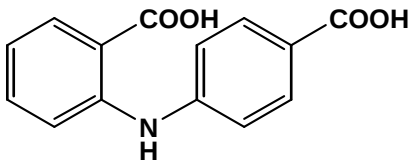
Abstract

The work in this thesis involves three parts.

Part I: Synthesis:

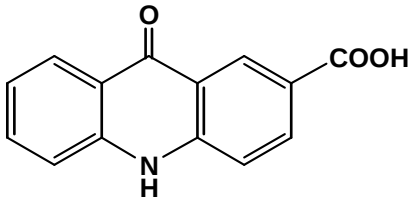
Acridone derivatives containing 1, 3, 4-oxadiazole and 1, 3, 4-thiadiazole rings are synthesized according to the following steps:

Step one: Diphenylamine-2,4`-dicarboxylic acid [1] is obtained in a high yield by refluxing a mixture of 4-aminobenzoic acid and 2-chloro benzoic acid in the presence of catalytic amount of copper oxide.



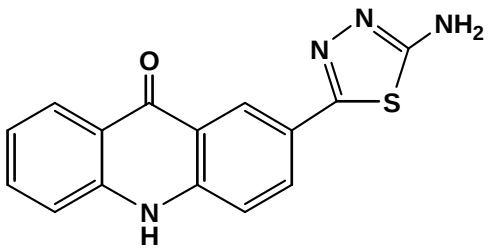
[1]

Step two: 9(10H)-Acridone-2-carboxylic acid [2] is synthesized in ring closure reaction by heating compound [1] in sulfuric acid followed by basic hydrolysis.



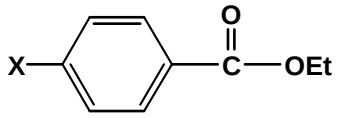
[2]

Step three: Reaction of compound [2] with thiosemicarbazide in the presence of phosphorus oxychloride gave 2-[5-amino-1, 3, 4-thiadiazole-2-yl]-9(10H)-acridone.



[3]

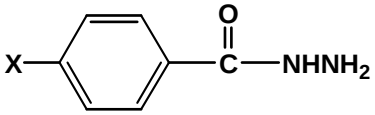
Step four: Ethyl benzoate, ethyl-4-nitrobenzoate, ethyl-4-chlorobenzoate and ethyl-4-hydroxybenzoate were prepared by the usual esterification method through the reaction of the corresponding acid with absolute ethanol in the presence of catalytic amount of sulfuric acid.



X = H , NO_2 , Cl , OH

[4] , [5] , [6] , [7]

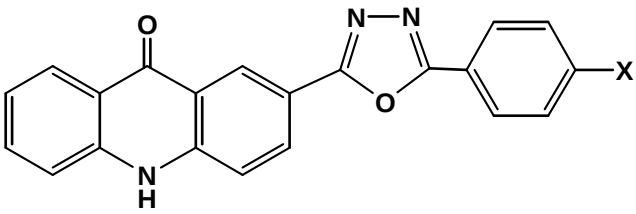
Aryl hydrazines [8-11] were obtained by refluxing of the corresponding esters [4, 5, 6, and 7] and hydrazine hydrate in absolute ethanol.



X = H , NO_2 , Cl , OH

[8] , [9] , [10] , [11]

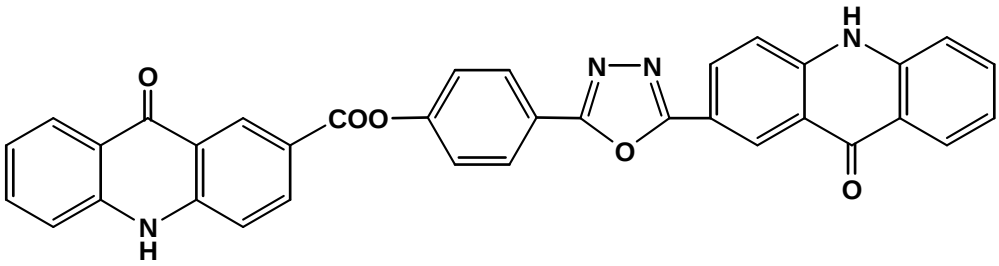
Step five: Three of 2-[5-(4-substituted benzene)-1, 3, 4-oxadiazole-2-yl]-9(10H)-acridone were prepared through the cycloaddition reaction of compound [2] with the appropriate acid hydrazide [8, 9 and 10] in the presence of phosphorus oxychloride.



X = H , NO_2 , Cl

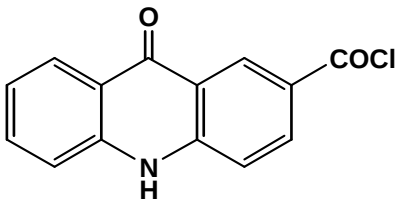
[12],[13],[14]

Step six: The condensation-cyclization reaction of 4-hydroxy benzoyl hydrazine with two equivalents of compound [2] in the presence of phosphorus oxychloride yielded the cyclized product .



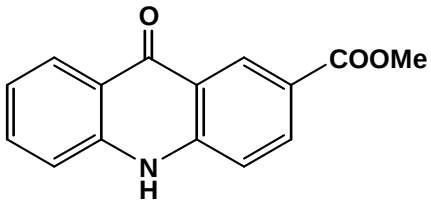
[15]

Step seven The following acid chloride [16] was obtained by the reaction of compound [2] with thionyl chloride.



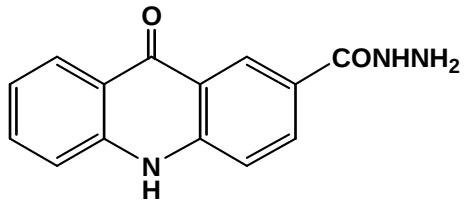
[16]

Esterification of compound [16] with absolute ethanol afforded the following ester [17] .



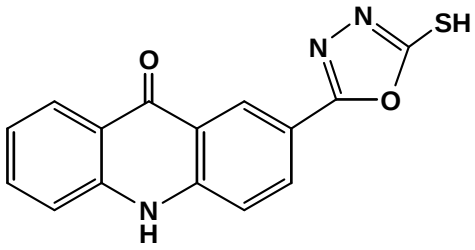
[17]

Thus on hydrazinolysis of this compound yielded the acid hydrazide derivative,[18].



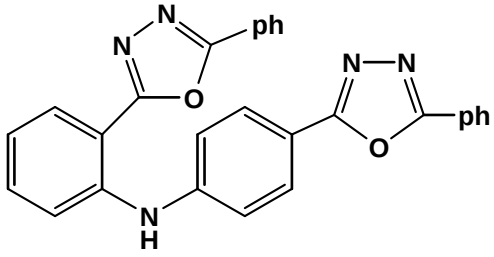
[18]

Compound [18] was subjected to cyclodehydration by means of carbon disulfide in basic medium leading to the formation of 2-[5-thiol-1, 3, 4-oxadiazole-2-yl]-9(10H)-acridone.



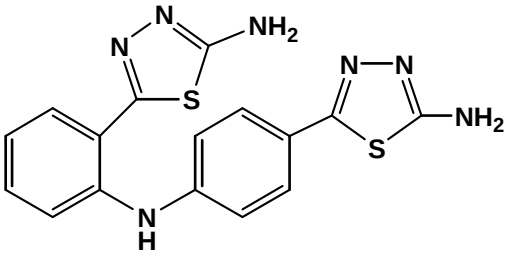
[19]

Step eight: 2,4`-bis [5- (phenyl) -1,3,4-oxadiazole-2-yl] diphenylamine synthesized by reaction compound [1] with two equivalents of benzoyl hydrazine [8] in the presence of phosphorus oxychloride.



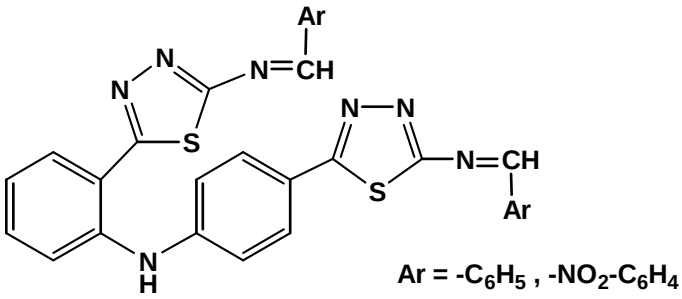
[20]

Step nine: Reaction of compound [1] with two equivalents of thiosemicarbazide in the presence of phosphorus oxychloride gives 2,4`-bis[5-(amino)-1,3,4-thiadiazole-2-yl]diphenylamine.



[21]

Step ten: Finally, two new Schiff bases [22,23] were synthesized by the reaction of compound [21] with two equivalents of benzaldehyde and 4-nitrobenzaldehyde , respectively .



Ar = $-C_6H_5$, $-NO_2-C_6H_4$

[22 , 23]

Part II: Characterization:

Structures of all these synthesized compounds have been confirmed by spectral (FTIR, UV) data. The results were discussed and found in agreement with the suggested structures.

Part III: Biological Activity:

Antibacterial behavior of some of the synthesized compounds against two strains of bacteria has been investigated; the results obtained are listed in Table (3- 2).

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التحصيل الدراسي: بكالوريوس علوم الكيمياء/ الجامعة المستنصرية (٢٠٠٠) و ماجستير من جامعة النهرين/ كلية العلوم/ قسم الكيمياء/ الاختصاص/ (كيمياء عضوية) (٢٠٠٦)

اسم الاطروحة: (تحضير بعض المركبات الحلقية غير المتجانسة الجديدة المحتوية على حلقات ٩(H١٠) - أكريدون ، و دراسة فعاليتها البايولوجية)

SYNTHESIS OF SOME NEW HETEROCYCLIC COMPOUNDS CONTAINING 9(10H)-ACRIDONE,AND STUDYING THEIR BIOLOGICAL ACTIVITY

تاريخ المناقشه: ٢٠٠٦/٧/١٧

العنوان: بغداد/ حي الخليج العربي، محلة/٧٢٧، شارع/٧٧، دار/١٢٤

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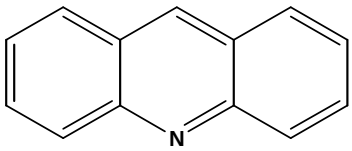
Chapter One

Introduction

1.1 Acridines:

Acridine [1] $C_{13}H_8N$, is a planer dibenzopyridine, resembling anthracene in structure with one of the mesomethine groups replaced by a nitrogen atom.



[1]

Acridine discovered in the crude anthracene fraction of coal-tar and gave it name on account of its irritating action, which causes sneezing and smarting of the skin and eyes. A number of useful basic and vat dyestuffs contain the acridine nucleus and some acridine derivatives have valuable medicinal properties. Acridine is used in the identification of adenosine triphosphate. (1)

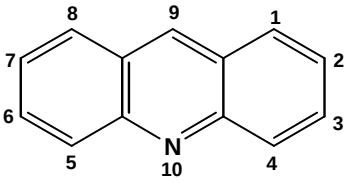
Acridine and its derivatives comprise a very extensive class of compounds that have been investigated by a wide variety of chemical and physical methods. As far as can be ascertained nuclear magnetic resonance (N.M.R.) techniques have been applied in a systematic fashion to a representative selection of acridine derivatives. Among the molecular properties which may be of relevance to an understanding of such mechanisms are the relative electrons densities and tautomerism of the compounds involved both of which may be studied by N.M.R. techniques(2).

Acridines are a well known groups of compounds with a wide variety of biological properties, DNA & RNA intercalating agents, anti carcinogenic, bactericidal, anti malarial, insecticides and anti fungus(3). Moreover the pharmacological activity of these intercalating drugs

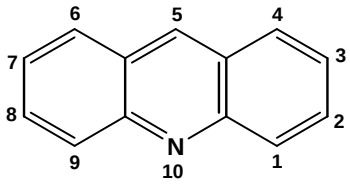
derives from their ability to inhibit the synthesis of nucleic acids by blocking the action of DNA metabolizing proteins [4].

1.1.1 Naming and Numbering [1, 5]:

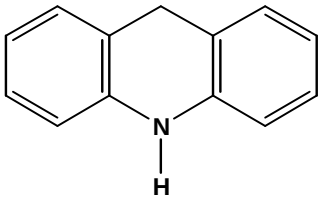
The two systems of numbering are most commonly used as the following:



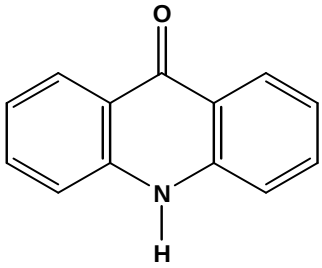
Acridine
American and German system



British system



Acridan

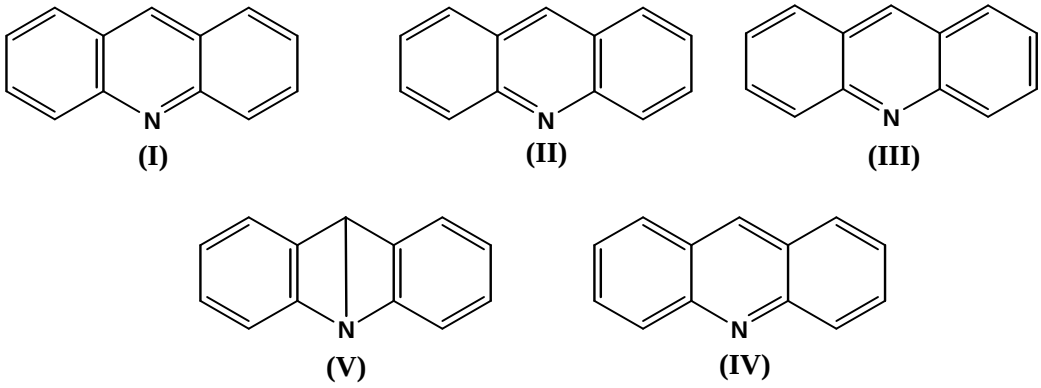


Acridone

The former system seems to be the more favored and has been recommended by the International Union of Pure and Applied Chemistry.

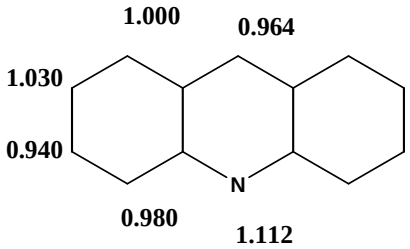
1.1.2 Resonance :[1]

Acridine accordingly is a resonance hybrid with contributing structures (I-IV) along with other structures containing an excited pyridine ring. The most important of these structures are (I) and (II), having two benzenoid rings in contrast to (III) and (IV) have two quinonoid nuclei. The older formula (V) with a Para linkage is no longer used.



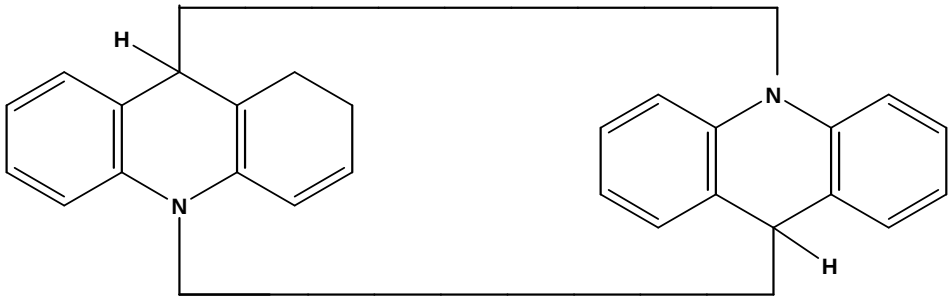
1.1.3 Electron Density Distribution [1, 6]:

More refined analysis by molecular orbital method allocates π-electrons to the ring atoms as shown.



1.1.4 Properties:

The acridines are weak bases Pka 5.60 in water at 20˚C. Acridine, by the action of sunlight undergoes dimerization to pale yellow substances [1] which form salts when reacts with acids such as hydrochlorides, nitrates and picrate, and their tertiary amino structure is shown by the formation of colored quaternary ammonium salts (acridinium compounds) and of N-oxides when treated with per benzoic acid.

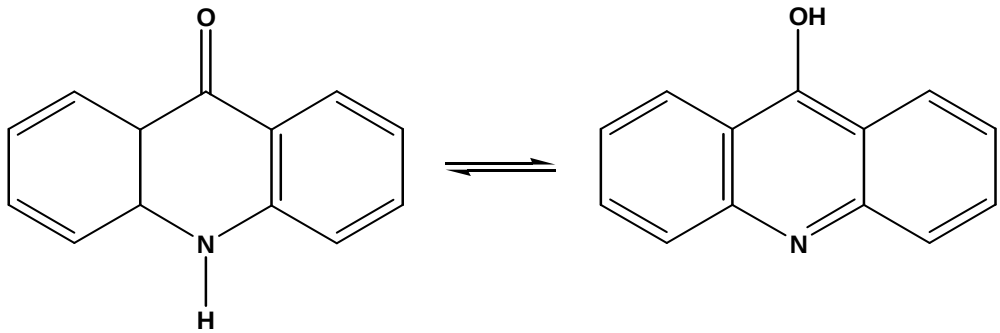


One of the most characteristic properties of the acridines is their fluorescence. Acridine salts in dilute solution exhibit a green fluorescence whilst further dilution results in hydrolysis and the fluorescence changes to the violet fluorescence of free acridine.

1.1.5 Acridones:

$C_{13}H_9NO$, m.p. 354˚C, sublimes and distils with out decomposition. It crystallizes, best from acetic acid and then amyl acetate, in yellow needles and is only very slightly soluble in the common organic solvents. It exhibits in ethanol an intense blue fluorescence.[1] Certain alkaloids such as Acronycine, a pyrano [2,3-a] acridone alkaloids and alkaloids based upon the isomeric [3 ,2-b] acridone ring system[7].

Acridone is very weak base, for although it dissolves in warm hydrochloric acid it separates unchanged when the solution cools[1]. The weakly basic nature of nitrogen atom of the acridone nucleus usually resists to N-alkylation with alkyl halides. However, it can be achieved in the presence of basic condensing agents like sodium amide or sodium hydride [8]. Acridone is tautomeric [formula (I) and (II)] [1].

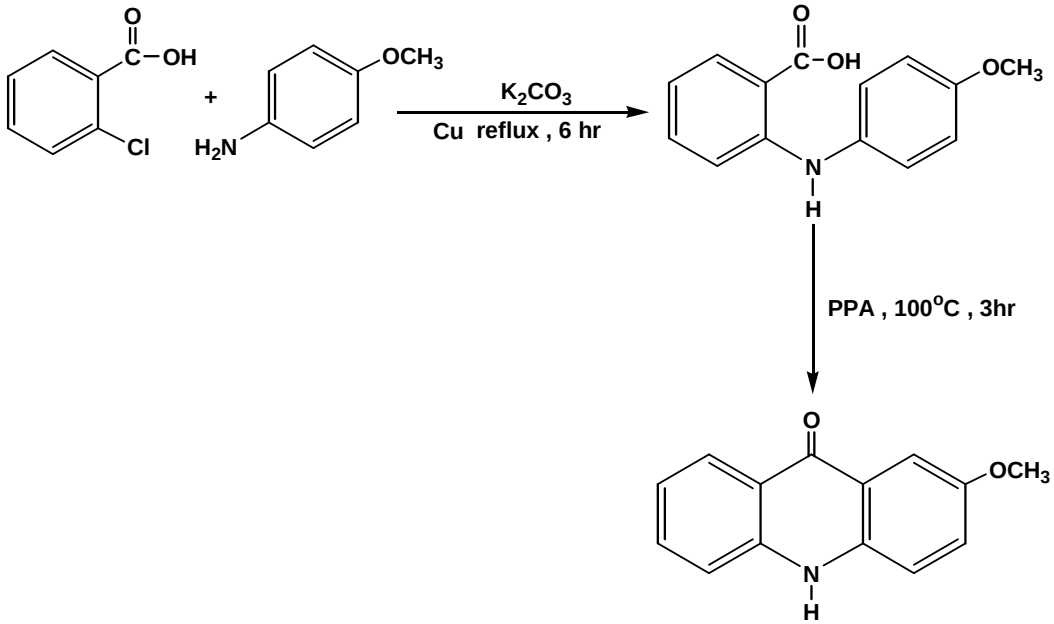


(I) **(II)**

1.2 Synthesis of 9(10H)-Acridone:

1.2.1 By Ullmann condensation:

2-Methoxyacridone was prepared by the condensation of *o*-chlorobenzoic acid and *p*-ansidine[8] in the presence of copper powder and potassium carbonate in iso amyl alcohol, followed by cyclization using sulfuric acid or poly phosphoric acid. Many of acridones were synthesized by ***Ullmann*** type condensation [4, 9-11].



A general method for the preparation of a bi-aryl consists of the condensation of two molecules of an aromatic halide in the presence of a metallic agent, with elimination of metal halide [12]:

$$RX + R`X + M \longrightarrow RR` + MX_2$$

Ullmann condensations (loosely defined as copper catalyzed nucleophilic aromatic substitutions on inactivated aryl halides) are classic examples:

$$NuH + ArX \xrightarrow{\text{"Cu" / base}} ArNu + HX$$

NuH = $ArNH_2$, Ar_2NH , ArOH , ArSH , $ArCO_2H$
$ArC{\equiv}CH$, ROH , RSH , H_2O , HX , HCN , etc.
X = Cl, Br , I
"Cu" = Cu metal , oxides , salts , alloys , complexes , etc.
base = K_2CO_3 , KOH , NaH , etc., or preformed Nu

These reactions have been catalyzed by a variety of forms of copper, including the metal itself (in various forms: copper, bronze, freshly precipitated, "activated", etc.), salts or complexes of cuprous or cupric ion, and insoluble oxides. For reasons which have not been well understood, one form of catalyst good for a certain reaction will be poor for another, and in general there is a wide variability in the rate and yield of ***Ullmann*** condensations using copper metal from different sources[13].The role of using copper as catalyst can be illustrated in the following figure .

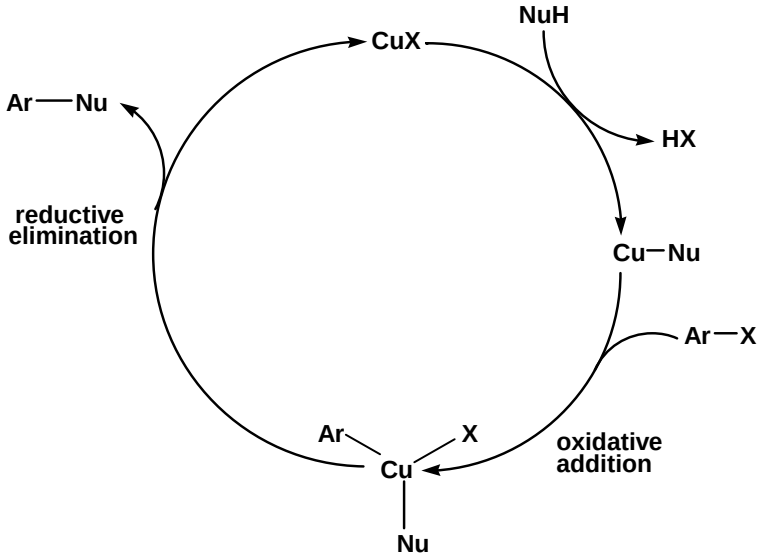


Figure (1-1): role of copper in the *Ullmann* condensation [14].

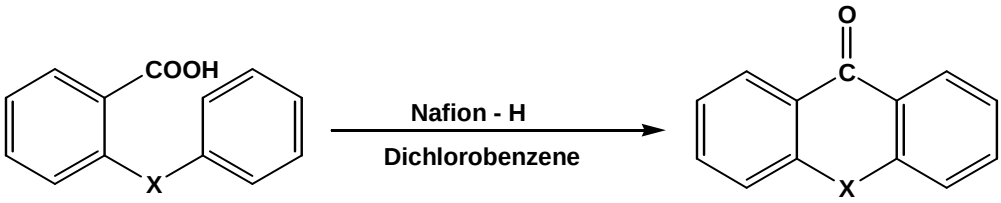
The ***Ullmann*** reaction has enjoyed continued use; for example, in the elucidation of structure of natural products and in the mechanisms of organic reactions, in the synthesis of biologically active substances, and in the preparation of symmetrical and unsymmetrical biaryls, biphenyls[12], and effect ring closures are discussed [15].

The activating effect of strongly electronegative substituents such as: $-NO_2$, -COOH, $-N(CH_3)_2$, -CN, $-SO_3H$, -CHO, -COR and –X groups is predominantly at ortho and para positions, thus resonance involving electron withdrawing groups strengthens the activation toward nucleophilic substitution caused by inductive effect[16]. For example, o-iodnitrobenzene is one of the most reactive aryl halides known in the ***Ullmann*** reaction. The result of study of the ***Ullmann*** reaction of the o-, m- and p-chloro, bromo and iodo nitrobenzene are presented.

The order of reactivity of halogens is I > Br > Cl, and the activating effect of the nitro group is o > p > m [12].

1.2.2 From Nafion-H catalyzed Intramolecular cyclization [17]:

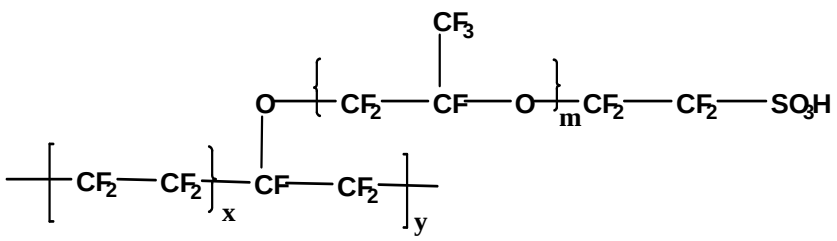
Aromatic hydrocarbons undergo direct aroylation with aryl carboxylic acid over ***Nafion***-H, per fluorinated resin sulfonic acid catalyst to give benzophenone and their derivatives .



X= -NH- , - O - , - CO - ,
$- CH_2 -$, $- CH_2CH_2 -$, etc .

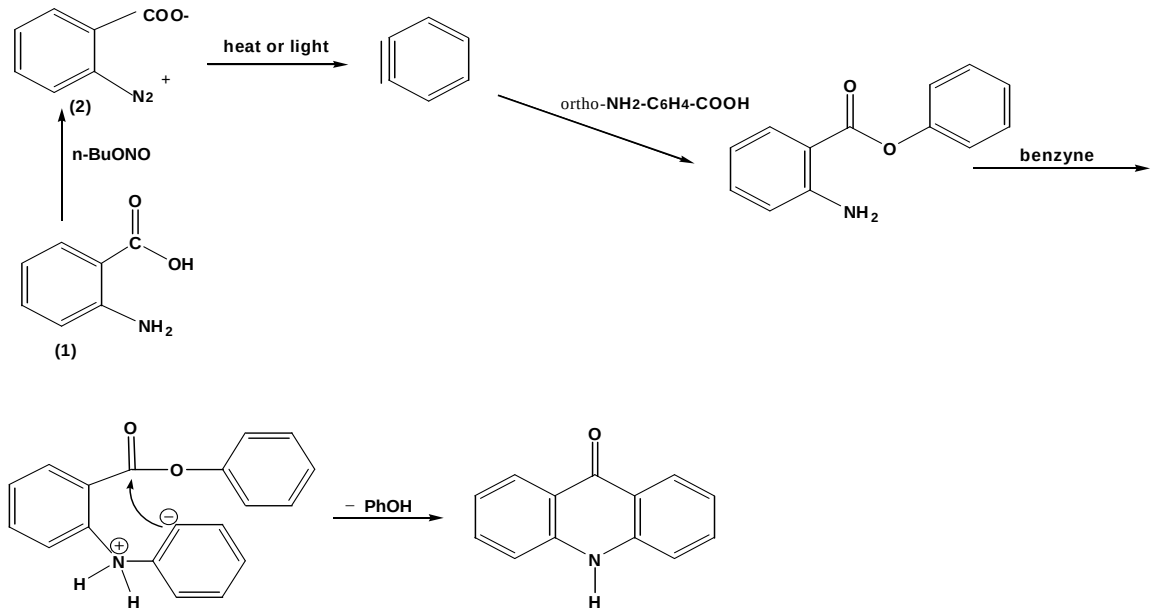
(82 - 95 %)

The structure of Nafion-H (solid Resin) per floroalkane sulfonic acid is:



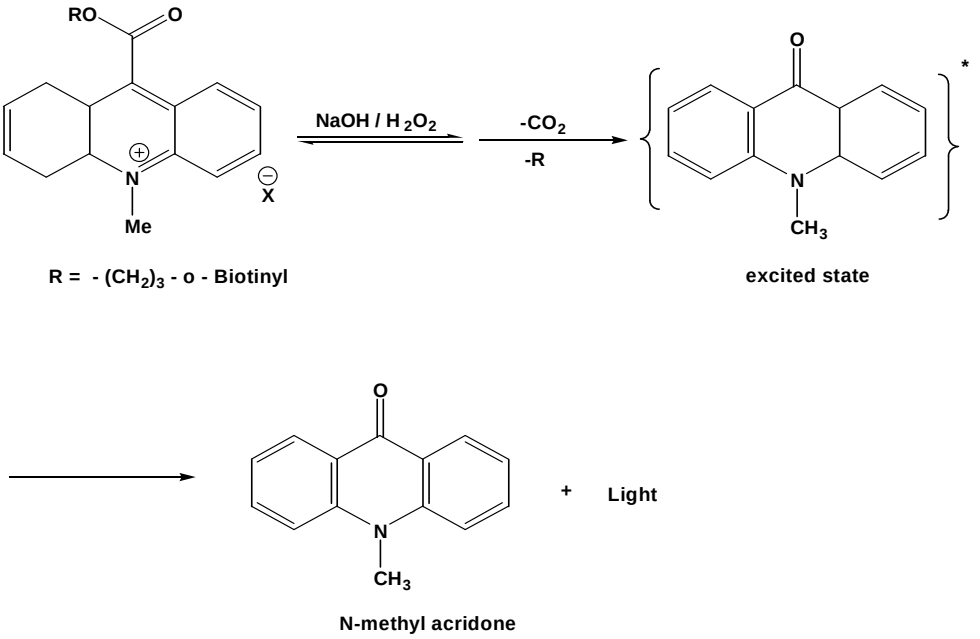
1.2.3 Diazotation of Anthraanilic acid [18]:

Benzyne generation by thermal or photolytic decomposition of benzenediazonium-2-carboxylate (2) which is obtainable from diazotization of anthranilic acid (1) with the n-butyl nitrite .



