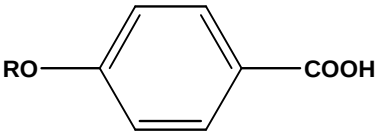
ABSTRACT

The present work consists of four parts. The first part deals with the synthesis of new series 1,3,5-tri-[5(4'-n-alkoxyphenyl)-1,3,4-thiadiazol-2-yl-]-trimesilydene $[7]_n$, involving four steps which were outlined as follows:

Step one: Preparation of 4-n-alkoxybenzoic acid$[2]_n$

The reaction of 4-hydroxybenzoic [1] acid with different n-alkyl halides afforded the corresponding 4-n-alkoxybenzoic acid$[2]_n$.

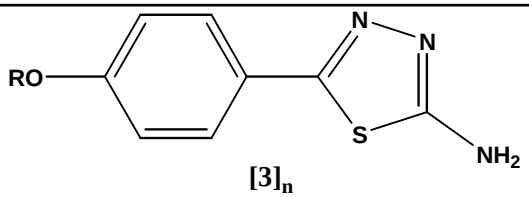


$[2]_n$

R: methyl$[2]_1$, ethyl$[2]_2$, n-propyl$[2]_3$, n-butyl$[2]_4$, n-pentyl$[2]_5$, n-hexyl$[2]_6$, n-heptyl$[2]_7$, n-octyl$[2]_8$

Step two: Synthesis of 2-amino-5-(4-n-alkoxyphenyl)-1,3,4-thiadiazole$[3]_n$

The reaction of thiosemicarbazide and different 4-n-alkoxy benzoic acid$[2]_n$, in $POCl_3$ afforded the corresponding 2-amino-5-(4-n-alkoxyphenyl)-1,3,4-thiadiazole$[3]_n$.

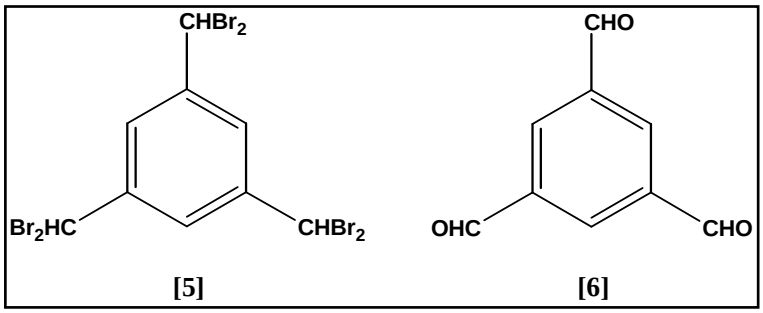


$[3]_n$

R: methyl$[3]_1$, ethyl$[3]_2$, n-propyl$[3]_3$, n-butyl$[3]_4$, n-pentyl$[3]_5$, n-hexyl$[3]_6$, n-heptyl$[3]_7$, n-octyl$[3]_8$

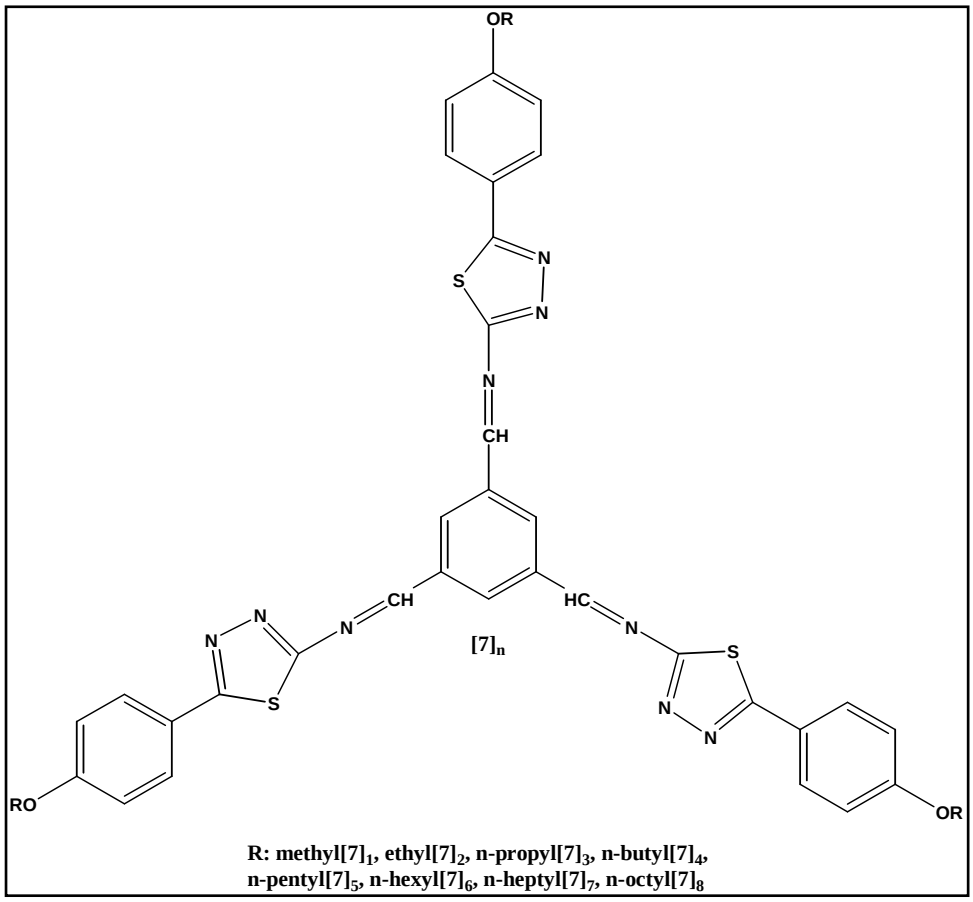
Step three: Preparation of 1,3,5-triformylbenzene[6]

First, step 3A the reaction of mesitylene with bromine under a source of UV light afforded α,α,α',α',α",α"-hexabromomesitylene[5]. Second, step 3B the reaction of α,α,α',α',α",α"-hexabromomesitylene[5] with morpholine and concentrated hydrochloric acid afforded 1,3,5-triformyl benzene[6].



Step four: Synthesis of 1,3,5-tri-[5(4'-n-alkoxyphenyl)-1,3,4-thiadiazol-2-yl-]-trimesilydene[7]$_n$

The reaction of 1,3,5-triformylbenzene [6] with different 2-amino-5-(4-n-alkoxyphenyl)-1,3,4-thiadiazole[3]$_n$ afforded the titled compounds [7]$_n$.



R: methyl[7]$_1$, ethyl[7]$_2$, n-propyl[7]$_3$, n-butyl[7]$_4$, n-pentyl[7]$_5$, n-hexyl[7]$_6$, n-heptyl[7]$_7$, n-octyl[7]$_8$

Part two ***Characterization***: The characterization of the synthesized compounds was elucidated by different spectroscopic methods e.g., (UV, IR,) spectroscopy. The results are in agreement with the suggested structures.

Part three ***Liquid crystals***: The liquid crystalline behavior of the Schiff's bases containing 1,3,4-thiadiazole[7]$_n$ ring system have been examined by means of hot-stage microscopy. Texture observations suggested the existence of LC phases for the compounds [7]$_4$, [7]$_5$,[7]$_6$,[7]$_7$, and [7]$_8$ while compounds [7]$_1$, [7]$_2$, [7]$_3$ do not form liquid crystals phases.

Part four ***Biological activity:*** The synthesized compounds were tested ***in vitro*** for antimicrobial activity. The results obtained indicated that some of these compounds are more active than the others. Table (3-5).

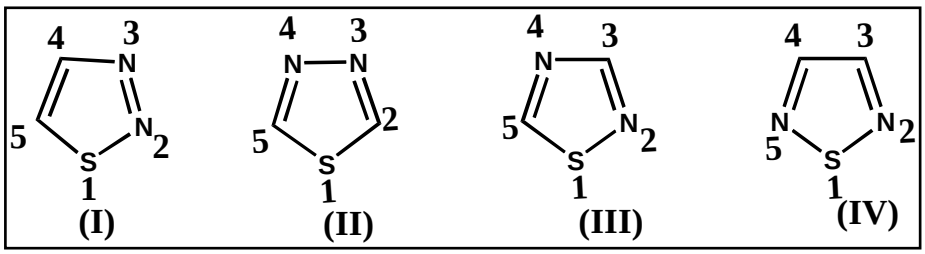
CHAPTER ONE
INTRODUCTION
PART ONE

1-1 What is the chemistry of heterocyclic compounds?

The chemistry of heterocyclic compounds is the most complex branch of organic chemistry. It is equally interesting for its theoretical implications, for the diversity of its synthetic procedures, and for the physiological and industrial significance of heterocyclic compounds[1]. Heterocyclic compounds, or heterocycles are cyclic compounds in which one or more of the atoms of the ring are hetero atoms. A hetero atom is an atom except carbon. The name comes from the Greek word *heteros*, which means "different". A variety of atoms, such as N, O, S, Se, P, Si, B and As can be incorporated into ring structures. In this work we will consider only the 1,3,4-thiadiazole compounds.

1-2 Thiadiazoles

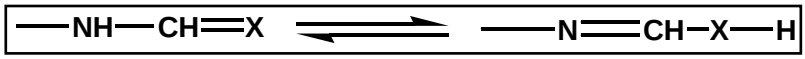
Thiadiazoles are five membered aromatic ring compounds with three hetero atoms; one sulfur atom and two nitrogen atoms. There are four isomeric types of thiadiazoles: 1,2,3-thiadiazole(I); 1,3,4-thiadiazole(II), 1,2,4-thiadiazole(III); and 1,2,5-thiadiazole (IV), as shown bellow[2]



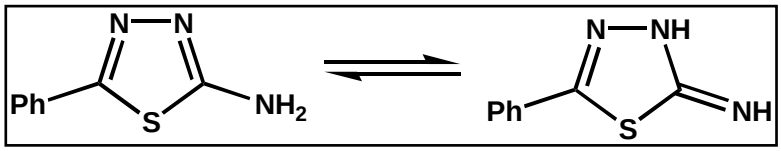
1-3 1,3,4-Thiadiazoles

The most thermally stable isomer is 1, 3, 4-thiadiazole, and its stability is controlled in general by the electron density at the C2 and C5 atoms, which is largely dependent on the substituents[3]. The stability of 1,3,4-thiadiazole is especially enhanced by alkyl and aryl substituents[4] on positions 2 and 5.

Thiadiazoles, like all other compounds containing (NHCH=X) moiety (X=N, O, and S), exist in two tautomeric forms:



It was established by ultra – violet, Infrared spectroscopy and fluorescence that 2-amino-5-phenyl-1,3,4-thiadiazole exists in a tautomeric equilibrium[5]:

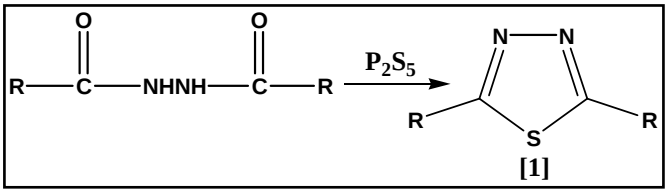


1-4 Synthesis of 1,3,4-thiadiazoles

Several methods have been used to synthesize 1,3,4-thiadiazoles, the most commonly used are:

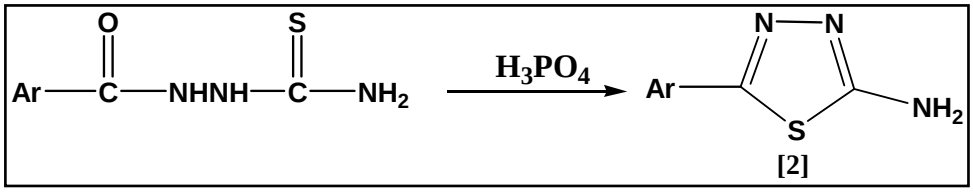
Stolle, Callaborators and Hille[6] prepared (2,5-dialkyl-1,3,4-thiadiazole),[1] by using 1,2-diacylhydrazine with phosphorus pentasulfide

.



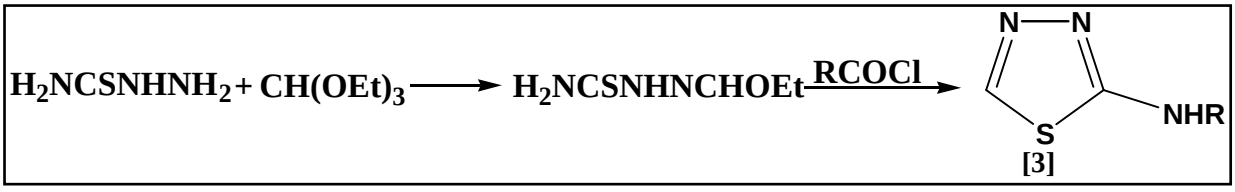
[1]

Hoggarth[7] prepared (2-amino-5-aryl-1,3,4-thiadiazole), [2] derivatives using thiosemicarbazide derivatives with phosphoric acid:



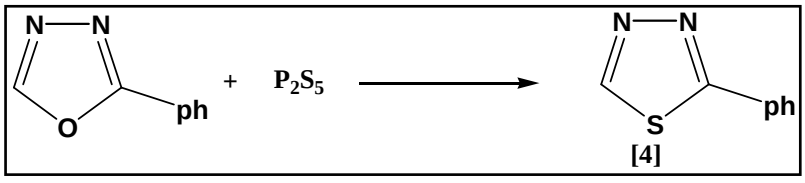
[2]

Anisworth[8] prepared derivatives (2-amino-1,3,4-thiadiazole),[3] by using thiosemicarbazide with triethoxy methane and the product was reacted with an acid chloride:



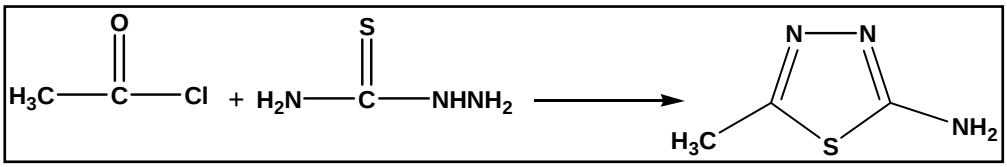
[3]

The compound (2-phenyl-1,3,4-thiadiazole),[4] was prepared by the reaction of (2-phenyl-1,3,4-oxadiazole) with P_2S_5[9] :

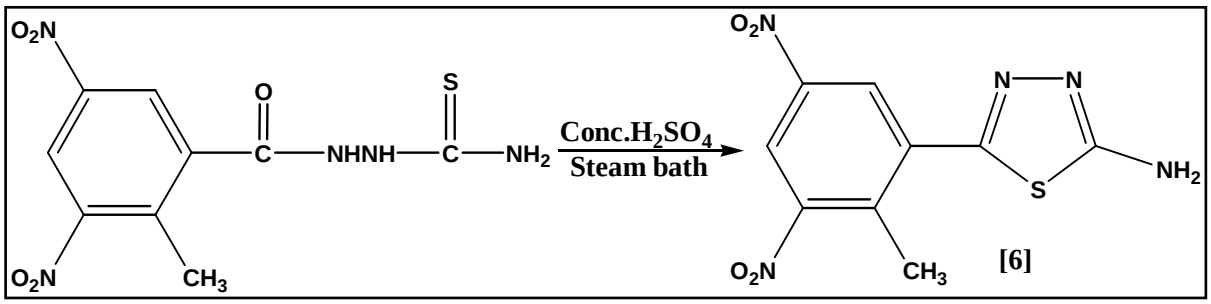


[4]

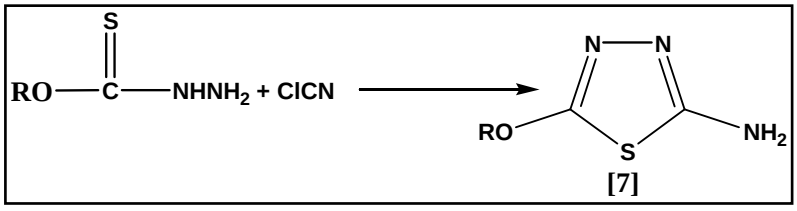
Freund [10] cyclized thiosemicarbazide directly to 2-amino-5-methyl-1,3,4-thiadiazole through the reaction with acetyl chloride.



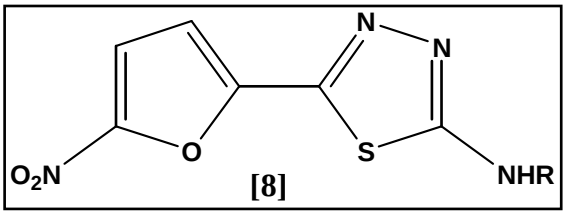
The compound (2-amino-5-dinitro-1-benzoyl thiosemicarbazide phenyl-1,3,4-thiadiazole),[6] were synthesized using the compound 2-methyl-3,5-dinitro-1-benzoyl thiosemicarbazide with concentrated sulfuric acid[11]:



The compounds (2-amino-5-alkoxy-1,3,4-thiadiazole)[12],[7] were prepared by reacting alkoxy thiosemicarbazide derivatives with chlorocyanide:

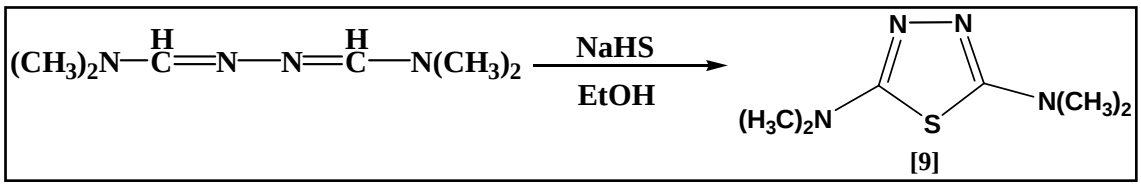


Skagins[13] prepared the compounds (2-(5-nitro furfuryl)-5-substituted amino-1,3,4-thiadiazole), [8]:



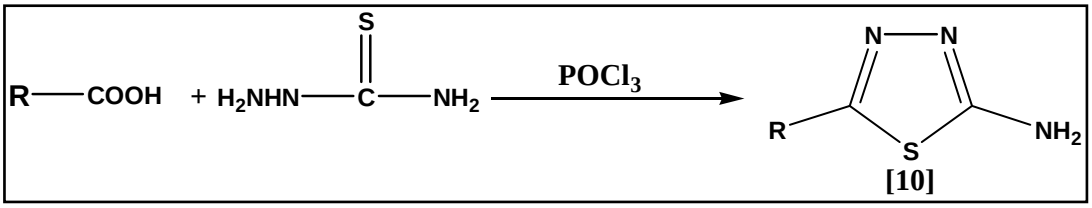
[8]

Fohlische[14] synthesized (1,3,4-thiadiazole derivatives), [9] by mixing an equal quantities of N,N-dimethyl formamide and phosgene to give N,N-dimethyl formamidazine, then this compound reacted with sodium hydrogen sulfide in the presence of ethanol to give the 1,3,4-thiadiazole derivatives.



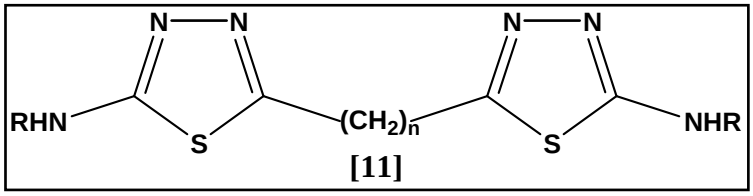
[9]

Carboxylic acids react with thiosemicarbazide in phosphorus oxychloride affording (2-amino-5-alkyl or aryl-1,3,4-thiadiazole)[15] [10].



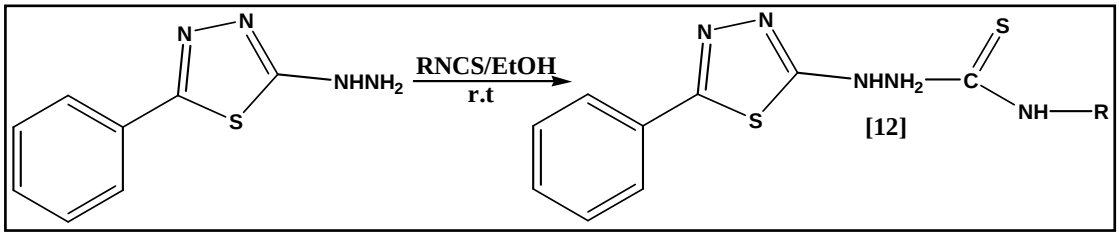
[10]

The compounds bis-(5-aryl amino-1,3,4-thiadiazol-2-yl)-alkanes [11] were prepared by using sulfuric acid and alkyl or aryl thiosemicarbazide[16]:

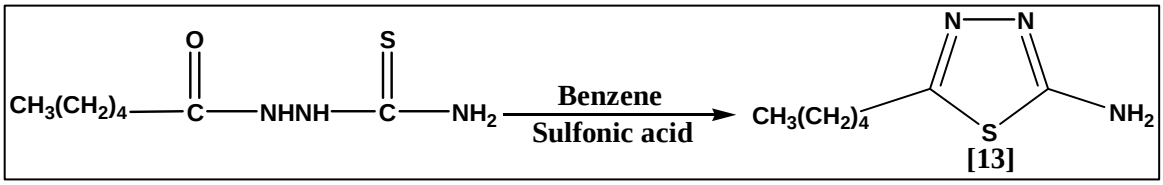


[11]

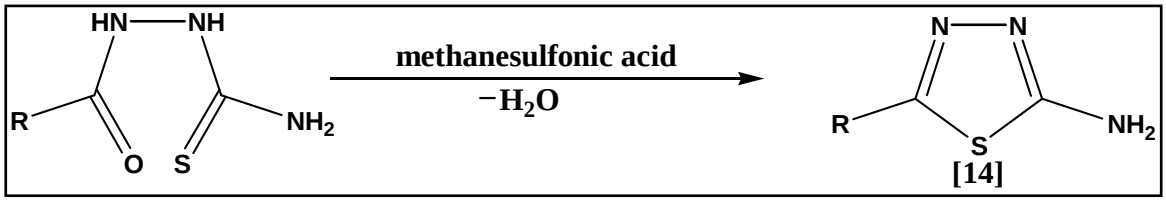
Mohsen[17] et. al., synthesized a novel series of (2-aryl thiocarbomyl hydrazine-5-phenyl-1,3,4-thiadiazoles[12].



Howard[18] prepared 2-amino-5-amyl-1,3,4-thiadiazole by using (1-acyl thiosemicarbazide), [13].



The treatment of 2-acylthiosemicarbazide with molar equivalents of methansulfonic acid in refluxing toluene afforded 1,3,4-thiadiazoles 2-amino-5-alkyl-1,3,4-thiadiazoles[19] [14].



1-5 Uses of 1, 3,4-thiadiazoles

The growing patent literature from the sixties demonstrates that the 1,3,4-thiadiazoles are becoming of great interest, this is primarily due to the large number of uses of 1,3,4-thiadiazoles in the most diverse areas, for example in drug synthesis, scintillation material, dyestuffs industry[20], photography[21], and corrosion inhibitors[22]. Numerous 1,3,4-thiadiazoles have been synthesized and reported to be biologically versatile compounds having bactericidal[23], fungicidal[24], muscle relaxent[25] properties …etc. Some 1,3,4-thiadiazole derivatives possess central nervous system (CNS) depressant activity[26]. Liquid crystals were initially of interest as examples of a new state of matter and until about 1965[27] most researches work involved the preparation of homologous series of compounds with particular core structure and a study of how the transition temperatures and types of mesophase changed within that series. Thiadiazoles were used in the preparation of liquid crystalline series in many mesogens; several examples were listed in the literature survey of the liquid crystalline materials containing heterocyclic units (page 26).

PART TWO

1-6 What are liquid crystals?

The liquid crystal (LC) phase[28] is a well-known state of matter, which lies between the solid and isotropic liquid phases. Liquid crystals have intermediate order, and are consequently sometimes known as mesophases. By definition, the LC state (**mesomorphic state**) is characterized by having a long-range *orientational order* and possible partial *positional order*. To specify quantitatively the amount of orientation order in the LC phase, the scalar order parameter S defined by equation is commonly used.

$$S=1/2 \langle 3\cos^2\theta - 1 \rangle \quad \ldots\ldots\ldots\ldots (1.1)$$

$(0 < S < 1)$. Where θ is the angle between the director (n) which is the preferred direction of molecules and the longaxis of each molecules[29].

