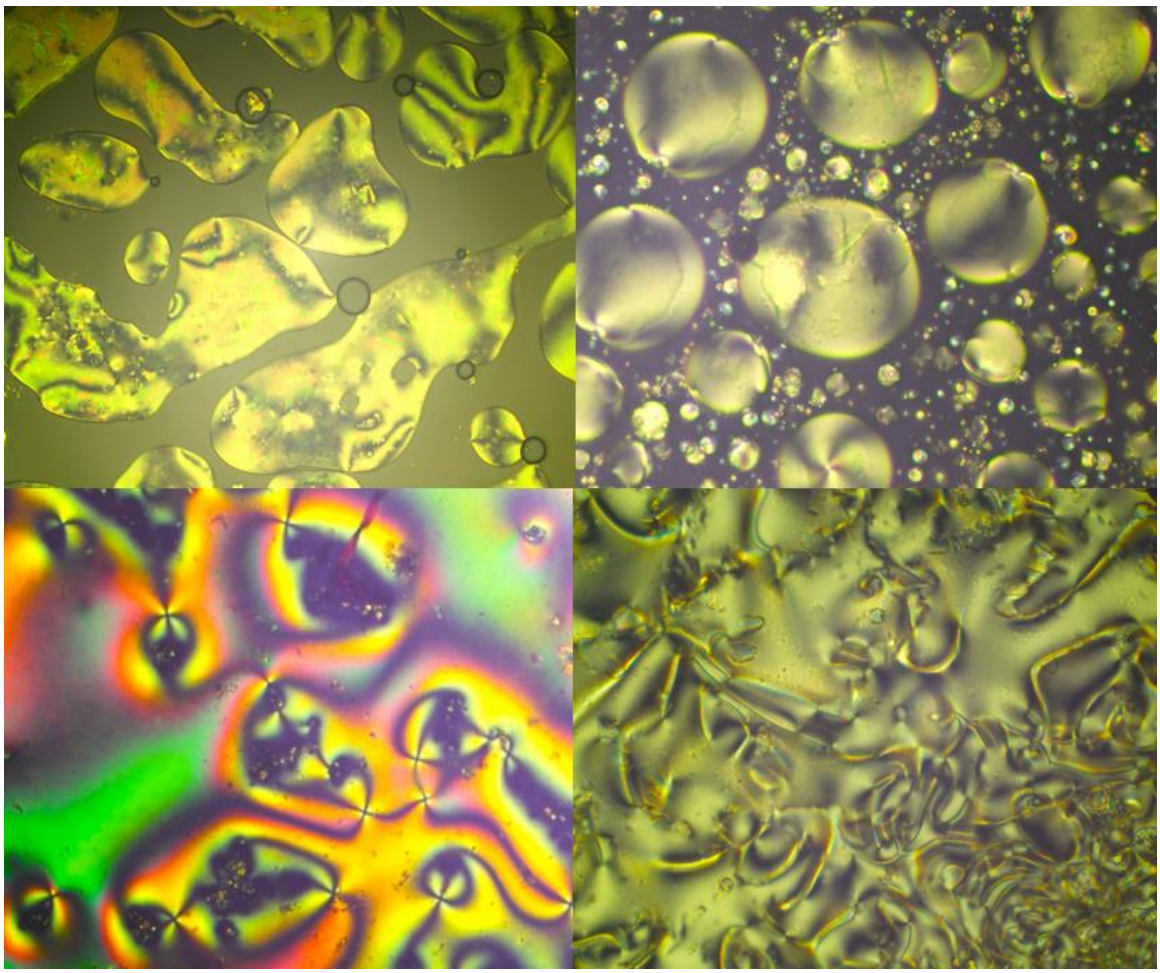


Figure 5. POM textures (left to right) of Schliren nematic phase, nematic marble-like texture, nematic textures with four brush defect, thread like nematic textures of coumarin based Schiff's-base derivatives upon heating and cooling cycles using untreated microscopic glass slides. All the microscopic textures were taken under the magnification of 10 X.

References

1. F. Reinitzer, *Wiener Monatsh. Chem.*, **9**, 421–44 (1888).
2. S. Setia, S. Sidiq, J. De, et al., *Liq Cryst.* **43** (13-15), 2009-2050 (2016).
3. R.K. Gupta, V. Manjuladevi, C. Karthik, et al., *Liq Cryst.* **43** (13-15), 2071-2091 (2016).
4. K.D. Katariya, K.J. Nakum, M. Hagar, *Liq Cryst.* **49** (3), 312-326 (2022).
5. R.R. Koshti, A. Vyas, K.A. Patel, et al., *Liq Cryst.* **49** (2), 248-263 (2022).
6. M.P. Brun, L. Bischoff, C. Garbay *Angew Chemie - Int Ed.* **43** 3432-3436 (2004).
7. Y.F. Sun, S.H. Xu, R.T. Wu, et al. *Dye Pigment.* **87** 109-118 (2010).
8. S. Inagaki, O. Ohtani, Y. Goto, et al. *Angew Chemie - Int Ed.* **48** 4042-4046 (2009).
9. V.C. Ezeh, T.C. Harrop, *Inorg Chem.* **51** 1213-1215 (2012).
10. M. Halim, M.S. Tremblay, S. Jockusch, et al. *J Am Chem Soc*. **129** 7704-7705 (2007).