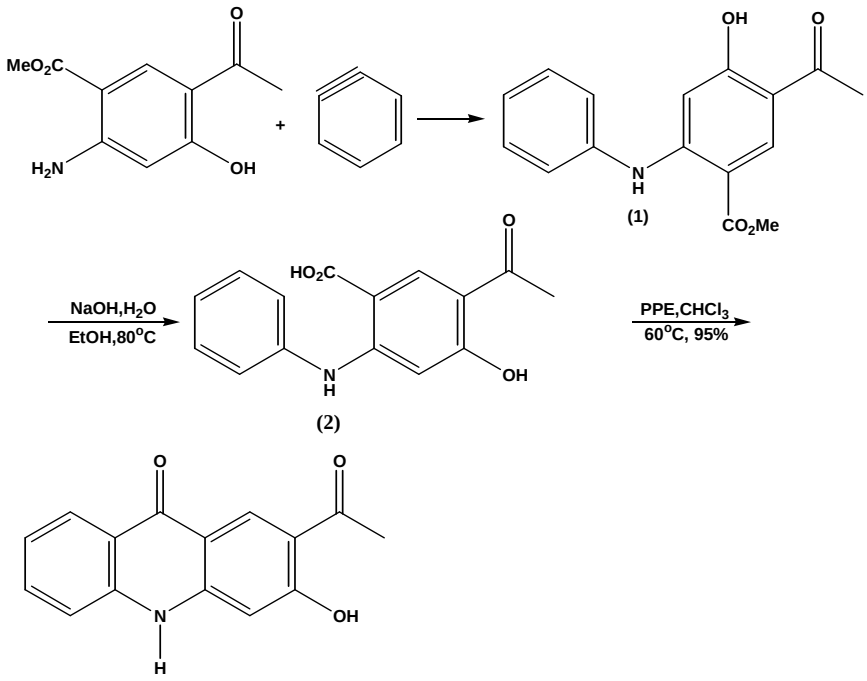
1.2.4 Chemiluminescence's reactions of Acridinium esters [19]:

The steps of the chemiluminescence's reaction of acridinium esters is provided by the injection of trigger solutions which causes the rapid chemiluminescent reaction to take place with emission is centered on 430 nm.



1.2.5 Regioselective addition of Aniline derivatives to benzyne [7]:

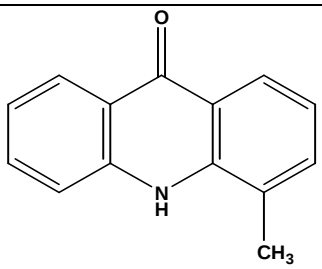
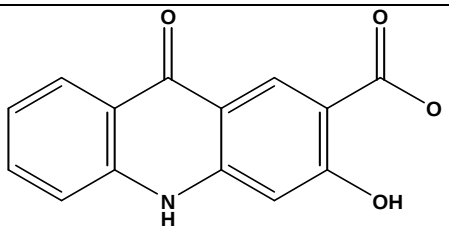
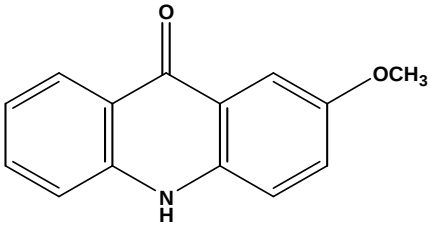
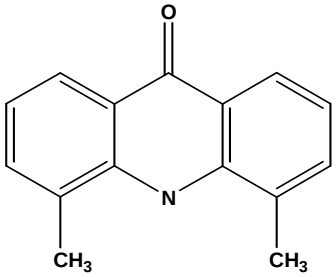
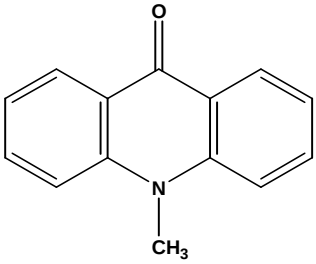
The regioselective addition of the known aniline derivatives to benzyne, then alkaline hydrolysis of the ester (1) followed by the addition of PPE (poly phosphate ester) mediated ring closure of the acid (2) to produce acridone derivatives in high yield .

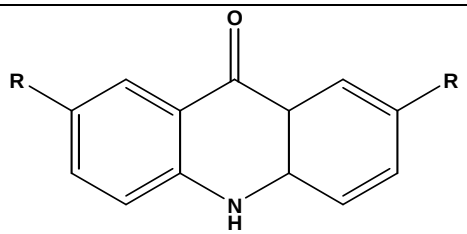
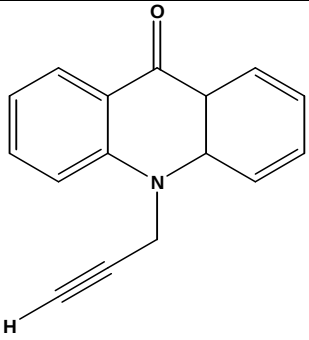
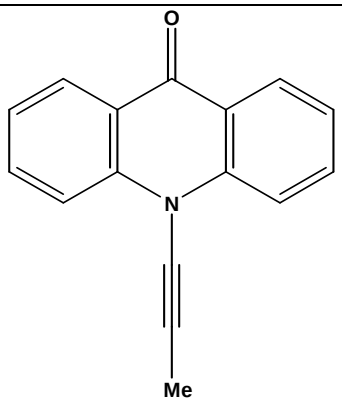
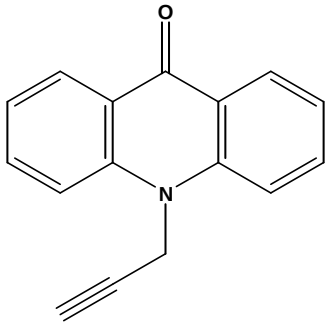
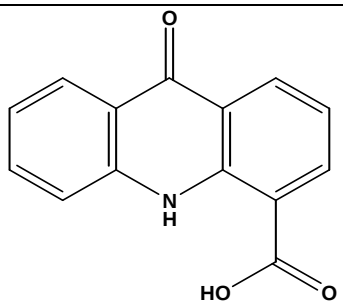


1.3 Uses of 9(10H)- Acridone:

New structures and uses of acridone derivatives are periodically reviewed as shown in table (1-1);

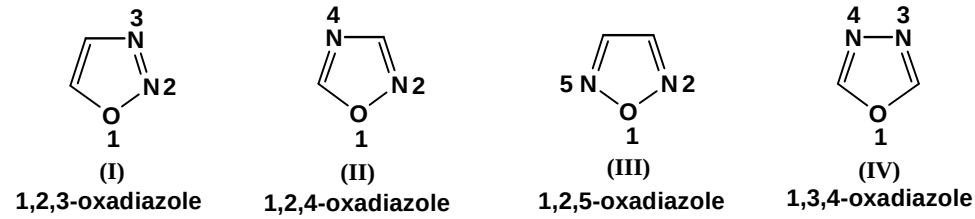
Table (1-1): Structures and uses of acridone derivatives .

NO	Acridone derivatives	Uses	Ref
1		**Synthesis of new Bis- and Tetra-acridines as therapeutic agents**	**4**
2		**Convenient and regioselective synthetic sequence for preparation of acronycine, a pyrano[2,3-a] acridones.**	**7**
3		**Synthesis of 2- methoxy N ^{10}- substituted acridones needed to reverse vinblastine resistance in multidrug resistant cancer cell.**	**8**
4		**Synthesis of acridine-based DNA bis-intercalating agents.**	**11**
5		**Light emitting species in the Chemiluminescence's reaction sequence of acridinium ester.**	**19**

6		**As a precursor to the synthesis of a new class of 'molecular tweezers'**	**20**
7		**The synthesis of a new series of fluorescent dinuclear and trinuclear metal complexes bearing acridone.**	**21**
8		**A highly Stereoselective of acrylic acid derivatives and 1, 3-Dienes using electron deficient variant of ynamine.**	**22**
9		**Synthesis of novel ynamides and allenamides.**	**23**
10		**Solid-phase synthesis of acridine-peptide conjugates.**	**24**

1.4 Oxadiazoles:

There are four isomeric types of oxadiazoles : 1,2,3-oxadiazole (I); 1,2,4-oxadiazole (II); 1,2,5-oxadiazole (III) and 1,3,4-oxadiazole (IV), as shown below[25].



1.4.1 1, 3, 4-Oxadiazoles:

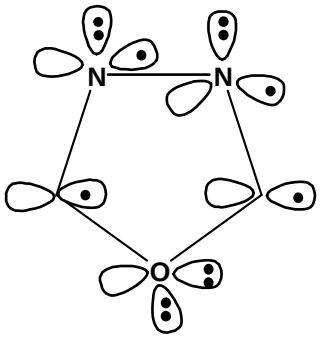


Figure (1-2): Orbital structure of 1, 3, 4-oxadiazole.

1, 3, 4-Oxadiazole ring has three pairs of delocalized π-electrons. Two of the pairs are shown as π-bonds through the overlapping of un hybridized *p*-orbital of nitrogen atom and one pair of non-bonding electrons on the hetero oxygen atom . 1, 3, 4-Oxadiazole has three pairs of non-bonding electrons that are not part of the π-cloud. These electrons are in sp^2 perpendicular to the *p*-orbital.

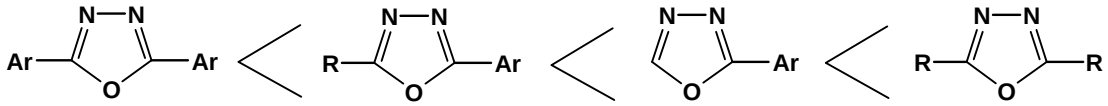
The growing literature in the past years demonstrates that 1,3,4-oxadiazoles are becoming of great interest, stems mainly from their wide range of applications.

The 1,3,4-oxadiazoles have been reported to be biologically versatile compounds having bactericidal[26], fungicidal[27], herbicidal[28], analgesic[29], hypoglycemic[30], anti-inflammatory[31] and transqualizing

agents[32,33]. More over, various 1, 3, 4-oxadiazoles are suitable for uses in photography [34], scintillation materials, dyestuffs industry [35], corrosion inhibitors [36] and as thermal stabilizers for rigid polyvinyl chloride [34].

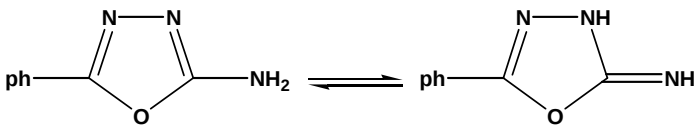
In agriculture, 1, 3, 4-oxadiazole derivatives are used as insecticides [37], in combating unwanted vegetation [38] and in preventing nitrification of the soil [39].

1, 3, 4-oxadiazole is the most thermally stable isomer and its stability is controlled in general by the electron density at the C-2 and C-5 atoms, which is largely dependent on the substituents. The stability of 1, 3, 4-oxadiazoles is especially enhanced by alkyl and aryl substitution on positions 2 and 5[40]. It has been established that the susceptibility to hydrolysis increases with increasing solubility, which is in the order given below [41]:



Oxadiazoles, like all other compounds containing (-NH-CH=X) moiety (X= N, O, S) exist in two tautomeric forms [42]:

It has established by ultra-violet, fluorescence and IR spectra that 2-amino-5-phenyl-1, 3, 4-oxadiazole exists in the tautomeric equilibrium [43].

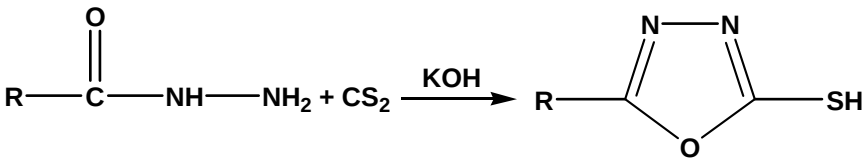


1.4.2 Synthesis of 1, 3, 4-Oxadiazoles:

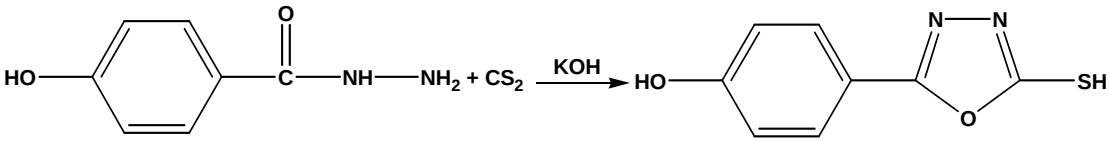
Several methods have been used to synthesize 1, 3, 4-oxadiazole the most commonly used:

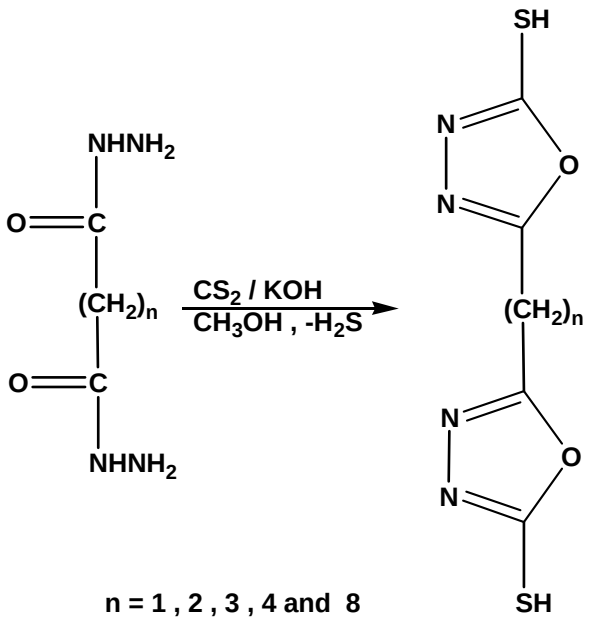
1.4.2.a Reaction of Acid hydrazide with Carbon disulfide:

The oxadiazole ring is obtained by following the general method of ***Young*** and ***Wood*** [42] i.e., by refluxing an ethanolic mixture of the appropriate acid hydrazide, carbon disulfide, and KOH to give 2-mercapto-1, 3, 4-oxadiazole, the general reaction is:



For example [50, 51].

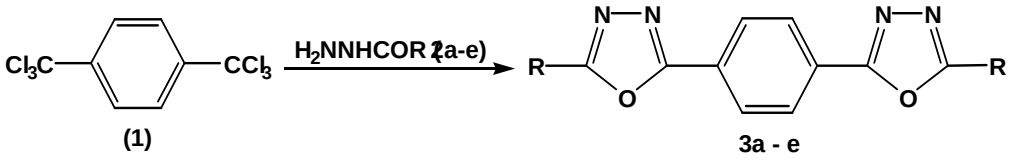




n = 1 , 2 , 3 , 4 and 8

1.4.2.b Reaction of Bis(Trichloromethyl)benzene with Acyl hydrazine:

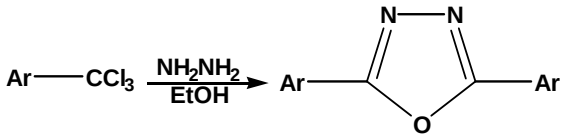
1, 4-Phenylene-bis-1, 3, 4-oxadiazoles (3) were prepared through reaction of bis (trichloromethyl) benzene with acyl hydrazines (2) were shown to be very simple route [45].



a R = ph , b R = 2-OHC$_6$H$_4$, c R = 4-O$_2$NC$_6$H$_4$
d R =4-C$_5$H$_4$N , e R =H

1.4.2.c Reaction Of Benztrichloride and its Derivatives With Hydrazine:

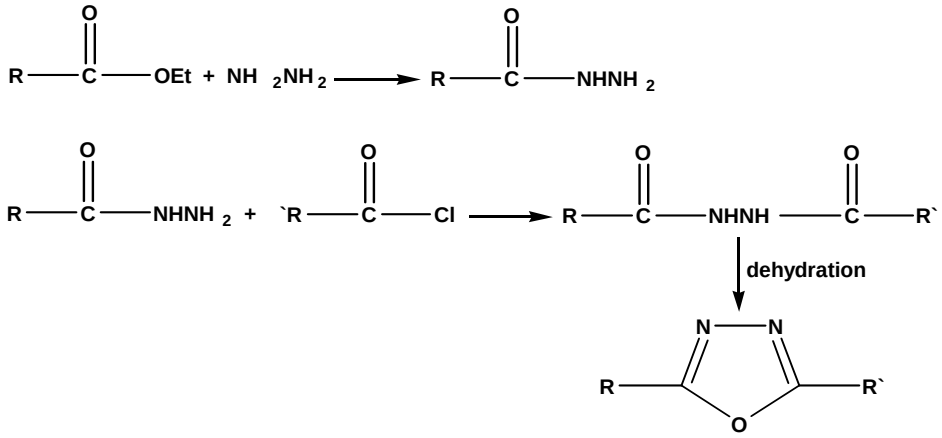
In alcohols as solvents benzotrichloride (1a) and its substituted derivatives 4-chlorobenzotrichloride (1b), 3-bromobenzotrichloride (1c), reacts with hydrazine to give 2,5-disubstituted-1,3,4-oxadiazoles(2a-2c) [45].



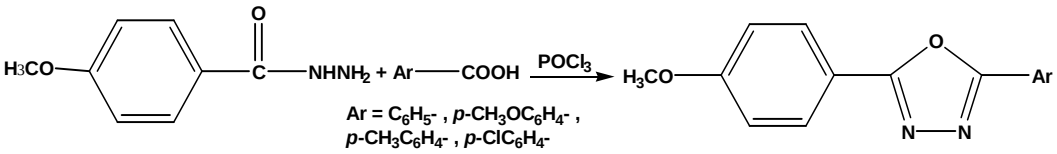
a) Ar = C$_6$H$_5$, b) Ar = 4-ClC$_6$H$_5$, c) Ar =3-Br-C$_6$H$_5$

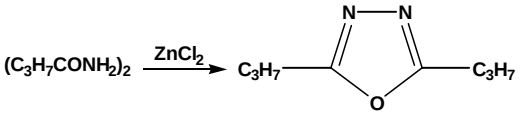
1.4.2.d Dehydration Of Di-acid hydrazide:

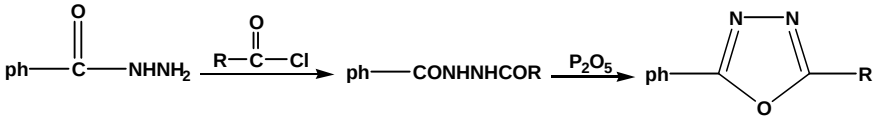
Acid hydrazides are usually prepared from the reaction of the corresponding esters with hydrazine hydrate. These hydrazides are converted to diacid hydrazides through their reaction with acyl chlorides. Dehydration of the di-acid hydrazide afforded 1, 3, 4-oxadiazoles [46].



The conversion of N,N`-diacid hydrazide to 2,5-dialkyl(aryl)-1,3,4-oxadiazole studied by using a different dehydrating agents, such as phosphorus oxychloride[47], phosphorus pentaoxide[48], zinc chloride, organic acid anhydride[49], thionyl chloride[50], phosphorus pentachloride[51]. The following examples illustrate the application of different dehydrating agents:

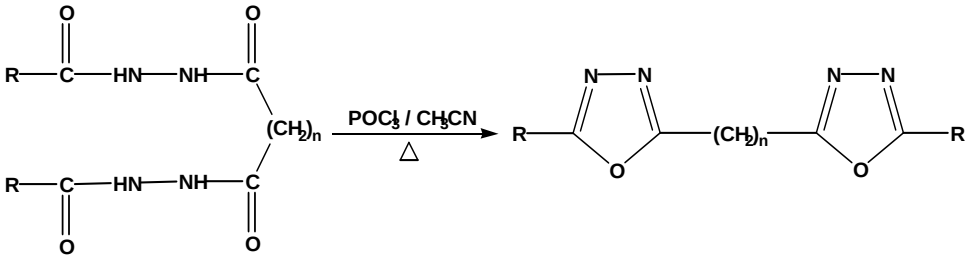






R = ethyl , hexyl

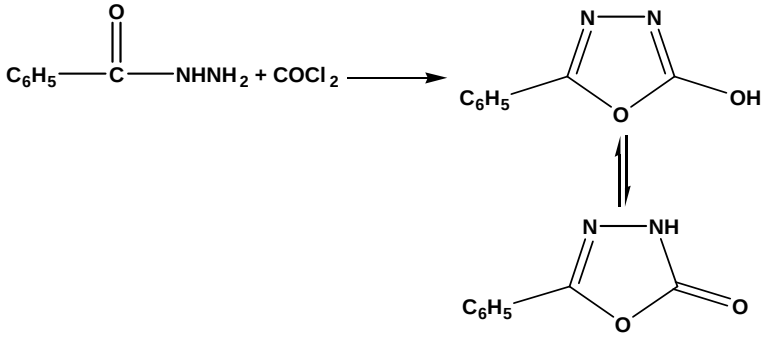
The most effective dehydrating agent used for this purpose was found to be phosphorus oxychloride in acetonitrile[52].



n =1 , 3 , 4 and 8 R = aryl , alkyl

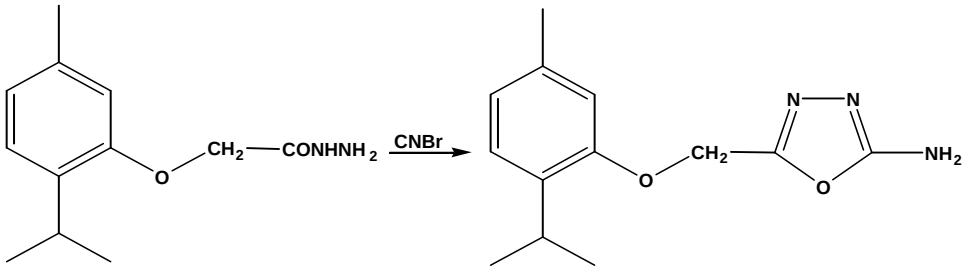
1.4.2.e Reaction Of Acid hydrazide with Phosgene:

Hydroxy-1, 3, 4-oxadiazoles or 3-substituted-1, 3, 4-oxadiazole-2-one are obtained from the reaction of the acid hydrazide with phosgene[53].



1.4.2.f Reaction of Acid hydrazide with Cyanogenbromide:

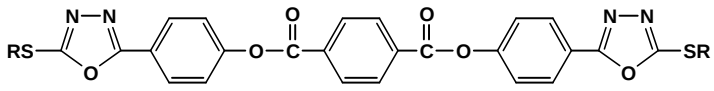
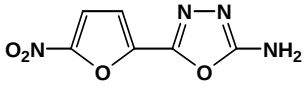
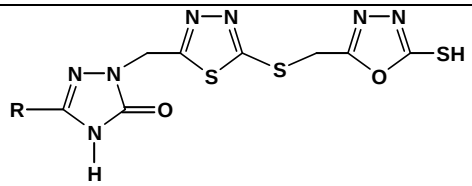
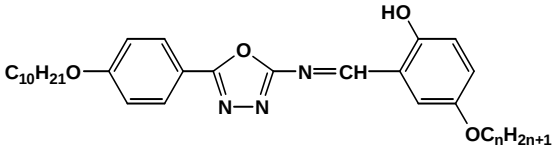
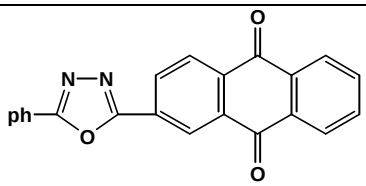
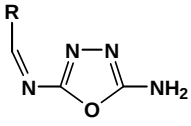
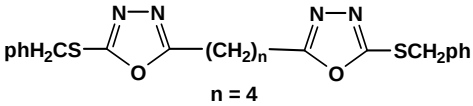
2-Amino-5-(2-isopropyl-5-methylphenoxymethyl)-1,3,4-oxadiazole was synthesized from reaction of acid hydrazide (1) with cyanogenbromide according to this method [54].



(1)

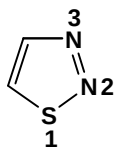
The following table shows further examples of using these methods

Table (1-2): Structure and method for the synthesis of some 1,3,4-oxadiazole derivatives.

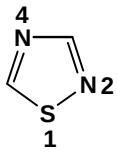
No.	Structure	Method	Ref.
1		**Reaction of acid hydrazide with carbon disulfide**	**55**
2		**Reaction of acid hydrazide with cyanogen bromide**	**56**
3		**Reaction of acid hydrazide with carbon disulfide**	**57**
4		**Dehydration of di-acid hydrazide**	**58**
5		**Dehydration of acid hydrazide**	**59**
6		**Reaction of acid hydrazide with cyanogen bromide**	**60**
7		**Reaction of acid hydrazide with carbon disulfide**	**61**

1.5 Thiadiazoles:

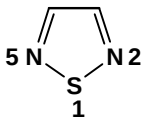
Compounds having five membered ring containing one sulfur and two nitrogen atoms are called thiadiazole. There are four classes of thiadiazoles corresponding to the four classes of oxadiazoles[62].



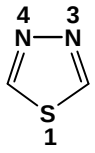
1,2,3-thiadiazole



1,2,4-thiadiazole



1,2,5-thiadiazole



1,3,4-thiadiazole

1.5.1 1, 3, 4-Thiadiazoles:

There are four pairs of non bonding electrons, two pairs on sulfur atom and two pairs on the two nitrogen atoms. These electrons are in sp^2 hybridized orbital that is perpendicular to the *p*-orbital. Since 1,3,4-thiadiazoles are cyclic planner molecules with three pairs of delocalized π electrons they fulfills the criteria for aromatic. ***Back*** et. al[63]., made a careful analysis of the microwave spectrum of 1,3,4-thiadiazole. They could determine the structure of molecule , figure (1-3).

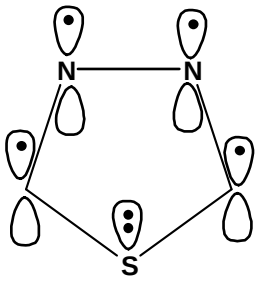
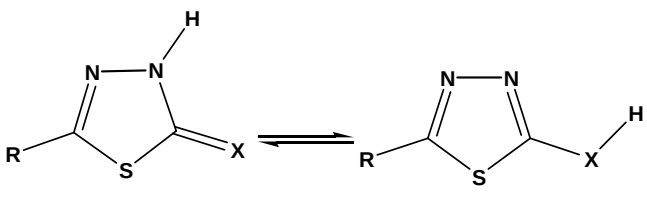


Figure (1-3): Orbital structure of 1, 3, 4-thiadiazole.