In a perfectly oriented system S = 1, and in anisotropic liquid state, where there is no orientational order, S = 0.In the crystal phase the molecules have a high degree of order, occupying fixed positions in the lattice, Therefore, the molecules are positioned in fixed orientations with no translational freedom. Conversely, in the isotropic liquid phase only a short-range order dominates, the molecules are mobile and have no orientation with respect to each other, as the molecular axes are able to tumble freely. The LC phase (**mesophase**) shares properties of both the crystal and liquid phases, possessing an intermediate molecular order between the perfect three-dimensional long-range positional and orientational order found in crystals, and the absence of long-range order found in the isotropic liquids (and amorphous solids).

LCs phases have orientational but not positional orders; they are neither liquids nor crystals. The molecules in the liquid crystal phase are not constrained within a lattice, but the molecular axes tend to be oriented[29] in a preferred direction (n), as shown in Figure (1-1) and (1-2)

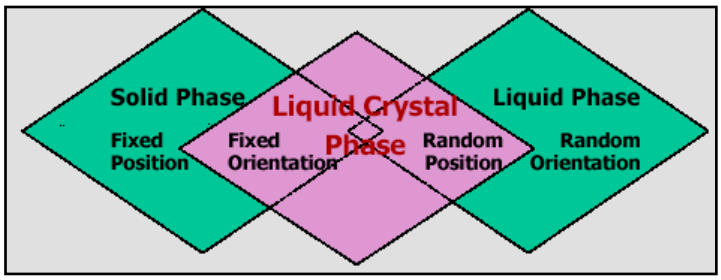


Figure (1-1): Solid, Liquid, and Liquid Crystal phases, With their positions and orientations.

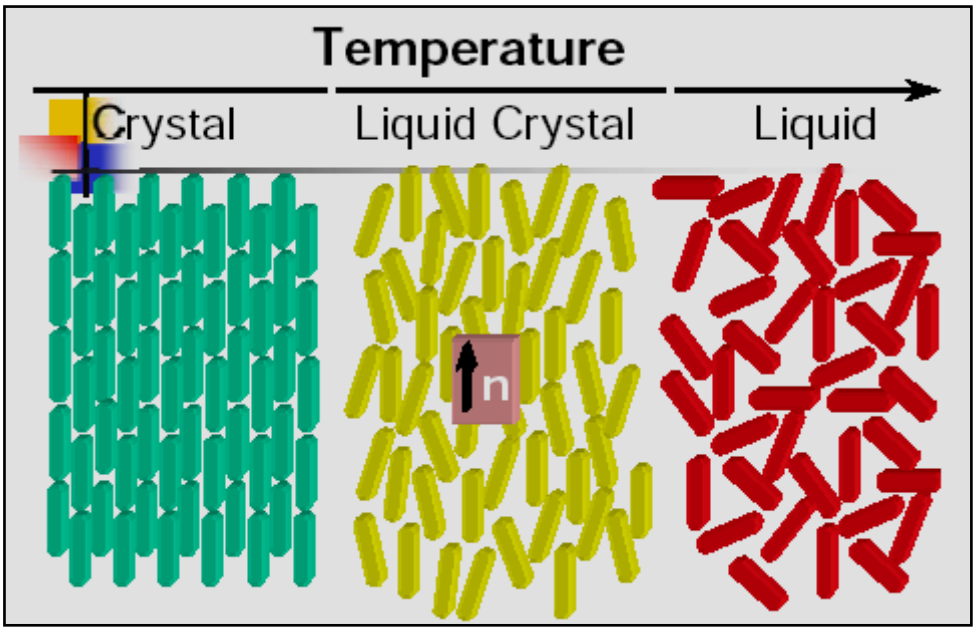


Figure (1-2): The effect of temperature increase on crystals

1-7 A brief History of LCs

The discovery of LCs in 1888 is commonly attributed to the Austrian botanist Friedrich Reinitzer[30], in the heating of cholesteryl benzoate; he observed "double melting" behavior of cholesteryl benzoate. The crystals of this material melted at 145.5 ^{o}C into a cloudy fluid, which upon further heating to 178.5 ^{o}C became clear. This discovery represented the first recorded documentation of the LC phase. Further investigations of this phenomenon were carried out by the German physicist Otto Lehmann[31] who observed and confirmed, using the first polarized optical microscope designed by himself, the existence of “crystals [which] can exist with softness that one could call them nearly liquid”. In 1922 the French scientist Friedel[32] produced the first classification scheme of LCs, dividing them into three different types of ***mesogens*** (materials able to sustain mesophases), based upon the level of order the molecules possessed in the bulk material:

1. ***Nematic(N)*** (from the Greek word *nematos* meaning “thread”), [33]
2. ***Smectic(S)*** (from the Greek word *smectos* meaning “soap”), [33]

and

3. ***Cholesteric(Ch)*** (better defined as *chiral nematic*)[33].

Following these first observations and discoveries, the scientific research turned attention towards a growing number of compounds, which displayed liquid crystalline properties. In order to establish a relationship between the molecular structure and the exhibition of liquid crystalline properties, a series of systematic

modifications of the structures of mesogens was undertaken, leading, in 1973, [34] to the discovery of the most technologically and commercially important class of LCs to date: the 4-alkyl-4'-cyanobiphenyl of which an example, 4-pentyl-4'-cyanobiphenyl [15] is illustrated in Figure (1-3)**.**

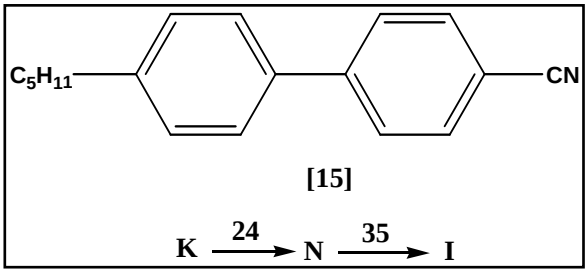


Figure (1-3): Molecular structure of 4-pentyl-4'-cyanobiphenyl [15]. (The transition temperatures are expressed in ^{0}C).

These are the materials, which still constitute the simple common displays found in calculators or mobile phones. However, the numerous and increasingly sophisticated applications, relying upon the use of liquid crystalline materials, require such a complexity of superior properties to achieve improved devices performance, that the quest for ever new LCs has grown enormously over the last three decades. Nowadays, LCs plays a dominant role in a large part of the display technology.

1-8 Types of LCs

Different types of molecules can form liquid crystalline phases. The common structural feature is that these molecules are form anisotropic: one molecular axis is much longer or wider than another one. The two major categories are:

1. ***Lyotropic LCs***, whose mesophase formation is concentration and solvent dependent, this thesis is concerned with thermotropic LCs, however a brief discussion is provided on lyotropic LCs.
2. ***Thermotropic*** *LCs*, whose mesophase formation is temperature (T) dependent.

1-8-1 Lyotropic LCs

Lyotropic LCs is two-component[29] systems where an amphiphile is dissolved in a solvent. Thus, lyotropic mesophases are concentration and solvent dependent. The amphiphilic compounds are characterized by two distinct moieties, a hydrophilic “head” and a hydrophobic “tail”. Examples of these kinds of molecules are soaps Figure (1-4 a) and various phospholipids like those present in cell membranes Figure (1-4 b).

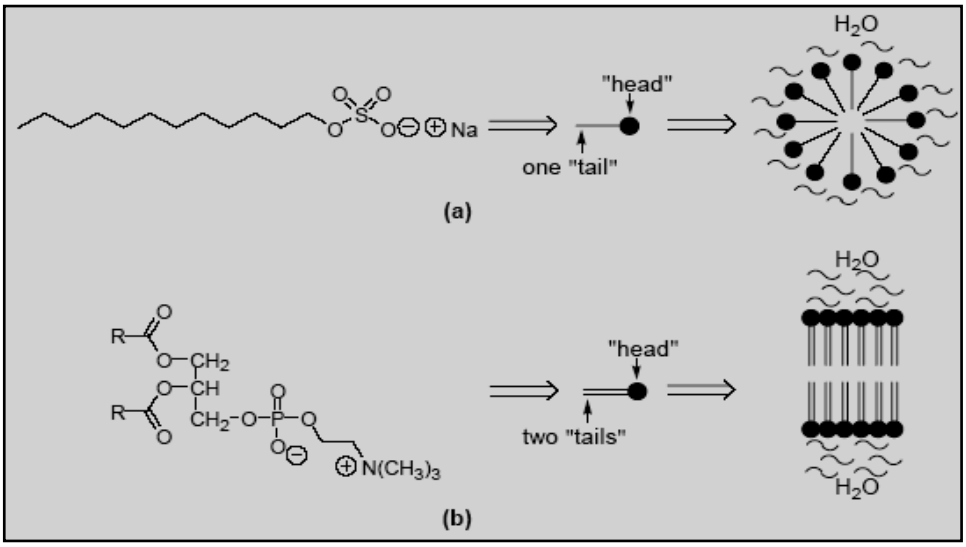


Figure (1-4): Chemical structure and carton representation of (a) Sodium dodecylsulfate (soap) forming micelles, and (b) a phospholipid (lecitine), present in cell membranes, in a bilayer lyotropic LC arrangement.

1-8-2 Thermotropic LCs

The essential requirement for a molecule to be a thermotropic LC is a structure consisting of a central rigid core (often aromatic) and a flexible peripheral moiety (generally aliphatic groups). This structural requirement[29] leads to two general classes of LCs:

1. Calamitic LCs, and

2. Discotic LCs

Both of which have other molecular subclasses.

1-8-2-1 Calamitic LCs

Calamitic[29] or rod-like LCs are those mesomorphic compounds that possess an elongated shape, responsible for the form anisotropy of the molecular structure, as the result of the molecular length (**l**) being significantly greater than the molecular breadth (**b**), as depicted in the cartoon representation in Figure (1-5). Calamitic mesogens usually follow the general structural formula shown in Figure (1-6).

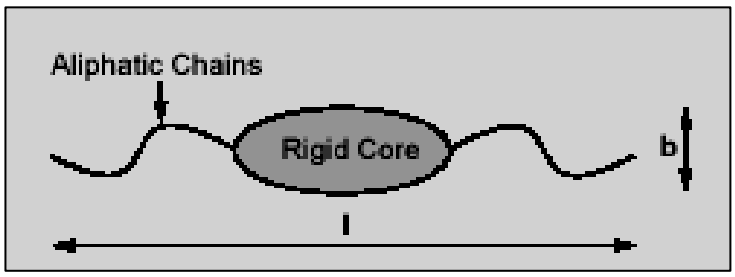


Figure (1-5): Cartoon representation of Calamitic LCs, where l>>b.

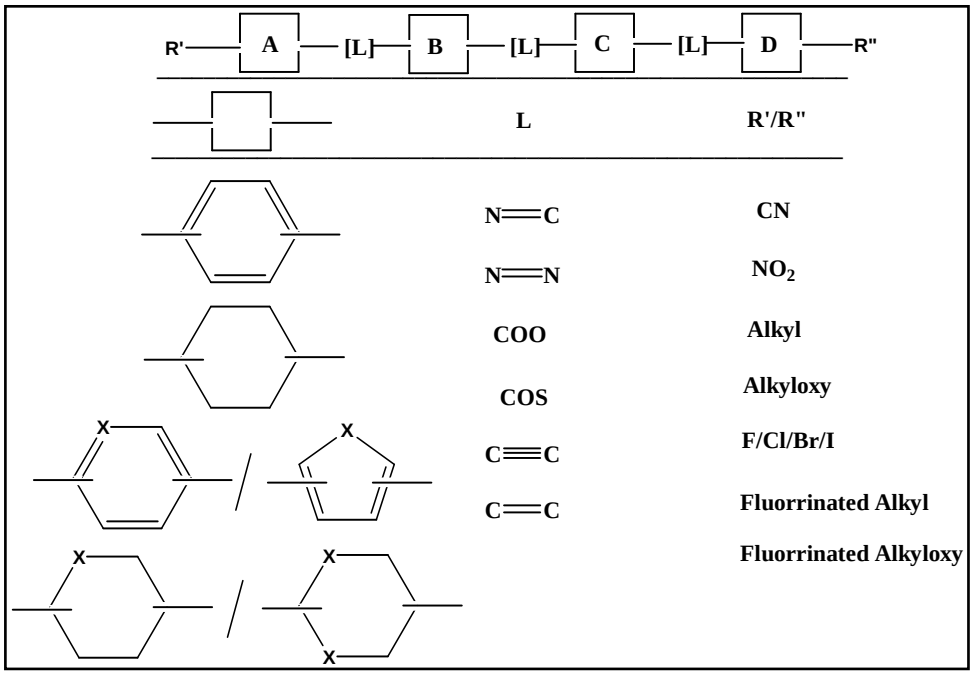


Figure (1-6): General structure of Calamitic LCs.

R’ and R” are often flexible terminal units such that at least one R group is an alkyl chain, (A, B, C, and D) are used to generally describe ring systems (phenyl, cyclohexyl, heteroaromatics, and heterocycles), and [L] represents the linking units, such as (CH=N, COO, or N=N) that can increase the length and flexibility of the molecule, whilst preserving a compatible linear shape suitable for mesophase formation. Calamitic LCs can exhibit two common types of mesophases:

1. Nematic, and
2. Smectic.

1-8-2-1-1 Nematic phases

The least ordered mesophase[33] (the closest to the isotropic liquid state) is the ***nematic*** (N) phase, where the molecules have only an orientational order. The molecular long axis points on average in one favored direction referred to as the director Figure (1-7). The classical example of LC displaying a nematic

mesophase is the [15] Figure (1-3).

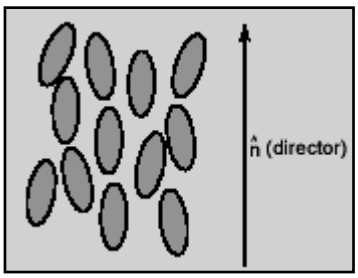


Figure (1-7): Cartoon representations of Nematic phase. The molecules are oriented, on average, in the same direction referred to as the director with no positional ordering with respect to each other.

1-8-2-1-2 Smectic phases

The next level of organization is classified as ***Smectic*** (S), where in addition to the orientational order the molecules possess positional order, such that the molecules organize in layered structures. The S phase has many subclasses[33] (S_A-S_I), which are illustrated in Figure (1-8).

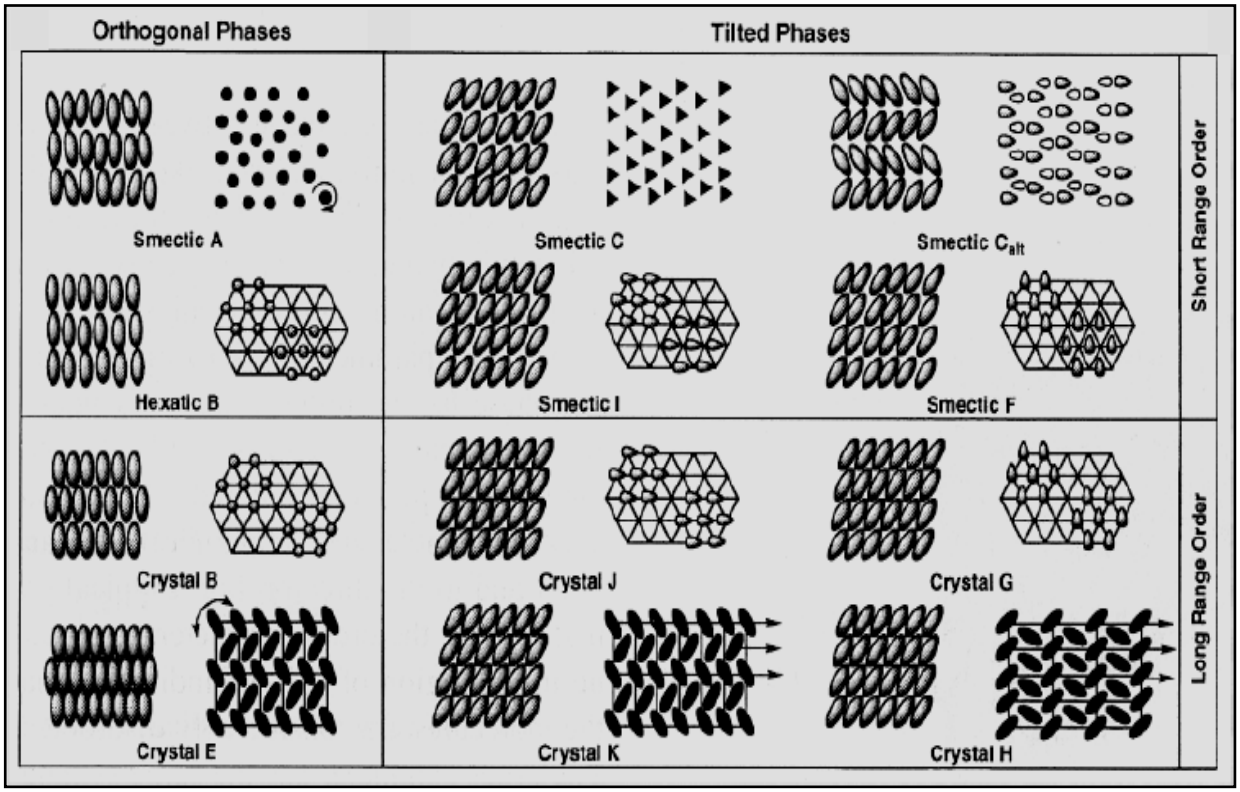


Figure (1-8): Cartoon representation of molecular arrangement in crystals and Smectic LC phases.

The smectic phase characterised by the least order is the orthogonal S_A phase, where the layers are perpendicular to the director Figure (1-9a). Otherwise when the director is tilted at an angle other than 0°, to the normal to the layers (z), the result is the S_C phase Figure (1-9b).

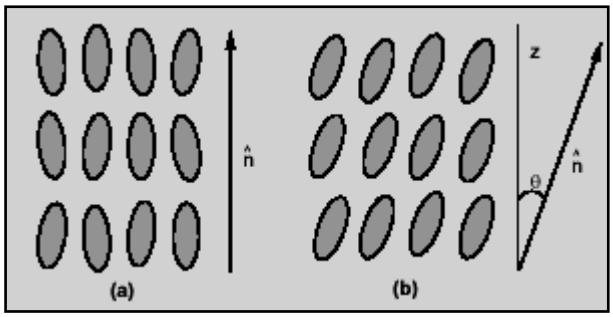
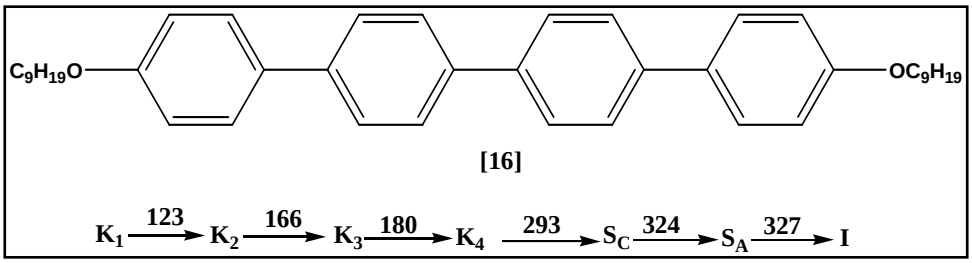


Figure (1-9): Cartoon representation of (a) the S_A phase, and (b) The S_C phase.

An example of a molecular structure displaying a smectic mesophase is given by the quaterphenyl derivative[16][35] illustrated in Figure (1-10), where the presence of such an extended

aromatic core, characterized by a large system, is responsible for the establishment of lateral stacking interactions between adjacent molecules, resulting in a layered organization (S_A and S_C).



Figure(1-10):4,4'''-Bis-nonyloxy-[1,1'',4',1'',4'',1''']quaterphenyl[16] exhibiting S_A and S_C phases. (The transition temperatures are expressed in ^{0}C).

1-8-2-2 Discotic LCs

In 1977, a second type of mesogenic structure, based on discotic (disc shaped) molecular structures was discovered. The first series of discotic compounds to exhibit mesophase belonged to the hexa-substituted benzene Derivatives[17] Figure (1-11) synthesised by Chandrasekhar[36] et. al.

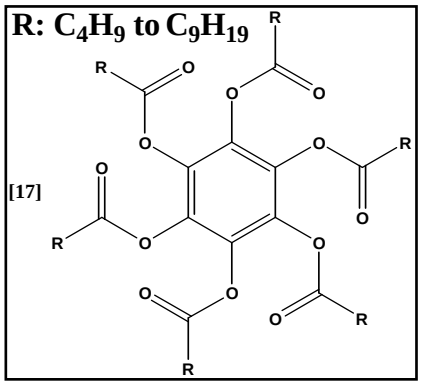


Figure (1-11): Molecular structure of the first series of discotic LCs discovered: The benzene-hexa-n-alkanoate derivatives[17].

Similarly to the Calamitic LCs, discotic[37] LCs possess a general structure comprising a planar (usually aromatic) central rigid core surrounded by a flexible periphery, represented mostly by pendant chains (usually four, six, or eight), as illustrated in the cartoon

representation in Figure (1-12). As can be seen the molecular diameter (**d**) is much greater than the disc thickness (**t**), imparting the form anisotropy to the molecular structure.

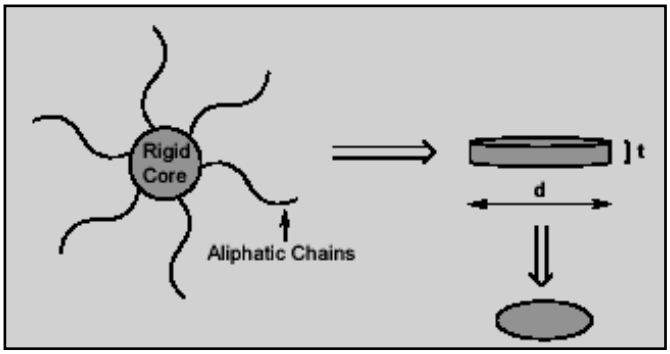


Figure (1-12): Cartoon representation of the general shape of discotic LCs, were d>>t.

Discotic[38] LCs, as well as calamitic LCs, can show several types of mesophases, with varying degree of organization. The two principle mesophases are:

1. Nematic discotic, and
2. Columnar.

1-8-2-2-1 Nematic discotic phases

Nematic[39] discotic (N_D) is the least ordered mesophase, where the molecules have only orientational order being aligned on average with the director as Illustrated in Figure (1-13). There is no positional order.

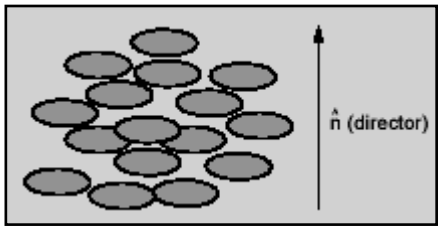


Figure (1- 13): Cartoon representation of the N_D phase, where the molecules are aligned in the same orientation, with no additional positional ordering.

1-8-2-2-2 Columnar phases

Columnar[40] (Col) phases are more ordered. Here the disc-shaped cores have a tendency to stack one on the top of another, forming columns. Arrangement of these columns into different lattice patterns gives rise to a number of columnar mesophases, namely columnar rectangular (Colr) and columnar hexagonal (Colh) in the fashion described in Figure (1-14).