Conferences/Symposiums/Quiz/Seminars/Training/Poster/Oral Presentations

1. Poster presented entitled "**Synthesis and study of Benzalazine Derivatives containing Ester Linkages**" in International Seminar on Advanced Materials and Applications organized by Applied Physics and Applied Chemistry Department, Faculty of Technology and Engineering, M.S.University of Baroda, Vadodara – 390001, India and Luminescence Society of India (Regd. No: GUJ/1156)
2. Poster presented entitled "**Synthesis and study of New Schiff-Base Derivatives containing Carbazole moiety**" in National Conference on Current Trends and Advances in Chemical Science Organized by Department of Chemistry, B.K.M. Science College Valsad, Gujarat – 396001
3. Oral Presentation entitled " **Synthesis and study of novel heterocyclic compounds containing oxazolone moiety**" in Virtual International Conference on Chemical Sciences in Sustainable Technology and Development (IC^2S^2TD-2020) organized by Applied Chemistry Department, S.V.National Institute of Technology, Surat 395007, Gujarat, India in Association with Department of Chemistry, Chung-Ang University, Seoul, South Korea.
4. Attended One Day Seminar on "**Recent Advances in Chemical Science-2023**" organized by the Department of Chemistry, Faculty of Technology and Engineering, The Maharaja Sayajirao University of Baroda, Vadodara-390001, India.
5. Attended an Online workshop on "**Challenges and Opportunities in Designing Nanoarchitectonics of Nanoporous Carbon for Industrial Applications**" organized by the Materials and Metallurgical Department of MANIT Bhopal from 16-20th September 2020.
6. Attended Five Day Faculty Development Programme on "**Accelerating Innovations in Material Science – Surface Characterization**" organized by the Department of Chemistry, BMS Institute of Technology and Management, Bengaluru, India from 18-22nd May 2021.
7. Registered Participant in the webinar on "**IPR issues and Patenting**" by Dr. Sunil Kumar Assistant Controller of Patents and Designs, Patent Office, Kolkata, West Bengal, India organized by the Department of Chemical Sciences, Maharaja Ranjit Singh College of Professional Sciences, Indore, MP, India on 24th June 2020.
8. Online Certification Course in "**Patent Searching for Beginners**" jointly organized by IP Moment and Department of Environmental Science and Department of Biotechnology of SRKI College, Surat – 395001.
9. Participation in International E-Quiz titled "**Chemistry Matters: A Novel Fight Against COVID-19**" organized from 13-23rd June 2020 under the aegis of the Department of Chemistry, Bherulal Patidar Govt. P.G. College, MHOW (M.P.), INDIA. CERTIFICATE ID: E0DXP0-CE000886.
10. **State Level Online Chemistry Quiz** organized by Govt. Science College, Gariyadhar, Department of Chemistry. (Passing Score – 56%)
11. **Online Interdisciplinary Quiz (Chemistry)** on 6th October 2020 organized by B N Patel Institute of Paramedical And Science. (Passing Score – 71%)
12. Participation in a One-week Training Program on R&D Equipment on the theme **CHARACTERIZATION OF MATERIALS/COMPOUNDS USING**

ADVANCED INSTRUMENTS from 11th-17th April 2023 at IIT Delhi Sonipat Campus jointly organized by CRF IIT Delhi & NIT Warangal.

List of Publications related to the Thesis

1. **Srujal Sonera**, Sagar Bairwa, R.C.Tandel An efficient synthesis of some novel oxazolone derivatives showing cytotoxic activity Journal of the Iranian Chemical Society, https://doi.org/10.1007/s13738-023-02918-3
2. **Srujal A. Sonera**, Sagar K. Bairwa & R.C.Tandel Nematogenic Homologous Series of Coumarin Derivatives Containing Azomethine-Ester Linkages: Synthesis, Characterization, Photophysical and Mesomorphic Properties Liquid Crystals (under review).[Submission ID: 231739537]
3. **Srujal A. Sonera**, Sagar K. Bairwa & R.C. Tandel Symmetrical homologous series of thiadiazole derivatives containing azomethine linkages: Synthesis, characterization and mesomorphic properties Molecular Crystals and Liquid Crystals (under review). [Submission ID: 238700911]
4. **Srujal A. Sonera**, Sagar K. Bairwa & R.C. Tandel Synthesis, characterization, and study of unsymmetrical homologous series of nematogenic liquid crystal compounds possessing imine linkage (under preparation).

Additional Publications non-related to the Thesis

1. Sagar K. Bairwa, **Srujal A. Sonera** & R.C. Tandel Cholesterol based mesogenic Schiff's base derivatives with carbonate linkage: Synthesis, characterization and photoluminescence study Liquid Crystals, DOI: 10.1080/02678292.2023.2260773
2. Sagar K. Bairwa, **Srujal A. Sonera** & R.C.Tandel Mesomorphic behaviour and photoluminescence study of homologous series of Schiff's based derived from cholesteryl carbonate and thiadiazole moiety Liquid Crystals (under review) [Submission ID 238582406]
3. Manoj J. Patel, **Srujal A Sonera,** Sagar K. Bairwa & Ramnik C. Tandel Monoazo Reactive Dyes: Synthesis and Application on cotton, silk and wool fibers Brazilian Journal of Science, 3(1), 175-182, 2024 ISSN: 2764-3417
4. Manoj J Patel, R C Tandel, **Srujal A Sonera** & Sagar K Bairwa Trends in the synthesis and application of some reactive dyes: A review Brazilian Journal of Science, 2(7), 14-29, 2023 ISSN: 2764-3417
5. Manoj J. Patel, R.C. Tandel, **Srujal A. Sonera**, Sagar K. Bairwa Bi-functional reactive dyes: A study of their dyeing properties on cotton fabric Eur. Chem. Bull. 2023,12(4), 1540-1553 ISSN 2063-5346

Srujalkumar Anilkumar Sonera

(Research Student)

Prof. R.C.Tandel

(Research Supervisor)

Head

Applied Chemistry Department

Dean

Faculty of Technology and Engineering