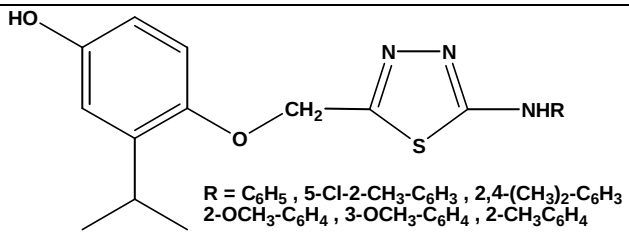
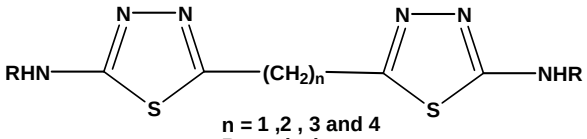
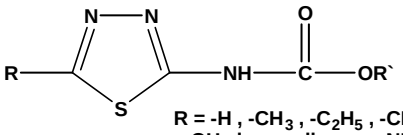
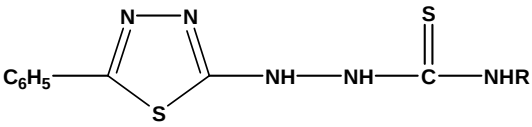
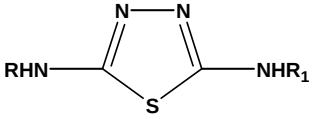
Potential 2-hydroxy and 2-mercapto-1, 3, 4-thiadiazole have been examined both by infrared and by ultraviolet spectra in solid state. These compounds exist mainly in the 2-oxo and 2-thione tautomeric form of thiadiazole derivatives respectively [64].



X = NH , O , S

The 1, 3, 4-thiadiazole nucleus which incorporates on N-C-S linkage exhibits a large number of biological activities [65], and the Table (1-3) shows some examples of these compounds.

Table (1-3): Some substitutes 1, 3, 4-thiadiazoles having biological activities.

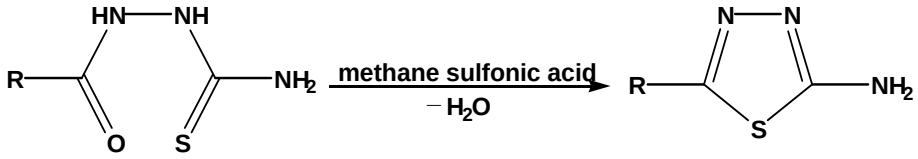
Structure	Ref.
 R = C_6H_5 , 5-Cl-2-CH_3-C_6H_3 , 2,4-$(CH_3)_2$-C_6H_3 2-OCH_3-C_6H_4 , 3-OCH_3-C_6H_4 , 2-$CH_3C_6H_4$	66
 n = 1 ,2 , 3 and 4 R = anisyl	67
 R = -H , -CH_3 , -C_2H_5 , -CF_3 R` = OH , lower alkoxy or NH_2	68
	69
 R = R_1 = alkyl or alkyl halides	70

Substituted thiadiazoles have been reported display diverse applications as oxidation inhibitors, cyanine dyes and metal complexing agent too [71].

1.6 Synthesis of 1, 3, 4-Thiadiazole:

1.6.1 Reaction of Acyl thiosemicarbazide with Methane sulfonic acid:

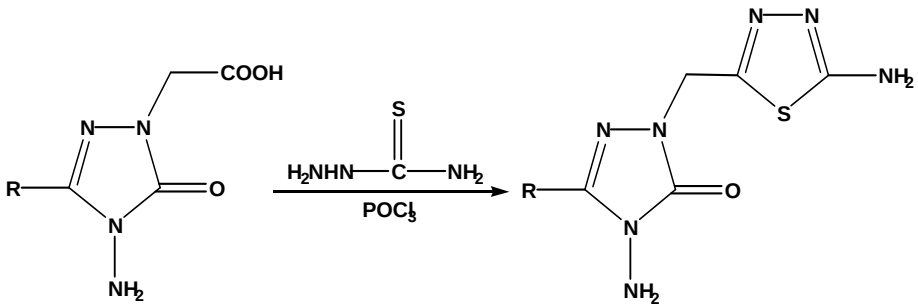
Treatment of 2-acyl thiosemicarbazide with molar equivalent of methane sulfonic acid as dehydrating agent in refluxing toluene afforded good yields of the thiadiazoles [72].



R = *p*-CF_3-C_6H_5- , *p*-Cl-C_6H_5- , $C(CH_3)_3$

1.6.2 Reaction of Thiosemicarbazide with Carboxylic acids:

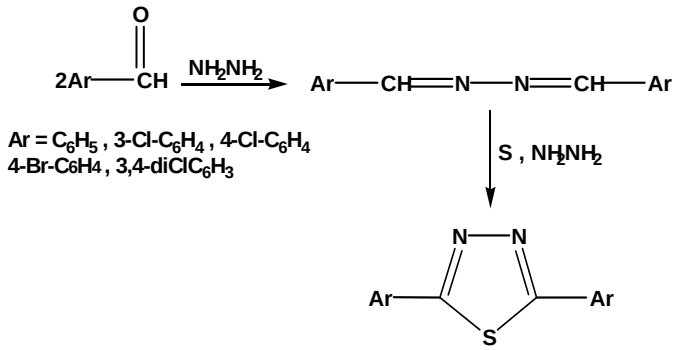
Refluxing a mixture of carboxylic acid and an equivalent amount of thiosemicarbazide in phosphorus oxychloride give the desired product of 1, 3, 4-thiadiazoles [57].



R = -CH_3 , -$CH_2C_6H_5$, -C_6H_5

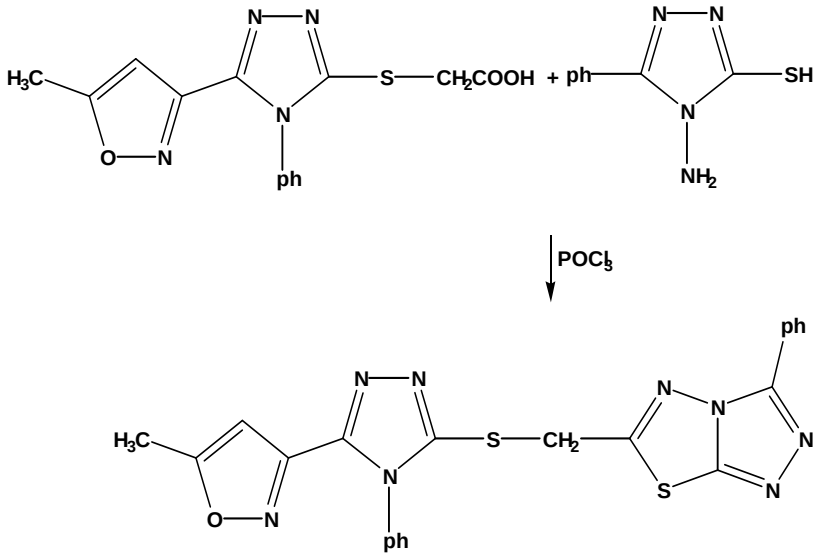
1.6.3 Treatment of Aromatic aldehydes with Sulfur and Hydrazine hydrate:

Numbers of thiadiazoles were synthesized in an easier fashion by treatment of aromatic aldehyde with sulfur and hydrazine hydrate, in ratio 1:2:3 respectively, in steel autoclave at 150 ^{o}C for 12 h. [73].



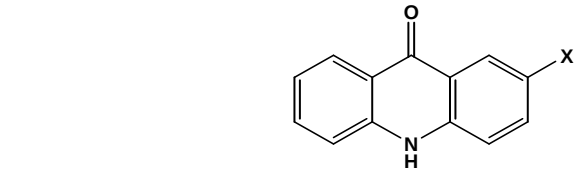
1.6.4 Cyclo condensation of the –SH and –NH$_2$ functions of Triazole derivatives with Carboxylic acids:

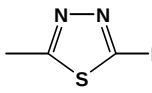
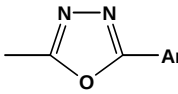
The fused 1,3,4-triazole [3,4-b]-1,3,4-thiadiazole derivatives can be synthesized by the cyclo condensation of –SH and –NH$_2$ functions of 4-amino-5-mercapto-3-substituted-1,2,4-triazole with carboxylic acids under reflux in the presence of POCl$_3$ [74].

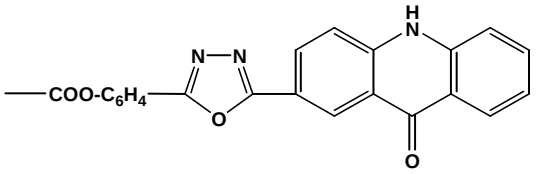
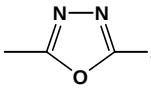


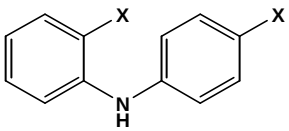
Aim of the work:

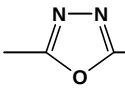
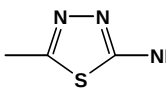
Acridones are a well known group of compounds with a wide variety of biological properties: anti carcinogenic, bactericidal, anti malarial, insecticides and antifungus . Further, Five-membered heterocyclic like 1,3,4-oxadiazoles, 1,3,4-thiadiazoles constitute a potential class of compounds which possess a broad spectrum of biological activity, furthermore, the synthetic utility of acridone in building up the bis heterocyclic compounds containing the above heterocyclic units is not reported in the literature, keeping the above facts in view, we made an attempt to condense the acridone with 1,3,4-oxadiazole and 1,3,4-thiadiazole . In addition to synthesis of new bis-1,3,4-oxadiazole and bis-1,3,4-thiadiazole derived from diphenylamine 2,4`-dicarboxylic acid as shown bellow for their characterization and evaluation of their antibacterial activities .

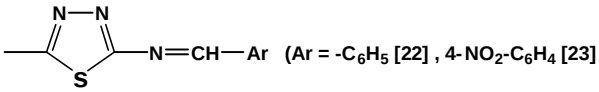


X =  [3] ,  (Ar = -C_6H_5 [12] , 4-NO_2-C_6H_4 [13], 4-Cl-C_6H_4 [14]) ,

 [15] ,  [19] .



X =  [20] ,  [21] ,

 (Ar = -C_6H_5 [22] , 4-NO_2-C_6H_4 [23]

Chapter Three

Results and Discussion

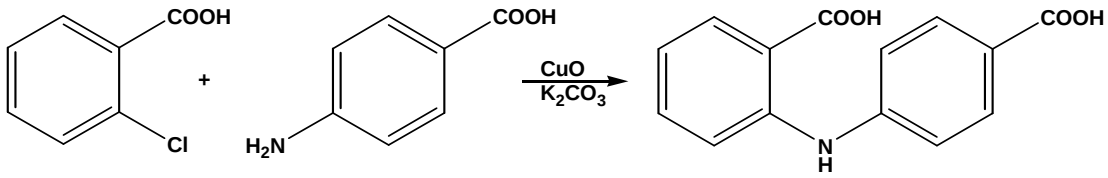
3.1 Introduction:

Biologically significant heterocyclic compounds bearing three hetero atoms in the ring such as, 1, 3, 4-oxadiazole, 1, 3, 4-thiadiazole, have already been well documented in the literature [78, 79].

Additionally, the synthetic utility of 9(10H)-acridone for building the above heterocycles has not been reported in the literature. Combining these facts an attempt was made to condense the acridone with 1, 3, 4-oxadiazole and 1, 3, 4-thiadiazole as shown in Scheme (2-1).

3.2.1 Synthesis of Diphenylamine-2,4`-dicarboxylic acid [1]:

Ullmann-type condensation of 2-chlorobenzoic acid with 4-aminobenzoic acid by refluxing the reactants in the presence of copper oxide and potassium carbonate in amyl alcohol medium afforded diphenylamine-2,4`-dicarboxylic acid [1], equation (3-1) . In this reaction as copper catalyzed nucleophilic aromatic substitution on aryl halide bearing electron withdrawing group.



equation (3-1)

Any mechanism proposed for the ***Ullmann*** reaction must be agreement with two facts: (1) the activity of a series aromatic halides increases in the order Ar-Cl < Ar-Br < Ar-I ; (2) activity is increased by electronegative substituents in the ortho- and para- positions. The facts that these electronegative substituents produce a residual plus charge on

the ortho-position and para-positions suggests that a nucleophilic attack by the copper at the activated position may be rate determining step.

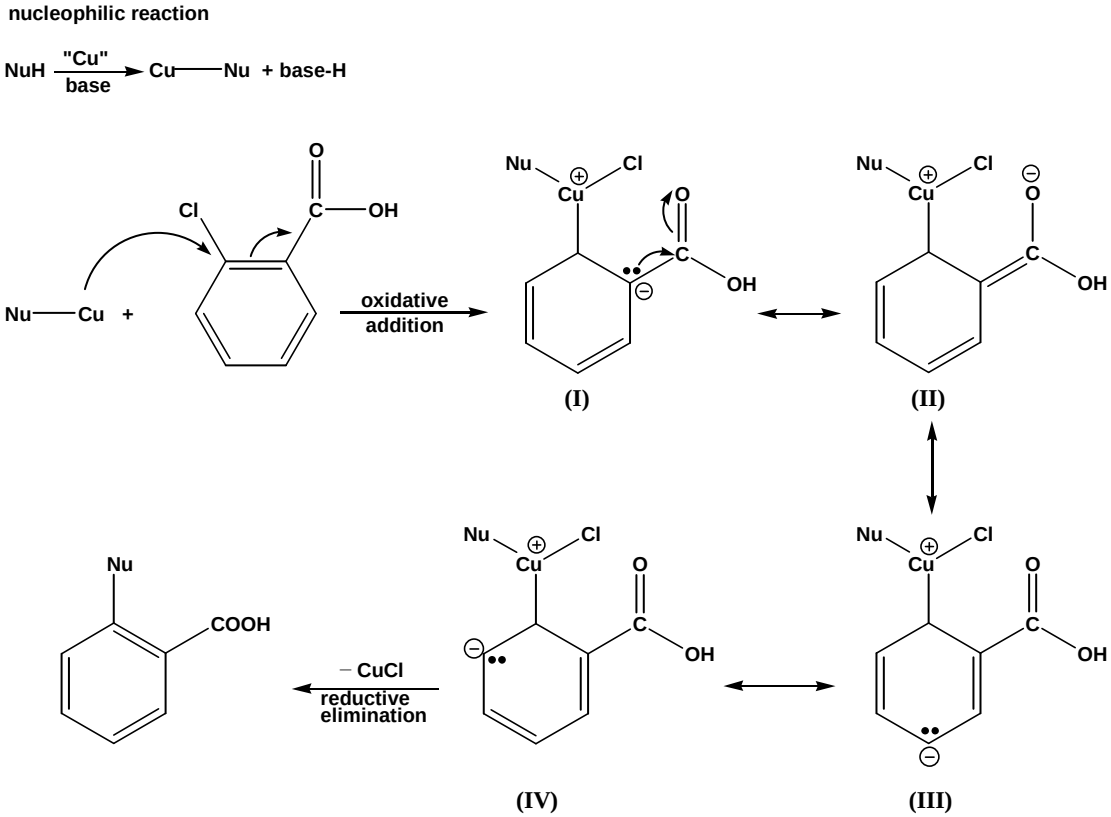
The combination of these two effects must be such that the polarization of Ar-X bond. We may conclude that a possible mechanism consists in three steps:

1) A nucleophilic reaction of NuH (4-amino benzoic acid) with copper oxide ("Cu") to form a complex Cu-Nu at the metal surface .

2) The oxidative addition of complex Cu-Nu to aromatic halide Ar-Cl (2-chloro benzoic acid) produce the complex Ar-Cu-NuCl

3) The reductive elimination of copper halide (Cu-Cl) to form Ar-Nu ,molecule (diphenyl amine-2,4`-dicarboxylic acid)[12,15].

The proposed mechanism for the formation of this compound is shown in Scheme (3-1) below:

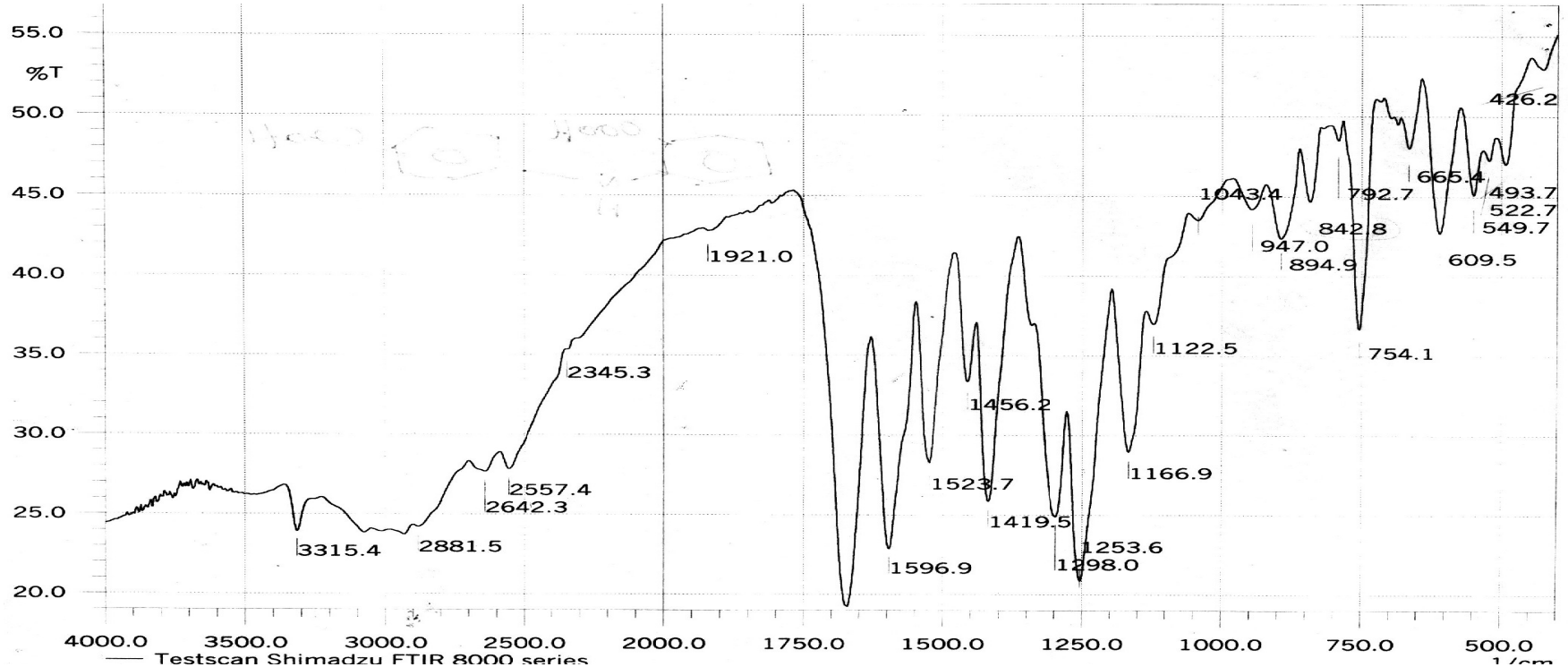


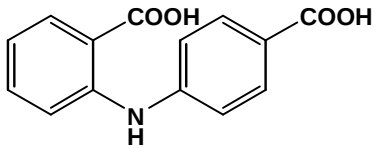
Scheme (3-1)

The authenticity of this product was confirmed by its melting point (208-210^{o}C) and by F.T.IR spectrum Figure (3-1), which showed the

disappearance of absorption bands due to NH_2 stretching of amino group in *p*-amino benzoic acid and the appearance of a band at 3315.4 cm^{-1} for (N-H) .

The presence of a carboxyl group (-COOH) is recognizable by the presence of O-H stretching absorption band at (2500-3500 cm^{-1}), as well as the C=O absorption at 1685 cm^{-1}. Evidence of the presence of aromatic ring was the presence of (C=C) aromatic stretching band at (1596.9 cm^{-1}) and also a sharp bands at (754.1 cm^{-1}) and (842.8 cm^{-1}) that were assigned to the out of plane bending of *o*- and *p*-disubstituted benzene ring, respectively.



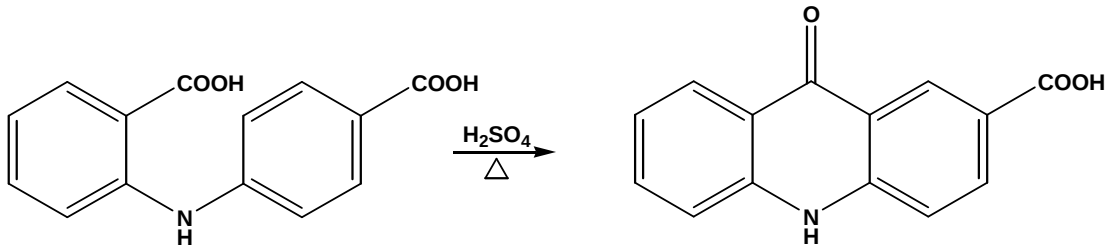
Analysis data (%) calculated				IR (KBr cm^{-1}) spectral data
C	**H**	**N**	**O**	**1. N-H stretch., 3315.4** **2. O-H stretch., near 2500-3300** **3. C=O stretch., of acid 1685** **4. C=C stretch., 1596.9** **5. Out-of-plane C-H bend., (*p*-disub. benzene) 842.8** **6. Out-of-plane C-H bend., (*o*-disub. benzene) 754.1**
65.37	**4.31**	**5.44**	**24.88**	
				

M.P. (^{o}C)	Yield (%)	Color	Molecular formula
208-210	**62**	**White**	**$C_{14}H_{11}NO_4$**

Figure (3-1): F.T.IR spectrum of Diphenylamine-2,4`-dicarboxylic acid [1].

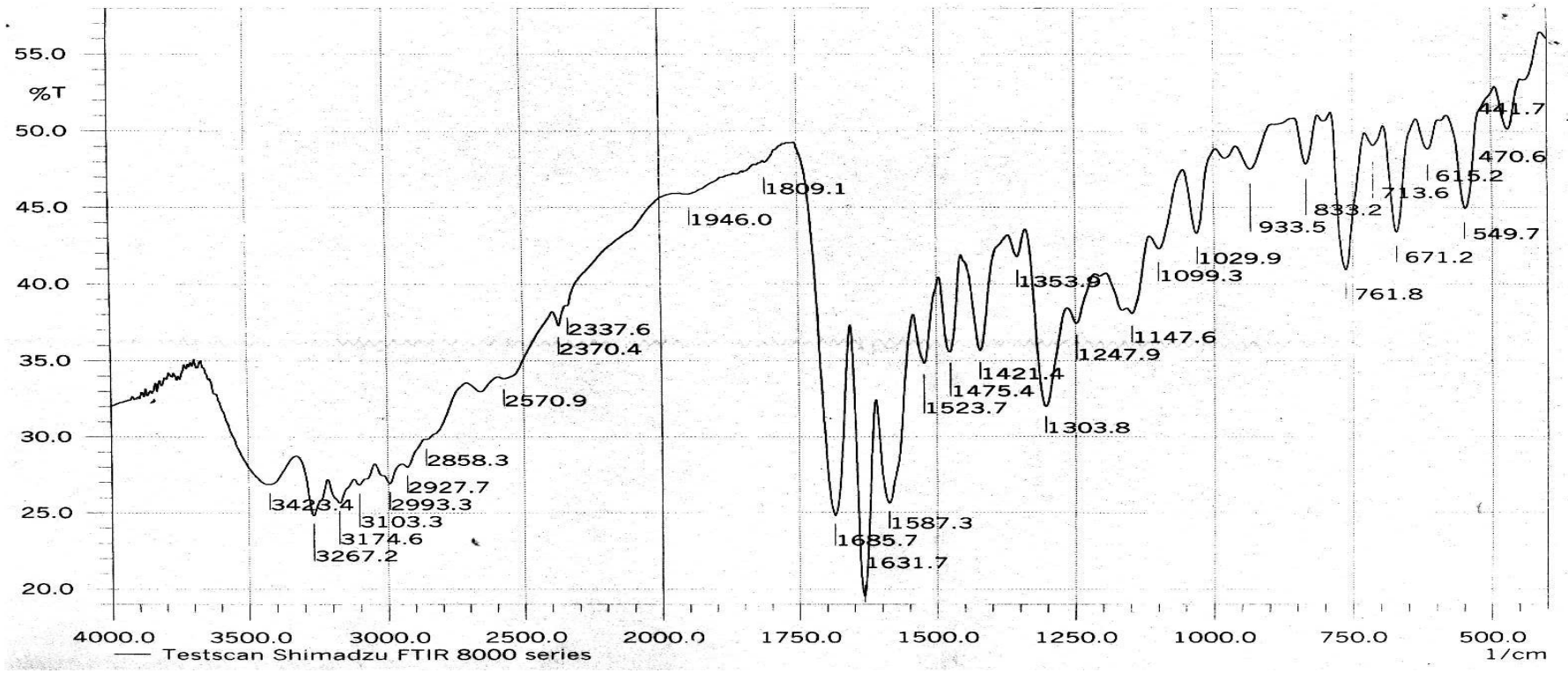
3.2.2 Synthesis of 9(10H)-Acridone-2-carboxylic acid [2]:

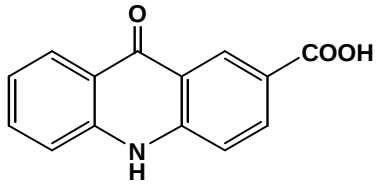
Compound [1] should undergo Intramolecular cyclization [Fridel-Crafts acylation] with sulfuric acid at 100°C to give 9(10H)-acridone-2-carboxylic acid, equation (3-2):



equation (3-2).

The structure of this acid was confirmed by its very high melting point (>330°C), the melting point agrees well with that reported in the literatures [1, 4, 10, 13]. Also by F.T.IR spectrum, which displays a broad (O-H) stretching absorption band in the region of (3267.2 cm^{-1}) as well as the carboxylic acid (C=O) absorption band at (1685.7 cm^{-1}) , also ketone (C=O) aromatic , (C=C) and amine (N-H) absorption band at (1631.7 cm^{-1}), (1587.3 cm^{-1}) and (3423.4 cm^{-1}) respectively. The F.T.IR spectrum of this compound is shown in Figure (3-2).



Analysis data (%) calculated				IR (KBr cm^{-1}) spectral data
C	H	N	O	1. N-H stretch., 3423.4 2. O-H stretch., 3267.2 3. Aromatic C-H stretch.,3103 4. C=O stretch., of acid 1685.7 5. C=O stretch., of ketone 1631.7 6. C=C stretch., 1587.3
70.29	3.79	5.86	20.06	
				

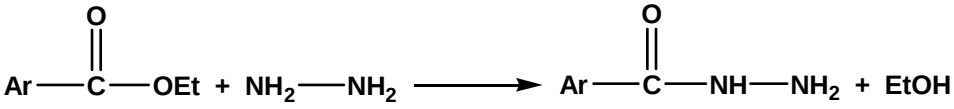
M.P. (^oC)	Molecular formula
>330	$C_{14}H_9NO_3$

Figure (3-2): F.T.IR spectrum of 9(10H)-acridone-2-carboxylic acid [2].

3.3.0 Synthesis of 1,3,4-Oxadiazole derivatives:

3.3.1 Synthesis of 2-[(5-(4-Substituted benzene)-1,3,4-oxadiazol-2-yl]-9(10H)-acridone [12-14

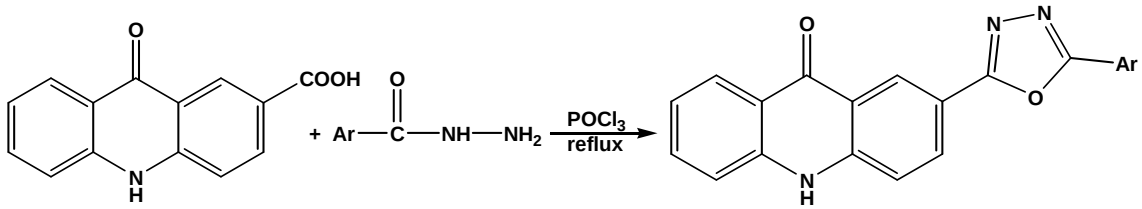
Aryl hydrazines [8, 9, and 10] were prepared by the reaction of appropriate esters with hydrazine hydrate, equation (3-3).