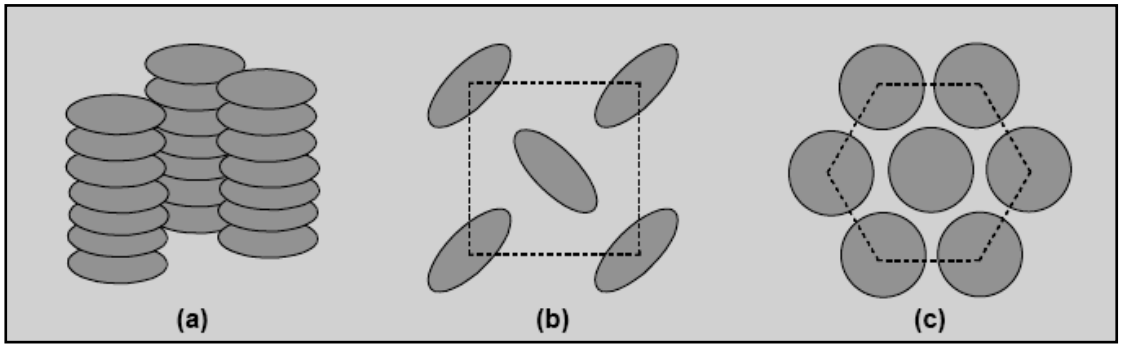
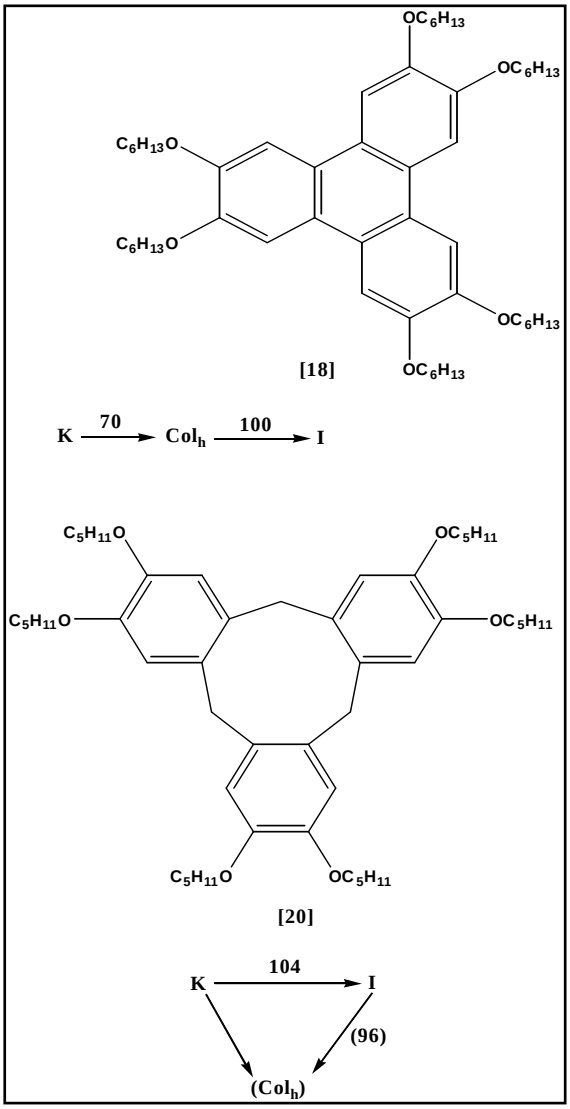


Figure (1-14): Cartoon representation of (a) the general structure of Col phases, where the molecules are aligned in the same orientation and, in addition, form columns, (b) representation of (Col_r), and (c) representation of (Col_h).

In the years following the discovery of the first discotic mesogens, further investigations[41] lead to the synthesis of a vast number of new discotic LCs[42-43] (18 to 21) Figure (1-15).



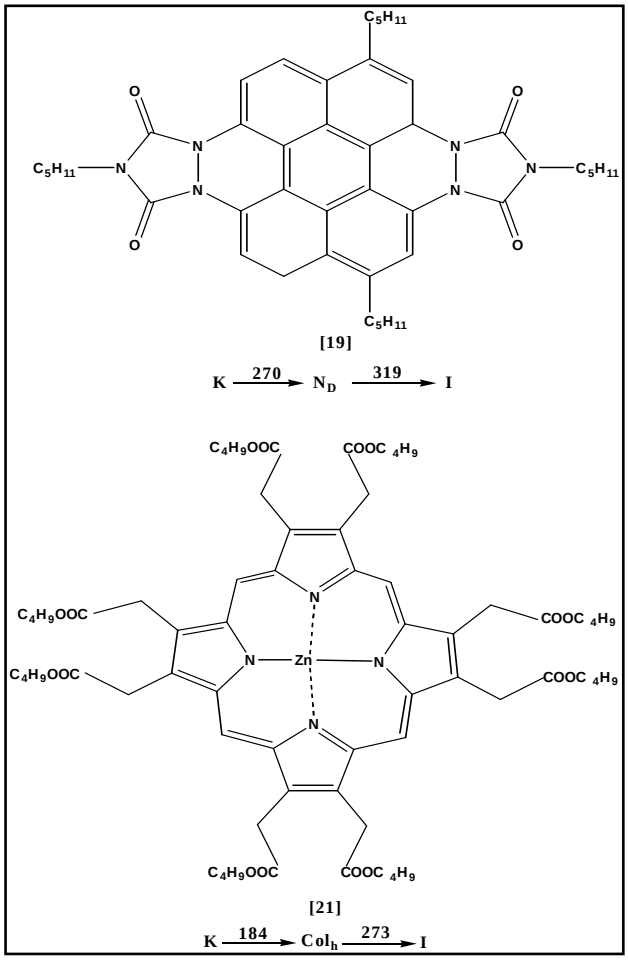


Figure (1-15): Molecular structure of some discotic mesogens: 2,3,6,7,10,11-hexabishexyloxytriphenylene[18],3,10-dipentylperylene discogen derivative [19] ,2,3,7,8,12,13-hexabispentyloxy-10,15-dihydro-5H-tribenzo [a,d,g] cyclononene (bowl-shaped discotic) [20], porphyrin metallomesogen [21] . (The transition temperatures are expressed in ºC, and the mesophase in brackets represents a monotropic transition).

1-9 Polycatenar LCs

Polycatenar mesogens[44] represent a hybrid class of thermotropic LCs, which can be described with intermediate molecular features between classical rod-like and disc-like mesogens. Schematically the central core of polycatenar LCs comprises a calamitic region, with half-discs on the extremities Figure (1-16). This hybrid molecular structure allows both calamitic and columnar phases to be generated, depending on the specific molecular structure of the components.

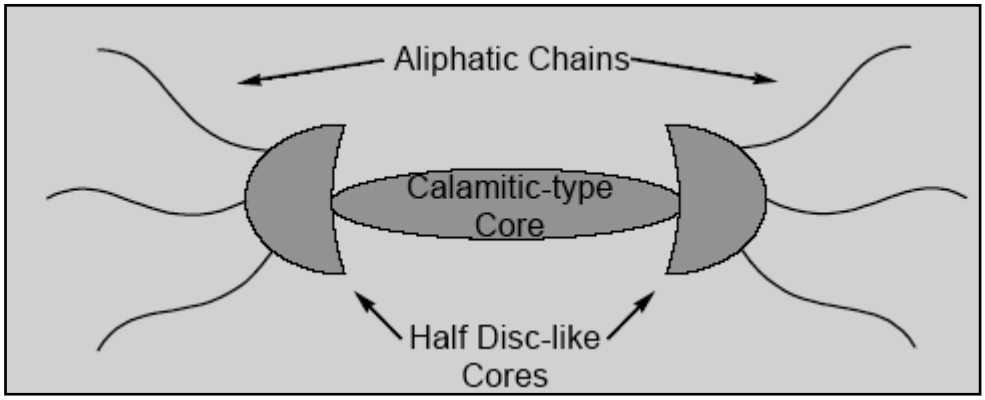


Figure (1-16): Cartoon representation of the architectural molecular structure of polycatenar LCs.

Polycatenar molecules possess a number of flexible alkyl chain substituents, which varies from two to six (bi- to hexa-catenar compounds). Bi-catenar LCs is in most of the cases classical rod-like molecules, like compound [22], 4-pentyl-4'-pentyl biphenyl Figure (1-17). Examples of bi-[45], tri-[45], tetra-[46] and hexa-catenar[47] LCs ([22] to[27]) are shown in Figures (1-17) to (1-20).

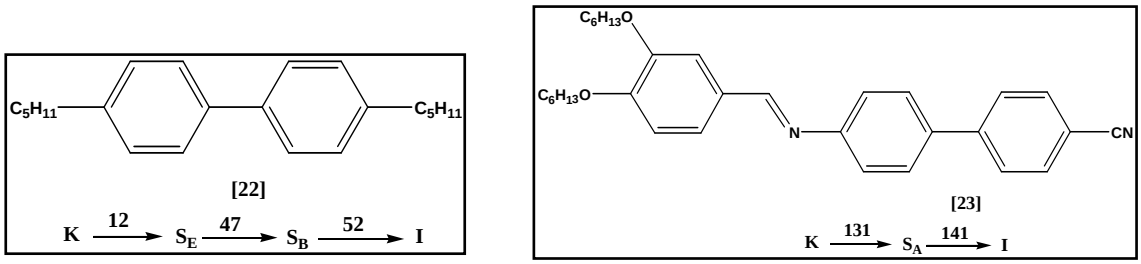


Figure (1-17): Molecular structure of two bi-catenar mesogens 4-pentyl-4'-pentyl biphenyl [22] and 4'-[(3",4"-bis-hexyloxy-benzylidene)-amino]-4- nitrile biphenyl [23].

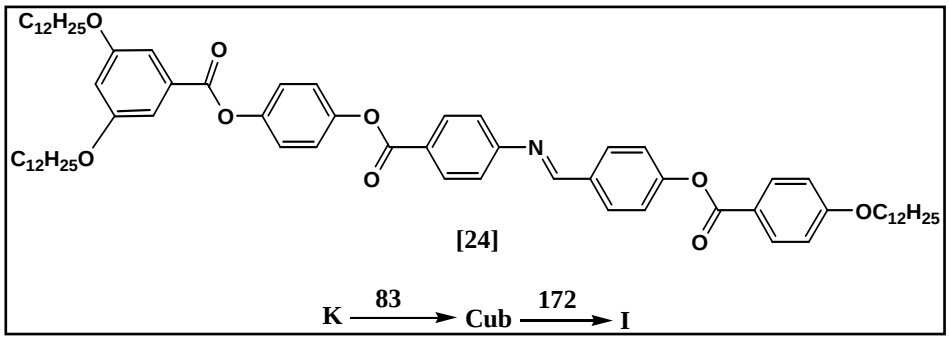


Figure (1-18): Molecular structure of a tri-catenar mesogen [24].

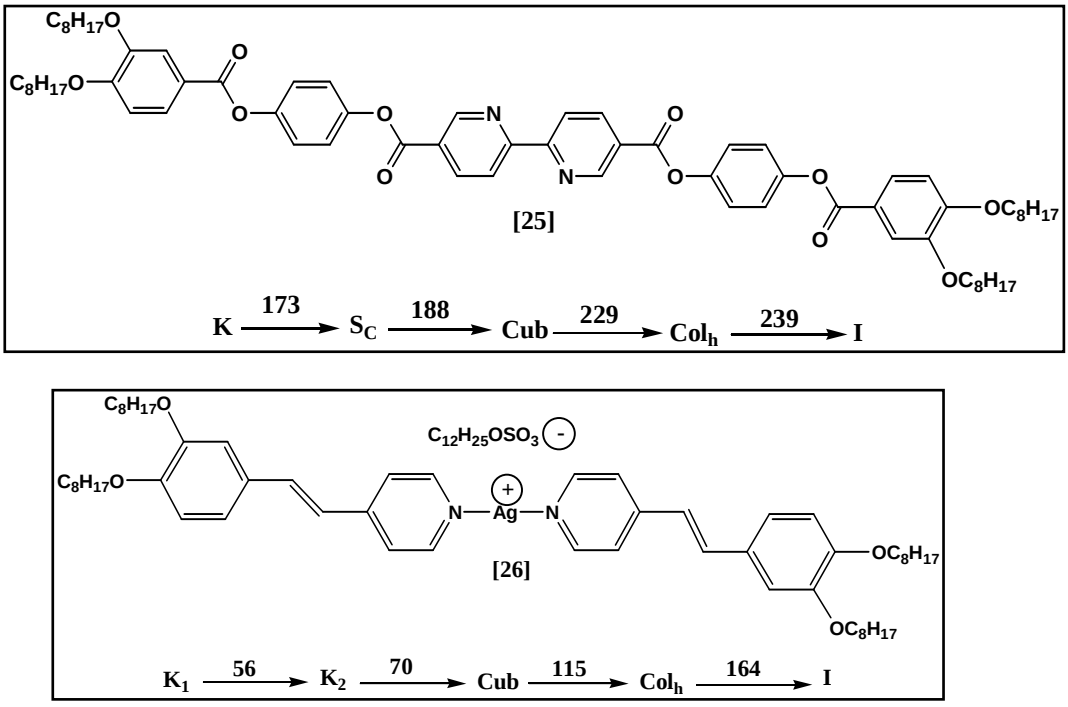


Figure (1-19): Molecular structure of tetra-catenar mesogens 2,2'-bipyridine derivative [25] and liquid crystalline 3,4-dioctyloxystilbazole silver complex [26].

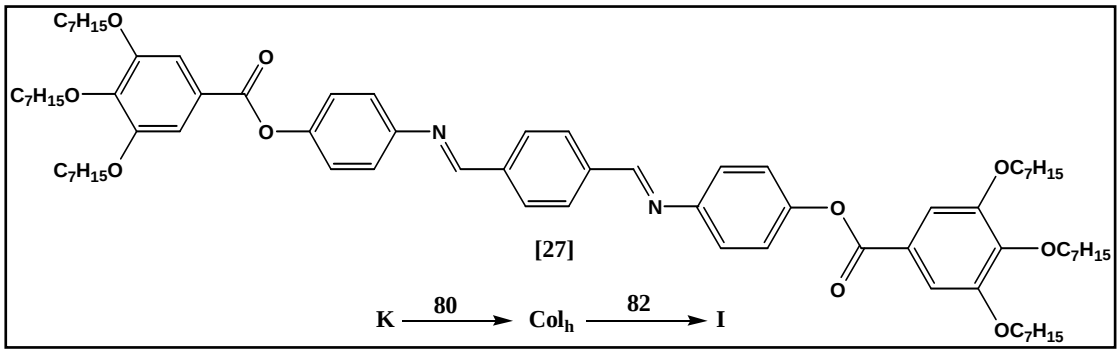


Figure (1-20): Molecular structure of a hexa-catenar mesogen [27].

Compound [23] and [24] show close similarity to the class of LCs named swallow-tailed LCs and compounds [25] and [26] show similarity to the bi-swallow-tailed LCs[48].

1-10 Applications of liquid crystals

Liquid crystals have a large number of applications due to their electro-optical, magneto-optical, electro-chromic and thermo-chromic properties, which are important in industrial and medical applications. These application include

1. Display-device technology.
2. Medical applications.
3. Gas-liquid chromatography.
4. Cosmetics applications.

The major use of liquid crystal displays[49] is currently in watches and small portable calculators …. etc. Liquid crystal displays have visibility in high ambient light, easily changed pattering and size, variation in color, operation in Transmissive or reflective mode and more.

Liquid crystals have gained a great interest as stationary phase in gas liquid chromatography (G.L.C.) [50]. They are used in the separation of close boiling compounds on the bases of their

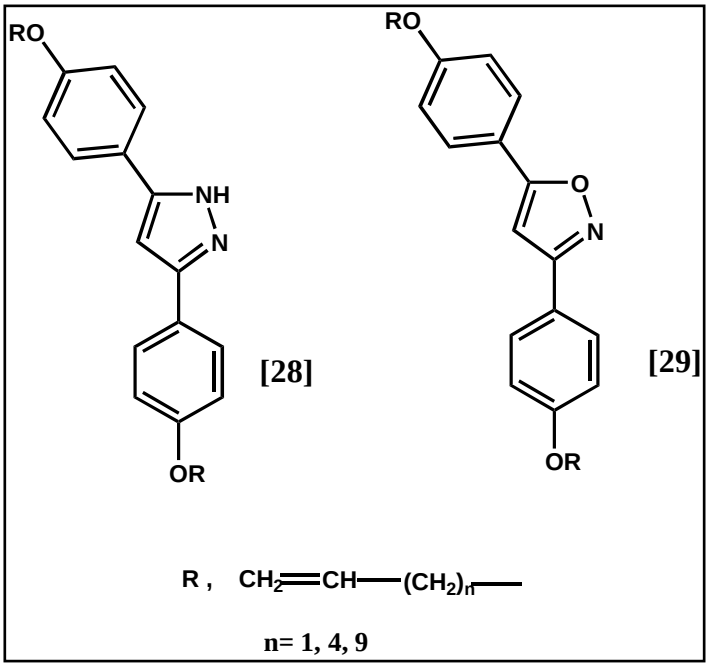
molecular shape. One of the most interesting separations that have been achieved on liquid crystals is in separation of optical[50] isomers. Certain liquid crystal stationary phases are suitable for programmed-temperatures gas chromatography and for work at temperature of about 300^{o}C.

The medical applications[51] of liquid crystals such as cholesteric nematic type, include disposable oral thermometry, neurology, encology, pediatrics surgery, and podiatry. To be more specific these medical applications include detection of breast cancer, location of the placenta, blood flow patterns in extremities of the human anatomy and observation of skin temperature change following blockage of the sympathetic nervous system. Liquid crystals used in many skin care products. The first and probably most successful product is Eyzon[51], which incorporates very attractive coils of iridescent liquid crystal in a clear gel. It is probable that vitamin A palmitate is mixed with the liquid crystal.

1-11 Literature Survey of Liquid Crystalline Materials Containing Heterocyclic Units

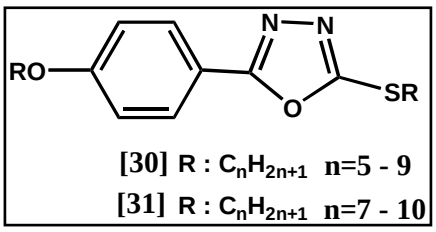
During the last century, tens of thousand of liquid crystalline materials have been prepared giving wide applications in many fields. Yet ambition enormously grows for preparing a new liquid crystal with different heterocyclic unit having higher quality and more wide applications.

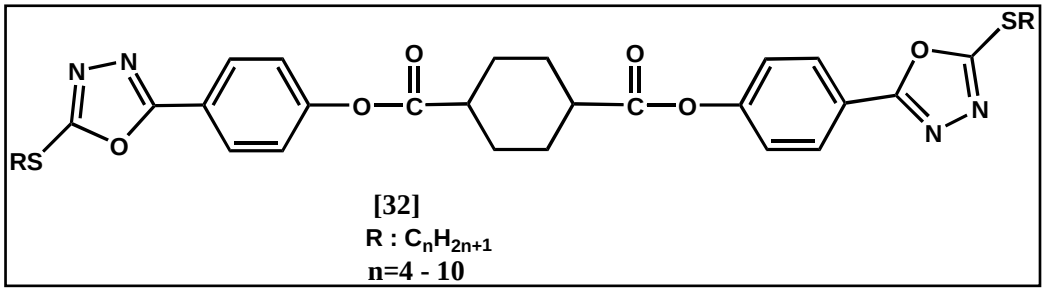
In 1992, ***Seguel***[52] et. al., synthesized new mesogenic alkyloxy pyrazole [28] and isoxazole [29] derivatives.



Series [28] shows smectic (S_A) mesophase for (n=4), and smectic (A, C, X)for(n=9) where (S_X) is undetermined smectic phase. While series [29] shows nematic mesophae for (n=1), nematic and smectic (S_A) for (n=4), and smectic (S_A) for (n=9).

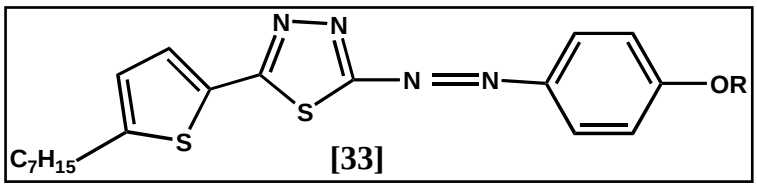
In 1995, ***parra***[53] et.al, synthesized and investigated the mesomorphic behaviour of the following types of new 1,3,4-oxadiazole derivatives ([30],[31], and [32]).



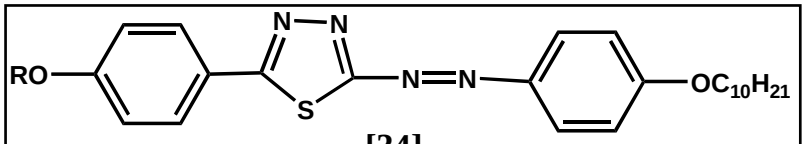


Oxadiazole derivatives [31] show a monotropic liquid crystalline behavior with nematic and smectic monotropic mesophases. The 1,3,4-oxadiazole derivatives [32] exhibit nematic and smectic (S_C) liquid crystalline properties. While the 2-alkyl-1,3,4-oxadiazole derivatives [30] do not show liquid crystalline properties.

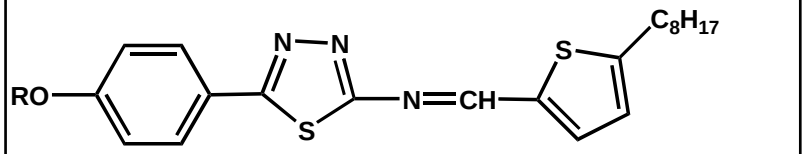
In 1997, ***Parra***[54] et.al., reported the synthesis and mesomorphic behavior of two homologous series of new azo compounds containing thiophene and 1,3,4-thiadiazole rings ([33] and [34] respectivily). All compounds of series [33] exhibit enantiotropic nematic mesophase and the higher homologues (n= 9-10) also show monotropic smectic (S_C) phase. Series [34] show dimorphism (S_C) and (N) (for n=5-7 the S_C is monotropic). These series is compared with the Schiff-bases analogues ([35] and [36]), the imine bond gives raise to similar liquid crystals phase but larger mesomorphic range.



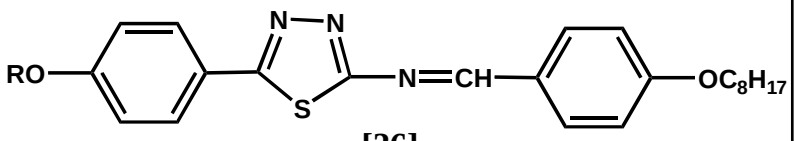
[33]



[34]



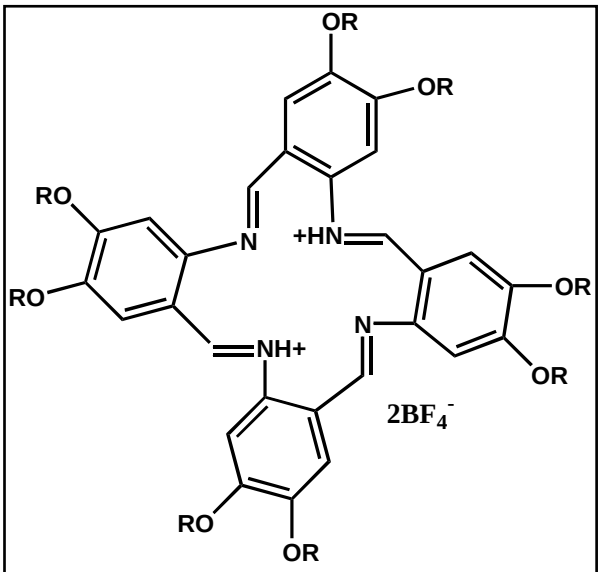
[35]



[36]

R : C_nH_{2n+1} **n 5-10**

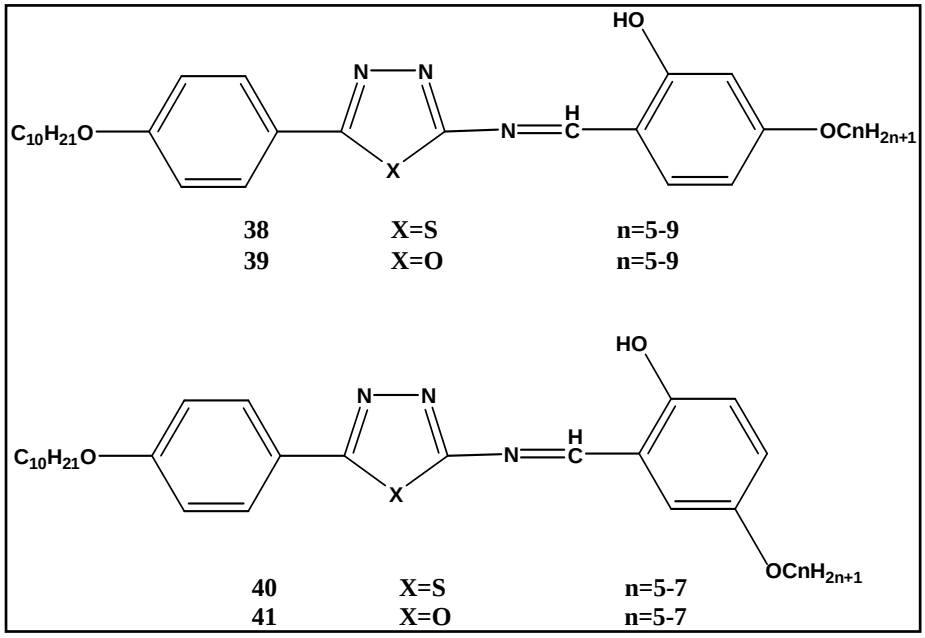
In 1998, ***Kang*** [55] et.al., reported that the self-condensation of 3,4-dialkoxy-2-aminobenzaldehyde (alkoxy=n-$C_8H_{17}O$, n-$C_{10}H_{21}O$ and n-$C_{12}H_{25}O$) [37] in the presence of HBF_4 gives the tetrafluoroborate salt of diprotonated octaalkoxy-TAAB which exhibits a hexagonal columnar mesophase (discotic mesogen) over a wide range of temperature.