Ar = C_6H_5- , *p*-O_2N-C_6H_4- , *p*-Cl-C_6H_4-

equation (3-3)

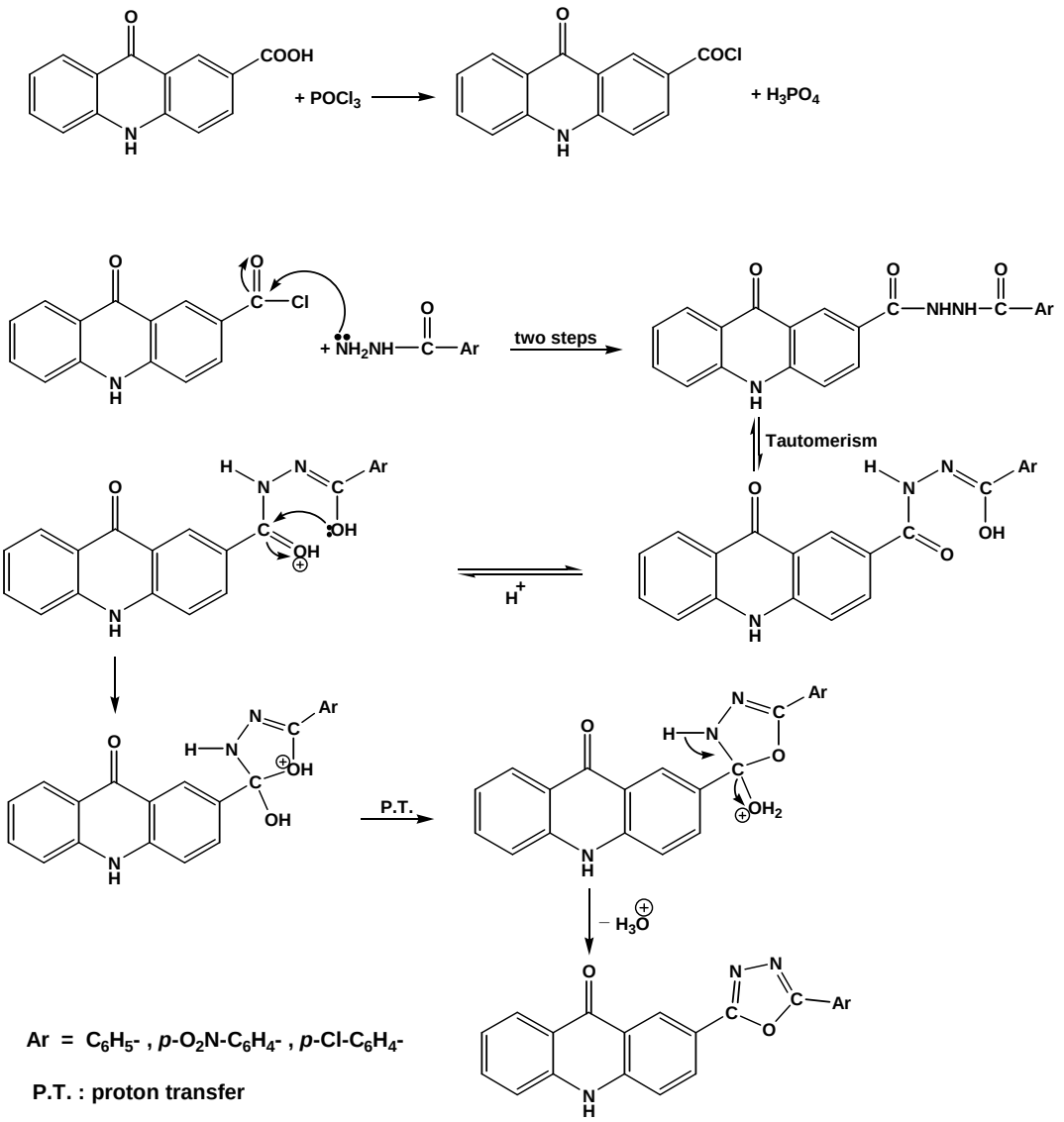
The title compounds [12,13,and 14] bellow were synthesized by refluxing appropriate aroyl hydrazines with phosphorus oxychloride and one equivalent of 9(10H)-acridone-2-carboxylic acid [2], according to equation (3-4).



Ar = C_6H_5- , *p*-O_2N-C_6H_4- , *p*-Cl-C_6H_4-

equation (3-4).

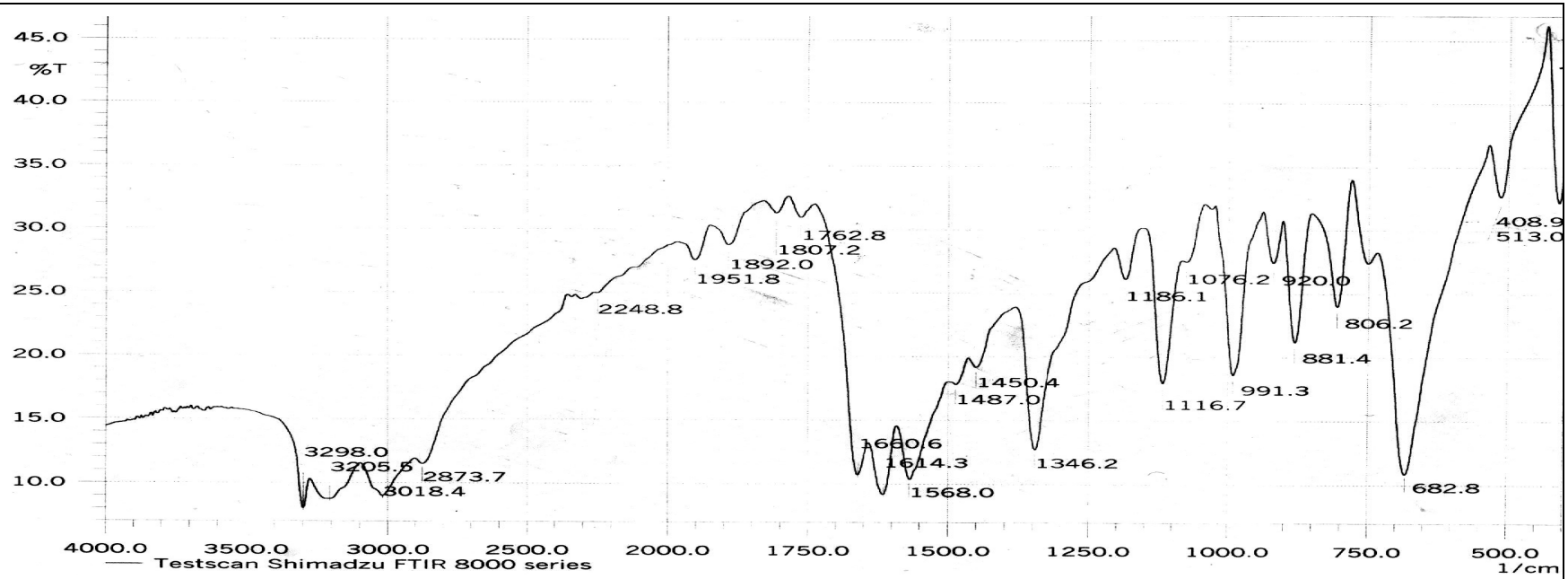
The mechanism of the reaction is depicted in the following steps; Scheme (3-2).

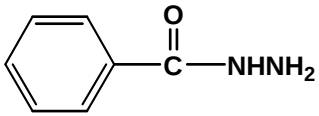


Scheme (3.2)

The synthesized compounds were characterized by melting points, UV and F.T.IR spectral data.

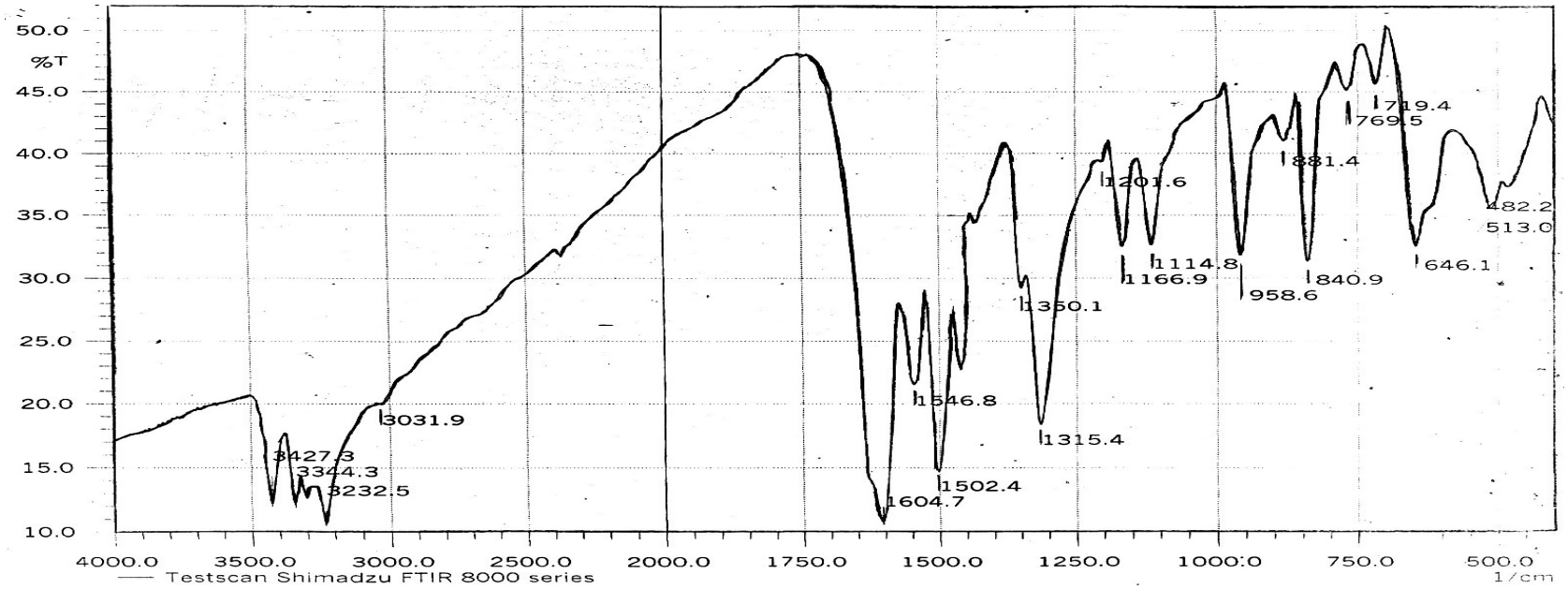
The F.T.IR spectra of compounds [12,13 and 14] Figures (3-6), (3-7) and (3-8) were devoid of the amide bands present in the spectrum of the aryl hydrazines [8,9 and 10] Figures (3-3), (3-4) and (3-5) in regions between (3427.3-3184.3 cm^{-1}) of asymmetric and symmetric N-H stretching of (NH_2) , as well as the disappearance of O-H band at (3267.2 cm^{-1}) of compound [2]. The appearance of bands near (1600 cm^{-1}) assigned to (C=N) band of oxadiazole moiety and bands near (1260 and 1035 cm^{-1}) assigned for (C-O-C) cyclic grouping in oxadiazole are good evidence for the presence of 1,3,4-oxadiaozle ring in compounds [12,13 and 14].

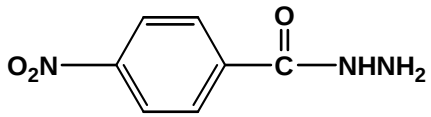


Analysis data (%) calculated				IR (KBr cm^{-1}) spectral data
C	H	N	O	1. Asym., and sym., of N-H stretch., 3298, 3205.5 2. Aromatic C-H 3018.4 3. C-N stretch., 1450.4 4. C=O stretch., of amide 1660.6 5. Ring C=C stretch., 1568 6. Out-of-plane bend., (mono sub. benzene 682.8
61.75	5.92	20.58	11.75	
				

M.P. (^{o}C)	Yield (%)	Color	Molecular formula
113-115	68	White	$C_7H_8N_2O$

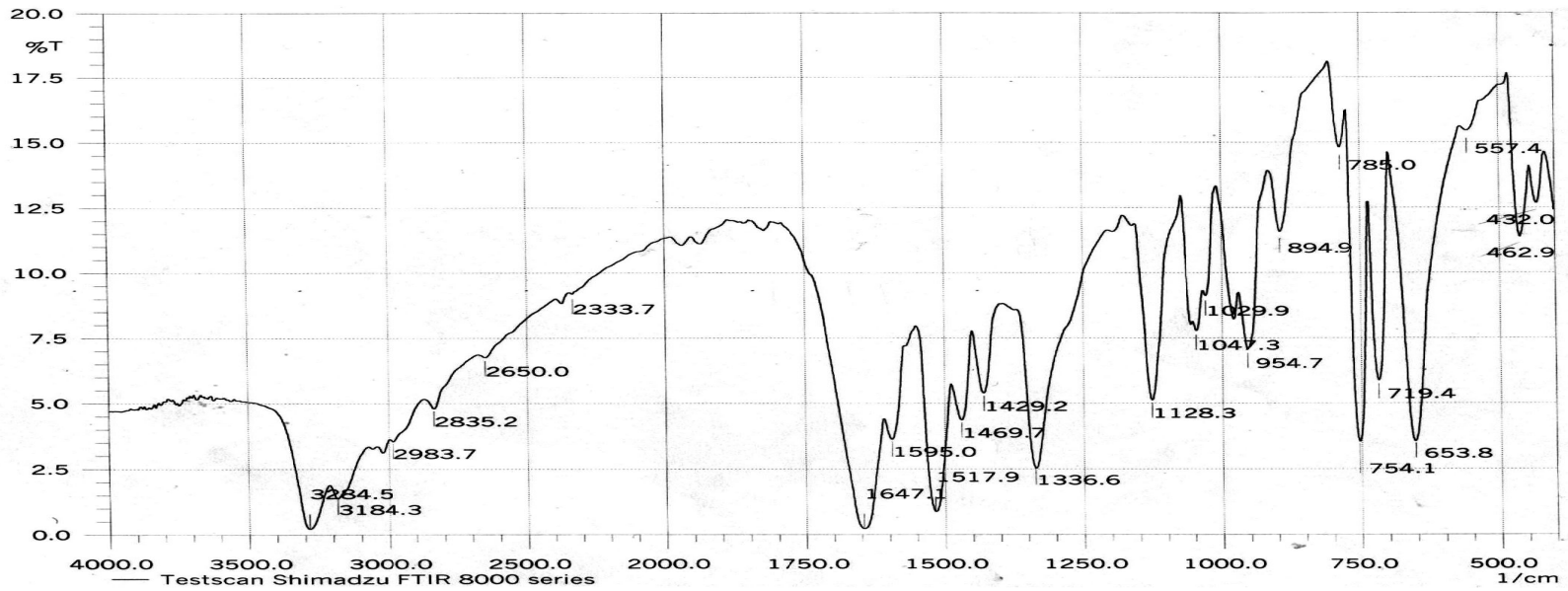
Figure (3-3): F.T.IR spectrum of benzoyl hydrazine [8].

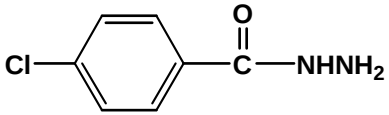


Analysis data (%) calculated				IR (KBr cm^{-1}) spectral data
C	**H**	**N**	**O**	**1. Asym., and sym., of N-H stretch., 3427.3, 3232.5** **2. Aromatic C-H stretch. 3031.9** **3. C=O stretch., shoulder near 1640** **4. Asym (Ar-NO_2) N-O stretch. 1546.8** **5. C-N stretch. near 1450** **6. Sym. (Ar-NO_2) N-O stretch. 1350.1** **7. Out-of-plane bend.,(p-disub.) 840.9**
46.41	**3.89**	**23.20**	**26.50**	
				

M.P. (^oC)	Yield (%)	Color	Molecular formula
220 (dec.)	**69**	**Yellow**	**$C_7H_7N_3O_3$**

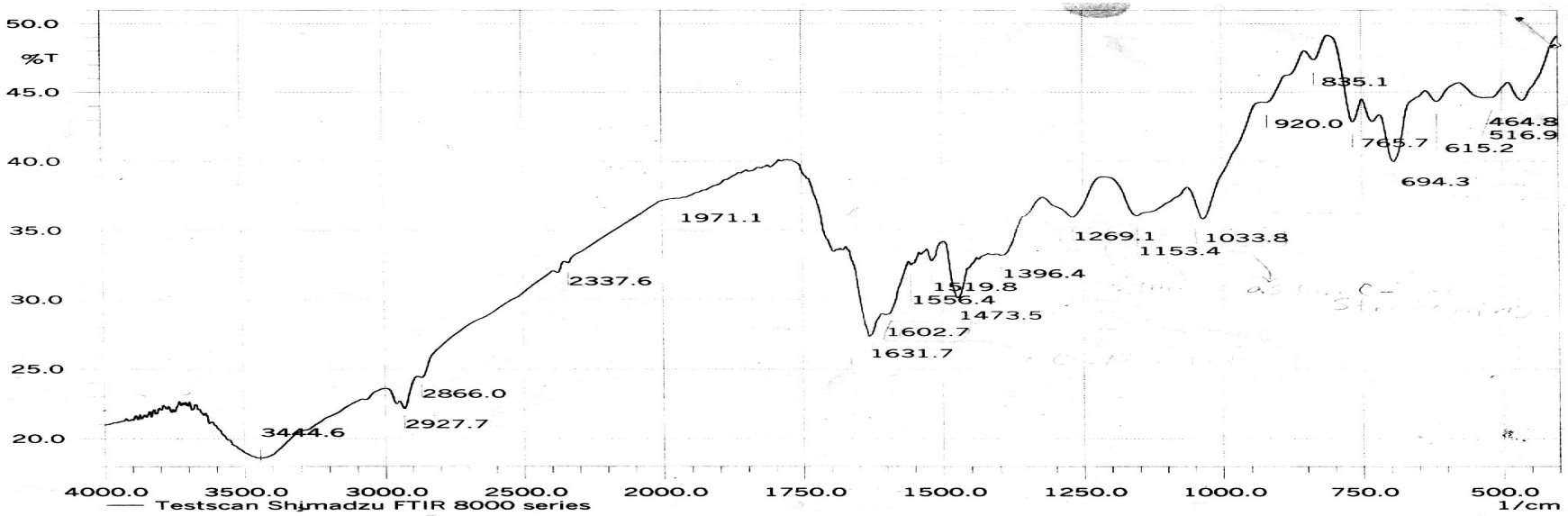
Figure (3-4): F.T.IR spectrum of 4-nitro benzoyl hydrazine [9].

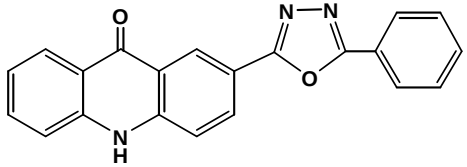


Analysis data (%) calculated				IR (KBr cm^{-1}) spectral data
C	**H**	**N**	**O**	**1. Asym., and sym., of N-H stretch., 3284.5, 3184.5** **2. C=O stretch., of amide 1647.1** **3. C-N stretch., 1469.7** **4. Out-of-plane C-H bend., (*p*-disub. benzene) 894.9**
49.28	**4.14**	**16.42**	**9.38**	
				

M.P. (^{o}C)	Yield (%)	Color	Molecular formula
166-168	**66**	**White**	**$C_7H_7N_2OCl$**

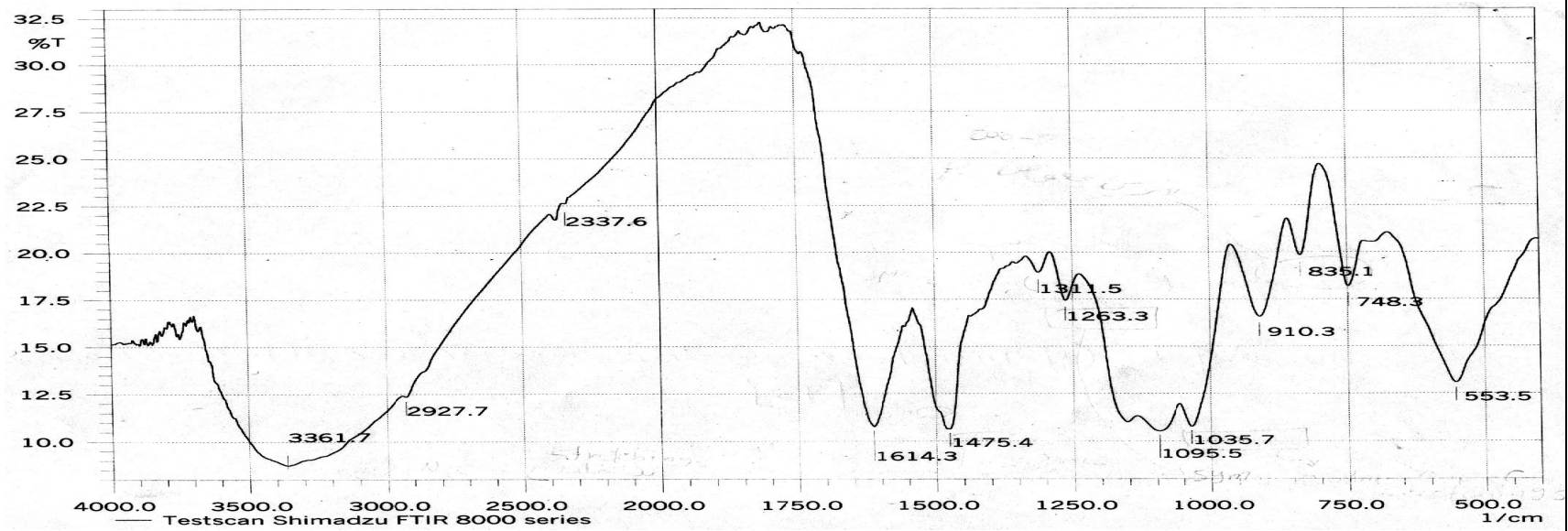
Figure (3-5): F.T.IR spectrum of 4-chlorobenzoyl hydrazine [10].



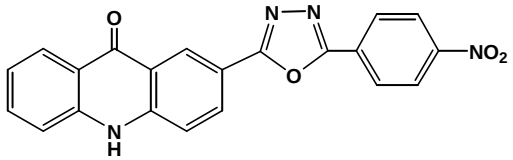
Analysis data (%) calculated				IR (KBr cm^{-1}) spectral data
C	**H**	**N**	**O**	**1. N-H stretch., 3444.6** **2. C=O stretch., of ketone 1631.7** **3. C=N stretch., 1602.7** **4. Ring C=C stretch., 1556.4** **5. Asym. and sym. C-O-C stretch., 1269.1, 1033.8** **6. Out-of-plane C-H bend., (mono-sub. benzene) 694.3**
74.33	**3.86**	**12.38**	**9.43**	
				

M.P. (^{o}C)	Yield (%)	Color	Molecular formula
296-298	**66**	**Red**	**$C_{21}H_{13}N_3O_2$**

Figure (3-6): F.T.IR spectrum of 2-[5-(phenyl)-1,3,4-oxadiazol-2-yl]-9(10H)-acridone [12].

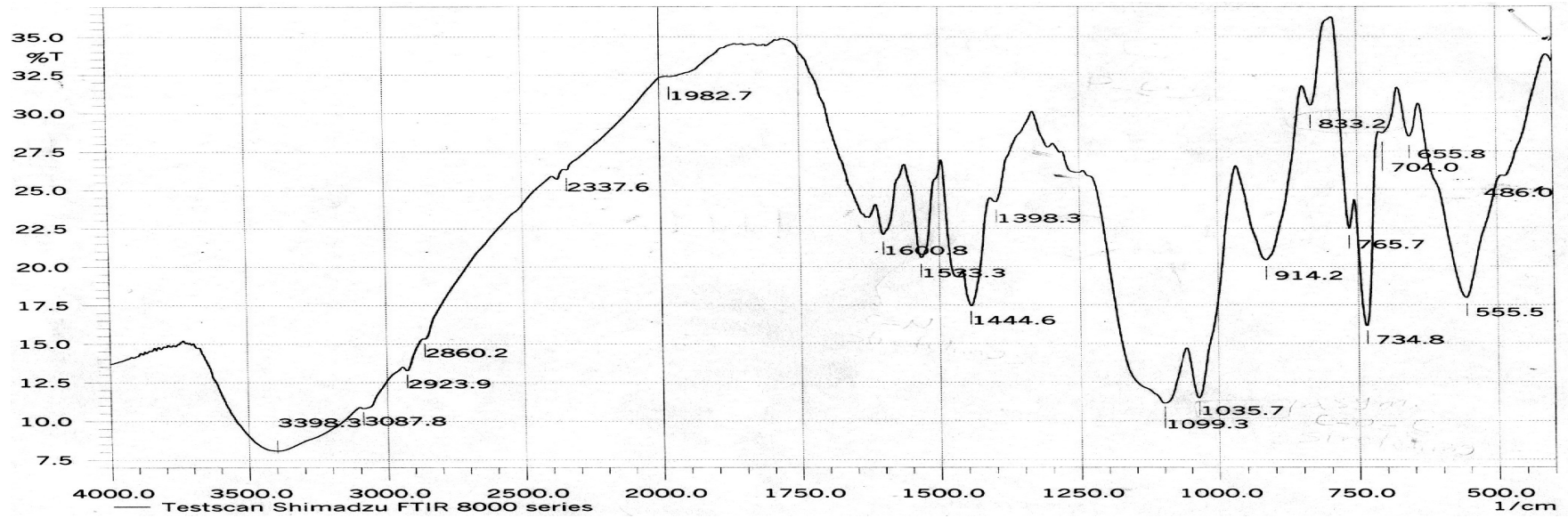


Analysis data (%) calculated				IR (KBr cm^{-1}) spectral data
C	**H**	**N**	**O**	**1. N-H stretch., 3361.7** **2. C=N stretch., 1614.3** **3. Asym. and sym. C-O-C stretch., 1263.3, 1035.7** **4. Asym. (Ar-NO_2) N-O stretch., near 1500** **5. Sym. (Ar-NO_2) N-O stretch., 1311.5** **6. Out-of-plane C-H bend., (*p*-disub. benzene) 835.1**
65.62	**3.15**	**14.58**	**16.65**	



M.P. (^oC)	Yield (%)	Color	Molecular formula
302-304	**74**	**Reddish-Brown**	**$C_{21}H_{12}N_4O_4$**

Figure (3-7): F.T.IR spectrum of 2-[5-(4-nitrobenzene)-1,3,4-oxadiazol-2-yl]-9(10H)-acridone [13].



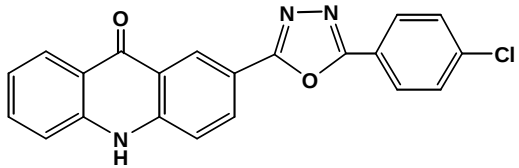
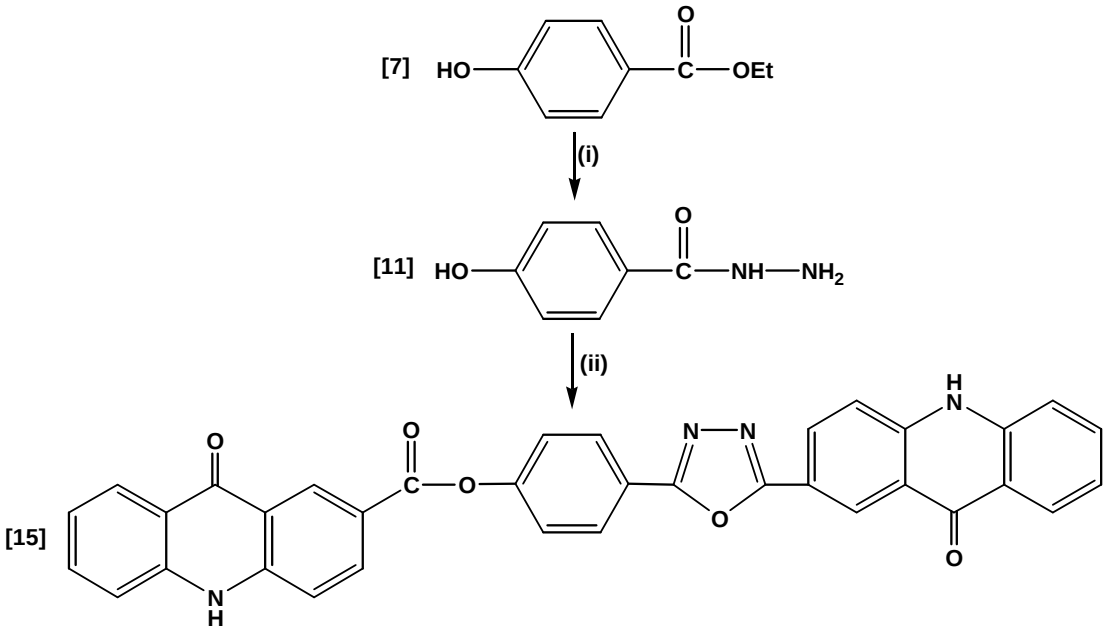
Analysis data (%) calculated				IR (KBr cm^{-1}) spectral data	
C	H	N	O	1. N-H stretch., 3398.3 2. Aromatic C-H stretch., 3087.8 3. C=N stretch., 1600.8 4. Asym. and sym. C-O-C stretch., 1260, 1035.5 5. Out-of-plane C-H bend., (*p*-disub. benzene) 833.2	
67.48	3.24	11.24	8.56		
					
M.P. (^{o}C)		**Yield (%)**		**Color**	**Molecular formula**
>330		**68**		**Brown**	**$C_{21}H_{12}N_3O_2Cl$**

Figure (3-8): F.T.IR spectrum of 2-[5-(4-chlorobenzene)-1,3,4-oxadiazol-2-yl]-9(10H)-acridone [14].

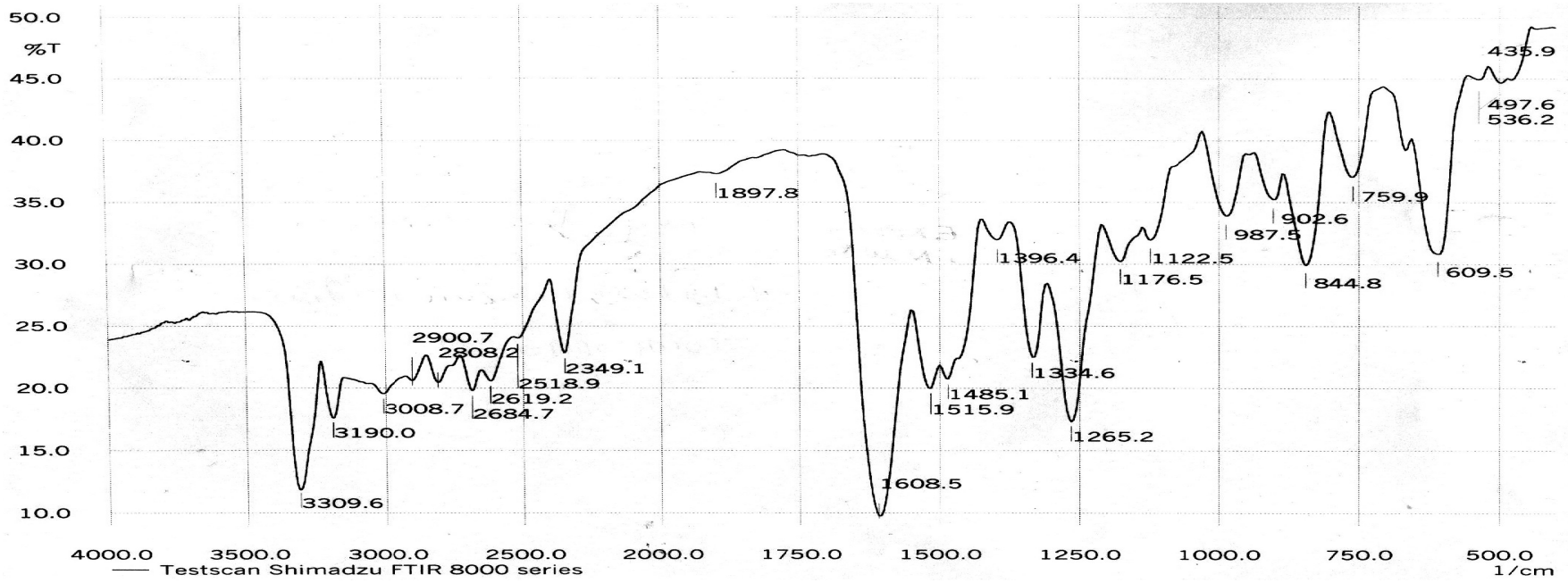
3.3.2 Synthesis of 2-[9(10H)-Acridone-2-yl]-5[4-(9(10H)-acridone-2-yl-carboxy) phenyl]-1, 3, 4-oxadiazole [15]:

The synthesis route used to prepare this compound is shown in Scheme (3-3). The convenient starting material was 4-hydroxy benzoyl hydrazine [11] which in turn was prepared from ethyl-4-hydroxy benzoate and hydrazine hydrate. Compound [11] on condensation with two equivalents of acridone-2-carboxylic acid in phosphorus oxychloride gave the compound [15].



Scheme (3-3): Reagents and conditions: (i) NH_2-NH_2, EtOH, reflux 7hr.; (ii) Ar-COOH (Ar = acridone), $POCl_3$, reflux 24hr.

The structure of this compound was established on the melting point (324-326 ^oC), UV and F.T.IR spectral data. The F.T.IR absorption bands show disappearance of the broad band at (3300-3170 cm^{-1}) assigned to O-H stretching and appearance of the carbonyl stretching at (1732 cm^{-1}) are good evidence to the success of the esterification step. Beside this, the F.T.IR spectrum of the compound was devoid of both amide and amino bands present in the spectrum of compound [11]. The above data agree with the proposed structure assigned to this compound. Figure (3-10) show F.T.IR of compound.



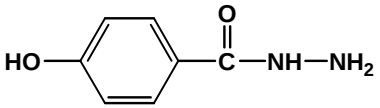
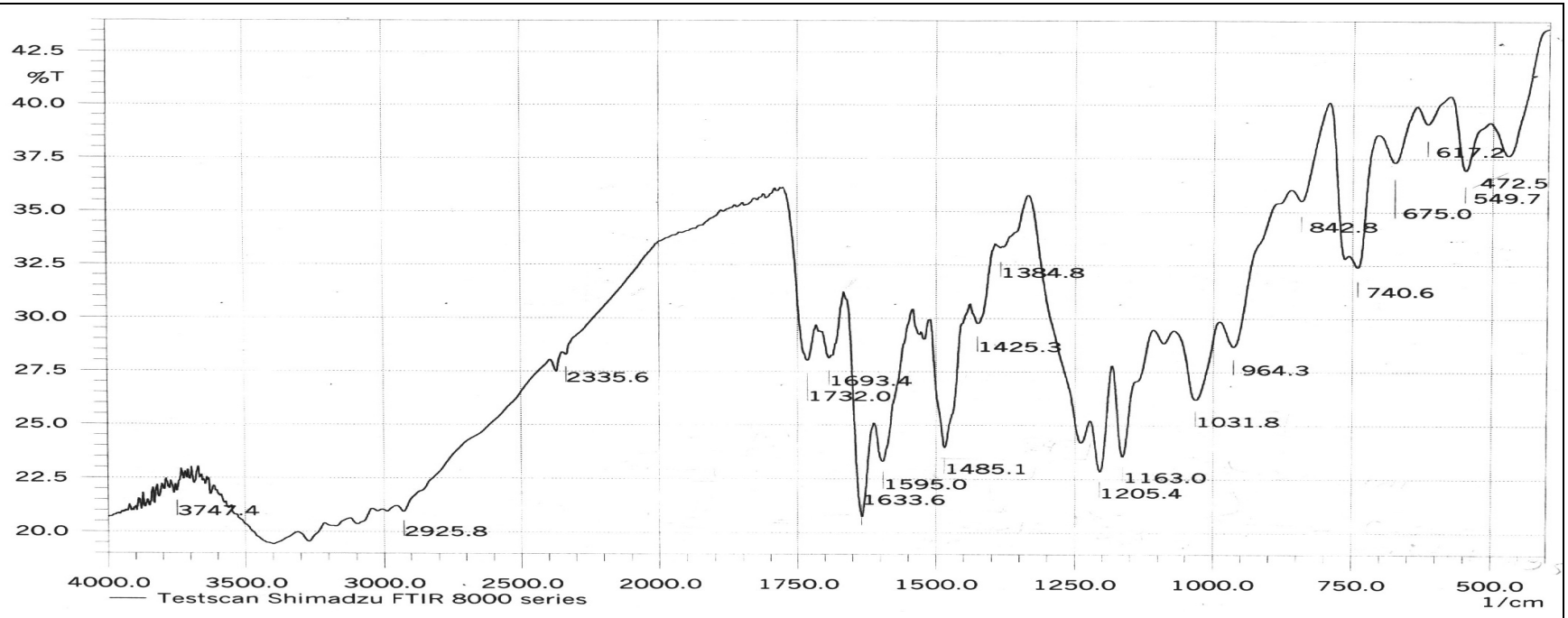
Analysis data (%) calculated				IR (KBr cm^{-1}) spectral data	
C	H	N	O	1. O-H stretch., 3300-2500 2. Asym. and sym. of N-H stretch., 3309 and 3190 3. C=O stretch. of amide 1608 4. Ring C=C stretch.,1515.1 5. C-N stretch.,1485.9 6. Out-of-plane C-H bend, (*p*-disub. benzene) 844	
55.26	5.30	18.41	21.03		
					
M.P. (^oC)		Yield (%)		Color	Molecular formula
266-268		74		White	$C_7H_7N_7O_2$

Figure (3-9): F.T.IR spectrum of 4-hydroxy benzoyl hydrazine [11].



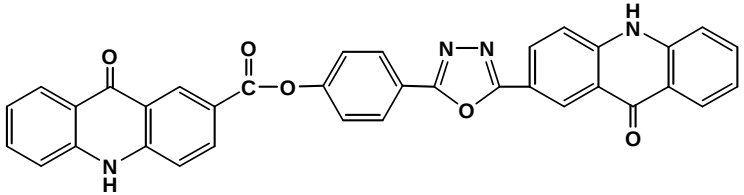
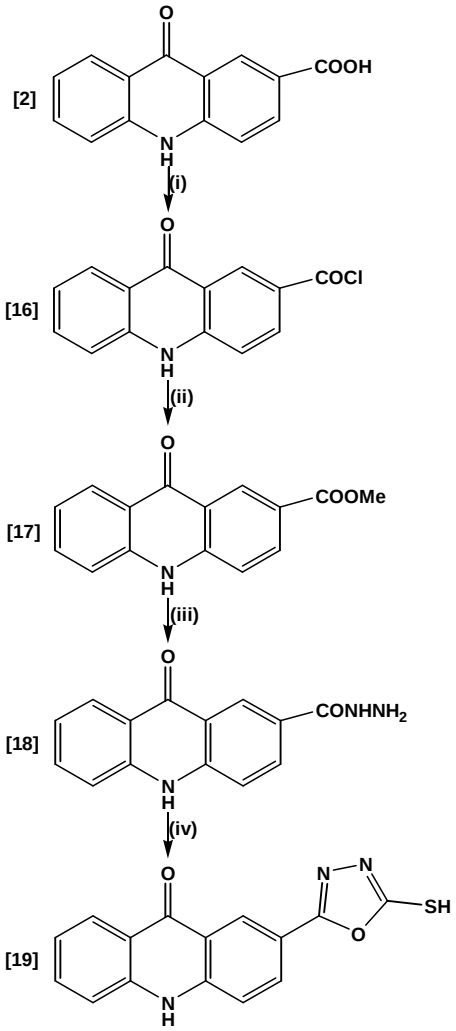
Analysis data (%) calculated				IR (KBr cm^{-1}) spectral data	
C	H	N	O	1. N-H stretch. near 3400 2. Aromatic C-H stretch. Near 3050 3. C=O stretch. of ester 1732.0 and 1693.4 4. C=O stretch. of ketone , 1633.6 5. C=N stretch. 1595.0 6. Ring C=C stretch. 1485.1 7. Asym and sym. C-O-C stretch. near 1250, 1031.8	
72.91	3.50	9.72	13.87		
					
M.P. (^{o}C)		Yield (%)		Color	Molecular formula
324-326		60		Yellow	$C_{35}H_{20}N_4O_5$

Figure (3-10): F.T.IR spectrum of 2-[9(10H)-Acridone-2-yl]-5-[4-(9(10H)-acridone-2-yl-carboxy)phenyl]-1,3,4-oxadiazole [15].

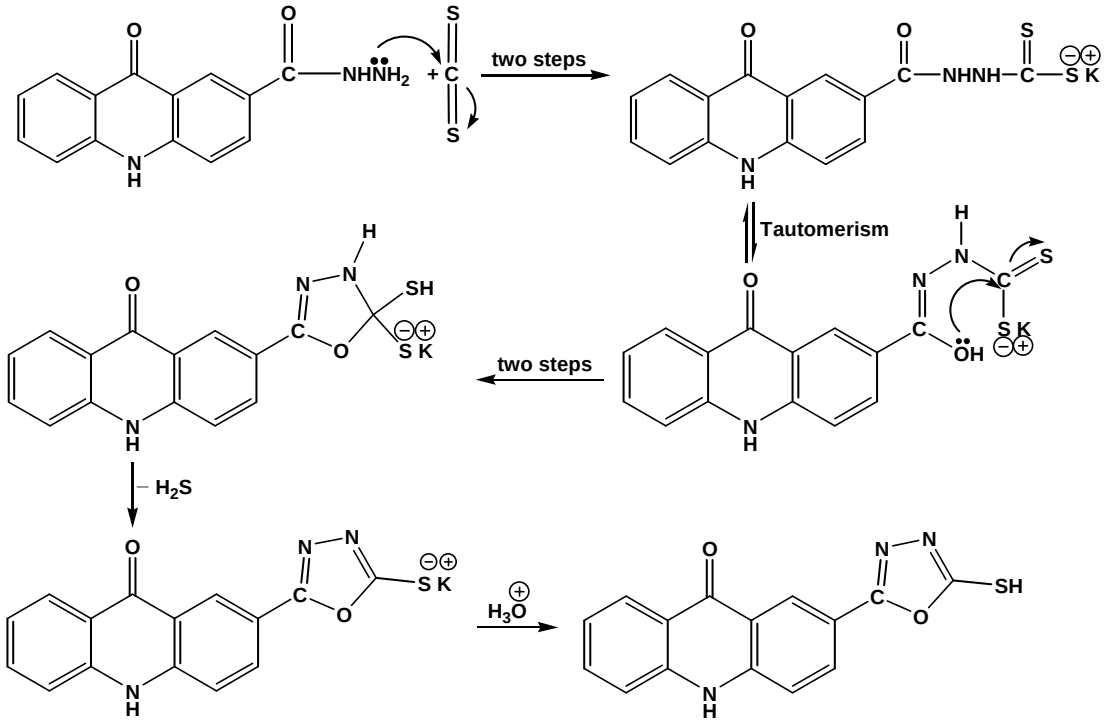
3.3.3 Synthesis of 2-[5-Thiol-1,3,4-oxadiazol-2-yl]-9(10H)-acridone [19]:

The preparation of compound [19] was carried out according to Scheme (3-4). 9(10H)-acridone-2-methylcarboxylate [17] ,obtained by condensation of 9(10H)-acridone-2-acid chloride [16] with methanol, on hydrazinolysis by refluxing with hydrazine hydrate furnished the compound 9(10H)-Acridone-2-carboxylic acid hydrazide [18]. The structure of this compound was verified from its melting point and F.T.IR spectrum. Reaction of compound [18] with carbon disulfide in basic medium of potassium hydroxide yielded the compound [19].

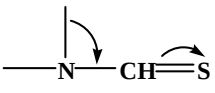


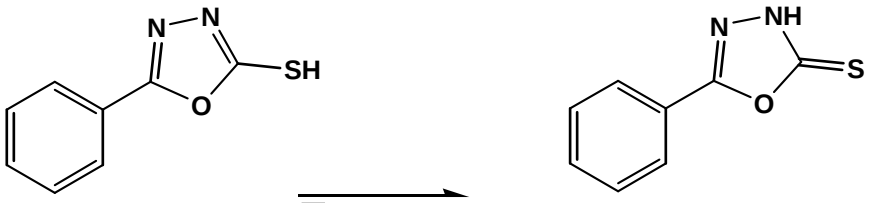
Scheme (3-4): Reagents and Conditions: (i) $SOCl_2$, reflux 3hr.; (ii) MeOH, (iii) NH_2-NH_2, DMSO, reflux 24hr.; (IV) CS_2, KOH, EtOH, reflux 24hr.

The mechanism of the reaction is depicted in the following steps: Scheme (3-5).



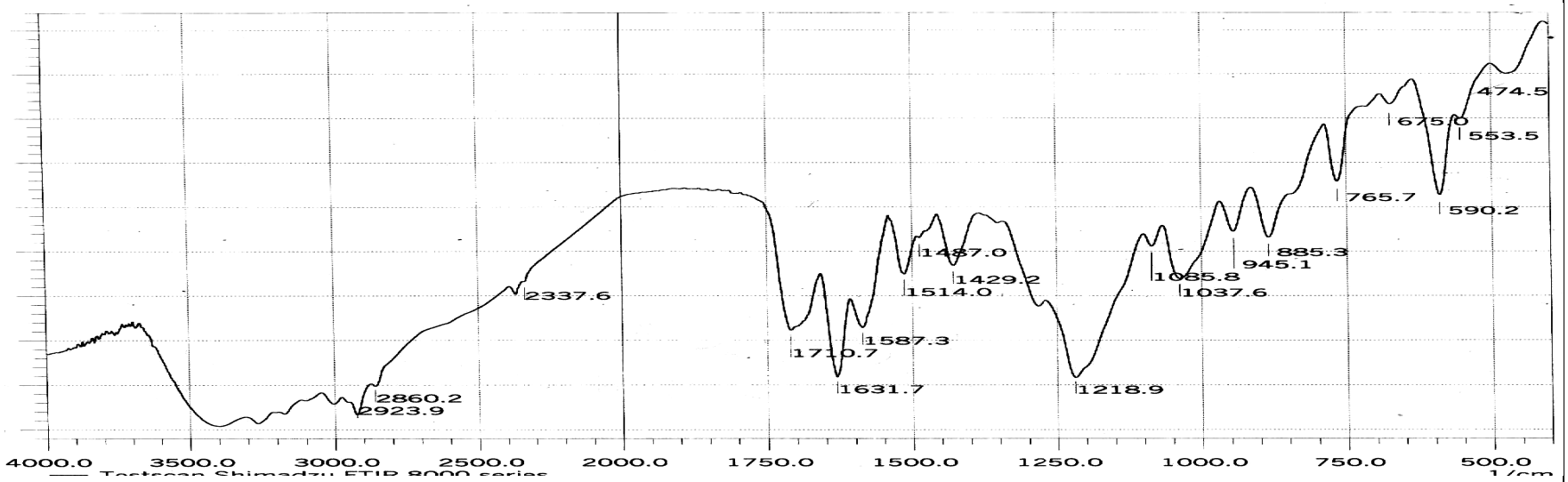
Scheme (3-5)

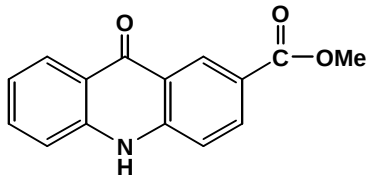
Compound [19], like all other compounds containing  moiety could exist in two equilibrium tautomeric forms enol form (I) and keto form (II). Despite the fact, that keto form is comparatively more stable [80].



Thiol (I) **Thion (II)**

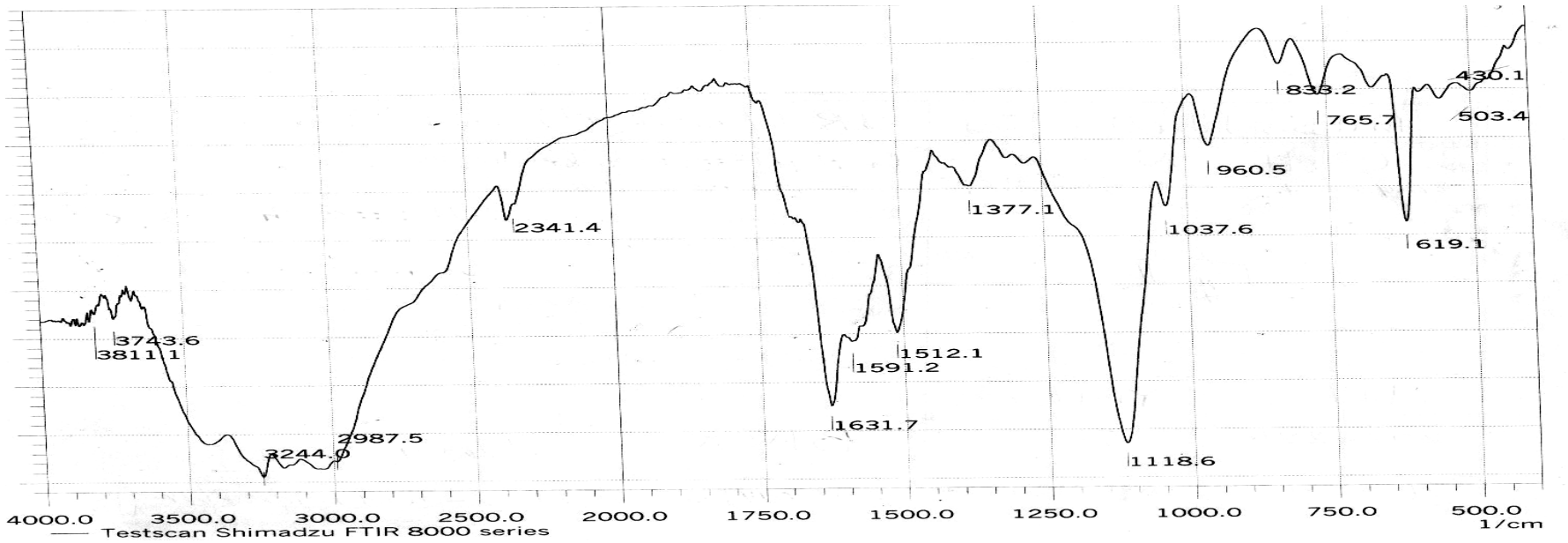
The structure of this compound was elucidated on the basis of its melting point and F.T.IR spectral data. The F.T.IR spectrum of this compound figure (3-13) reveled a sulfohydryl absorption band (S-H) at (2586.4 cm^{-1}) and absorption of (C=S) band at (1332.5 cm^{-1}). Also F.T.IR show a typical absorptions of oxadiazole ring endo cyclic C-O-C asymmetrical and symmetrical at (1278.7 and 1041.5 cm^{-1}) and absorption band of (C=N) near (1580 cm^{-1}).



Analysis data (%) calculated				IR (KBr cm^{-1}) spectral data
C	H	N	O	1. N-H stretch. near 3400 2. Aromatic C-H stretch. near 3000 3.C=O stretch. of ester,1710.7 4. C=O stretch. of ketone,1631.7 5. Ring C=C stretch.,1587.3
71.14	4.38	5.53	18.95	
				

M.P. (^{o}C)	Yield (%)	Color	Molecular formula
> 340	71	Black	$C_{15}H_{11}NO_3$

Figure (3-11): F.T.IR spectrum of 9(10H)-Acridone-2-methylcarboxylate [17].



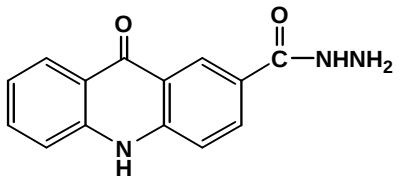
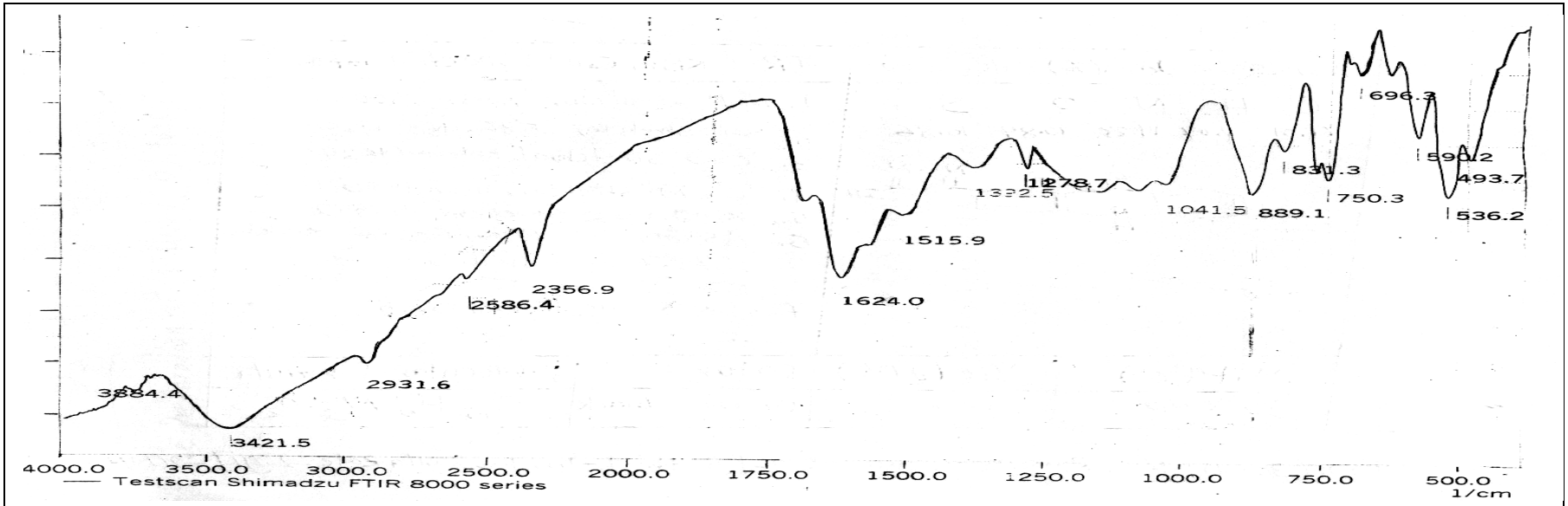
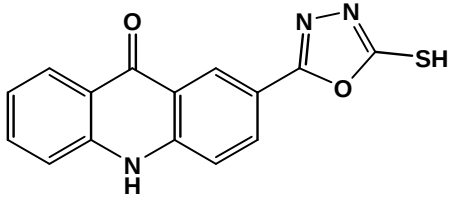
Analysis data (%) calculated				IR (KBr cm^{-1}) spectral data	
C	H	N	O	1. N-H stretch. of heterocyclic ring near 3400 2. Asym. and sym. N-H stretch. 3244 and near 3150 3. Aromatic C-H stretch. near 3100 4.C=O stretch. of amide and ketone, 1631.7 5. Ring C=C stretch. ,1591.2	
66.40	4.38	16.59	12.63		
					
M.P. (^{o}C)		**Yield (%)**		**Color**	**Molecular formula**
292-294		**70**		**Black**	**$C_{14}H_{11}N_3O_2$**

Figure (3-12): F.T.IR spectrum of 9(10H)-Acridone-2-acid hydrazide [18].