[37]

R : C_8H_{17},$C_{10}H_{21}$,$C_{12}H_{25}$

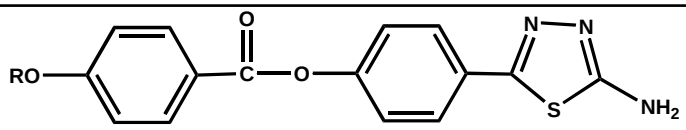
In 2000, ***Parra***[56] et.al., synthesized novel Schiff-base incorporating the five membered 1,3,4-thiadiazole (series [38],[39]) and 1,3,4-oxadiazole (series [40],[41]) rings. All compounds of series [38] exhibit an enantiotropic smectic (S_C) phase. No liquid crystalline properties were observed for the compounds of series ([39], [40], and [41]).



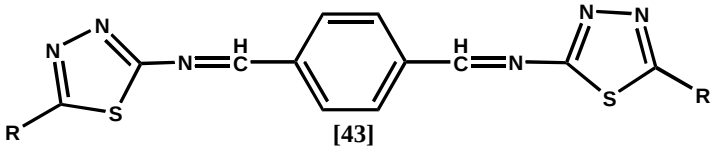
38 **X=S** **n=5-9**
39 **X=O** **n=5-9**

40 **X=S** **n=5-7**
41 **X=O** **n=5-7**

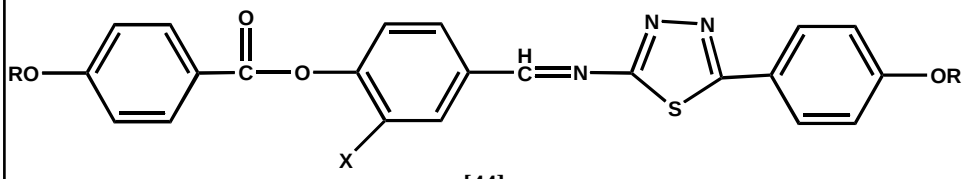
Atto[57] et.al., synthesized 1,3,4-thiadiazole derivatives having the structural formula ([42], [43], [44], and [45]). All these series showed nematic phase except series [45], which did not form liquid crystals.



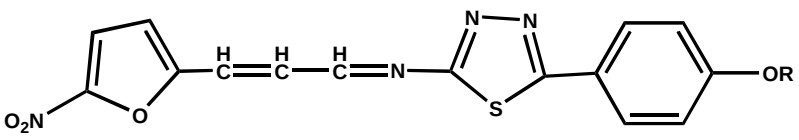
[42]
R : methyl, propyl



[43]
R : methyl-hexyl

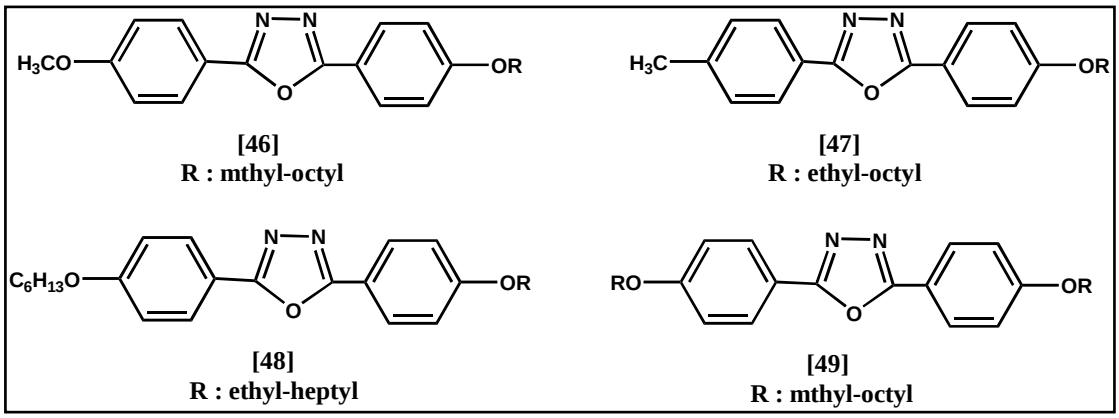


[44]
R : methyl- hexyl
X=H,OCH_3,CH_3



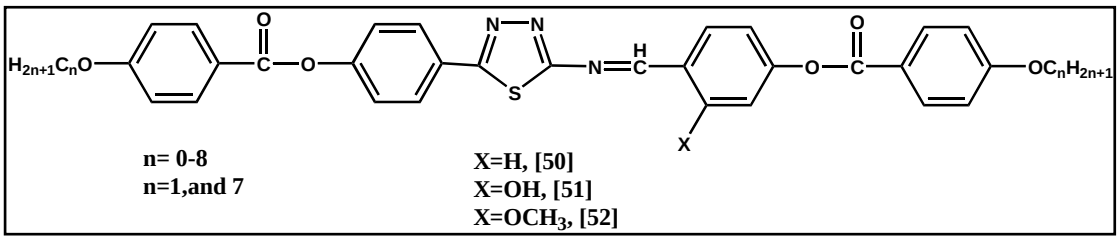
[45]
R : methyl- hexyl

Al-Dujaili[58] et.al., synthesized new homologous series of 2,5-disubstituted-1,3,4-oxadiazole and 3,5-disubstituted-4-amino-4H-1,2,4-triazole derivatives ([46] to [49]) having the following structural formula:

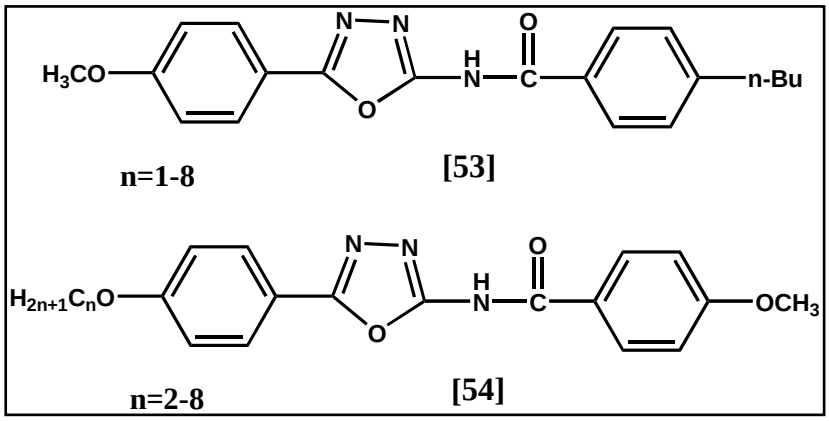


It was shown that except for the compound having (R=ethyl) group in series [46] and the four last compounds in the series [47] giving nematic and smectic mesomorphic properties, all the other compounds in the series ([46], [47], [48] and [49]) showed no liquid crystalline behavior.

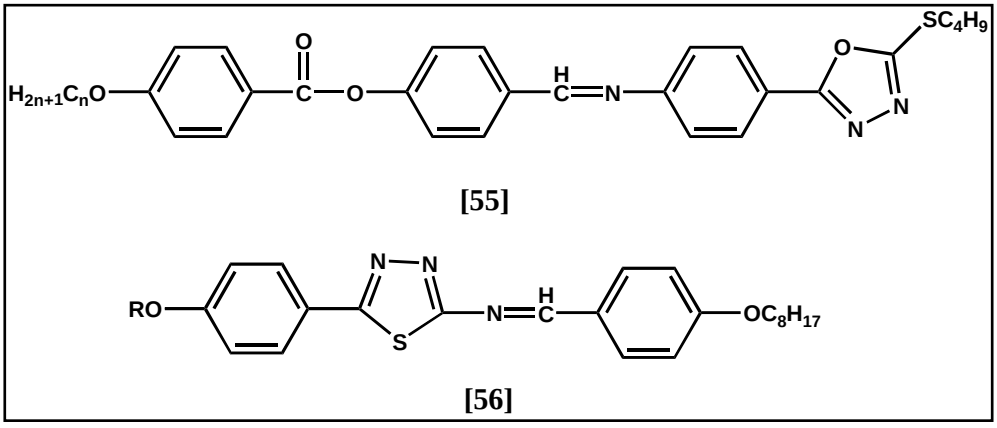
Al-Zubadi[59] synthesized three homologues series containing 1,3,4-thiadizole heterocyclic ring. These compounds contain ester and azomethine linkage, these series ([50], [51], and [52]) having the below structural formula, all exhibit nematic phase with the exception of the first homologue of both series ([50], and [51]).



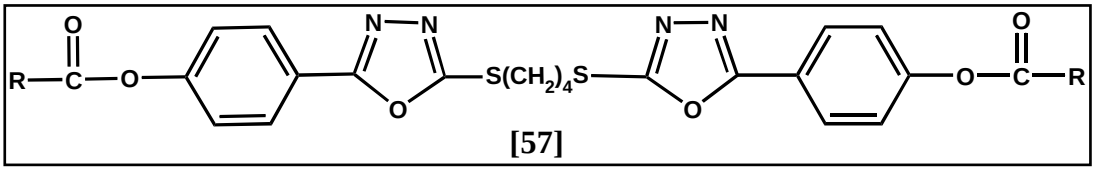
Al-Dujaili[60] et.al., studied the liquid crystalline properties of some amide compounds containing 1,3,4-oxadizole units ([53] and [54]) using differential scanning calorimetry (DSC) and hot stage polarizing microscopy. It was found that the tautomeric isomerization plays the important rule in the occurrence of the mesomorphic phases.



Mesomorphic behavior of some Schiff-base esters containing 1,3,4-oxadiazole [55] and thiadiazole [56] units was studied by ***Al-Dujaili***[61,62]and ***Tomma***. All compounds except compound (n=7) showed mesomorphic properties. Compounds with (n=1) show enantiotropic nematic phase, (n=2-3) show enantiotropic smectic (S_C), while compounds (n=4-6) show polymesomorphic nematic and smectic phases. The higher homologue compounds (n=8, 9, 12) show purely smectic (S_C) phase.



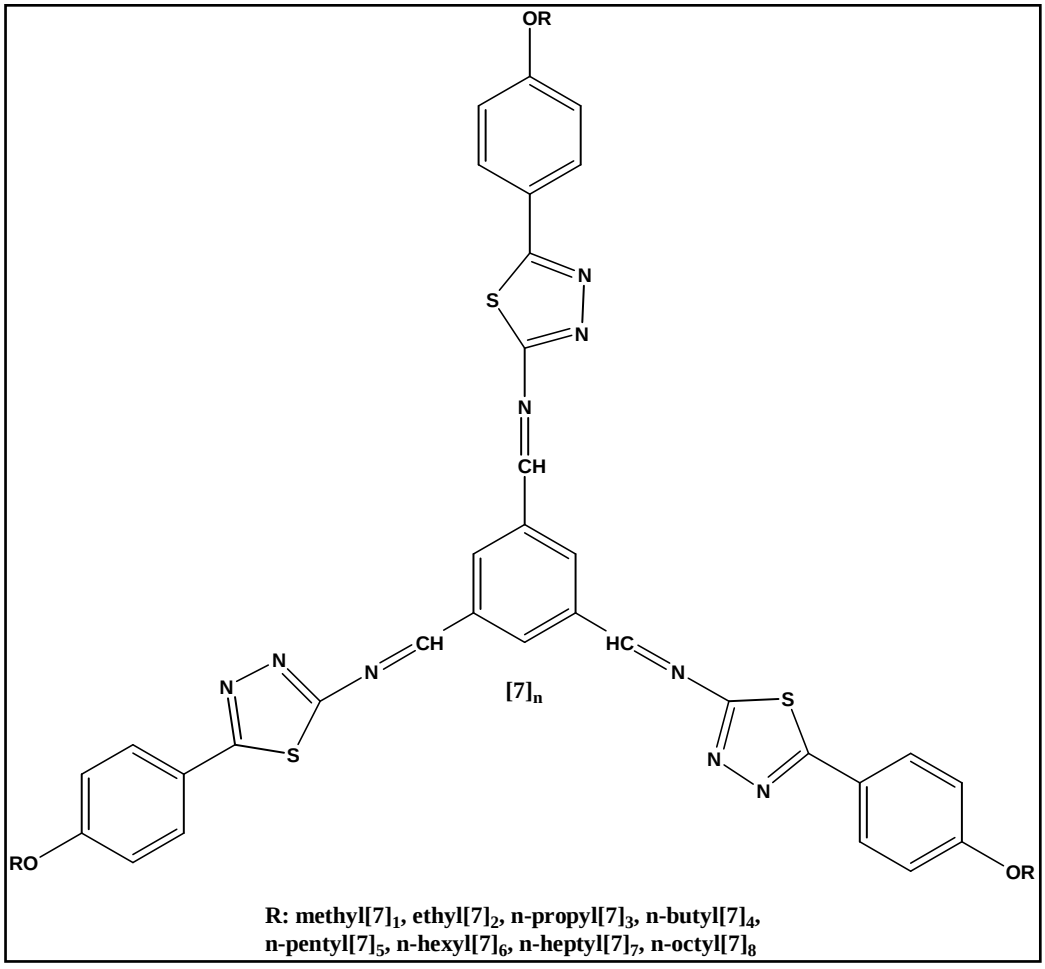
Al-Dujaili[63] et.al., synthesized a homologous series of 1,4-bis-[5-(4-n-alkoxybenzoyloxy)phenyl-1,3,4-oxadiazole-2-yl]butylenes disulphide [57]. All the homologous compounds showed enantiotropic nematic phase by examination with differential scanning calorimetry (DSC) and hot stage polarizing microscopy.



[57]

1-12 The Aim of the work

Substituted 1,3,4-thiadiazoles have attracted considerable attention in organic synthesis due to their broad range of biological, medicinal, and industrial, agricultural applications. In addition, recently many series containing 1,3,4-thiadiazole moieties showed unique liquid crystalline properties. Despite the Intensive research on substituted mono-, bis-1,3,4-thiadiazole little is known about tris-1,3,4-thiadiazole derivatives, and to our knowledge no attempt has been made to study the liquid crystalline properties of tris-1,3,4-thiadiazole derivatives. Thus, the object of this work is the study of the liquid crystalline behaviour of new series $[7]_n$ containing tris-1,3,4-thiadiazoles having the following structural formula:



[7]$_n$

R: methyl[7]$_1$, ethyl[7]$_2$, n-propyl[7]$_3$, n-butyl[7]$_4$, n-pentyl[7]$_5$, n-hexyl[7]$_6$, n-heptyl[7]$_7$, n-octyl[7]$_8$

Our object was also extended to evaluate the biological activity of the above series.

CHAPTER TWO
EXPERIMENTAL PART

2-1 Chemicals

The chemicals used and the manufacturers are listed in Table (2-1). Some of which were used directly while others were purified to obtain the highest purity.

Table (2-1): Chemicals and their manufacturers.

Compounds	Supplied from
Bromine	Chem-Supply
Bromobutane	Hopkin and Williams
Chlorofotrm	Hopkin and Williams
Dimethyl sulphoxide(DMSO)	BDH
Ethanol (96%)	BDH
Ethanol(absolute)	BDH
Heptan-1-ol	Hopkin and Williams
Hexane	Hopkin and Williams
Hexan-1-ol	BDH
Hydrobromic acid	BDH
Hydrochloric acid	BDH
4-Hydroxybenzoic acid	BDH
Iodoethane	Hopkin and Williams
Iodomethane	Hopkin and Williams
Iodopropane	Hopkin and Williams
Mesitylene	Riedel and Hean
Methanol	BDH
Morpholine	BDH
Pentan-1-ol	Hopkin and Williams
Phosphorus oxychloride	Fluka
Potassium hydroxide	BDH
Sulphuric acid	BDH
Thiosemicarbazide	Fluka

2-2 Techniques

2-2-1 Melting point

Melting points were recorded on hot stage Gallen Kamp melting point apparatus and were uncorrected.

2-2-2 Infra-Red Spectrophotometer (IR)

Infrared spectra were recorded on a Perkin Elmer 1310 infrared spectrophotometer and F.T.IR-8300 Fourier Transform Infrared Spectrophotometer Shimadzu using potassium bromide disc.

2-2-3 Ultra-violet-visible Spectrophotometer (UV)

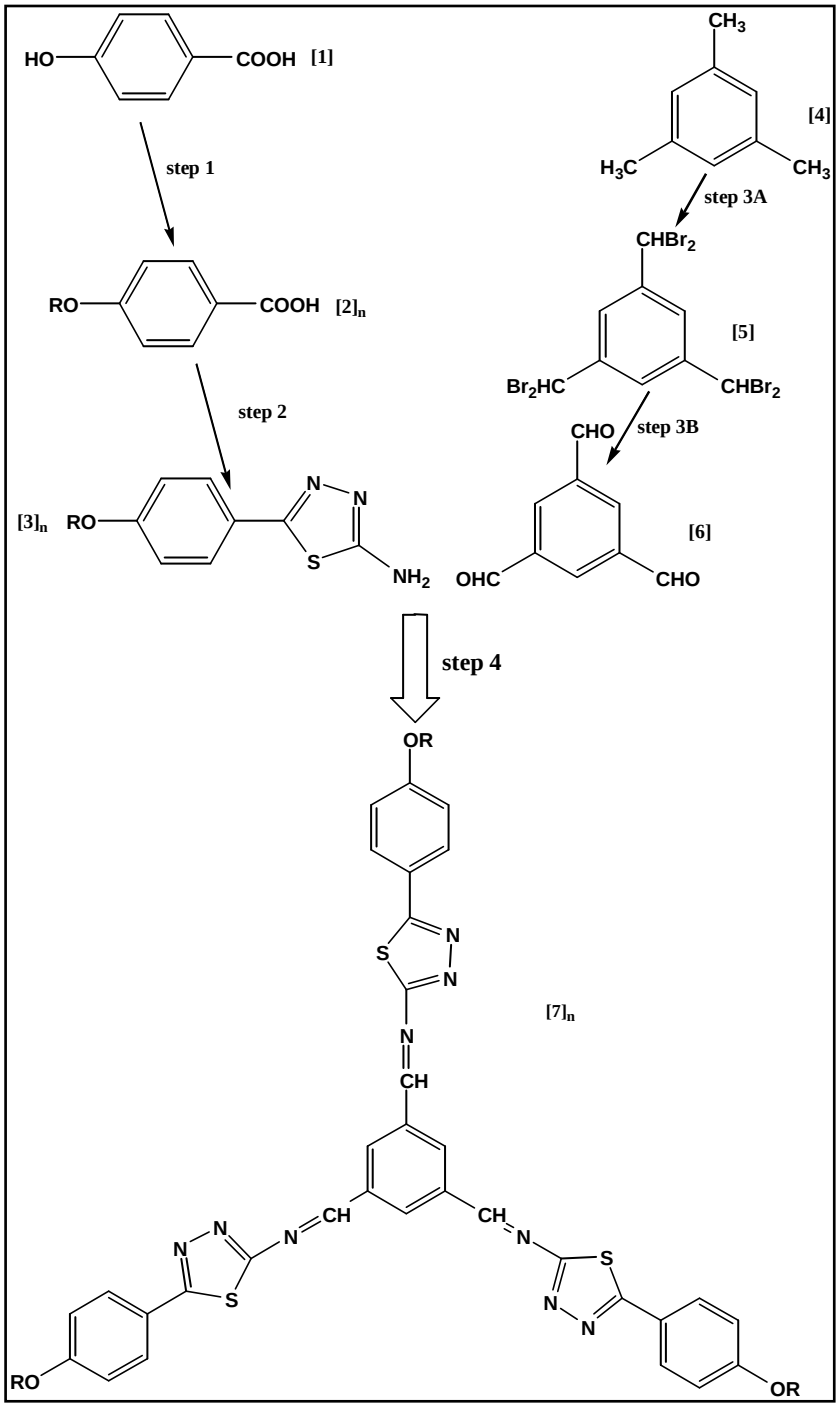
UV-Vis. Absorbance measurements were recorded on a cintra 5 UV-Visible Spectrophotometer

2-2-4 Hot-Stage Polarizing Microscopy

Texture observations were made using Leitz Laborlux microscope type 12 pol equipped with photomicrographic system type vario. Orthmate 2, Hot-Stage type Leitz-350 manufactured by Leitz, Switzerland.

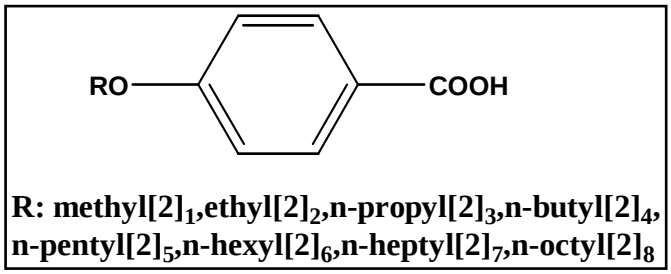
2-3 Procedures of the step-wise synthesis

The steps of the synthesis of homologous series ***1,3,5-tri-[5-4'-n-alkoxyphenyl-1,3,4-thiadiazol-2-yl-]-trimesilydine [7]$_n$***. are shown in the sequence of reactions depicted in scheme (2-1).



Scheme (2-1): Reagents and Conditions (step 1) MeOH, KOH, appropriate RX, reflux overnight ;(step 2) $POCl_3$, thiosemicarbazide,reflux(5hrs.);(step 3A) Br_2 , UV light, reflux (9hrs.); (step 3B)Morpholine, reflux (4hrs.) at (40 ^{0}C); (step 4) 1,3,5-triformylbenzene, EtOH absolute, reflux (24hrs.).

2-3-1 Preparation of 4-n-alkoxybenzoic acid [2]$_n$



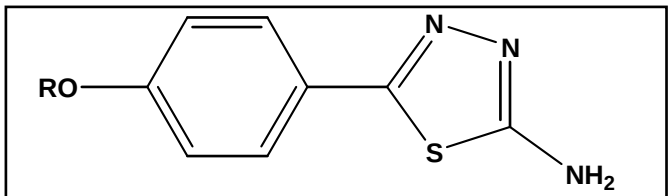
R: methyl[2]$_1$,ethyl[2]$_2$,n-propyl[2]$_3$,n-butyl[2]$_4$, n-pentyl[2]$_5$,n-hexyl[2]$_6$,n-heptyl[2]$_7$,n-octyl[2]$_8$

4-Hydroxybenzoic acid (11.25 g, 0.08 mol) was dissolved in (75mL) of methanol at (25^{o}C) with stirring, after the acid was dissolved, (13.12 g, 0.2 mol) of potassium hydroxide in (10mL) of distilled water was added dropwise, the reaction mixture was heated to reflux and (0.1mol) of n-alkylhalide was then added over (2hrs.).The reaction mixture was refluxed over night, and then (50mL) of methanol was removed by evaporation. The remained of reaction mixture was cooled at (25^{o}C) and then added to (250ml) of distilled water. Hexane (25mL) was added to extract organic impurities. After discarding organic phase, the aqueous phase was heated to (40^{o}C) and neutralized with (20%) HCl. The product precipitated during the neutralization was collected by filtration and purified by recrystallization from ethanol. The physical properties of the prepared compounds [2]$_n$ are listed in Table (2-2).