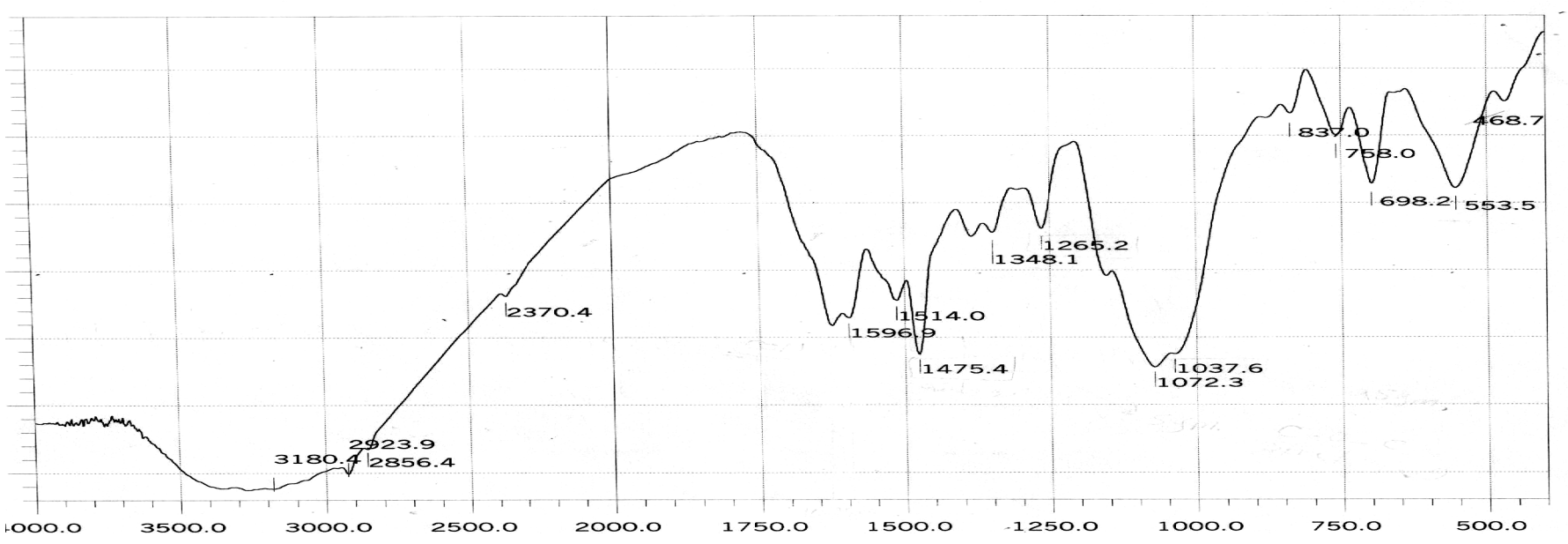
Analysis data (%) calculated					IR (KBr cm^{-1}) spectral data
C	H	N	O	S	1. N-H stretch., near 3400 2. S-H stretch.,2586.4 3. C=O stretch. of ketone,1624 4. C=N stretch. near 1580 5. Ring C=C stretch.,1515.9 6. Asym. and sym. C-O-C stretch., 1278.7 and 1041.5 7. C=S stretch.,1332.5
61.01	3.07	14.23	10.84	10.86	
					

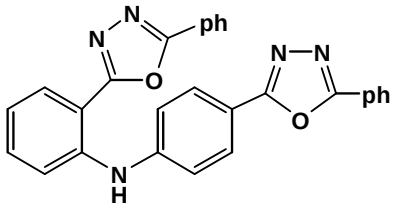
M.P. (^{o}C)	Yield (%)	Color	Molecular formula
> 340	69	Greenish-Black	$C_{15}H_9N_3O_2S$

Figure (3-13): F.T.IR spectrum of 2-[5-thiol-1,3,4-oxadiazole-2-yl]-9(10H)-acridone [19].

3.3.4 Synthesis of 2,4`-Bis[5-phenyl-1,3,4-oxadiazol-2-yl]diphenyl amine [20]:

The reaction of compound [1] with two equivalents of benzoyl hydrazine [8] in the presence of phosphorus oxychloride under the same conditions used for synthesis other 1,3,4-oxadiazole previously, afforded the 2,4`-bis[5-phenyl-1,3,4-oxadiazol-2-yl]diphenyl amine [20]. Figure (3-14) includes melting point and F.T.IR spectral data of this compound. The Figure showed the disappearance of the two absorption bands of (C=O) and $-NHNH_2$ stretching of benzoyl hydrazine [8] and appearance of a typical absorption of 1, 3, 4-oxadiazole near (1600 cm^{-1}) of (C=N) stretching and (asym., 1265.2; sym., 1072.3 cm^{-1}) of endo cyclic C-O-C.



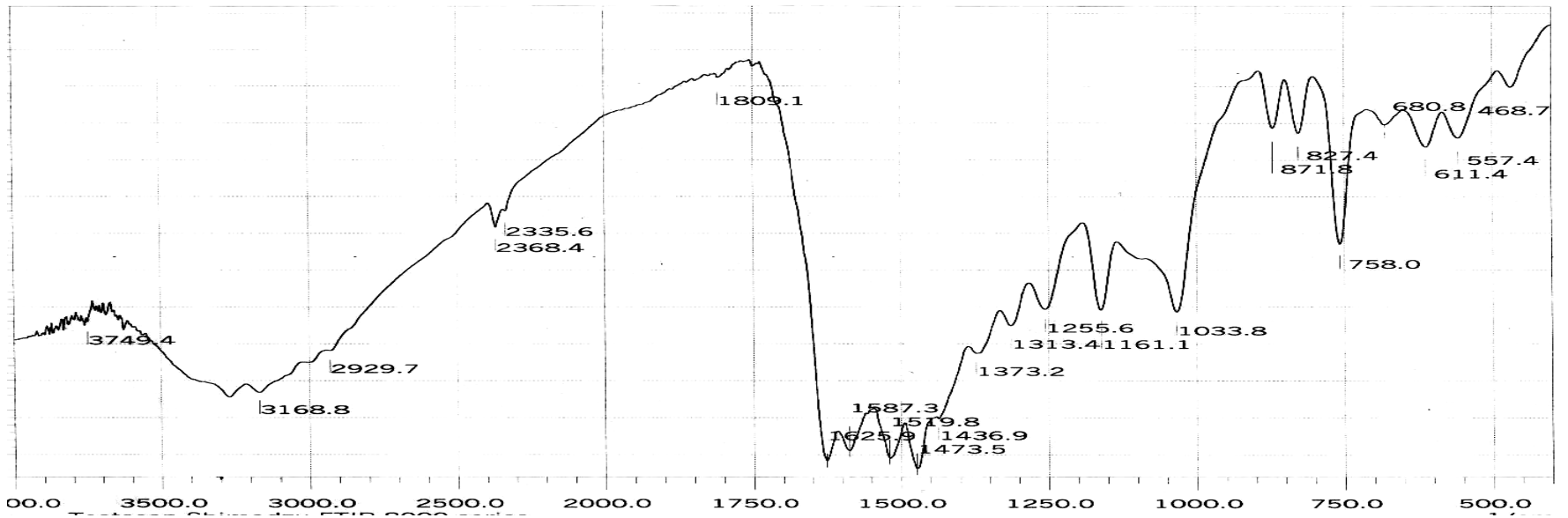
Analysis data (%) calculated				IR (KBr cm^{-1}) spectral data
C	**H**	**N**	**O**	**1. N-H stretch. 3200-3500** **2. C=N stretch. near 1600** **3. Ring C=C stretch. 1596.9** **4. Asym and sym. C-O-C stretch. 1265.2 and 1037.3** **5. Out-of-plane C-H bend.(*p*-disub. benzene) 837** **6. Out-of-plane C-H bend.(o-disub. benzene) 758 and 698.2**
63.37	**2.99**	**23.09**	**10.55**	
				

M.P. (^{o}C)	Yield (%)	Color	Molecular formula
278	**70**	**Reddish-Brown**	**$C_{28}H_{19}N_5O_2$**

Figure (3-14): F.T.IR spectrum of 2,4`-bis[5-(phenyl)-1,3,4-oxadiazole-2-yl]diphenylamine [20].

3.4.1 Synthesis of 2-Amino-1, 3, 4-thiadiazole derivatives [3, 21]:

The reaction of one equivalent of thiosemicarbazide with compound [2] and two equivalents of thiosemicarbazide with compound [1], in the presence of phosphorus oxychloride under conditions reported previously [81] , afforded 2-[5-(amino)-1,3,4-thiadiazol-2-yl]-9(10H) acridone [3] , 2,4`-bis[5-(amino)-1,3,4-thiadiazol-2-yl]diphenylamine [21] respectively. The structural assignments to the products were based on their m.p. and F.T.IR spectral data. Melting points are (>340 for [3]and 288-290^{o}C for [21]) respectively. F.T.IR spectra of compounds [3, 21] figures (3-15) and (3-16) exhibited significant two bands about (~3300, 3168.8 cm^{-1}) for [3] and (3325, 3085.9 cm^{-1}) for [21], which could be attributed to asymmetric and symmetric stretching of NH_2 group. Beside this, a band at (1620 cm^{-1}) due to C=N stretching is also observed.



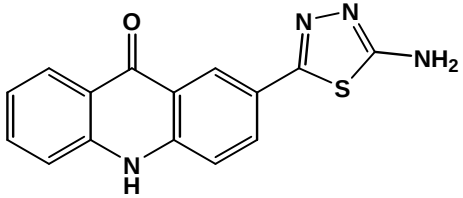
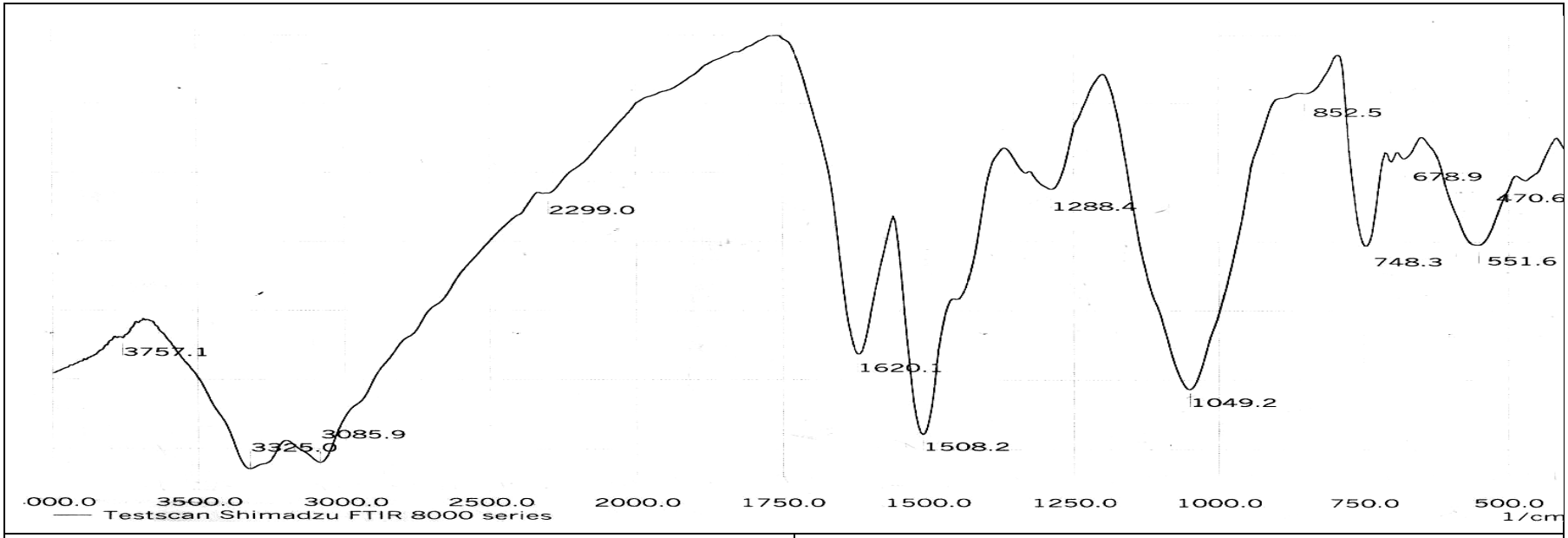
Analysis data (%) calculated					IR (KBr cm^{-1}) spectral data	
C	H	N	O	S	1. N-H stretch. I^o amine coupled doublet, asym near 3250 sym.,3168 2. Aromatic C-H stretch. about 3000 3. C=N stretch. overlapped with C=O stretch. of ketone, 1625.9 4. Ring C=C stretch., 1587.3	
61.21	3.42	19.04	5.44	10.89		
						
M.P. (^{o}C)		Yield (%)			Color	Molecular formula
> 340		48			Reddish-Brown	$C_{15}H_{10}N_4OS$

Figure (3-15): F.T.IR spectrum of 2-[5-amino-1,3,4-thiadiazole-2-yl]-9(10H)-acridone [3].



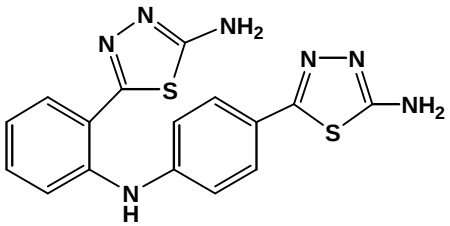
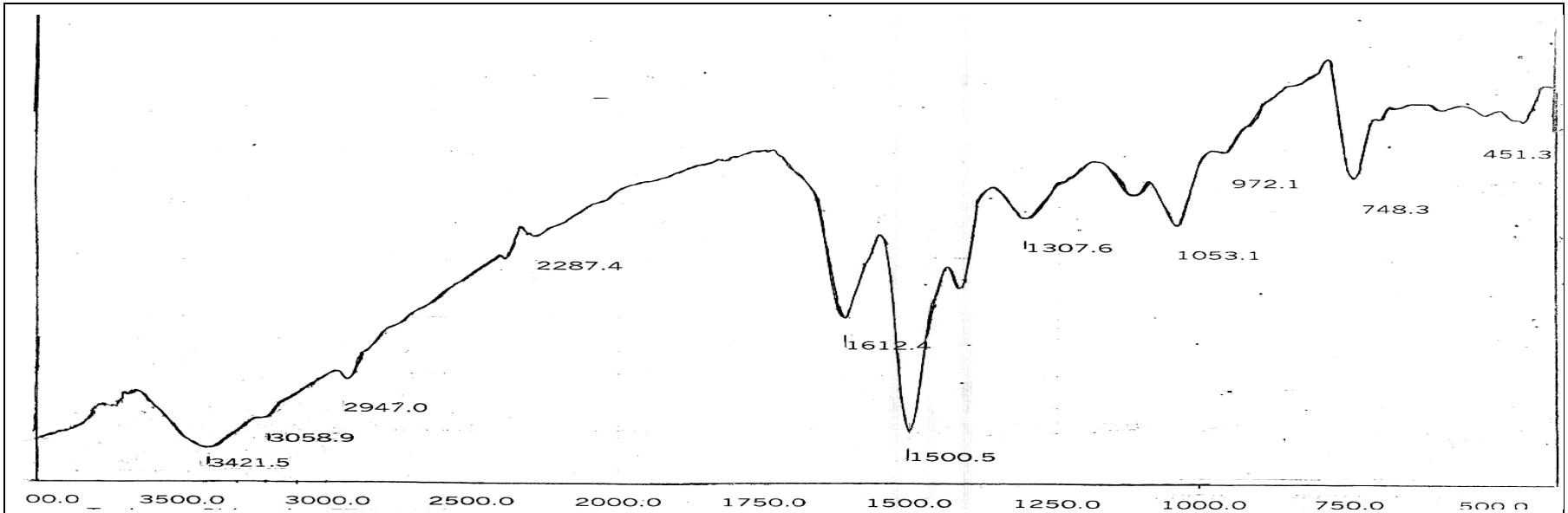
Analysis data (%) calculated				IR (KBr cm^{-1}) spectral data	
C	**H**	**N**	**S**	**1. N-H stretch. I^{o} amine coupled doublet, asym near 3325 sym. 3085.9** **2. Aromatic C-H stretch. overlapped with sym. N-H, 3085.9** **3. C=N stretch., 1620.1** **4.Ring C=C stretch.,1508.2** **5. Out-of-plane C-H bend. (*p*-disub. benzene) 852.5** **6. Out-of-plane C-H bend. (o-disub. benzene) 748.3**	
52.30	**3.57**	**26.68**	**17.45**		
					
M.P. (^{o}C)		**Yield (%)**		**Color**	**Molecular formula**
288-290		**45**		**Brown**	**$C_{16}H_{13}N_7S_2$**

Figure (3-16): F.T.IR spectrum of 2,4`-bis[5-(amino)-1,3,4-thiadiazole-2-yl]diphenylamine [21].

3.4.2 Synthesis of Schiff bases derived from 2-Amino-1,3,4-thiadiazole [22,23]:

The two Schiff bases namely, 2,4`-bis[5-benzylideneimino-1,3,4-thiadiazol-2-yl]diphenylamine and 2,4`-bis[5-(4-nitrobenzylideneimino)-1,3,4-thiadiazol-2-yl]diphenylamine were synthesized by refluxing the compound [21] with benzaldehyde and 4-nitrobenzaldehyde , respectively . The synthesized compounds were characterized by melting points and F.T.IR spectra.

The characteristic F.T.IR absorption bands Figure (3-17) and (3-18) showed disappearance of two absorption bands due to (NH_2) stretching of amino-thiadiazole, it also shows a stretching band around (1600 cm^{-1}) which is assigned to ν (C=N).



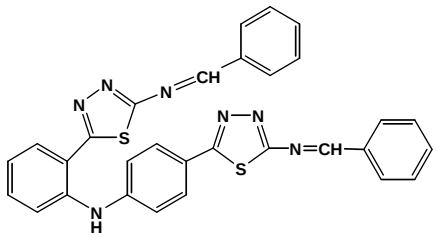
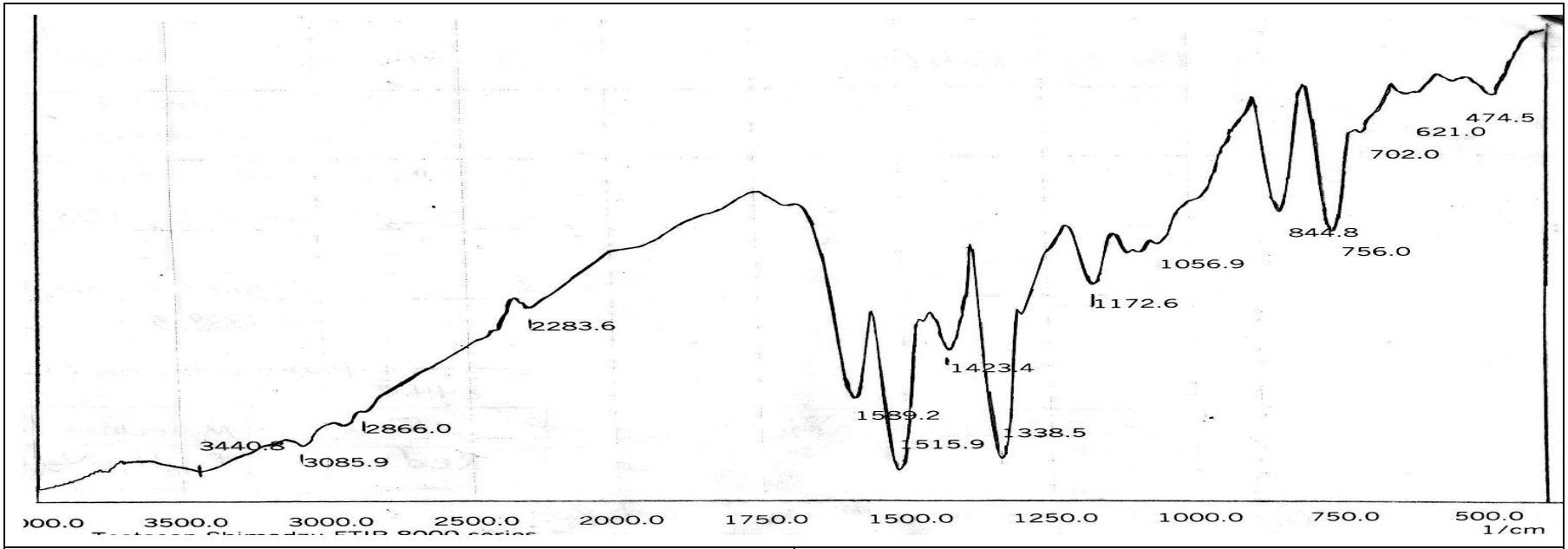
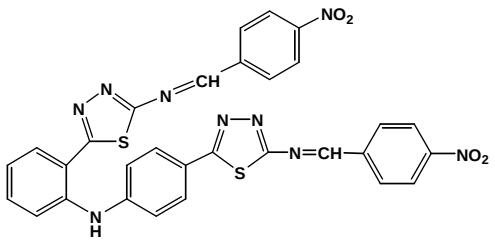
Analysis data (%) calculated				IR (KBr cm^{-1}) spectral data	
C	**H**	**N**	**S**	**1. N-H stretch.,3421.5** **3. Aromatic C-H stretch., 3058.9** **3. Aliphatic C-H stretch., 2947.0** **4. C=N stretch.,1612.4** **5. C=C ring stretch.,1500.5** **6. Out-of-plane C-H bend. (o-disub. benzene) 748.3**	
66.52	**4.54**	**18.10**	**11.84**		
					
M.P. (^{o}C)		**Yield (%)**		**Color**	**Molecular formula**
178-182		**40**		**Red**	**$C_{30}H_{21}N_7S_2$**

Figure (3-17): F.T.IR spectrum of 2-4`-bis[5-benzylideneimino-1,3,4-thiadiazol-2-yl]diphenylamine [22].



Analysis data (%) calculated					IR (KBr cm^{-1}) spectral data
C	**H**	**N**	**O**	**S**	**1. N-H stretch., 3440.8** **2. Aromatic C-H stretch., 3085.9** **3. Aliphatic C- stretch., 2866.0** **4. C=N stretch., 1589.2** **5. Asym. and sym. (Ar-NO_2) stretch., 1515.9 and 1338.5** **6. Out-of-plane C-H bend. (*p*-disub. benzene) 844.8** **7. Out-of-plane C-H bend. (*o*-disub. benzene) 756.0**
56.86	**3.02**	**19.89**	**10.10**	**10.12**	



M.P. (^oC)	Yield (%)	Color	Molecular formula
216-218	**50**	**Red**	**$C_{30}H_{19}N_9O_4S_2$**

Figure (3-18): F.T.IR spectrum of 2,4`-bis[5-(4-nitrobezylideneimino)1,3,4-thiadiazol-2-yl]diphenylamine [23].

3.5 The UV-Visible spectral data:

The ultra-violet spectrophotometry technique is also used to characterize the synthesized compounds in dimethyl sulfoxide as a solvent. The Ultra-Violet electronic spectra of compounds [2,3,12, 13,14,15,19,20,21,22 and 23] are shown in figures from (3-19) to (3-29) respectively. These spectra showed bands at regions (250-538 nm) .

These **λ max** could be assigned to (π-π*),(n-π*) [(acridone, thiadiazole, oxadiazole, C=N (azomethine)] transitions.

The spectra data table (3-1) is found to be quite similar to other acridone derivatives reported earlier literature **(1, 8, 16, 82-84)**.

Table (3-1): The UV-Visible absorption maxima (λ nm) of diphenylamine-2,4`-dicarboxylic acid derivatives.

Comp. no.	UV-Visible (λ nm)
2	**538, 396, 378, 325, 286, 262, 239**
3	**488, 396, 377, 324, 286, 259, 213**
12	**381, 261**
13	**411, 329, 258**
14	**402, 381, 364, 345, 288, 259, 232**
15	**396, 378, 324, 287, 259**
19	**397, 379, 361, 327, 286, 267**
20	**515, 402, 342, 250**
21	**499, 314**
22	**315**
23	**321**

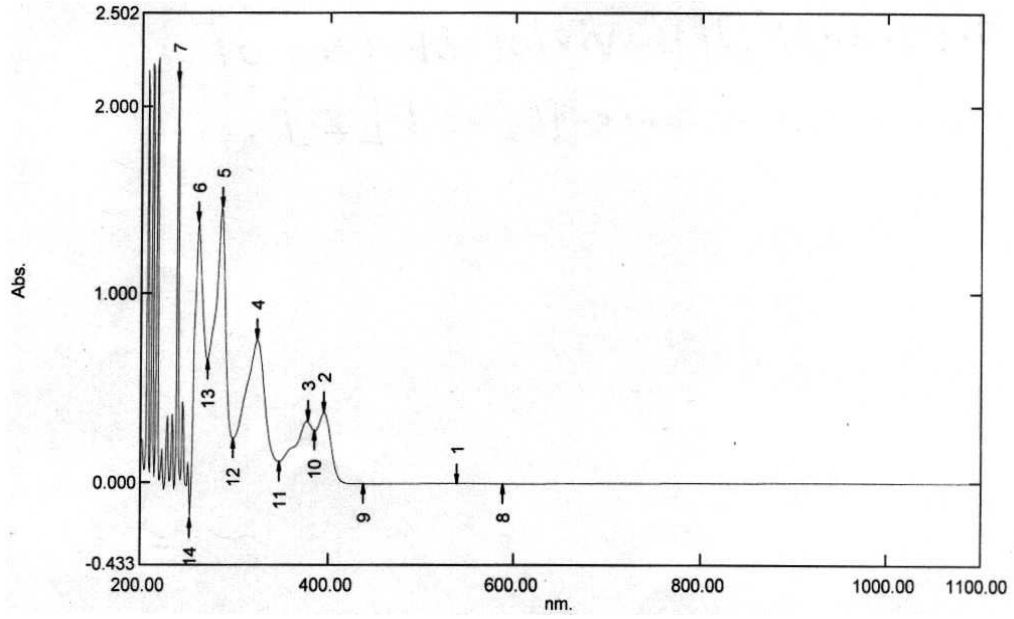


Figure (3-19): Ultraviolet spectrum of 9(10H)-Acridone-2-carboxylic acid [2].

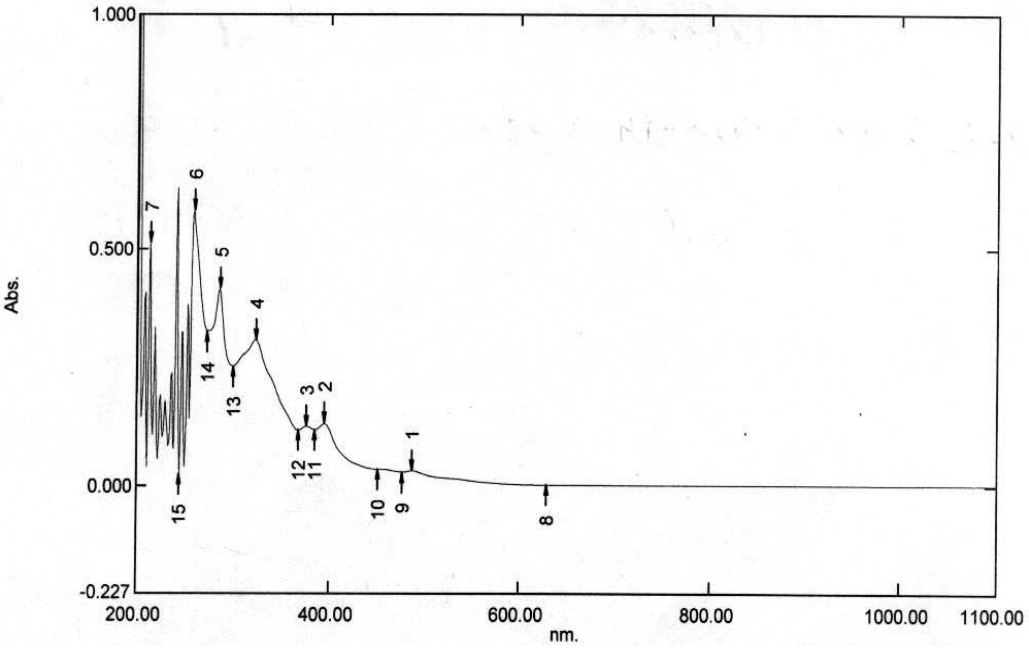


Figure (3-20): Ultraviolet spectrum of 2-[5-Amino-1, 3, 4-thiadiazol-2-yl]-9(10H)-acridone [3].

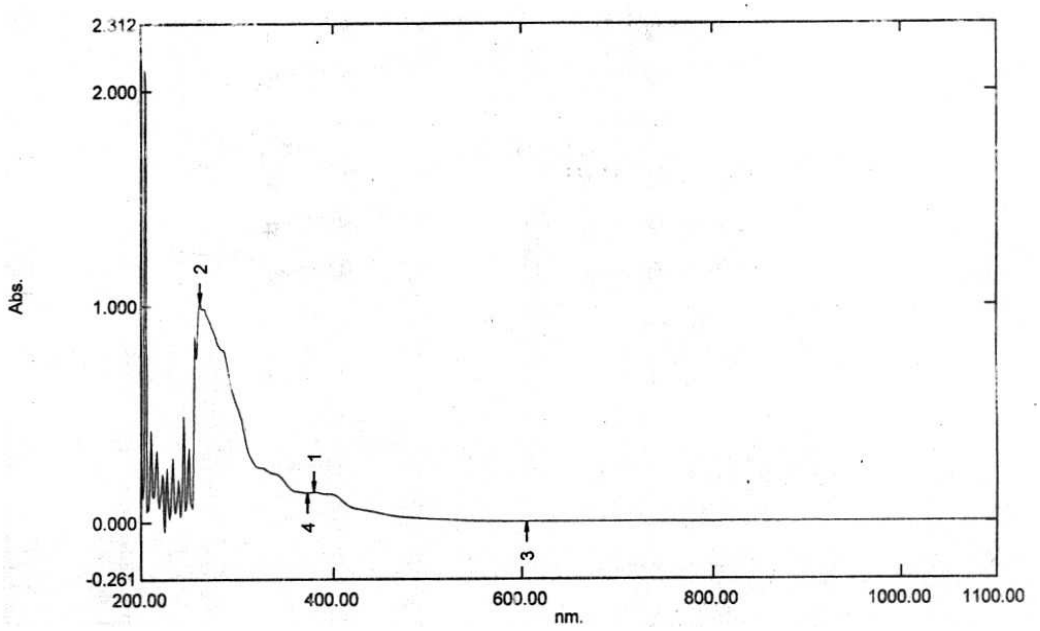


Figure (3-21): Ultraviolet spectrum of 2-[5-(Phenyl)-1, 3, 4-oxadiazol-2-yl]-9(10H)-acridone [12].

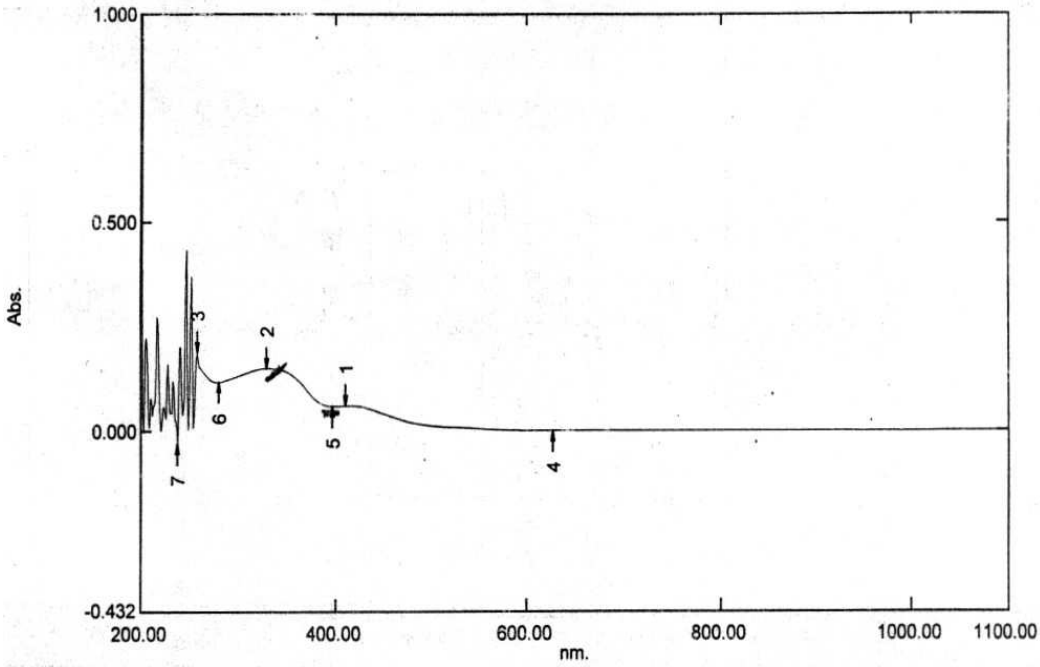


Figure (3-22): Ultraviolet spectrum of 2-[5-(4-Nitrobenzene)-1, 3, 4-oxadiazol-2-yl]-9(10H)-acridone [13].

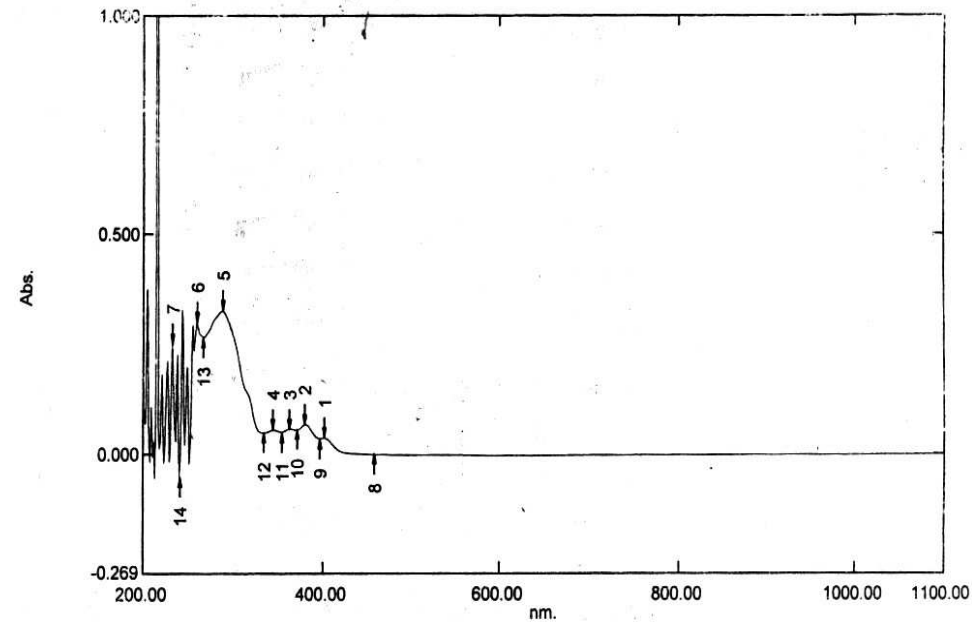


Figure (3-23): Ultraviolet spectrum of 2-[5-(4-Chlorobenzene)-1, 3, 4-oxadiazol-2-yl]-9(10H)-acridone [14].

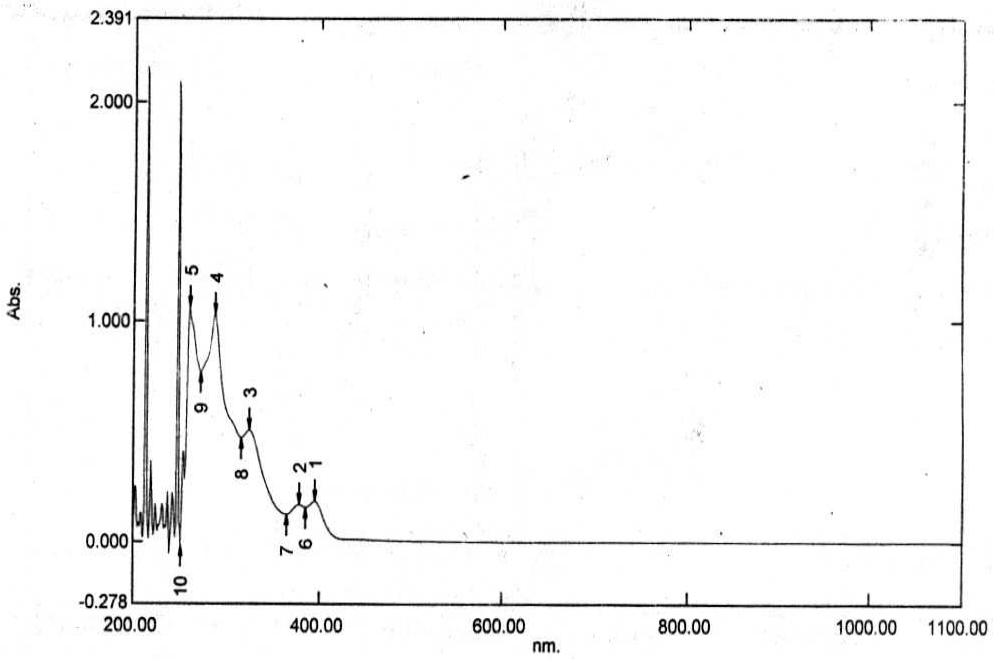


Figure (3-24): Ultraviolet spectrum of 2-[9(10H)-Acridone-2-yl]-5-[4-(9(0H)-acridone-2-yl-carboxy) phenyl]-1, 3, 4-oxadiazole [15].

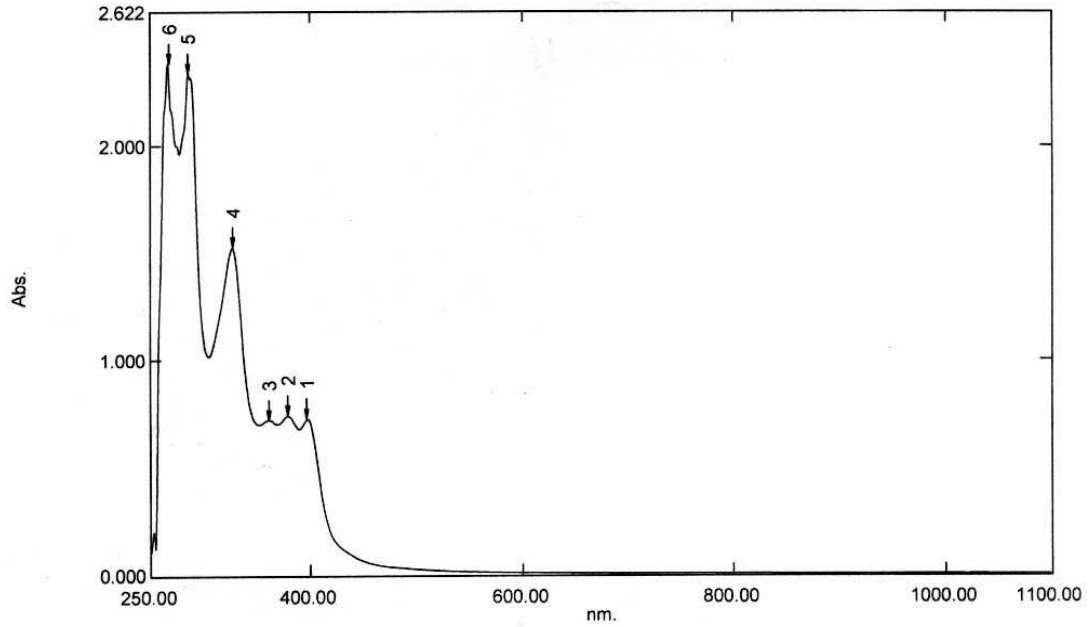


Figure (3-25): Ultraviolet spectrum of 2-[5-Thiol-1, 3, 4-oxadiazol-2-yl]-9(10H)-acridone [19].

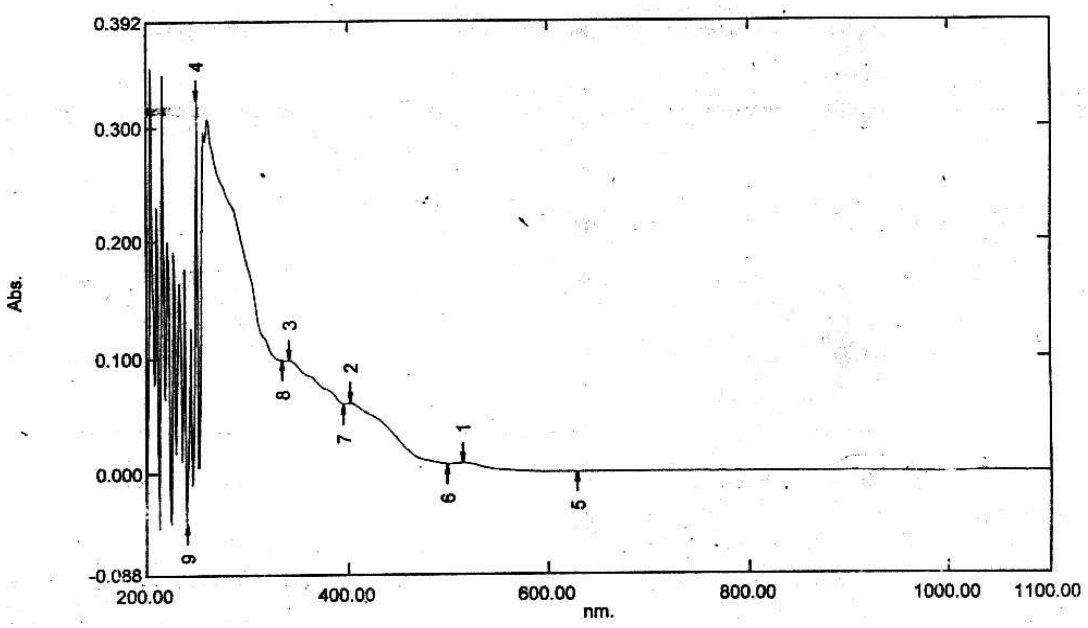


Figure (3-26): Ultraviolet spectrum of 2,4`-bis-[5-phenyl-1, 3, 4-oxadiazol-2-yl] diphenylamine [20].

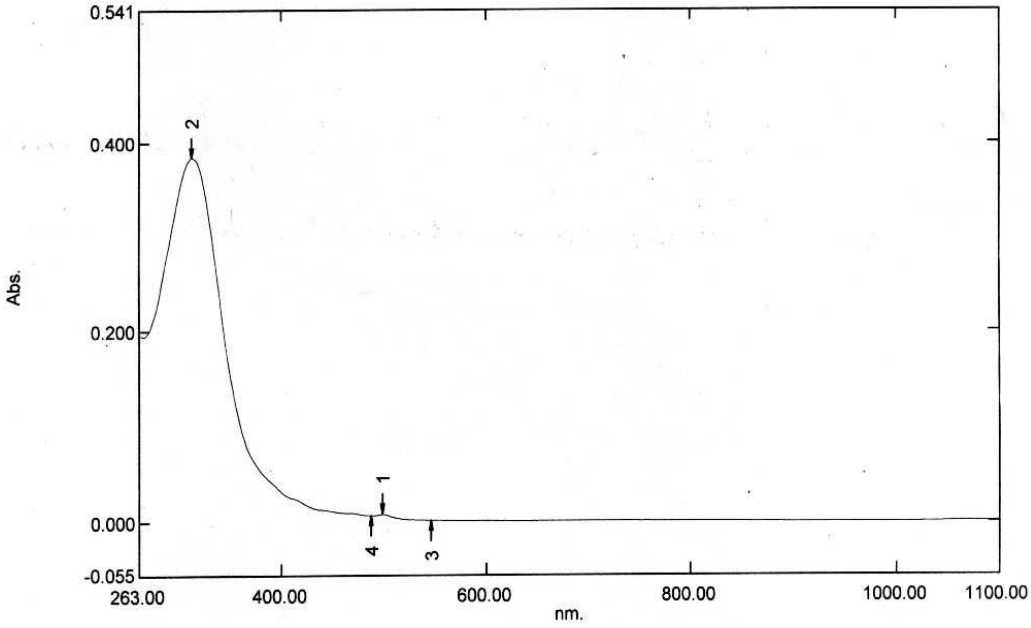


Figure (3-27): Ultraviolet spectrum of 2, 4`-bis-[5-amino -1,3,4-thiadiazol-2-yl] diphenylamine [21].

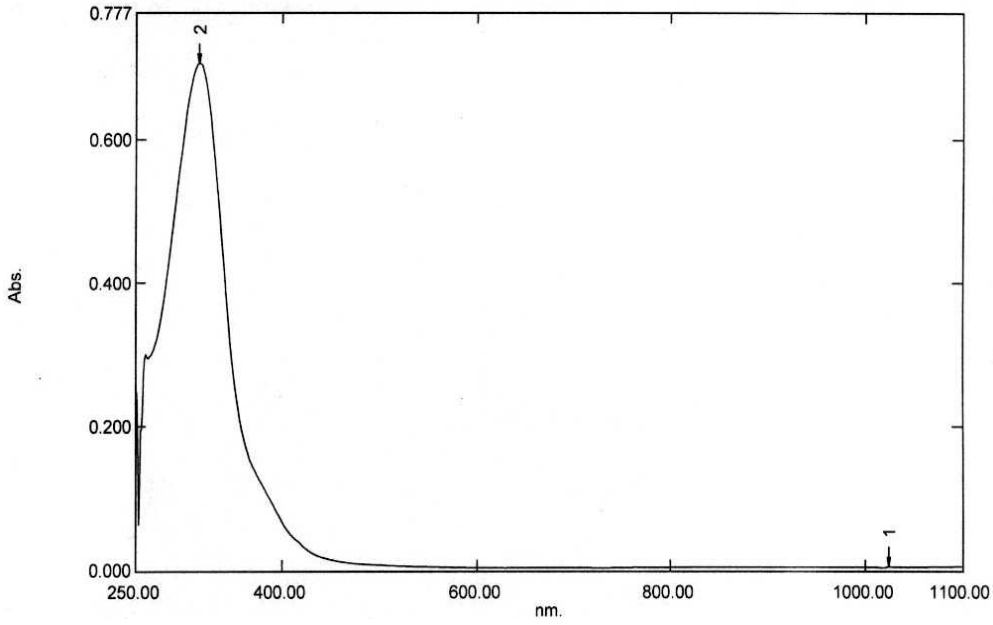


Figure (3-28): Ultraviolet spectrum of 2,4`-bis[5-bezylideneimino-1,3,4-thiadiazol-2-yl]diphenylamine [22].

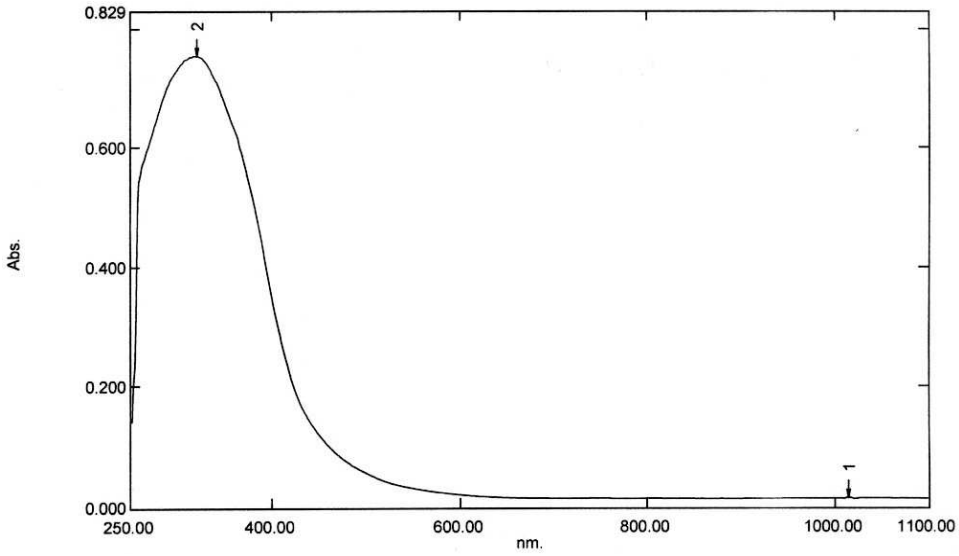


Figure (3-29): Ultraviolet spectrum of 2,4`-bis[5-(4-nitrobenzelideneimino)-1,3,4-thiadiazol-2-yl]diphenylamine [23].

3.6 Antibacterial Activity:

Acridines were mainly tested against bacterial infections, malaria and other protozoa infections. From a structural point of view, acridines and acridones bearing fused benzene or heterocyclic rings will be presented as analogous because of close similarities of their chemical, physiochemical or biological properties with acridine derivatives [(85)].

1,3,4-Oxadiazole are well known to have a wide range of biological activities. Examples of such activities are anti-inflammatory [(86)], antifungal [(87)], anti parasitic[(88)] and antimicrobial effects[(89)]. Some bis-1,3, 4-oxadiazoles have also been tested for antibacterial activity [(90)]. The 1,3, 4-thiadiazole nucleus which incorporates an N-C-S linkage has been attracting wide spread attention due to their diverse pharmacological properties such as antimicrobial, anti-inflammatory, analgesic and antitumoral activities [(91-97)]. The antibacterial activity of the synthesized compounds was determined ***in vitro*** using paper disc method [(98)] (agar plate diffusion method).The representative compounds [1-3,12-15,19-23] were test against two pathogenic microorganism, ***Staphylococcus aureus***

(Gram +ve) and ***Escherichia coli*** (Gram –ve). In this method the solution of our tested compounds were prepared by dissolving in dimethyl sulfoxide (1mg per 1ml), a standard 5mm diameter sterilized filter paper impregnated with the compound was placed on agar plate seeded with the test organism . The plates were incubated for 24 hours at 37^{o}C . The zone of inhibition of bacterial growth produced by diffusion of the compounds from the disc into the surrounding medium was measured in mm as shown in table (3-2) and figures (3.30-3.33) respectively. Compounds [12-15,21-23] showed considerable activities against both kinds of microorganisms. Compounds [1,2 and 3] showed good activities against *Staph.aureus* (Gram +ve)only. Compound [19] showed well activity against *Esch. Coli* (Gram -ve) only. Compound [20] has low activity against two pathogenic bacteria .

Table (3-2) Antibacterial activities of the tested compounds .

Comp. no. DMSO (solvent) 1mg/mL	*Staphylococcus* **(G +ve)**	*Esch. Coli* **(G -ve)**
[1]	**20mm**	**10 mm**
[2]	**13mm**	**9mm**
[3]	**15mm**	**10mm**
[12]	**17mm**	**12mm**
[13]	**21mm**	**18mm**
[14]	**13.5mm**	**14mm**
[15]	**14mm**	**18mm**
[19]	**10mm**	**12mm**
[20]	**10mm**	**9mm**
[21]	**18mm**	**17mm**
[22]	**15mm**	**17mm**
[23]	**15mm**	**11.5mm**

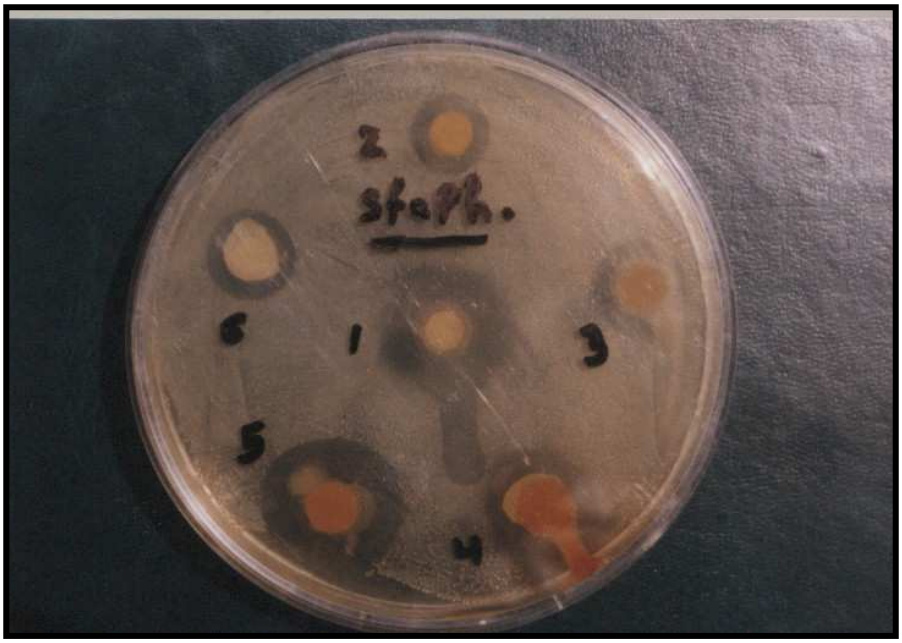


Figure (3-30): Effect of [1,2,3,12,13 and 14] on *Staph.aureus*,1=effect of [1], 2=effect of [2], 3=effect of [3], 4=effect of [12], 5=effect of [13], 6=effect of [14].

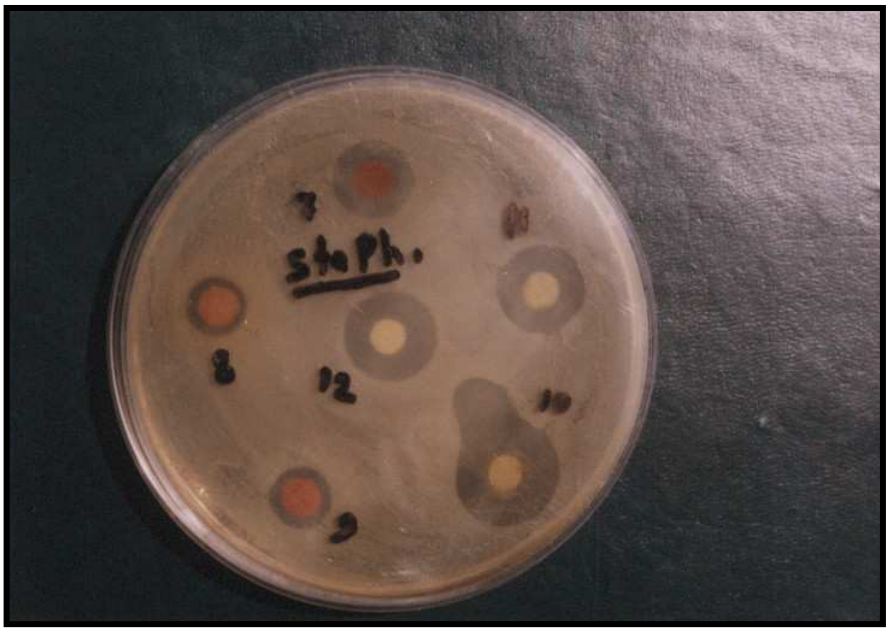


Figure (3-31): Effect of [15,19,20,21,22 and 23] on *Staph.aureus*,7=effect of [15], 8=effect of [19], 9=effect of [20], 10=effect of [21], 11=effect of [22], 12=effect of [23].

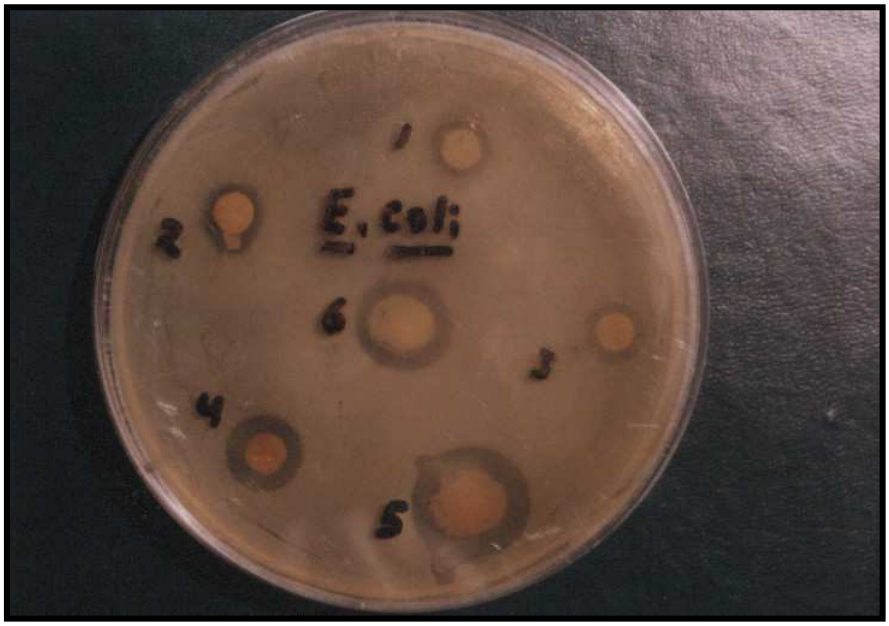


Figure (3-32): Effect of [1,2,3,12,13 and 14] on *Esch.coli.*,1=effect of [1], 2=effect of [2], 3=effect of [3], 4=effect of [12], 5=effect of [13], 6=effect of [14].

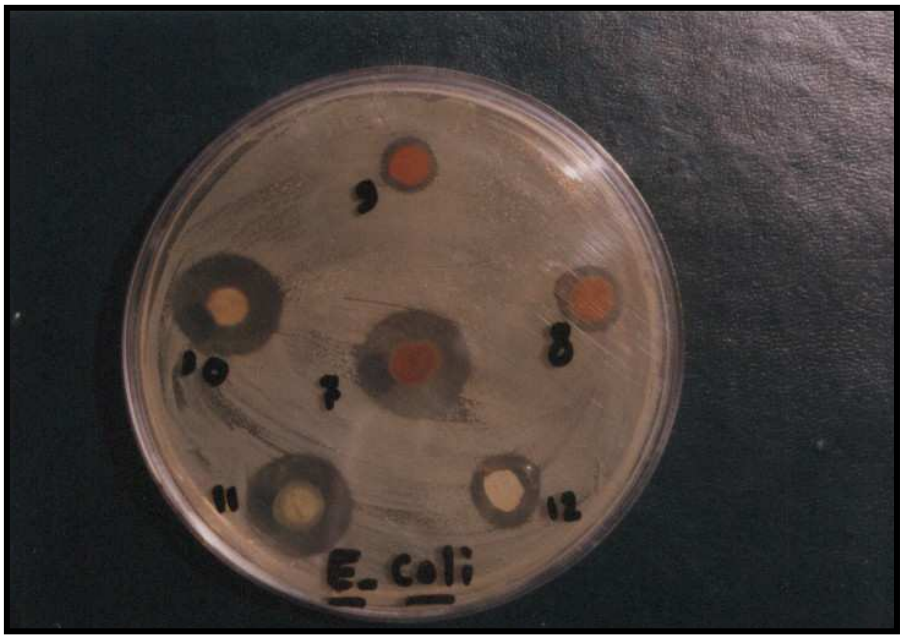
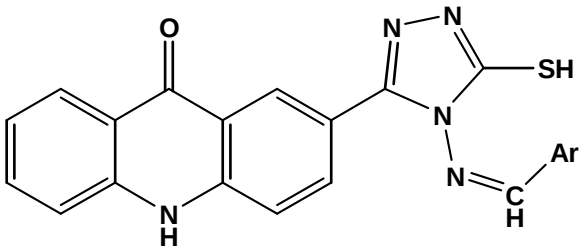


Figure (3-33): Effect of [15,19,20,21,22 and 23] on *Esch.coli.*,7=effect of [15], 8=effect of [19], 9=effect of [20], 10=effect of [21], 11=effect of [22], 12=effect of [23].