Table (2-2): The melting points of 4-n-alkoxybenzoic acid $[2]_n$.

Compound no.	R	Yield (%)	M.P.(°C)
$[2]_1$	methyl	70	184
$[2]_2$	ethyl	75	196
$[2]_3$	n-propyl	68	145
$[2]_4$	n-butyl	75	147
$[2]_5$	n-pentyl	70	124
$[2]_6$	n-hexyl	55	105
$[2]_7$	n-heptyl	60	92
$[2]_8$	n-octyl	50	101

2-3-2 Synthesis of 2-amino-5-(4-n-alkoxyphenyl)-1,3,4-thiadizole $[3]_n$



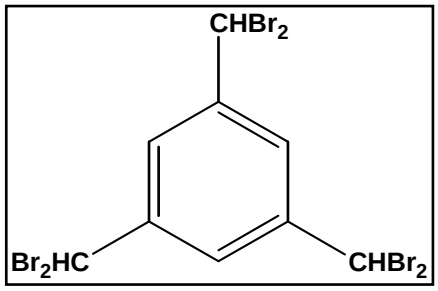
R: methyl$[3]_1$,ethyl$[3]_2$,n-propyl$[3]_3$,n-butyl$[3]_4$, n-pentyl$[3]_5$,n-hexyl$[3]_6$,n-heptyl$[3]_7$,n-octyl$[3]_8$

A mixture of appropriate 4-n-alkoxybenzoic acid (0.01mol) and (0.91g ,0.01 mol) of thiosemicarbazide with (5mL) of phosphorus oxychloride was refluxed gently for (5 hrs.). After cooling (50mL) of water was added, the mixture was then refluxed for (7hrs.) and filtrated, neutralized with potassium hydroxide. The Precipitate was washed with water and recrystallized from (ethanol-water) to give the titled compounds $[3]_n$. The physical properties of the synthesized 1,3,4-thiadiazole derivatives are listed in Table (2-3).

Table (2-3): The melting points of 2-amino-5-(*4*-n-alkoxyphenyl)-1,3,4-thiadizole $[3]_n$.

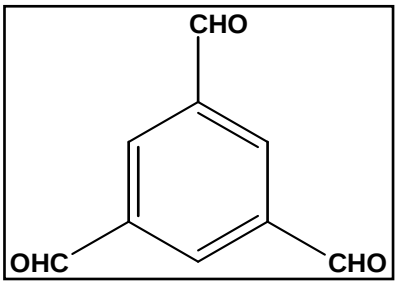
Compound no.	R	Yield (%)	M.P.(C^0)
$[3]_1$	methyl	65	188
$[3]_2$	ethyl	64	190
$[3]_3$	n-propyl	60	195
$[3]_4$	n-butyl	65	200
$[3]_5$	n-pentyl	63	197
$[3]_6$	n-hexyl	66	180
$[3]_7$	n-heptyl	50	170
$[3]_8$	n-octyl	45	165

2-3-3 Preparation of α,α,α′,α′,α″,α″-hexabromomesitylene [5]



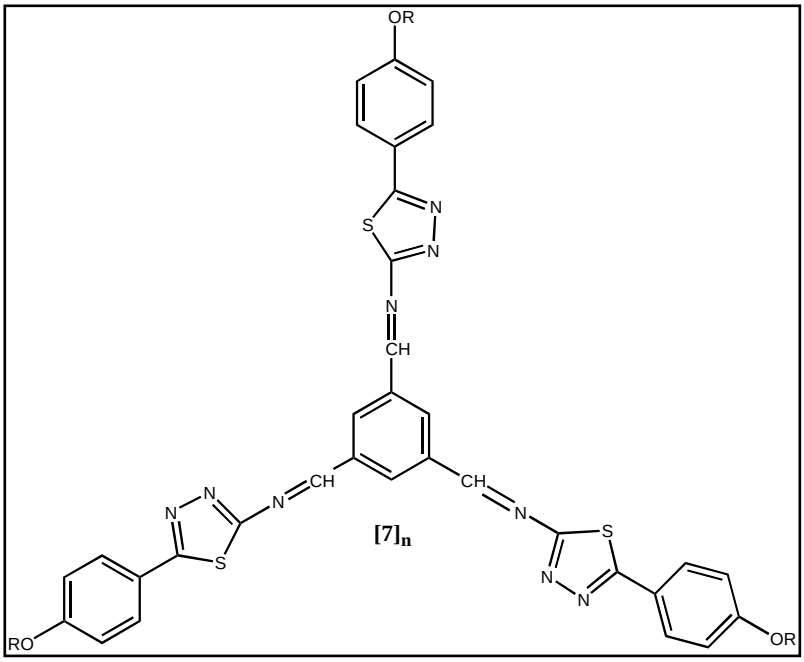
To a (100mL) round bottom flask containing (23mL) of mesitylene, (15mL) of bromine was added within (2hrs.) at (155^{o}C), another (15mL) of bromine was added also within (6hrs.) at (170-180)^{o}C. The addition of bromine was administrated under UV light. The mixture was then refluxed for another (1hr.) at (170^{o}C). After cooling to room temperature the mixture was filtrated to give (80%) of the titled compound[68] [5]. m.p. = 183^{o}C.

2-3-4 Preparation of 1,3,5-triformylbenzene [6]



A (2.97g) of α,α,α',α',α'',α''-hexabromomesitylene was dissolved in (22 mL) of anhydrous morpholine. The solution was then refluxed for (4 hrs.) by using water bath, after that the solution was poured into a (30g) of concentrated hydrochloric acid (d= 1.19 g/mL) with ice, the solution was then filtered, and the precipitate was then dissolved again in (200mL) boiled water. The solution was neutralized by Potassium hydroxide, (60% from the titled compound[68] [6] was formed by cooling to room temperature). M.p. = 154^{o}C.

2-3-5 Synthesis of 1,3,5-tri-[5(4'-n-alkoxyphenyl)-1,3,4-thiadiazol-2-yl]-trimesilydene $[7]_n$



$[7]_n$

A mixture of appropriate 2-amino-5-(4-n-alkoxyphenyl)-1,3,4-thiadizole $[3]_n$ (0.03 mol) and of 1,3,5-triformylbenzene (0.01 mol) [6] dissolved in (35 mL) of absolute ethanol. The mixture was then refluxed for (24 hrs.) with stirring. After cooling to room temperature the solvent was evaporated, and the precipitate was recrystallized from ethanol. The physical properties of the synthesized compounds $[7]_n$ are listed in Table (2-4).

Table (2-4): The melting points of homologous series $[7]_n$.

Compound no.	R	Yield (%)	M.P.(C^0)
$[7]_1$	methyl	60	**200**
$[7]_2$	ethyl	61	**210**
$[7]_3$	n-propyl	50	**215**
$[7]_4$	n-butyl	55	**219**
$[7]_5$	n-pentyl	65	**220**
$[7]_6$	n-hexyl	60	**215**
$[7]_7$	n-heptyl	45	**237**
$[7]_8$	n-octyl	44	**212**

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Republic of Iraq
Ministry of Higher Education
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Al-Nahrain University
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SYNTHESIS, LIQUID CRYSTALLINE PROPERTIES, AND BIOLOGICAL ACTIVITY OF SOME NOVEL TRIS-SCHIFF'S BASES CONTAINING 1,3,4-THIADIAZOLE RING SYSTEM

A Thesis submitted to the College of Science Al-Nahrain University in partial fulfillment of the requirements for the Degree of Master of Science in Chemistry

By
Mustafa Kadtan Shneshil Al-Malki
(B.Sc 2002)

May 2005 *Rabee Al –Thani 1426*

Supervisor certification

We certify that this thesis was prepared under our supervision at the Department of Chemistry, College of Science, Al-Nahrain University as a partial requirements for the Degree of Master of Science in Chemistry.

Professor **Lecturer**

Dr. Ammar H. Al-Dujaili **Dr.Ayad S. Hameed**

In view of the available recommendation, I forward this thesis for debate by the Examining Committee.

Assistant Professor

Dr. Shahbaz A. Maki

Head of the Department of Chemistry College of Science Al-Nahrain University

Examining Committee's Certification

We, the Examining Committee, certify that we read this thesis and have examined the student *Mustafa Kadtan Shneshil Al-Malki*, in its contents and that, in our opinion; it is adequate as a thesis for the Degree of Master of Science, in Chemistry.

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(Chairman) .

Signature:

Name: Assistant Prof. Sawsan H. Shawkat
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Approved for the College of Graduate Studies

Assistant Professor
Dr. Laith Abd Al-Aziz
Dean of College of
Science Al-Nahrain
University

In the Name of Allah the most Merciful, the most Compassionate

"Allah will exalt those of you who believe, and those who are given knowledge, in high degrees"

[58:11]

الإهداء

إلى الذين أحبوا و تمنوا لي النجاح

الى من أمرنا الله بطاعتهم و موالاتهم

الى الذين صبروا و تحملوا لأجل ذلك الكثير

أعز الناس والدي و والدتي

الى عالم يزهو حبا و عطاء أستاذي

الى من أشد بهم أزري في الحياة أخوتي

الى رفاق الدرب الطويل أصدقائي

أهدي بحثي المتواضع ....

مصطفى

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Praise is to God the Lord of the worlds and peace and blessings be upon the master of mankind Muhammad and his pure Progency and his relatives and may God curse their enemies until the Day of Judgment.

I would like to express my deepest thanks to my respected Supervisors Proff. Dr. Ammar H. Al-Dujaili and Dr. Ayad S. Hameed for their great help and assistance provided during this work. I am especially grateful to Dr. Emad Al-Sarage.

I am especially grateful to Mr. Jamal O. Stephan for his great help. Special thank to the department of chemistry Al-Basrah University for processing texture observations and to Ahmed Nuri (Department of Biotechnology) for processing biological part of the work.

I am especially grateful to my friends Osama Muhammad, Bassam Faron and Mutaz Adnan for their help in justifying this thesis.

Sincere thanks are also to the Dean of the college of science and the head of department of chemistry Dr. Shahbaz A. Maki and the staff member of the department of chemistry.

Finally to all my friends…….. I present my thanks.

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Mustafa 2005

REFERENCES

1. H. L. Yale and K. Losee, *J. Med. Chem*., **9**, 478 (1966).

2. C. Anisworth, *J. Am. Chem. Soc*., **87**, 5800 (1965).

3. R. C. Elderfield, “Heterocyclic compounds”, C. E. Robert, Editor, 7, Wiley, NewYork (1971).

4. A. Grekov and R. Azen, *Zh. Obshch, Khim*, **31**, 1919 (1961).

5. R. C. Elderfield, “Heterocyclic compounds”, 7, Wiley, NewYork (1971).

6. R. Stolle, H. Hille and Callaborators *J. Prakt, Chem*., **69**, 481(1904).

7. E. Hoggarth, *J. Chem. Soc*.,**5**, 1163 (1949).

8. C. Ainsworth, *J. Am. Chem. Soc*. **78**, 1937 (1956).

9. C. Ainsworth, *J*. *Am. Chem. Soc*., **80**, 5201, (1958).

10. R. C. Elderfield, "Heterocyclic Compound" Academic Press, London (1962).

11. R.C.Elder Field, “Heterocyclic Compound”, Acadimic Press London (1962).

12. British Patent, 916,061(1963), Chem. Abs. **59**, 1650 (1963).

13. D. Compbull, Kiskagins, Chem. Abs. **74**, 100068z (1971).

14. B. Fohlisch, R. Bann and K. W. Schultze, *Angew. Chem*., **79**, 318 (1976).

15. T. J. Kress and S. M. Costantino, *J*. *Heterocyclic Chem*., **17**, 607 (1980).

16. V. K. Mishra and S. C. Bahel, *J*. *Indian Chem*. *Soc*., **59**, 867-870 (1983).

17. A. Mohsen, M. E. Omar and O. M. Aboulwafa, *J. Heterocyclic Chem*., **23**, 1339 (1977).

18. S. Howard. *J. Heterocyclic Chem*., **22**, 361 (1985).

19. T. J. Kress and S. M. Costantino., *J. Heterocyclic Chem*., **17**, 607 (1980).

20. A. Hetzheim and K. Mockel, "Advances in Heterocyclic Chemistry", A. R. Katrizky and A. J. Boulton (Editors), Vol. **7**, Academic Press, NewYork, 224 (1966).

21. V. K. Mishra and S. C, Bahel, Indian *J. Chem. Soc*., **LX**, 867 (1983).

22. F. Bentiss and M. Traisnel, Corrosion Science, **42**, 1, 146 (2000).

23. S. Giri, H. Singh and L. D. S. Yadva, *Agr. Biol. Chem*. **40**, 17 (1976).

24. V. J. Ram and H. N. Fanday, *J. Indian Chem. Soc*., **51**, 634 (1974).

25. I. Angelini and F. Sparaco, British Pat., 161, 801 (1969);[C. A., 71, 112936g (1969)].

26. H. Najer, R. Cindicelli and J. *Menin, Bull. Soc. Chim., France*, **25**, 153 (1966).

27. S. K. Chaudhary and S. S. Parmar, J. *Pharm. Sci*., **67**, 1507 (1978).

28. D. Demus, J. Goodby, G.W. Gray, H.W. Spiess and V.Vill, "Handbook of Liquid Crystals", (Eds), Wiley-VCH, Weinheim, Vol1, Chapter VII (1998).

29. D. Demus, J. Goodby, G.W. Gray, H.W. Spiess and V.Vill, “Handbook of Liquid Crystals”, (Eds), Wiley-VCH, Weinheim, Vol2, Chapter VI (1998).

30. F. Reinitzer, *Liq. Cryst*., **5**, 7-18 (1888).

31. O. Lehmann, *Z. Phys. Chem*., **8**, 462-472 (1889).

32. G. Friedel, *Ann. Physique*, **18**, 273 (1922).

33. H. Sackmann, *Liq. Cryst*., **5**, 43-55 (1989).

34. G.W. Gray, K.J. Harrison and J.A. Nash, *Electronics Lett*., ***9***, 130-131 (1973).

35. M. Sahara, S. Yano, K. Ikemoto and Z. Maejima, *Liq. Cryst*., **15**, 929-931 (1993).

36. S. Chandrasekhar, B.K. Sadashiva and K.A. Suresh, *Pranama*, **9**, 471-480 (1977).

37. D. Demus, J. Goodby, G.W. Gray, H.W. Spiess and V.Vill,(Eds),” Handbook of Liquid Crystals”, Wiley-VCH, Weinheim, Vol **2B**, Chapter VII (1998).

38. B.A. Gregg, M.A. Fox and A.J. Bard, *J. Chem. Soc., Chem. Commun*., **34**, 1134-1135 (1987).

39. M.T. Allen, S. Diele, K.D.M. Harris, T. Hegmann, B.M. Kariuki, D. Lose, J.A. Preece and C. Tschierske, *J. Mater. Chem*., **11**, 302-311 (2001).

40. C. Göltner, D. Pressner, K. Müllen and H.W. Spiess, *Angew. Chem*., *Int*. Ed., **32**, 1660-1662(1993).

41. R. Poupko, Z. Luz, N. Spielberg and H. Zimmermann, *J. Am. Chem. Soc*., **111**, 6094-6105(1989).

42. J. Maltêhte and A. Collect, *J. Am. Chem. Soc*., **109**, 7544-7545(1987).

43. B.A. Gregg, M.A. Fox and A.J. Bard, *J. Chem. Soc., Chem. Commun*., **11**, 1134-1135(1987).

44. H. T. Nguyen, C. Destrade and J. Maltêhte, *Adv. Mater*., **9**, 375-388(1997).

45. H. Bengs, O. Karthaus, H. Ringsdorf, C. Baehr, M. Ebert and J.H. Wendorff, *Liq. Cryst*., **10**, 161-168(1991).

46. B. Donnio, B. Heinrich, T. Gulik-Krzywicki, H. Delacroix, D. Guillon and D.W. Bruce, *Chem. Mater*., **9**, 2951-2965(1997).

47. D. Demus, J. Goodby, G.W. Gray, H.W. Spiess and V.Vill, "Handbook of Liquid Crystals", (Eds), Wiley-VCH, Weinheim, Vol **1**, Chapter VI.(1998).

48. K.E. Rowe and D.W. Bruce, *J. Mater. Chem*., **8**, 331-341(1998).

49.R. Cai., E. T. Samulski, *Liq. Cryst*., **9**, 617-619(1991).

50. G. W. Gray and P. Winsor, (Eds), "Liquid Crystals and the Plastic Crystals", 2, Ellis Horwood Press, New York (1972).

51. G. H. Brown and J. J. Wolken, (Eds), "Liquid Crystals and Biological Structures", Acadimic Press, P. 186, London (1979).

52. C. G. Seguel, B. Borchers, W. Haase and C. Aguilera, *Liq. Cryst*., **11**, 903 (1992).

53. M. Parra, J. Belmar, H. Zunza, C. Zúñiga, G. Fuentes and R. Martinez, *J. Prakt. Chem*., **337**, 241 (1995).

54. M. Parra, Sh. Villouta, V. Vera, J. Belmar, C. Zúñiga and H. Zunza, *Z. Naturforsch.,* **52b**, 1538 (1997).

55. S. H. Kang, M. Kim, H-K. Lee, Y-S. Kang, W-Ch. Zin and K. Kim, *Chem. Common.*, **8**, 94 (1999).

56. M. Parra, S. Hernandez, J. Alderete and C. Zúňiga, *Liq. Cryst.,* **27(8)**, 1000 (2000).

57. A. T. Atto, A. H. Al-Dujaili and A. S. Hameed, *J. Saddam University*., **4(1)**, 41 (2002).

58. A. H. Al-Dujaili, A. S. Hameed, and N. A. Saleh, *National J. Chem*., **5**, 121 (2002).

59. W. M. Al-Zubadi, Ph. D. Thesis, Saddem University, Iraq (2002).

60. A. H. Al-Dujaili, N. R. Jaber and A. T. Atto, *National J. Chem*., **8**, 542 (2002).

61. J. H. Tomma and A. H. Al-Dujaili, *Iraqi J. Sci*., **43A**, 35 (2002).

62. A. H. Al-Dujaili, and J. H. Tomma, *Iraqi J. Chem*., **28(2)**, 405 (2002).

63. A. H. Al-Dujaili, A. S. Hameed, and Y. Al-Thaif, *Iraqi J. Chem*., **28(2)**, 397 (2002).

64. A. C. Cope and S. W. Fenton, *J. Am. Chem. Soc*., **73**, 1972 (1951).

65. M. A. Apfel, H. Finkelman and G. M. Janini, *Anal. Chem*., **57**, 651 (1974).

66. M. Parra, J. Belmar, H. Zunza, C. Zúňiga, G. Fuentes and R. Martinez, *J. Prakt. Chem*., **249**, 350 (1998).

67. F. Suzuki, I. Kawkami, F. Motohash, S. Hayashi, N. Otoga, M. Hirose and Y. Iwabushi, Jap. Pat., 76, 09, 007 (1976); [C. A., 86, 55, 451d (1977)].

68. Peter Sykes, “A guidebook to mechanism in organic chemistry”, (Eds), John Wiley and Sons, Inc., New York (1986).

69. J. Thiele and O. Gunther, *Ann. Chem*., **347**, 107 (1966).

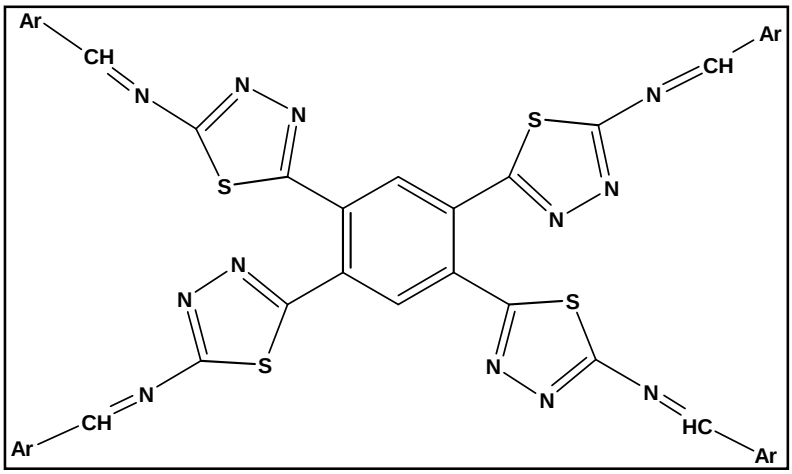
70. V. Kishore and S. S. Parmar, *Res. Commun. Chem., Patho.,***5**, 23 (1976).

71. M. M. Dutta and J. S. Kataky, *J*. Heterocyclic Chem., 23, 793 (1986).

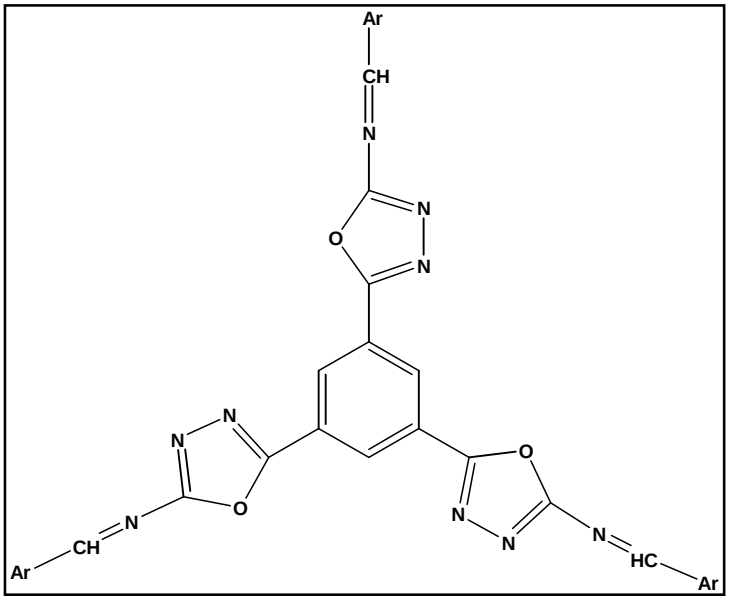
Suggestion for further work

In order to continue our extensive program directed towards the synthesis of novel heterocycles possessing liquid crystalline properties, we hope to prepare the following compounds in the future.

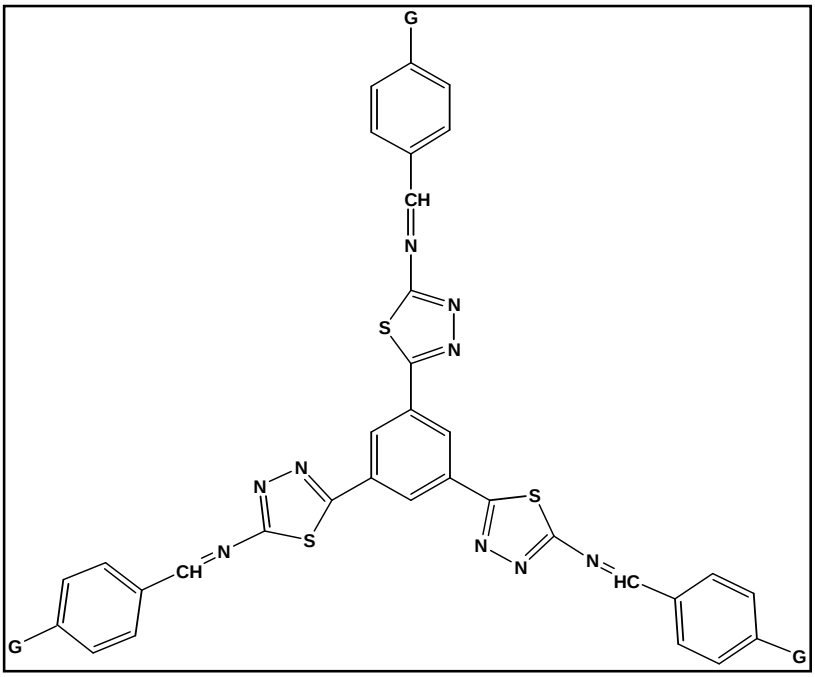
1. A series of new tris-Schiff's bases having the following structural formula will be synthesized.



2. A comparative study between 1,3,4-thiadiazole ring of our synthesized series with 1,3,4-oxadiazole ring which has the following structural formula.

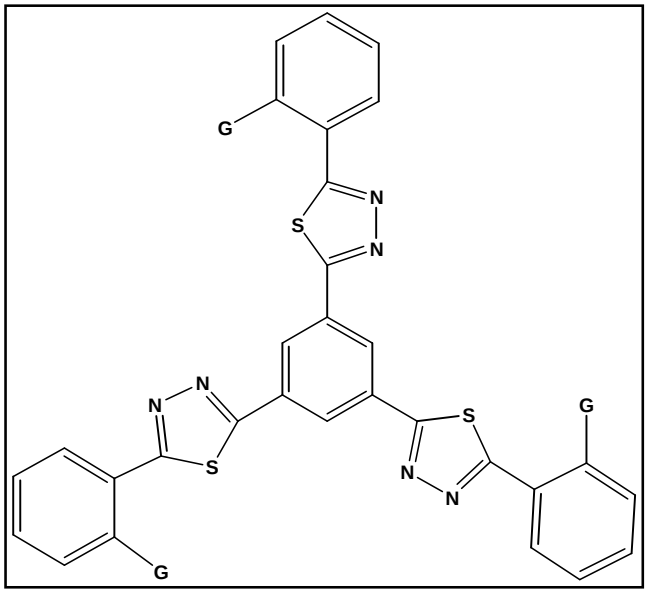


3. Studying the effect of replacing of terminal alkoxy group in our synthesized series by a polar terminal group.



G: -NO_2, Hal-, CH_3CO-, ROCO-, -NH_2, etc.

4. Introducing a lateral substituents group on our synthesized series and studying the effect of these groups on liquid crystalline properties.



CHAPTER THREE
RESULTS AND DISCUSSION

REFERENCES

CHAPTER TWO
EXPERIMENTAL PART

CHAPTER ONE
INTRODUCTION

جمهورية العراق
وزارة التعليم العالي والبحث العلمي
جامعة النهرين
كلية العلوم
قسم الكيمياء

تحضير ودراسة الصفات البلورية السائلة والفعالية البايلوجية لبعض قواعد شف الثلاثية الجديدة الحاوية على حلقة ١،٣،٤- ثاياديازول

رسالة
مقدمة الى كلية العلوم- جامعة النهرين
وهي جزء من متطلبات نيل درجة الماجستير في الكيمياء

من قبل
مصطفى كطان شنيشل المالكي
بكالوريوس ٢٠٠٢ (جامعة النهرين)

ربيع الثاني ١٤٢٦ **آيار ٢٠٠٥**

بسم الله الرحمن الرحيم

"يرفعُ اللهُ الذينَ آمنوا مِنكم والذينَ أوتوا العلمَ درجات"

"صدق الله العظيم"

سورة المجادلة الآية (١١) .

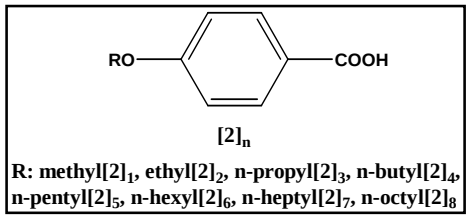
الخلاصة

البحث في هذه الأطروحة تضمن أربعة مراحل:

المرحلة الأولى: لقد تم خلال هذه المرحلة تحضير قواعد شف الثلاثية الحاوية على حلقة١،٣،٤- ثايادايازول و قد تضمن أربع خطوات وكما يلي:

الخطوة الأولى: تحضير مركبات ٤-ن-الكوكسي حامض البنزويك $[2]_n$:

أن تفاعل ٤-هيدروكسي حامض البنزويك [1] مع هاليدات الكيل معينة مستقيمة السلسلة بوجود هيدروكسيد البوتاسيوم يعطي مركبات ٤-ن-الكوكسي حامض البنزويك$[2]_n$.

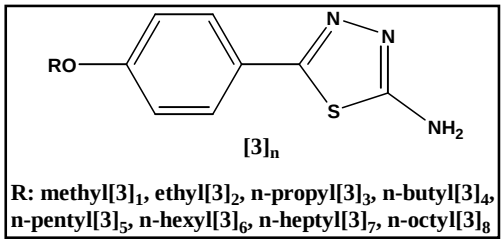


$[2]_n$

R: methyl$[2]_1$, ethyl$[2]_2$, n-propyl$[2]_3$, n-butyl$[2]_4$, n-pentyl$[2]_5$, n-hexyl$[2]_6$, n-heptyl$[2]_7$, n-octyl$[2]_8$

الخطوة الثانية: تحضير مركبات ٢-أمينو-٥-(٤-ن-الكوكسي فنيل)-٤،٣،١- ثايادايازول$[3]_n$:

أن تفاعل ٤-ن-الكوكسي حامض البنزويك $[2]_n$ مع مركب ثايوسيميكاربازايد بوجود ثلاثي كلوريد الفسفوريل اعطى مركبات ٢-أمينو-٥-(٤-ن-الكوكسي فنيل)-١،٤،٣-ثايادايازول$[3]_n$.



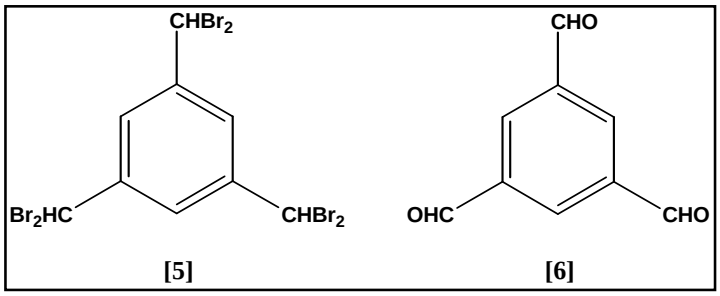
$[3]_n$

R: methyl$[3]_1$, ethyl$[3]_2$, n-propyl$[3]_3$, n-butyl$[3]_4$, n-pentyl$[3]_5$, n-hexyl$[3]_6$, n-heptyl$[3]_7$, n-octyl$[3]_8$

الخطوة الثالثة: تحضير مركب١،٣ ، ٥-ثلاثي فورميل البنزين [6]:

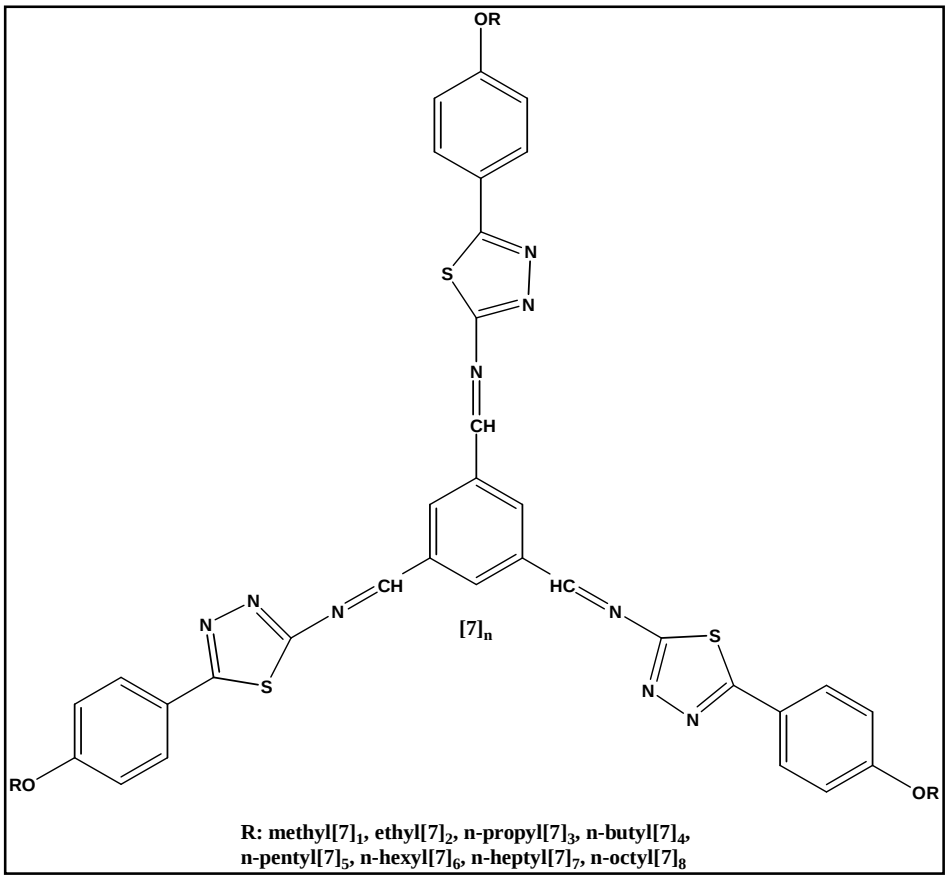
أ- تم تحضير المركب سداسي بروميد المسيتيلين [5] وذلك عن طريق مفاعلة المسيتيلين [4] مع البروم بوجود مصدر ضوئي يولد ألأشعة فوق البنفسجية.

ب- التحلل ألحامضي للمركب [5] بوجود المورفلين يعطي المركب [6].



الخطوة الرابعة: تحضير قواعد "شف" الثلاثية الحاوية على حلقة١ ، ٣ ، ٤-ثاياداياز‌ول $_n$[7]:

تم تحضير هذه القواعد عن طريق مفاعلة المركبات٢-أمينو-٥-(٤-ن-الكوكسي فنيل)-١،٣،٤-ثاياداياز‌ول $_n$[3] مع المركب ١، ٣، ٥-ثلاثي فورميل البنزين [6] بوجود الأيثانول المطلق.



R: methyl[7]$_1$, ethyl[7]$_2$, n-propyl[7]$_3$, n-butyl[7]$_4$, n-pentyl[7]$_5$, n-hexyl[7]$_6$, n-heptyl[7]$_7$, n-octyl[7]$_8$

المرحلة الثانية فقد تضمنت تشخيص المركبات التي تم تحضيرها وذلك عن طريق استخدام (طيف الأشعة تحت الحمراء والأشعة فوق البنفسجية) أضافة الى درجات الأنصهار وكانت النتائج مطابقة للتراكيب المقترحة.

المرحلة الثالثة تضمنت دراسة الصفات البلورية السائلة لقواعد "شف" الثلاثية الحاوية على حلقة١، ٣، ٤-ثايادايازول وذلك بأستخدام مجهر الضوء المستقطب.

أثبتت الدراسة أن المركبات([7]$_8$,[7]$_7$,[7]$_6$,[7]$_5$, [7]$_4$) أظهرت صفات بلورية سائلة بينما لم تظهر المركبات ([7]$_3$,[7]$_2$, [7]$_1$) أي صفة بلورية.

المرحلة الرابعة تضمنت دراسة الفعالية البايلوجية لقواعد "شف" الثلاثية الحاوية على حلقة١، ٣، ٤-ثايادايازول حيث كانت بعض المركبات لها فعالية بايلوجية ولم تمتلك مركبات أخرى هذه الفعالية أنظر جدول (٣-٥).

الأسم: مصطفى كطان شنيشل المالكي

العنوان: بغداد حي أشبيلية د١٨ ز٤٤ م٥١٩

تأريخ المناقشة: الأربعاء ١٣/٧/٢٠٠٥

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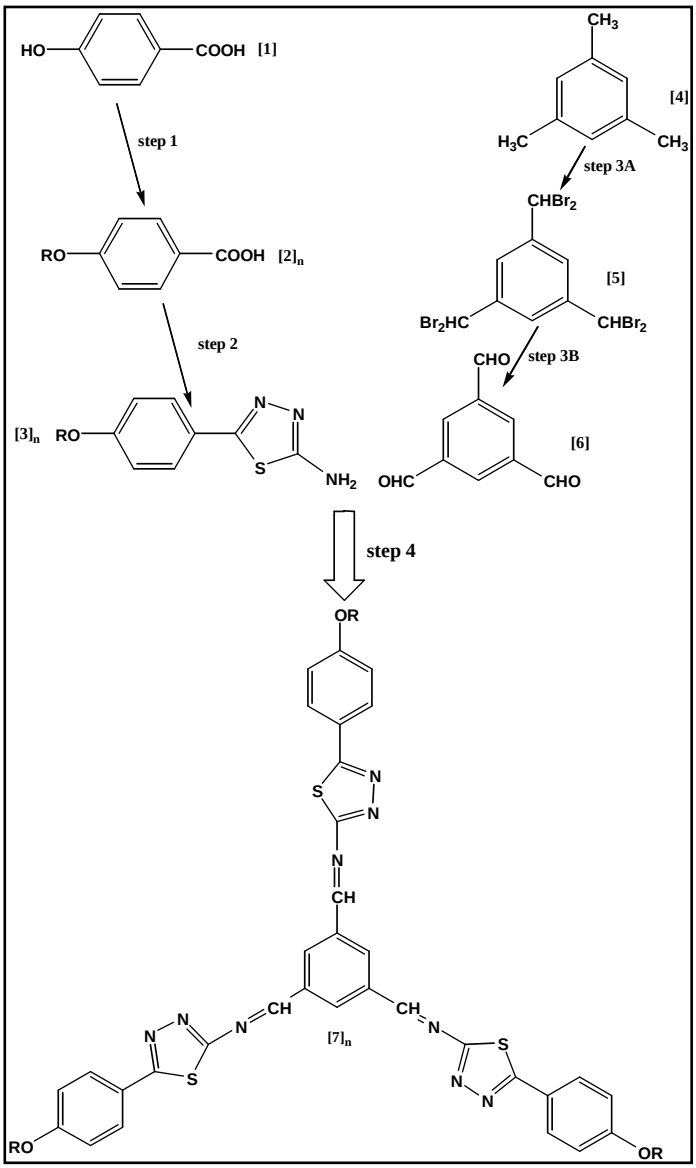
CHAPTER THREE
RESULTS AND DISCUSSION

3-1 Synthesis of 1,3,5-tri-[5(4'-n-alkokxyphenyl)-1,3,4-thiadiazol-2-yl]-trimesilydene[7]$_n$

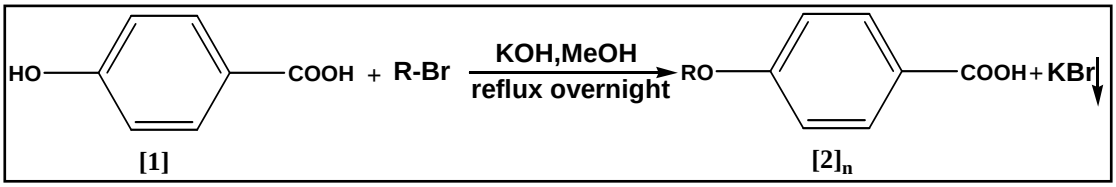
It is well established that the various derivatives of 1,3,4-thiadiazoles[64] exhibited interesting pharmalogical, liquid crystalline properties, and biological activity. In the light of these findings, we undertook the designing and synthesis of the titled compounds $[7]_n$ as shown in scheme (3-1).



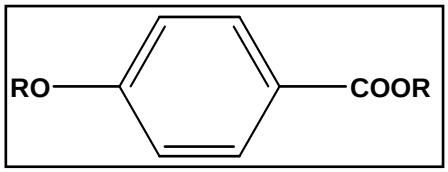
Scheme (3-1): The stepwise synthesis of the homologous series $[7]_n$.

3-1-1 Preparation of 4-n-alkoxybenzoic acid $[2]_n$

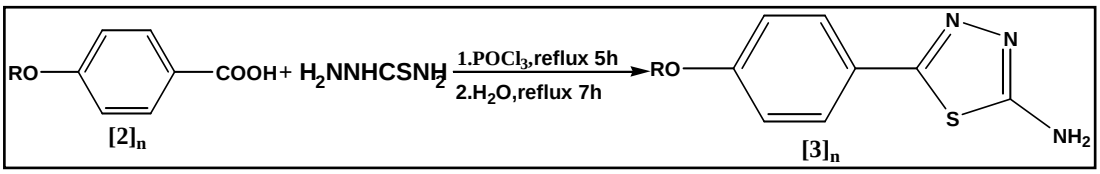
4-n-alkoxybenzoic acid was prepared by the refluxing of 4-hydroxybenzoic acid [1] with different alkylhalides (bromide, iodide) in strong basic media of potassium hydroxide.



The melting point of the compounds above agrees with that reported in the literature[65]. Through the preparation of 4-n-alkoxy benzoic acid $[2]_n$, n-hexane was added to dissolve the traces of the unreacted acid (4-hydroxybenzoic acid [1]), and another undesired products may be formed during the reaction which is n-alkyl-4-alkoxybenzoate



3-1-2 Synthesis of 2-amino-5-(4-n-alkoxyphenyl)-1,3,4-thiadiazole$[3]_n$



The reaction of appropriate 4-n-alkoxybenzoic acid, with thiosemicarbazide in the presence of phosphorus oxychloride under the conditions reported previously[66], afforded 2-amino-5-(4-n-alkoxyphenyl)-1,3,4-thiadiazole $[3]_n$.

The mechanism[67] of the reaction is shown in figure (3-1)

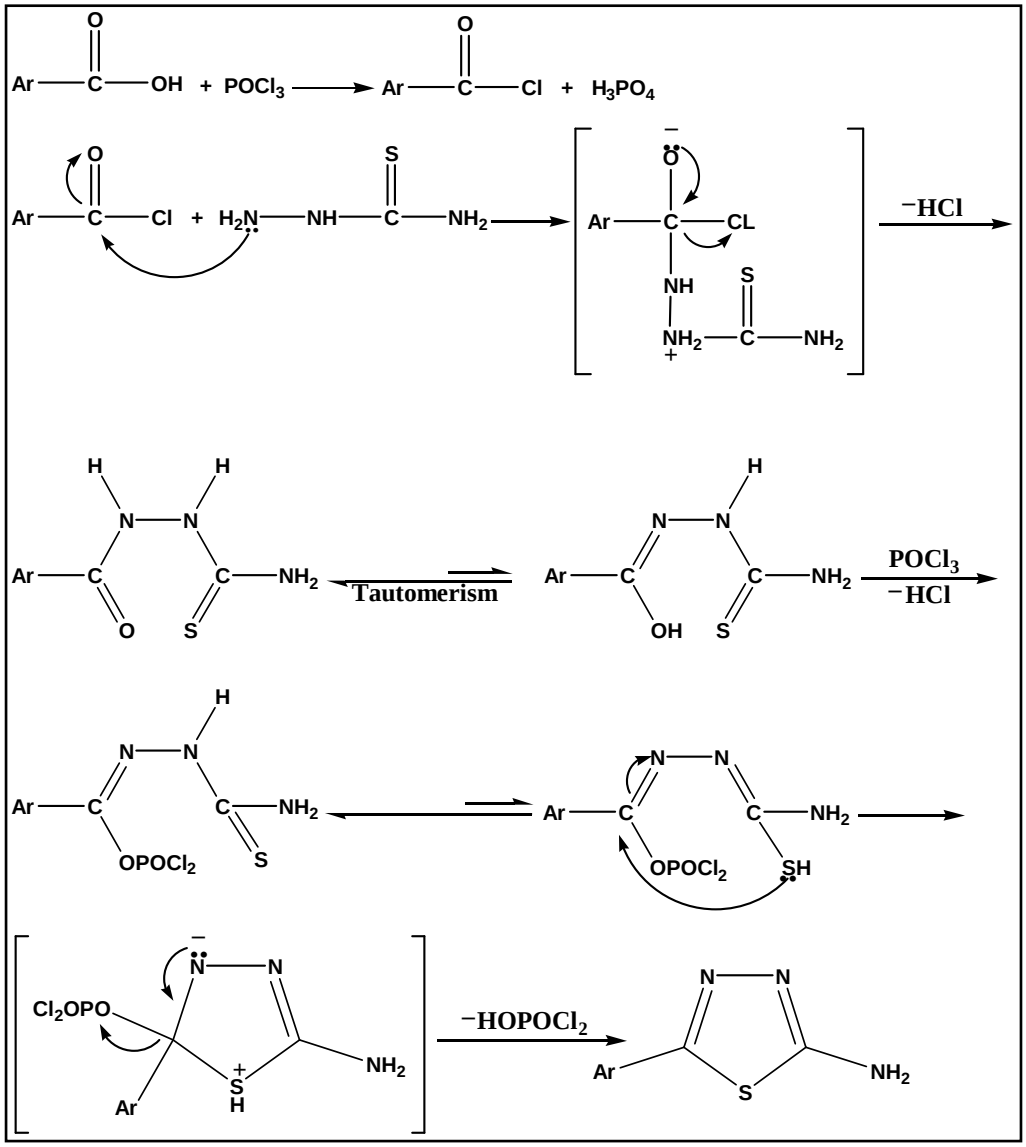


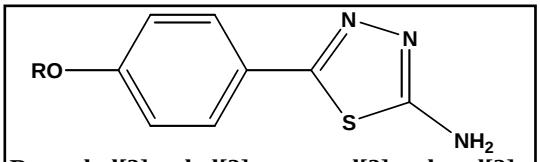
Figure (3-1): Mechanism steps for the synthesis of 2-amino-5-(4-n-alkoxyphenyl)-1,3,4-thiadiazoles.

The structures of these compounds were elucidated using melting point and infrared spectroscopy.

The F.T.IR spectra of 2-amino-5-(4-n-alkoxyphenyl)-1,3,4-thiadiazoles give the evidence for the formation of the titled compounds through, the disappearance of the two bands at (3550-2750 cm^{-1}), and (1687 cm^{-1}) attributed to the O-H stretching frequency, and C=O of 4-n-alkoxybenzoic acid together, with the appearance of the band at about (3300-3100 cm^{-1}) which could be assignable to NH_2 group, asymmetric and symmetric stretching vibrations.

Besides that, the band at about(1615-1600 cm^{-1}) due to the C=N group stretching frequency is also observed, the C-O-C group stretching vibrations (asymmetric and symmetric) appear at (1250-1020 cm^{-1}), also the γ C-H bending of *p*-disubstituted appears at about (830 cm^{-1}). The F.T.IR spectrum of 4-methoxy benzoic acid is shown in Figure (3-2), the spectroscopic data and charts of the synthesized 2-amino-5-(4-n-alkoxyphenyl)-1,3,4-thiadiazoles $[3]_n$ are shown in Figures (3-3) to (3-10) respectively. The spectroscopic data of the compounds 2-amino-5-(4-n-alkoxyphenyl)-1,3,4-thiadiazoles $[3]_n$ are shown in Table(3-1).

Table (3-1): The characteristic F.T.IR absorption bands of 2-amino-5-(4-n-alkoxyphenyl)-1,3,4-thiadiazole[3]$_n$.



R: methyl[3]$_1$,ethyl[3]$_2$,n-propyl[3]$_3$,n-butyl[3]$_4$, n-pentyl[3]$_5$,n-hexyl[3]$_6$,n-heptyl[3]$_7$,n-octyl[3]$_8$

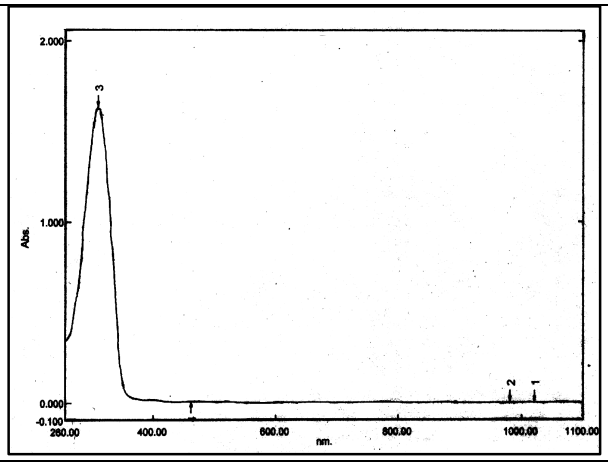
Compound No.	R	$\nu_{as.}$N-H	$\nu_{sy.}$N-H	νC-H aromatic	$\nu_{as,sy}$C-H aliphatic	νC=N	$\nu_{as,sy}$ C-O-C	γC-H aromatic
[3]$_1$	methyl	3281	3105	3105	2928 2858	1611	1252 1042	831
[3]$_2$	ethyl	3410	3277	3092	2924 2856	1612	1248 1056	831
[3]$_3$	n-propyl	3269	3105	3105	2928 2858	1614	1252 1024	833
[3]$_4$	n-butyl	3269	3105	3105	2926 2858	1612	1252 1024	833
[3]$_5$	n-pentyl	3241	3101	3101	2936 2864	1609	1254 1018	831
[3]$_6$	n-hexyl	3273	3099	3099	2961	1611	1252 1036	831
[3]$_7$	n-heptyl	3279	3113	3113	2951 2930	1609	1252 1051	833
[3]$_8$	n-octyl	3210.2	3105	3105	2928 2858	1611	1252 1042	831

3. The electronic spectra of the synthesized Schiff's bases dissolved in (DMSO) gave the (λ_{max}) absorption bands at about (310-312 nm) for all compounds which attributed to the (π - π^*). The (n - π^*) were forbidden, therefore not appear .The (λ_{max}) and the type of electronic transitions of the Schiff's bases $[7]_n$ are listed in Table (3-3).

Table (3-3): The electronic transitions and the (λ_{max}) for $[7]_n$.

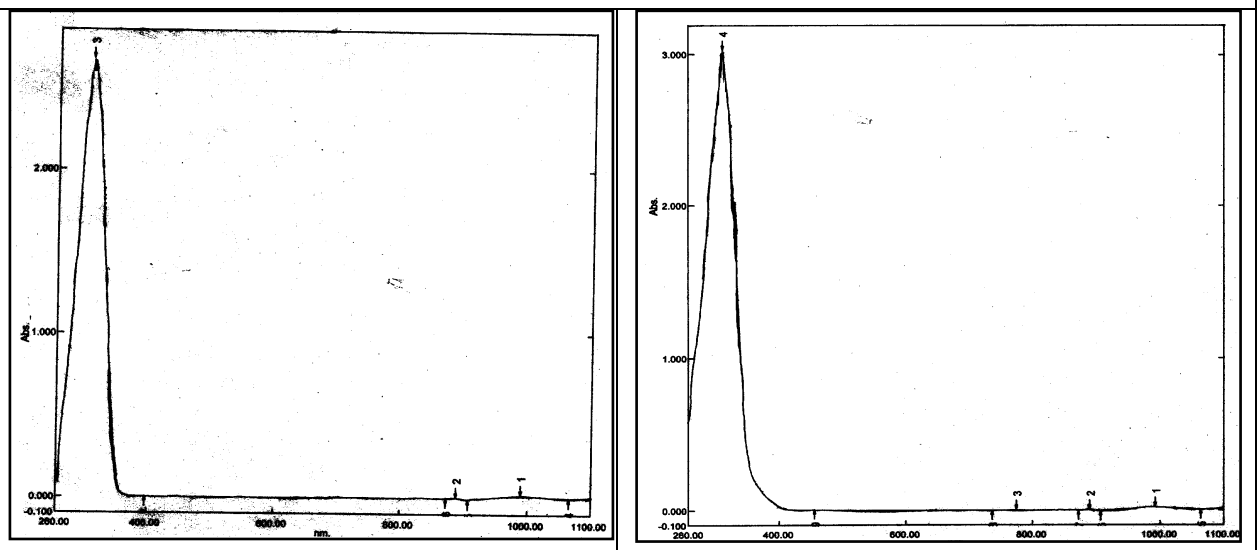
Compound no.	R group	λ_{max}(nm)
$[7]_1$	methyl	311
$[7]_2$	ethyl	312
$[7]_3$	n-propyl	311
$[7]_4$	n-butyl	310.5
$[7]_5$	n-pentyl	311
$[7]_6$	n-hexyl	311.5
$[7]_7$	n-heptyl	311.5
$[7]_8$	n-octyl	310.5

The (λ_{max}) for all Schiff's bases are approximately constant because the differences between each compound in these series is methylene group and this group is of no effect on the (λ_{max}). The UV-Vis. Spectra of the Schiff's bases are shown in Figures (3-28) to (3-31).



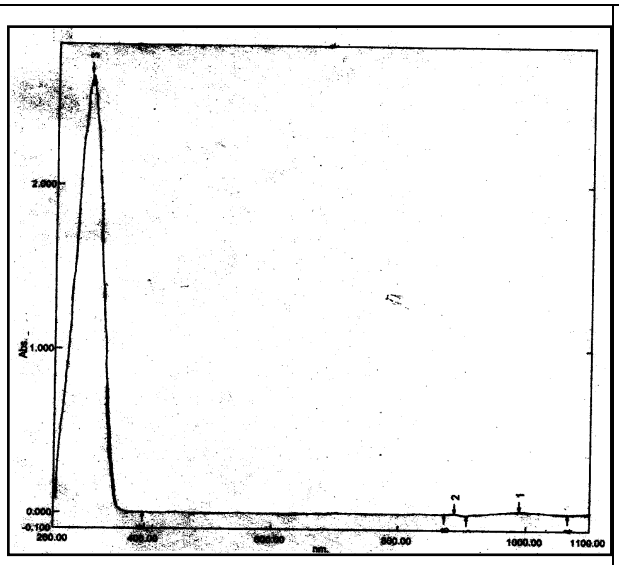
A B

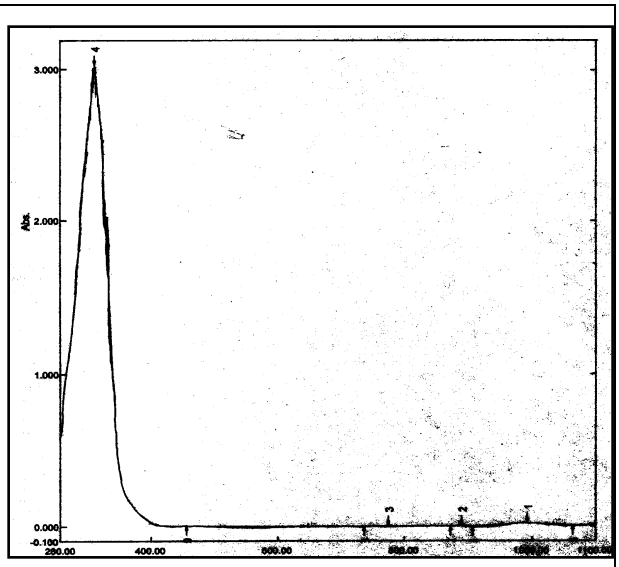
Figure (3-28): UV-Vis spectra of(A) $[7]_1$ and (B) $[7]_2$.



A B

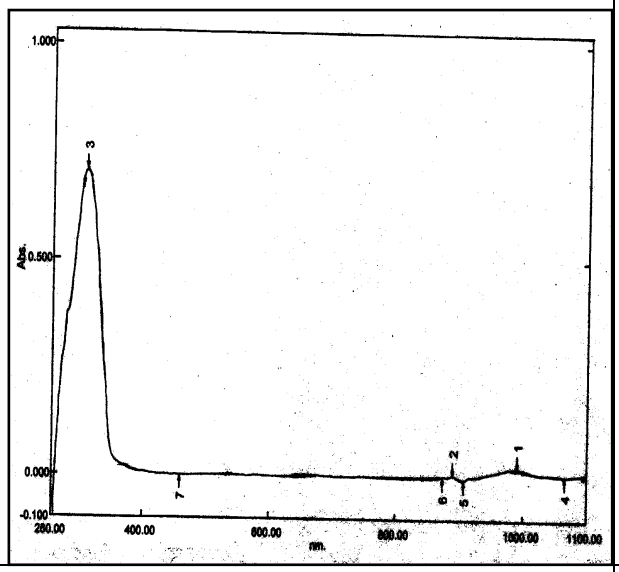
Figure (3-29): UV-Vis spectra of (A) $[7]_3$ and (B) $[7]_4$.

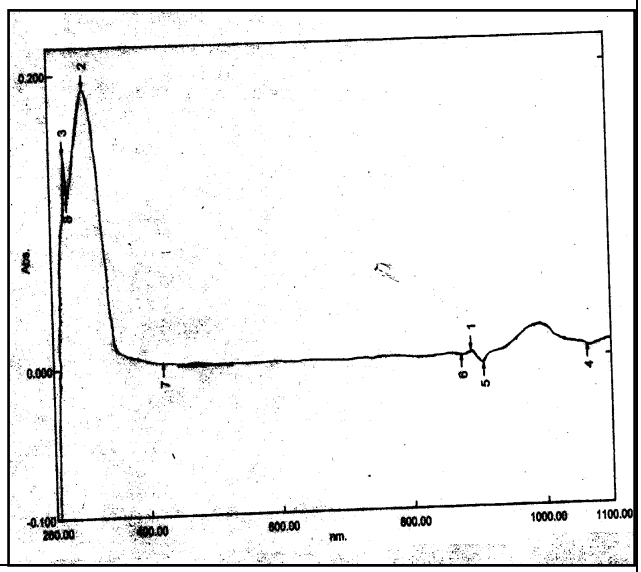




A **B**

Figure (3-30): UV-Vis spectra of (A) $[7]_5$ and (B) $[7]_6$.





A **B**

Figure (3-31): UV-Vis spectra of (A) $[7]_7$ and (B) $[7]_8$.

3-2 Liquid Crystalline behavior of the synthesized compounds

It is well established that the relationship between chemical structure and liquid crystalline properties of organic compounds is considered of particular importance to the organic chemist. A large number of liquid crystalline compounds containing 1,3,4-thiadiazole unit have been synthesized and interest in such structures constantly grows[70]. However, all liquid crystalline compounds described in the literature contain mono-, or bis-1,3,4-thiadiazole units. In this work we describe the first synthesized compounds containing tris-1,3,4-thiadiazole rings system. The syntheses of such compounds probably verify two goals. The first to show how these substituents act as structural disordering groups with respect to molecule rigidity consideration, which is an important factor for the formation of liquid crystalline compounds. The second, how these groups are considered as a part of the mesogenic system, the consequence on the liquid crystalline behavior should be of interest. Therefore, in this work a series $[7]_n$, of eight compounds (n=1-8) were synthesized and studied for their liquid crystalline properties. Normally, the liquid crystalline properties are examined by means of differential scanning calorimetry (DSC) and hot-stage microscopy. Unfortunately, we have been unable to use the (DSC) instrument since such facility is not available in the country. However, the hot-stage microscope furnish the transition temperatures to the different phases and reveals the type of these phases by texture observations. The Phase transition temperatures which were established by

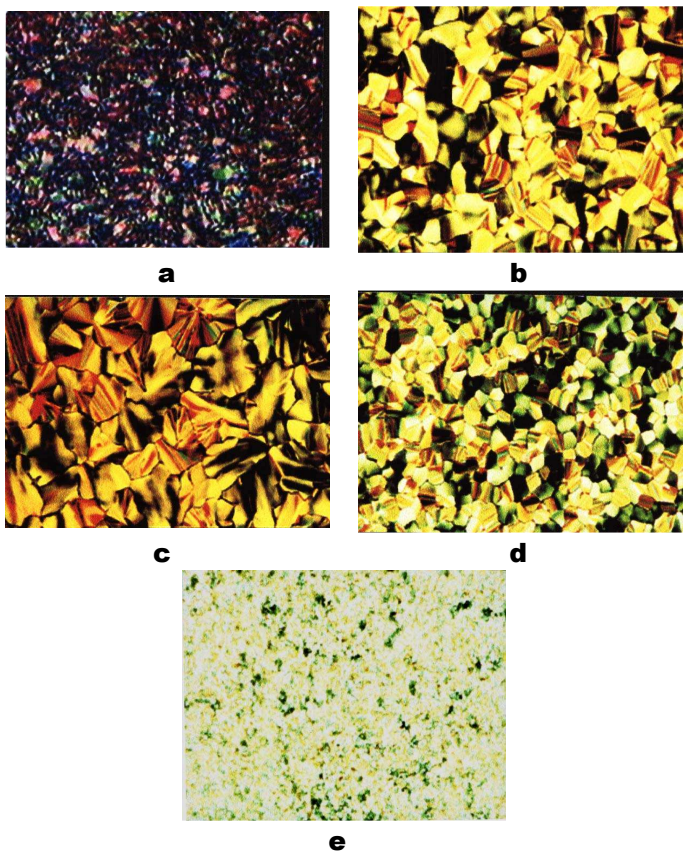
observations using a polarizing microscope are summarized in Table (3-4).

Table(3-4):Phase transition temperatures of compounds of series$[7]_n$.

Compounds symbol	Transition temperatures(^oC)	
	K to LC/^oC	LC to I/^oC
$[7]_1$	-	200
$[7]_2$	-	210
$[7]_3$	-	215
$[7]_4$	200	219
$[7]_5$	205	220
$[7]_6$	195	215
$[7]_7$	217	237
$[7]_8$	197	212

The first three homologous, (n = 1,2 and 3) do not reveal any liquid crystalline behavior, but simply changes from the solid crystalline state to the isotropic liquid at 200, 210 and 215 ^oC, respectively. The other last five compounds, (n = 4-8) show enantiotropic mesomorphic behavior (The phase transition from the solid to the liquid crystalline phase and from the liquid crystalline phase to the isotropic liquid phase occur respectively). Examination of the texture under polarizing microscope reveals that all five compounds exhibit smectic phase of type smectic A (S_A). Figure (3-32) displayed a planar focal conic texture typical of smectic A phase. The mesophase creation probably results from two competitive tendencies: stiffening of the molecular core by the dipole-dipole molecular interaction of highly polar methoxy, ethoxy and n-propoxy terminals substituent, which depresses the calamitic phases, and elongation of those substituents promoting these mesophases. The long alkoxy chains probably biased the

rotation of both molecular parts. However, this molecular core is less rigid than that in compounds n = 1,2,3, resulting in the formation of the columnar hexagonal phase, which is stable in a narrow temperature range. The mesophase's stability was found to be poor for the last five compounds. This suggests that the two strong stiffening of the molecular core depresses the calamitic phase formation. It is worth wide to mention that an increase in the molecular length with little or no change in the width allow an increase in the anisotropy of the polarizability for molecules with three thiadiazole rings, which favours molecular interaction and liquid crystalline properties for these compounds (n = 4-8).



Figure(3-32): Fanlike texture of Smectic A (S_A) of compounds a $[7]_4$, b $[7]_5$, c $[7]_6$, d $[7]_7$, e $[7]_8$, under crossed polars (x320).

3-3 Biological Activity of the synthesized compounds

The idea of the present investigation came from the promising effects of both mono- and bis-1,3,4-thiadiazole derivatives that were published in the literature, in addition to our previous interest in these compounds. Therefore, the tris-1,3,4-thiadiazole compounds synthesized in this work were evaluated for their antimicrobial activities.

The test was performed according to the disk diffusion method[71]. The prepared compounds were tested against one strain of Gram +ve bacteria (***Staphylococcus Aureus***), and Gram –ve bacteria (***Pseudo***). Prepared agar and Petridishes were sterilized by autoclaving for (15min) at 121 ^{o}C. The agar plates were surface inoculated uniformly from the broth culture of the tested microorganisms. In the solidified medium suitably spaced apart holes were made all (6mm) in diameter, were filled with 100µl of the prepared compounds (1mg of the compound dissolved in 1ml of DMSO solvent). These plates were incubated at (37^{o}C) for (24hrs.). The inhibition zones caused by the various compounds on the bacteria were examined. The results of the preliminary screening test are listed in Table (3-5). From the data obtained in Table (3-5), it is very clear that compounds $[7]_1$ and $[7]_3$ were found to have the highest activity against ***Pseudo***, and the compounds $[7]_1$, $[7]_2$, $[7]_4$, $[7]_6$ were found to have the highest activity against ***Staphylococcus Aureus*** , while the other compounds showed either slight or no activity. Figures (3-33) and (3-34) show the inhibition zones of the synthesized compounds $[7]_n$ on bacteria.

Table(3-5): Antibacterial activity of tris-Schiff's bases$[7]_n$ compounds.

Compound no. in figure		***Staphylococcus Aureus (G+)***	***Pseudo (G-)***
$[7]_1$	1	++	++
$[7]_2$	2	+	++
$[7]_3$	3	++	+
$[7]_4$	4	-	++
$[7]_5$	5	-	+
$[7]_6$	6	-	++
$[7]_7$	7	-	-
$[7]_8$	8	-	+

Key to symbols:
Highly active = +++ (inhibition zone > 20mm).
Moderately active = ++ (inhibition zone 11-20mm).
Slightly active = + (inhibition zone 5-10mm).
Inactive = - (inhibition zone <5mm).

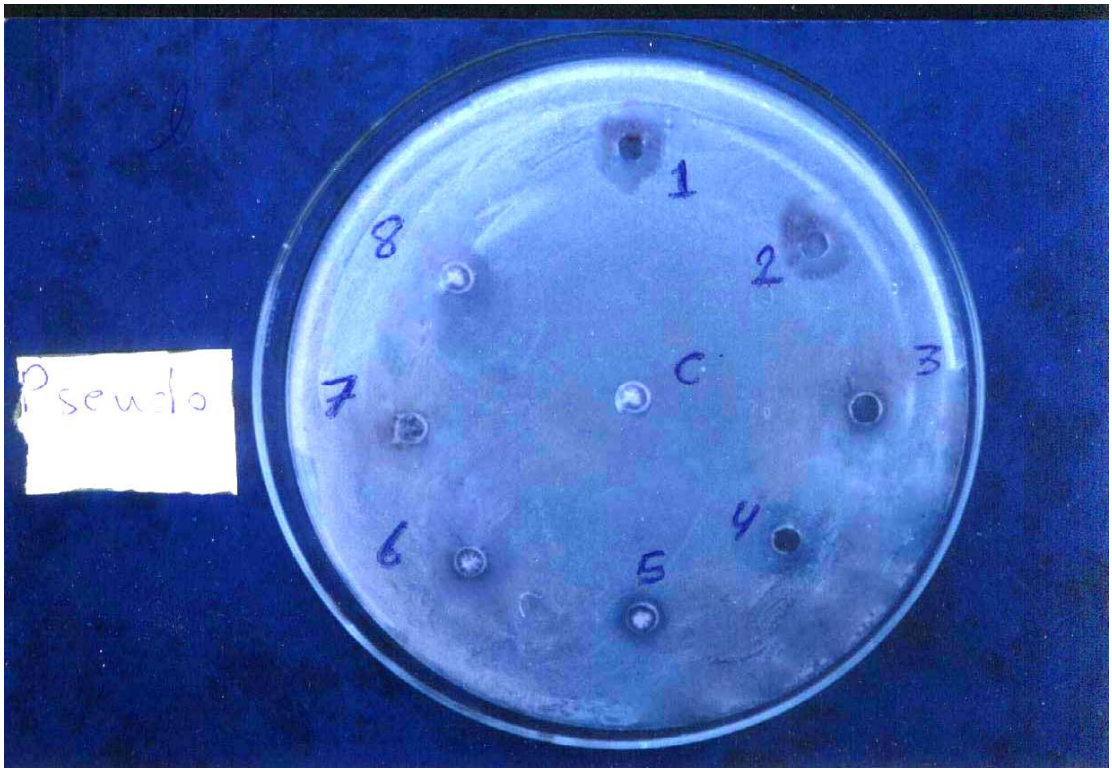


Figure (3-33): Inhibition zones of the prepared compounds on the gram positive bacteria (Pseudo).

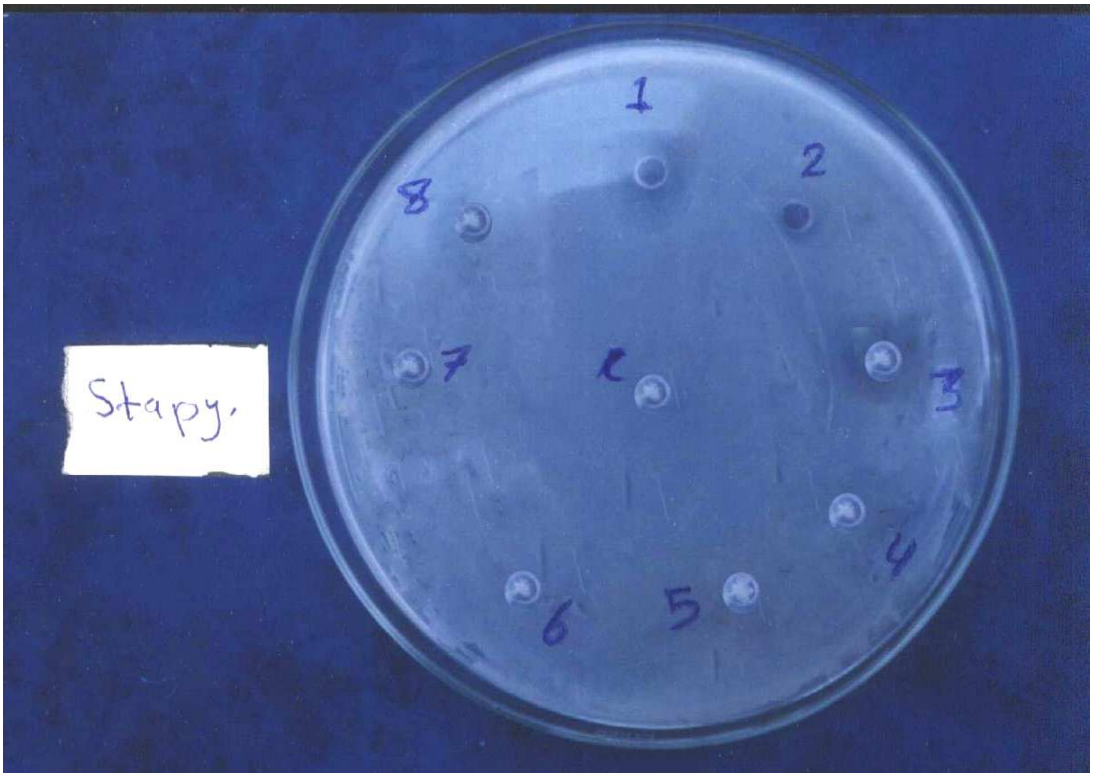
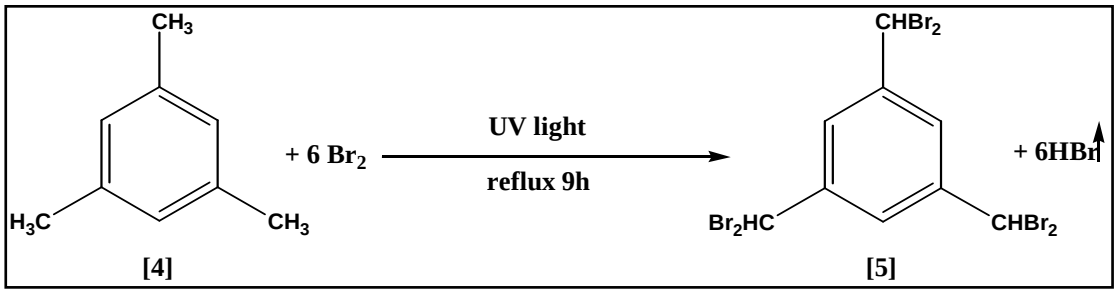


Figure (3-34): Inhibition zones of the prepared compounds on the gram negative bacteria (Staphylococcus Aureus).

3-1-3 preparation of α,α,α',α',α'',α''-hexabromo mesitylene[5]

α,α,α',α',α'',α''-Hexabromomesitylene [5] was prepared by the free radical bromination under a source of UV light of refluxed mesitylene.



The structure of the compound α,α,α',α',α'',α''–hexabromo mesitylene [5] was established by:

1. Melting point. The melting point of the [5] agrees with that reported in the literature[68] which is (183^{o}C).

2. Infrared spectroscopy. The F.T.IR spectrum assures the formation of [5] through the presence of the band at (3050.5 cm^{-1}) attributed to the C-H stretching band of aromatic ring and the peak at (1529 cm^{-1}) of C=C show that the aromatic ring of mesitylene is still found, and (2910.5 cm^{-1}) of C-H aliphatic and the C-Br vibration frequencies appeared at (536.2 cm^{-1}). The F.T.IR spectrum of α,α,α',α',α'',α''-hexabromomesitylene [5] is shown in figure (3-11) and for mesitylene [4] in Figure (3-12).

The proposed mechanism[68] of the reaction is shown in Figure (3-18).

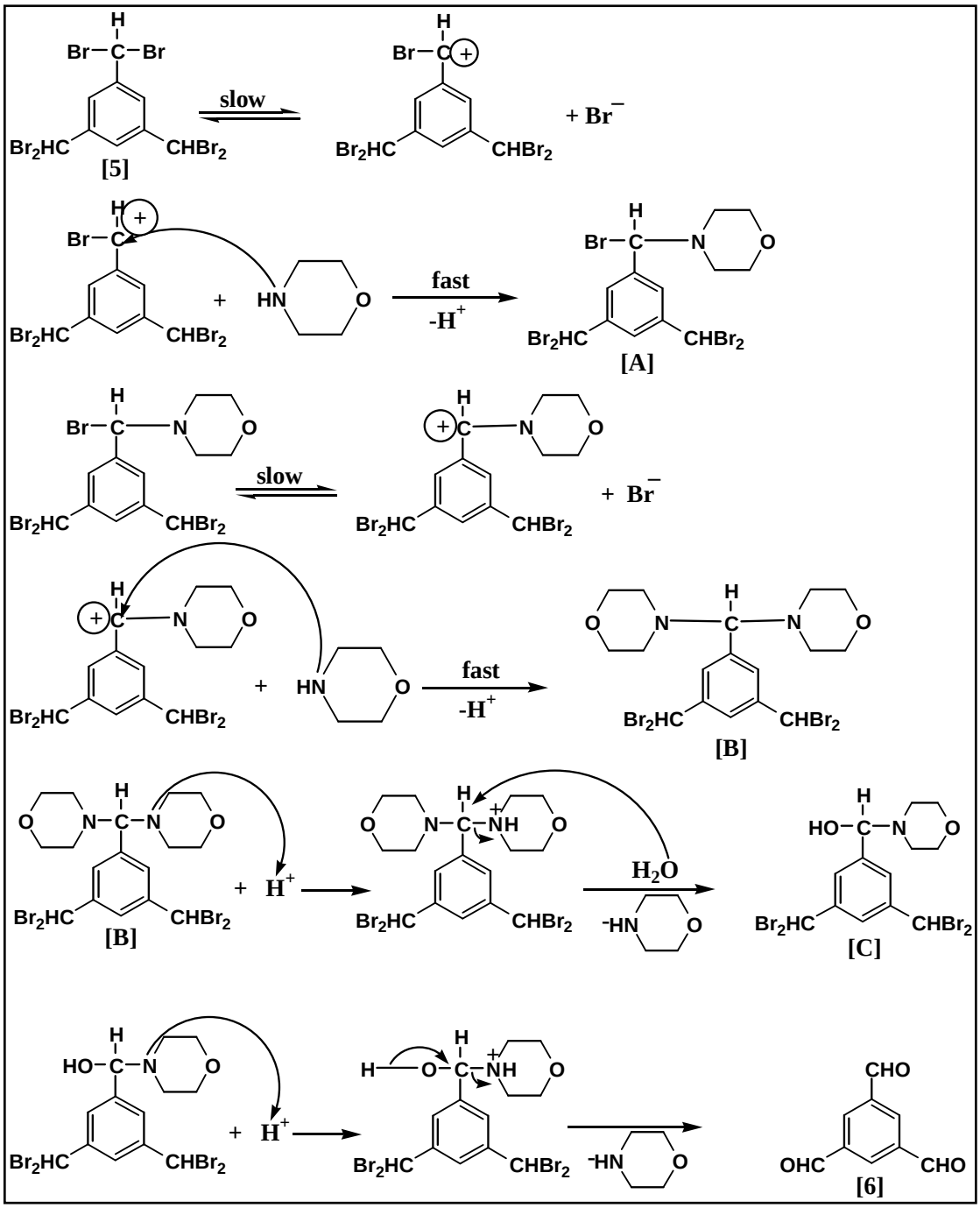
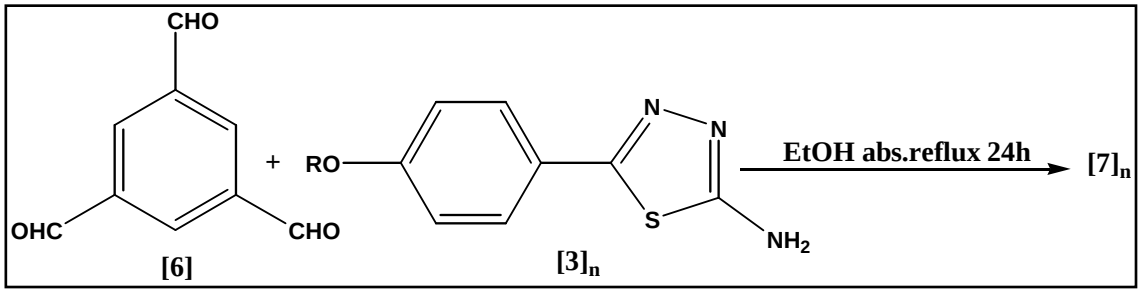


Figure (3-18): Mechanism steps for the preparation of 1,3,5-triformylbenzene [6].

Through the steps of the proposed mechanism[68] there are some evidence assure the affording of the product 1,3,5-trifomyl benzene [6]. The first step takes place on all ($CHBr_2$) groups forming compound [A] through a nucleopholic substitution reaction (S_N1), by the attacking of morpholine to the ($CHBr_2$) group. The same steps are repeated to form the compound [B], compound [C] is probably formed by nucleopholic displacing of morpholine molecule finally, acid catalyzed demorpholation lead to the formation of compound [6].

3-1-5 Synthesis of Schiff's bases derived from 2-amino-5-(4-n-alkoxyphenyl)-1,3,4-thiadiazole $[7]_n$

The Schiff's bases $[7]_n$ were synthesized by refluxing appropriate 2-amino-5-(4-n-alkoxyphenyl)-1,3,4-thiadiazole$[3]_n$ with 1,3,5-triformylbenzene [6] in absolute ethanol.



The proposed mechanism[69] of the reaction is shown in Figure (3-19).

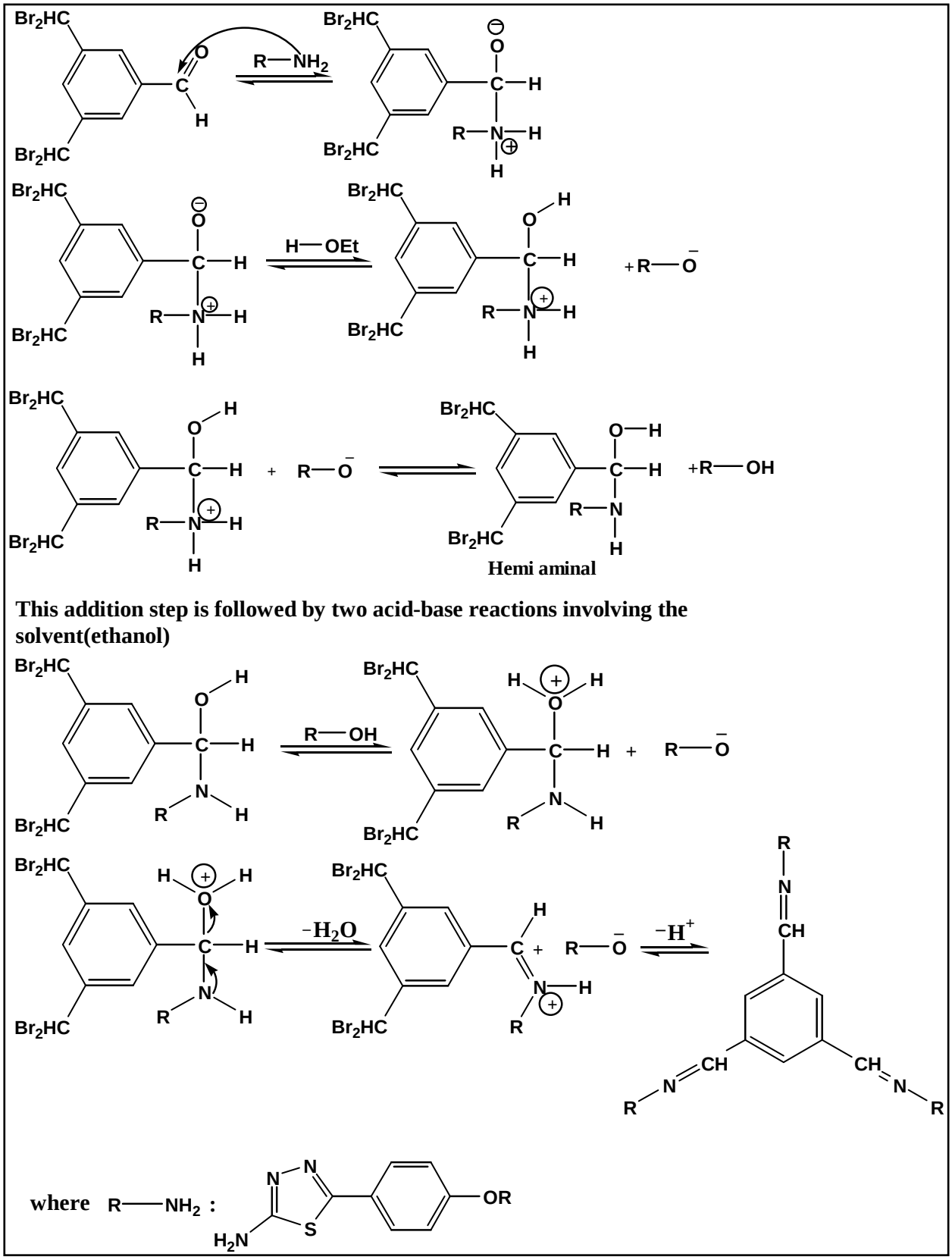


Figure (3-19): Mechanism steps for the synthesis of homologous series $[7]_n$.

The synthesized Schiff's bases $[7]_n$ were characterized using:

1. Melting point: The melting points of the synthesized Schiff's bases are shown in Table (2-4).

2. Infrared spectroscopy: The F.T.IR spectra of Schiff's bases synthesized assures the formation of Schiff's bases through the disappearance of two absorption bands due to NH_2 stretching of amino-thiadiazole, and the disappearance of the absorption band of C=O stretching frequency at (1718.5 cm^{-1}), for 1,3,5-triformyl benzene[6], and the appearance of stretching band at about (1610 cm^{-1}) which was assigned to C=N. The F.T.IR spectroscopic data of $[7]_n$ are shown in Table (3-2). The F.T.IR spectra of compounds $[7]_n$ are illustrated in Figures (3-20) to (3-27).

Table (3-2): The characteristic F.T.IR absorption bands of Schiff's bases$[7]_n$.

Compound No.	R	νC-H aromatic	$\nu_{as,sy}$ C-H aliphatic	νC=N	$\nu_{as,sy}$ C-O-C	γC-H aromatic
$[7]_1$	methyl	3092	2923 2855	1612	1248 1055	831
$[7]_2$	ethyl	3105	2926 2858	1612	1252 1024	831
$[7]_3$	n-propyl	3106	2927 2858	1610	1252 1042	831
$[7]_4$	n-butyl	3092	2923 2857	1613	1248 1055	831.3
$[7]_5$	n-pentyl	3100	2961 2930	1609	1252 1024	834
$[7]_6$	n-hexyl	3050	2934 2864	1607	1252 1024	827
$[7]_7$	n-heptyl	3000	2961 2839	1603	1259 1022	845
$[7]_8$	n-octyl	3100	2934 2868	1605	1246 1040	831.3

3. Ultra-Violet-Visible Spectrophotometery: The electronic spectrum of mesitylene [4], Figure (3-13) displayed band at (261nm) assigned to ($\pi - \pi^*$) transition.

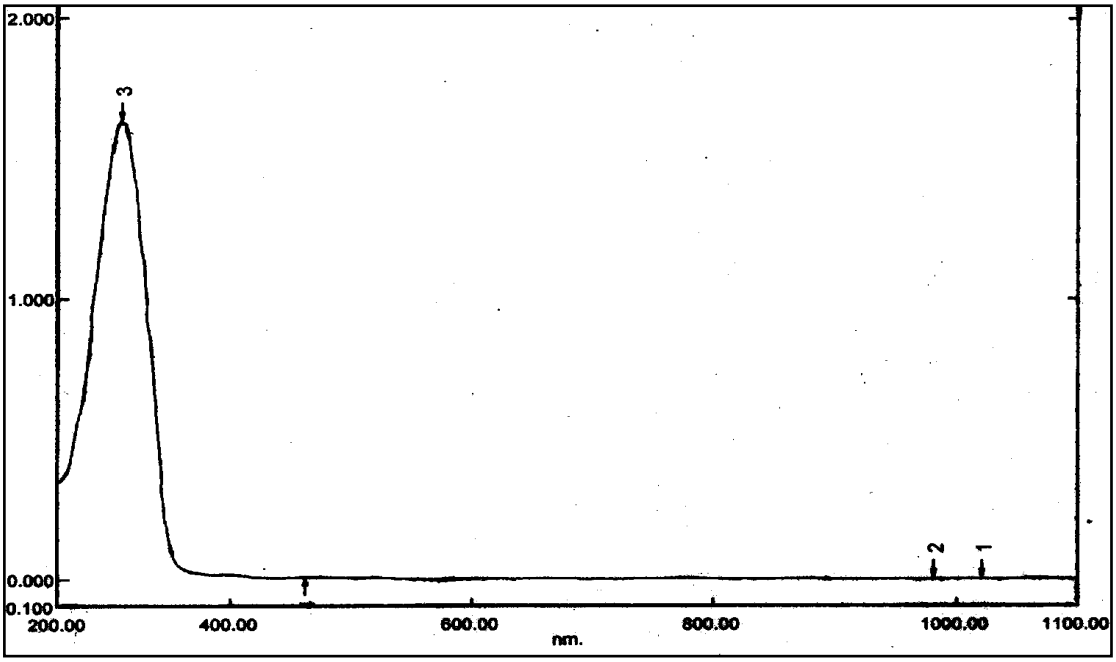
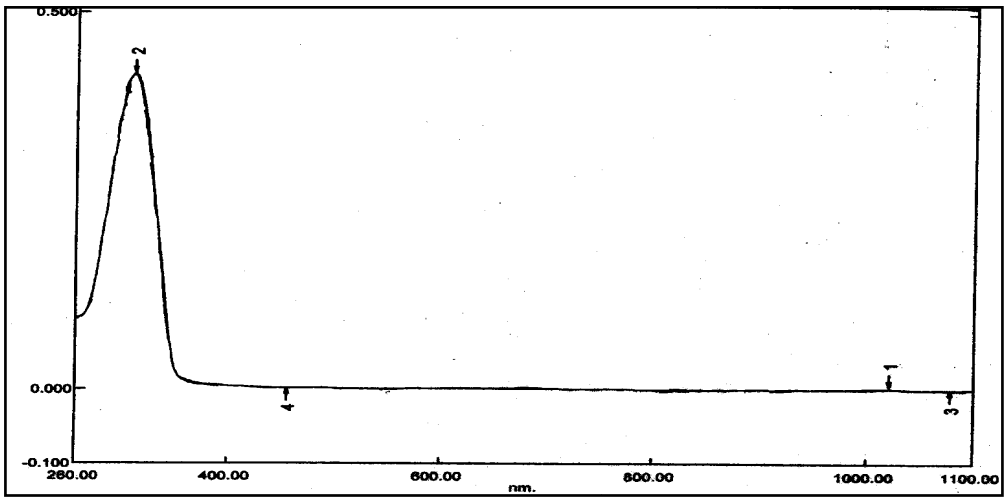


Figure (3-13): Ultraviolet spectrum of mesitylene[4].

The electronic spectrum of α,α,α',α',α",α"-hexabromo mesitylene [5] showed the corresponding transition at (300 nm) which assigned to ($\pi - \pi^*$) transition, the shifting of the ($\pi - \pi^*$) in this compound [5] with transition in compound [4] is because of the presence of the six bromine atoms Figure(3-14).



Figure(3-14):Ultraviolet spectrum of α,α,α',α',α",α"-hexabromomesitylene[5].

The proposed mechanism[68] steps of the reaction is shown in Figure (3-15).

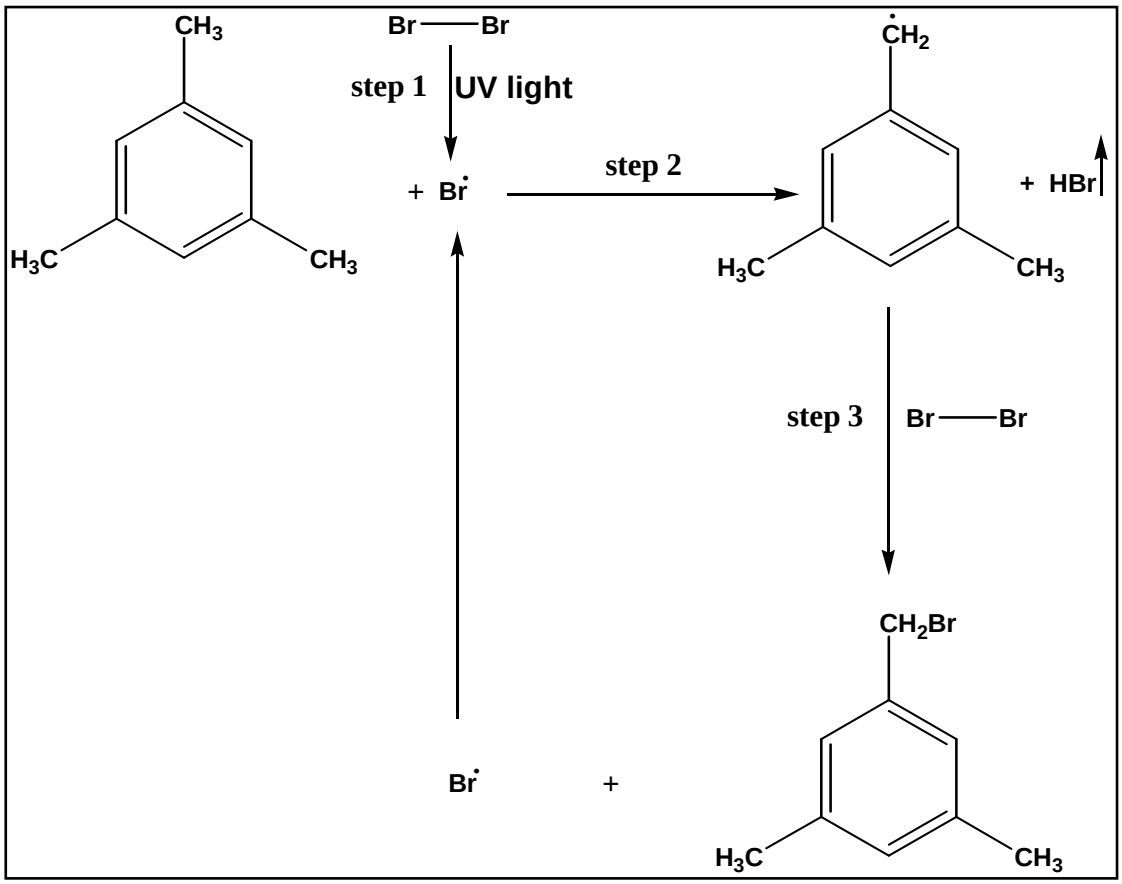
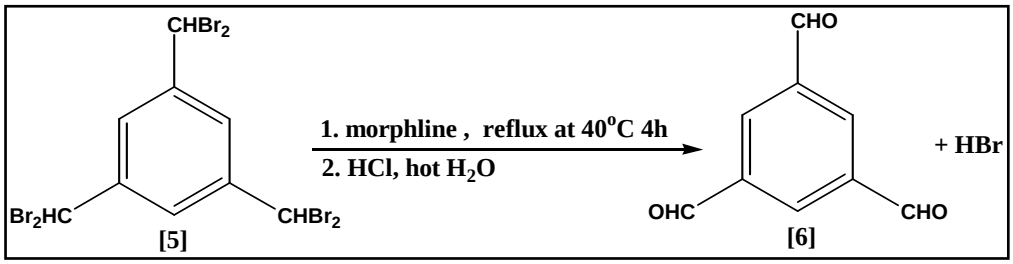


Figure (3-15): Mechanism steps for the preparation of α,α,α',α',α",α"-hexabromomesitylene.

The net displacement occurring at the methyl group on bromination of mesitylene consists (after the photolytic homolysis of bromine step 1) of abstraction from (Ar-CH_2-H) by ($Br^{\cdot}$) Step 2, followed by Br-abstraction from (Br-Br) by (Ar-$CH_2^{\cdot}$) step 3, and the chain reaction is repeated for the other two methyl groups in mesitylene. It's believed that the second displacement of H by ($Br^{\cdot}$) to form (Ar-$CHBr_2$) is markedly influenced by the presence in the substrate polar substituents ($Br^{\cdot}$); this is because ($Br^{\cdot}$), owing to the electronegativity of bromine, is markedly electrophilic and will therefore attack preferentially at sites of higher electron density.

3-1-4 preparation of 1,3,5-triformylbenzene [6]

The 1,3,5-triformylbenzene was prepared through the hydrolysis of α,α,α',α',α",α"-hexabromo mesitylene in anhydrous morpholine, then this solution was hydrolyzed with concentrated hydrochloric acid.



The structure of 1,3,5-triformyl benzene was elucidated using melting point and (UV-Vis. and F.T.IR) spectroscopy. The melting point of 1,3,5-triformylbenzene is (154 ^{o}C) and this melting point agrees very well with that reported in the literature[68] .The electronic spectrum of 1,3,5-triformylbenzene [6], displayed band at (320 nm), assigned to (π – π*) transition, Figure (3-16).

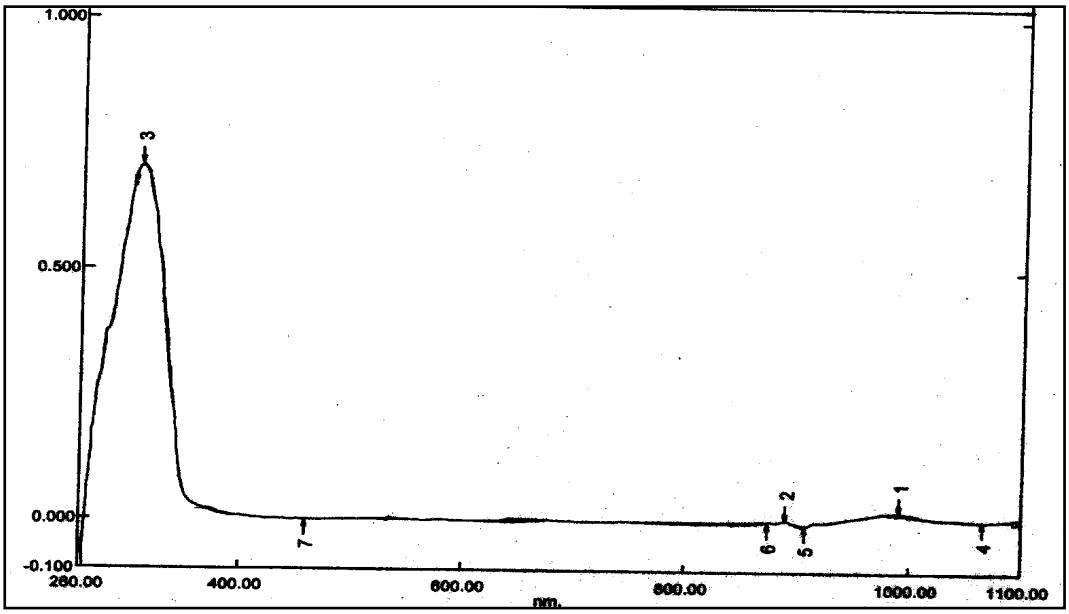


Figure (3-16): Ultraviolet spectrum of 1,3,5-teiformylbenzene [6].

The F.T.IR spectroscopic results assure the formation of 1,3,5-triformyl benzene through the disappearance of the peaks at (2910.5 cm^{-1}) attributed to the C-H aliphatic stretching frequency and the presence of the C=O of aldehyde at (1718.5 cm^{-1}) the peak at (2727.0 cm^{-1}) for C-H stretching of aldehyde, and the peak at (3050.5 cm^{-1}) for the C-H aromatic stretching frequency. All these evidences give us the prompt for the formation of 1,3,5-triformylbenzene. The F.T.IR spectrum of 1,3,5-triformylbenzene is shown in Figure (3-17).