3.7 Suggestion for further work:

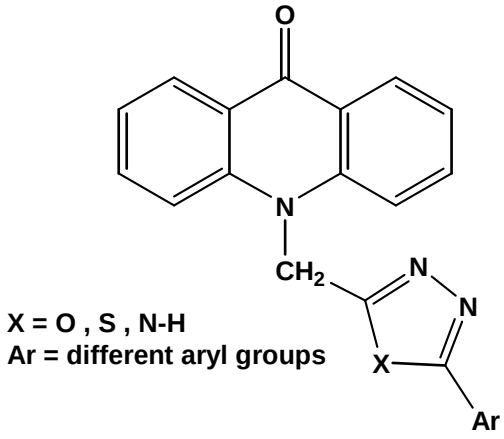
The following work will be done in near future:

1) Synthesized a new series having the following structural formula



Ar = different aryl groups

2) Synthesized the following compounds :



X = O , S , N-H
Ar = different aryl groups

3) Studying the photostability of the above two series for polystyrene and polyvinyl chloride .

4) Studying the Fluorescence properties of our synthesized compounds and the above two series .

5) The good results obtained for biological activity encouraged us to studying the biological activity of the above two series .

Chapter Two
Experimental Part

2.0 Chemicals and Techniques:

2.1 Chemicals:

The following chemicals were obtained from different companies.

Compounds (purity)	Supplied from
2-Chlorobenzoic acid (98%)	BDH
4-Aminobenzoic acid (99%)	BDH
Copper oxide powder (98%)	Merck
Amyl alcohol (99%)	BDH
n-Butanol (99.5%)	BDH
Potassium carbonate (99%)	BDH
Hydrochloric acid (37%)	BDH
Sodium hydroxide (97%)	Fluka
Activated charcoal (high purity)	BDH
Sulfuric acid (95%)	BDH
Methanol (99+%)	BDH
Ethanol (absolute)	BDH
Phosphorus oxychloride (99 %)	Fluka
Chloroform (99+%)	BDH
4-Chlorobenzoic acid (99%)	BDH
Benzoic acid (99%)	Fluka
4-Nitrobenzoic acid (99+%)	Merck
4-Hydroxybenzoic acid (99%)	BDH
Hydrazine hydrate (85%)	Merck
Thiosemicarbazide (99%)	Fluka
Potassium hydroxide (85%)	BDH
Thionyl chloride (99+%)	Fluka
Dimethyl sulfoxide, DMSO (99.9%)	BDH
Carbon disulfide (99+%)	Merck
Diethyl ether (distilled over a sodium wire)	BDH
Sodium bicarbonate (99.7%)	BDH
Benzaldehyde (99+%)	Fluka
4-Nitrobenzaldehyde (99.55%)	Merck

2.2 Techniques:

- Melting points were measured using Gallen Kamp melting point apparatus and were uncorrected.

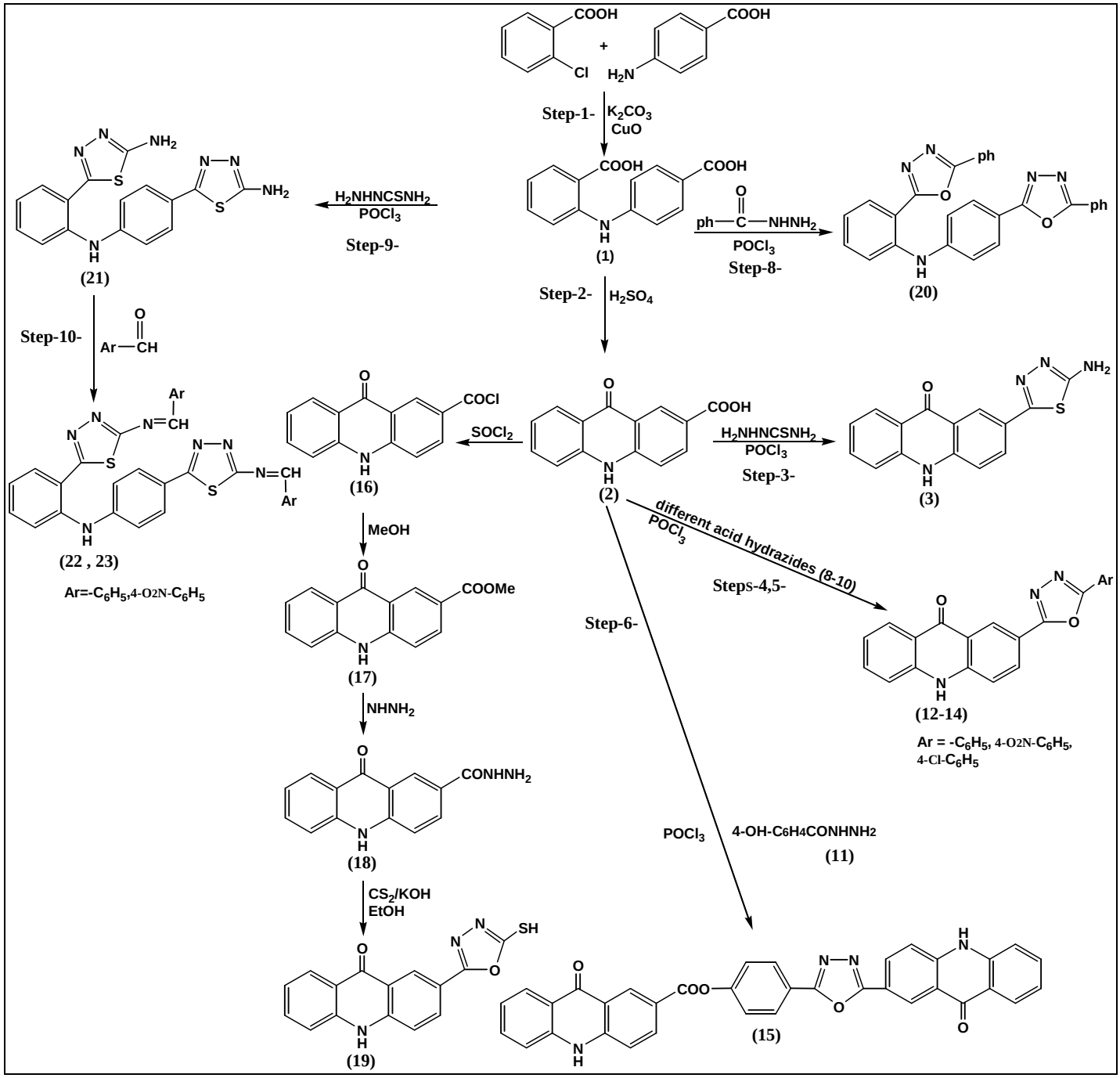
- Infrared spectra were recorded on F.T.IR-8300 Fourier transforms infrared spectrophotometer ***SHIMADZU*** as potassium bromide disc in the (600-4000) cm^{-1} spectral range.

- The electronic spectra of the compounds were obtained using (***SHIMADZU*** UV-Vis. 160A) ultraviolet spectrophotometer.

- The elemental analysis (C.H.N) were calculated theoretically by using chem. office program .

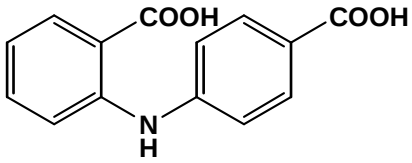
2.3 Stepwise synthesis of Diphenylamine-2,4`-dicarboxylic acid derivatives:

The synthesis of target heterocyclic compounds [2,3,12-15,19-23] derived from diphenylamine-2,4`-dicarboxylic acid are shown in Scheme (2-1).


Step-1- K2CO3 CuO
(1)
Step-2- H2SO4
(2)
Step-3-
(3)
Step-8-
(20)
Step-9-
(21)
Step-10-
(22 , 23)
Ar=-C6H5,4-O2N-C6H5
(16)
SOCl2
MeOH
(17)
NHNH2
(18)
CS2/KOH
EtOH
(19)
different acid hydrazides (8-10)
POCl3
Steps-4,5-
(12-14)
Ar = -C6H5, 4-O2N-C6H5, 4-Cl-C6H5
Step-6-
POCl3
4-OH-C6H4CONHNH2
(11)
(15)

Scheme (2-1) .

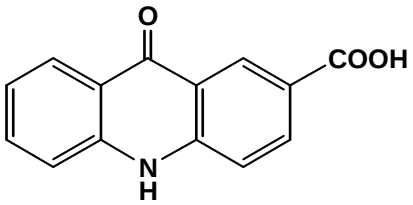
2.3.1 Preparation of Diphenylamine-2, 4'-dicarboxylic acid [1], Ullmann condensation:



$C_{14}H_{11}NO_4$
Exact Mass: 257.07
Mol. Wt.: 257.24
C, 65.37; H, 4.31; N, 5.44; O, 24.88
M.P. : 208 - 210 ^oC

To a mixture of 2-chlorobenzoic acid (12.5g, 0.08mol), 4-aminobenzoic acid (10.97g, 0.08 mol) and copper oxide powder (0.2g) in (60 ml) of amyl alcohol, dry potassium carbonate (12g) was slowly added and the contents were allowed to reflux for (6h) at about (100^{o}C). The amyl alcohol was removed by evaporation and the mixture poured into (250 ml) of hot water , cooling and acidified with concentrated hydrochloric acid. The greenish black precipitate which formed was filtered, washed with cold water and collected. The crude acid was dissolved in aqueous sodium hydroxide solution, boiled in the presence of activated charcoal and filtered, on acidification of the filterate with concentrated of hydrochloric acid white precipitate of [1] was obtained which was washed with water and recrystallized from ethanol . [8 with modification]. Yield (62%) . Figure (3-1)

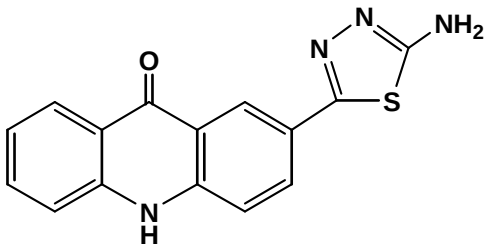
2.3.2 Preparation Of 9(10H)-Acridone-2-carboxylic acid [2]:



$C_{14}H_9NO_3$
Exact Mass: 239.06
Mol. Wt.: 239.23
C, 70.29; H, 3.79; N, 5.86; O, 20.06
M.P. : > 330 ^oC

compound [1] (5g) was placed in a round bottom flask which was added in (50 ml) of concentrated sulfuric acid, shaken well and heated on water bath at (100^{o}C) for (3hrs). Appearance of yellow color indicated the completion of the reaction. Then, it was poured into (250 ml) of hot water. The yellow precipitate which formed was filtered, washed with water and collected. The sample of 9(10H)-acridone-2-carboxylic acid [2] was recrystallized from methanol [8 with modification]. Yield (72%) . Figure (3-2)

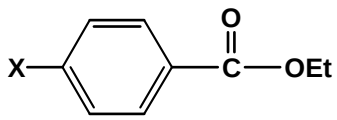
2.3.3Preparation of 2-[(5-Amino)-1, 3, 4-thiadiazol-2-yl]-9(10H)-acridone [3]:



$C_{15}H_{10}N_4OS$
Exact Mass: 294.06
Mol. Wt.: 294.33
C, 61.21; H, 3.42; N, 19.04; O, 5.44; S, 10.89
M.P. : > 340 ^{o} C

A mixture of 9(10H)-Acridone-2-carboxylic acid (1g, 0.004 mol) , thiosemicarbazide (0.364g, 0.004 mol) and phosphorus oxychloride (5 ml) was refluxed gently overnight. After cooling, water was added (50 ml). The mixture was refluxed for (3 hrs) and filtered. The solution was neutralized with potassium hydroxide. The precipitate was filtered and washed with distilled water and recrystallized from ethanol to give the title compound [3] [71 with modification] . Yield (48%) .Figure (3-15)

2.3.4 Preparation of 4-Substituted Ethyl benzoates [4-7]:



X = H , NO_2 , Cl , OH

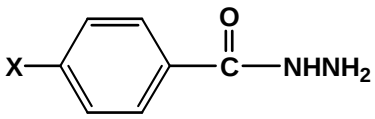
[4],[5],[6],[7]

These compounds were prepared by condensation of appropriate 4-substituted benzoic acid (10g) with absolute ethanol (50 ml) in the presence of concentrated sulfuric acid (1 ml) and treated according to the procedure described in the literature [75]. The physical properties of these compounds are given in Table (2-1).

Table (2-1): The physical properties of the 4-substituted ethyl benzoate .

Comp. No.	X	Yield%	m.p.(^{o}C)	b.p.(^{o}C)	Color
4	H	84	_	213-215	Colorless
5	NO_2	76	54-56	_	Yellow
6	Cl	78	_	238	Pale-Yellow
7	OH	80	114-116	_	White

2.3.5 Preparation of 4-Substituted Benzoyl hydrazines [8-11 :



X = H , NO_2 , Cl , OH

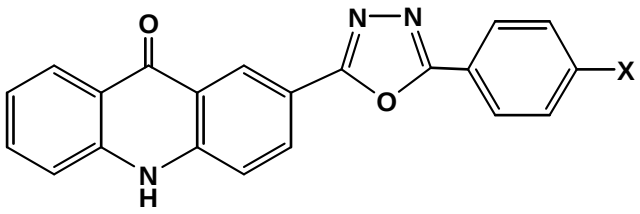
[8],[9],[10],[11]

A mixture of 4-Substituted ethyl benzoate (0.05 mol) and excess of hydrazine hydrate (10 ml) were refluxed for (2 hrs), ethanol (15 ml) was added and refluxed for (5-7 hrs). The precipitate which separated on cooling was filtered and washed with cold water (76 with modification). The physical properties of these compounds are given in Table (2-2). Figures (3-3) to (3-5) and (3-9).

Table (2-2): The physical properties of the 4-substituted benzoyl hydrazines .

Comp. No.	X	Yield%	m.p.(^{o}C)	Color
8	H	68	113-115	White
9	NO_2	69	220	Yellow
10	Cl	66	166-168	White
11	OH	74	266-268	White

2.3.6 Preparation of 2-[5-(4-Substituted benzene)-1,3,4-oxadiazol-2-yl]-9(10H)- acridone [12-14]:



X = H , NO_2 , Cl

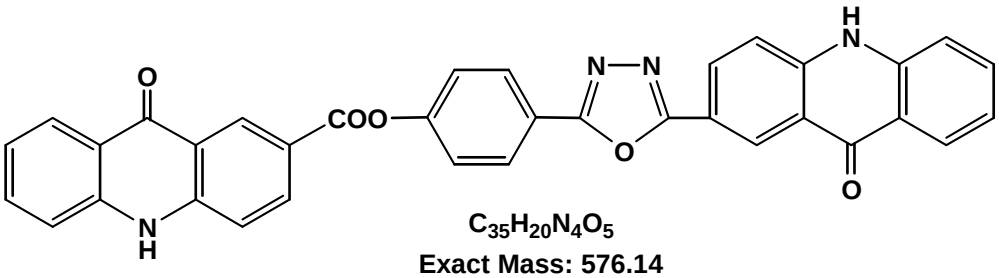
[12],[13],[14]

A mixture of 9(10H)-Acridone-2-carboxylic acid [2] (0.004 mol), 4-substituted benzoyl hydrazine (0.004 mol) and phosphorus oxychloride (5 ml) was refluxed overnight. The cold reaction mixture was poured on the crushed ice and made basic by adding sodium bicarbonate solution. The resulting solid was filtered, dried to give the desired product [46 with modification]. The physical properties of these compounds are given in table (2-3). Figures (3-6) to (3-8) .

Table (2-3): The physical properties of 2-[5-(4-substituted benzene)-1,3,4-oxadiazol-2-yl]-9(10H)-acridone.

Comp. No.	X	Molecular Formula	M.Wt.	Yield%	m.p.(°C)	color
12	H	$C_{21}H_{13}N_3O_2$	339	66	296-298	Red
13	NO_2	$C_{21}H_{12}N_4O_4$	384	74	302-304	Reddish-Brown
14	Cl	$C_{21}H_{12}N_3O_2Cl$	373.5	68	>330	Brown

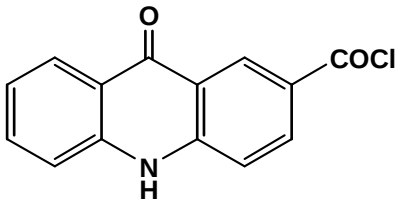
2.3.7 Preparation of 2-[9(10H)-Acridone-yl]-5-[4(9(10H)-acridone-2-yl-carboxy) phenyl]-1,3,4-oxadiazole [15]:



$C_{35}H_{20}N_4O_5$
Exact Mass: 576.14
Mol. Wt.: 576.56
C, 72.91; H, 3.50; N, 9.72; O, 13.87
M.P. : 324 - 326 °C

A mixture of compound [2] (0.5g, 0.004 mol), 4-hydroxybenzoyl hydrazine [11] (0.304g, 0.002 mol) and phosphorus oxychloride (7.5ml) was refluxed overnight. Procedure (2.3.6) was followed for the synthesis of this compound. Yield (60 %) . Figure (3-10).

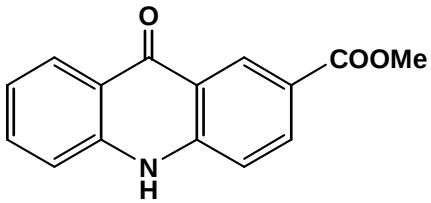
2.3.8 Preparation of 9(10H)-Acridonyl chloride [16]:



$C_{14}H_8ClNO_2$
Exact Mass: 257.02
Mol. Wt.: 257.67
C, 65.26; H, 3.13; Cl, 13.76; N, 5.44; O, 12.42
M.P. : 234 - 236^oC

A mixture of (1g, 0.004 mol) 9(10H)-Acridone-2-carboxylic acid [2] and excess thionyl chloride (10 ml) was refluxed for (3 hrs), and then the excess of thionyl chloride was evaporated [46 with modification] . Yield (64 %) .

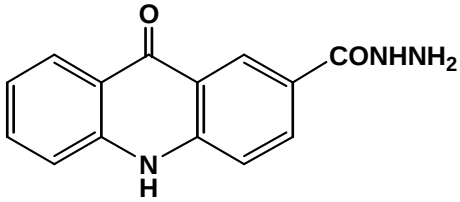
2.3.9 Preparation of 9(10H)-Acridone-2-methylcarboxylate [17]:



$C_{15}H_{11}NO_3$
Exact Mass: 253.07
Mol. Wt.: 253.25
C, 71.14; H, 4.38; N, 5.53; O, 18.95
M.P. : >340 ^oC

To the compound [16] (0.5g, 0.00194 mol), cold methanol (10 ml) was added almost readily and an instantaneous reaction occured to give the title product. The crystals of ester were collected, filtered and washed with cold solution of 10% $NaHCO_3$, then with cold water [46 with modification] . Yield (92 %) . Figure (3-11) .

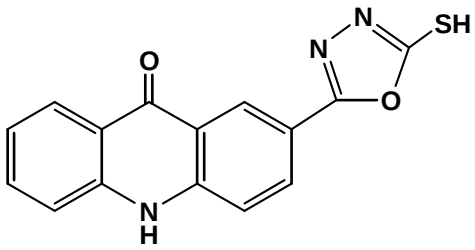
2.3.10 Preparation of 9(10H)-Acridone-2-carboxylicacid hydrazide [18]:



$C_{14}H_{11}N_3O_2$
Exact Mass: 253.09
Mol. Wt.: 253.26
C, 66.40; H, 4.38; N, 16.59; O, 12.63
M.P. : 318 - 320 ^{o}C

A mixture of ester [17] (0.5g, 0.00197 mol) and excess (85%) hydrazine hydrate (10ml) was refluxed for (3 hrs), DMSO (1ml) was added and the reflux continued for another (24 hrs). The crude product which was obtained after distilling off the excess DMSO. Cooling filtering then washing with a little cold water, this product was employed in the next step without further purification [76 with modification]. Yield (70 %) . Figure (3-12).

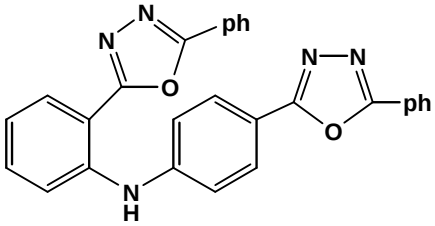
2.3.11 Preparation of 2-[5-Thiol-1, 3, 4-oxadiazol-2-yl]-9(10H)-acridone [19]:



$C_{15}H_9N_3O_2S$
C, 61.01 ; H, 3.07 ; N,14.23 ; O, 10.84 ; S,10.86
M.P. : > 340 ^{o}C

To a stirred solution of acid hydrazide [18] (0.5g, 0.00169 mol) in ethanol (10mL) and potassium hydroxide (0.0946g, 0.00169 mol), carbon disulfide (0.202ml, 0.00338 mol) was added slowly at (0^oC), and the mixture was refluxed for (6 hrs). The solvent was evaporated and the residue dissolved in water and acidified with dilute hydrochloric acid. The precipitate was filtered and washed with a litle cold water. The crude product was recrystallized from ethanol to give the desired product [77 with modification]. Yield (69 %).Figure (3-13).

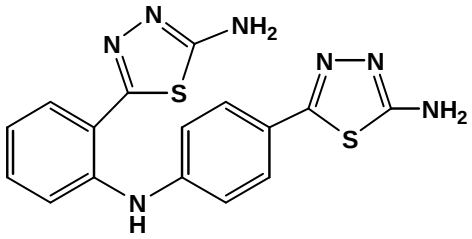
2.3.12 Preparation of 2,4`-Bis[5-phenyl-1,3,4-oxadiazol-2-yl] diphenylamine [20]:



$C_{28}H_{19}N_5O_2$
Exact Mass: 457.08
Mol. Wt.: 457.28
C, 63.37; H, 2.99; N, 23.09; O, 10.55
M.P. : 278 ^oC

A mixture of compound [1] (0.5g, 0.00194 mol) benzoyl hydrazine (0.263g, 0.00388 mol) and phosphorus oxychloride (5ml) was refluxed overnight. The cold reaction mixture was poured on crushed ice and then made basic by adding sodium bicarbonate solution. The resulting solid was filtered, dried and recrystallized from (chloroform-ethanol) to give the title oxadiazole. Yield (70%) . Figure (3-14).

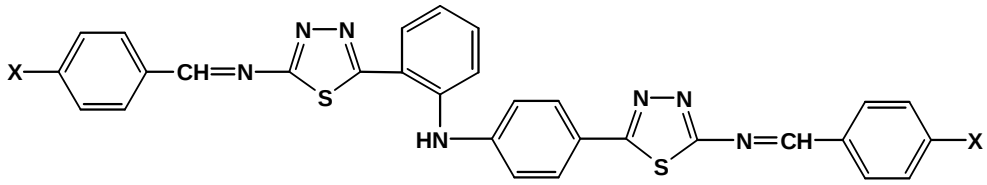
2.3.13 Preparation of 2, 4`-Bis [5-amino-1, 3, 4-thiadiazol-2-yl] diphenylamine [21]:



$C_{16}H_{13}N_7S_2$
Exact Mass: 367.07
Mol. Wt.: 367.45
C, 52.30; H, 3.57; N, 26.68; S, 17.45
M.P. : 288 - 290 ^oC

A mixture of diphenylamine-2,4`-dicarboxylic acid [1] (1g, 0.0038 mol), thiosemicarbazide (0.709g, 0.0076 mol) and phosphorus oxychloride (10ml) was refluxed. Procedure (2.3.3) was followed for synthesis of this compound Yield (45%). Figure (3-16).

2.3.14 Preparation of Schiff-bases [22,23]:



X = H , NO_2
$C_{30}H_{19}N_7S_2$
Exact Mass: 541.11
Mol. Wt.: 541.65
C, 66.52; H, 3.54; N, 18.10; S, 11.84

A mixture of compound [21] (0.01 mol), appropriate aldehyde (0.02 mol) and absolute ethanol (25ml), few drops glacial acetic acid, were refluxed for (3hrs.) with continuous stirring. Evaporation of ethanol gave a precipitate. The precipitate was filtered, dried and recrystallized from ethanol to give the desired product. m. p. = (188-190^{o}C if X=H and 216-218^o C if X=NO2), yields (40-50%).Figures (3-17) to (3-18) .

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

تحضير بعض المركبات الحلقية غير المتجانسة الجديدة المحتوية على حلقات $^{9}(H_{10})$- أكريدون ، ودراسة فعاليتها البايولوجية

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

من قبل
أياد كريم خان باوة
بكالوريوس ٢٠٠٠ (الجامعة المستنصرية)

تموز ٢٠٠٦

جمادي الثاني ١٤٢٧

Republic of Iraq
Ministry of Higher Education
and Scientific Research
Al-Nahrain University
College of Science
Department of Chemistry

SYNTHESIS OF SOME NEW HETEROCYCLIC COMPOUNDS CONTAINING 9(10H)-ACRIDONE, AND STUDYING THEIR BIOLOGICAL ACTIVITY

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
Ayad Kareem Khan Bawa
(B.Sc Al-Mustansiriah University, 2000)

July 2006 *Jumade Al-Thani 1427*

Supervisor certification

I certify that this thesis was prepared under my 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.**

Signature :
Name : Assist.Prof.Dr.Ayad S.Hameed
Date :

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

Signature:
Name: Assist. Prof. Dr. Afaf Al-Derzi
Head of Chemistry Department
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 *Ayad Kareem Khan Bawa* **, in its contents and that, in our opinion; it is adequate as a thesis for the Degree of Master of Science, in Chemistry.**

Chairman	**Member**
Signature:	**Signature:**
Name:	**Name:**
Date:	**Date:**
Member	**Supervisor**
Signature:	**Signature:**
Name:	**Name: Assist.Prof.Dr.Ayad S.Hameed**
Date:	**Date:**

Approved for the College of Graduate Studies

Signature:

Name: Assist. Prof. Dr. Laith Abdul Aziz Al-Ani

Address: Dean of the college of Science Al-Nahrain University

Date:

DEDICATION

TO MY PARENTS

, BROTHERS

AND SISTERS

AYAD

بِسمِ اللّه الرَحمن
الرَحِيم
يَرفَعُ اللّه آلذِينَ
آمنُوا مِنكُم
وَ آلذِينَ أُوتُوا
آلعِلمَ دَرَجاتٍ
صَدَقَ اللّه العَظيِم
سُورَة المُجادَلَة الآيَة (١١)

Acknowledgment

I would like to express my deepest thanks to my respected supervisor Dr. Ayad S. Hameed for the great help and assistance that provided during this work .

My thanks are also extended to Miss. Batool Al-Kadi and Beadaa Al-Samra`e for the processing of biological part of the work .

Sincere thanks are also to the Dean of the college of science and the head of chemistry department and the staff members of the chemistry department.

Finally to all my friends . I present my thanks .

Ayad

2006

CHAPTER ONE

INTRODUCTION

CHAPTER TWO

EXPERIMENTAL PART

CHAPTER THREE

RESULTS AND DISCUSSION

REFERENCES

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Chapter one: Introduction

Chapter two: Experimental part

Chapter three: Results and Discussion

List of abbreviations

FTIR : Fourier transforms infrared
UV : Ultraviolet
NMR : Nuclear magnetic resonance
DNA : Deoxynucleotides
RNA : Ribonucleotides
Pka : Acid dissociation constant
Nu : Nucleophile
PPE : Poly phosphate ester
PPA : Poly phosphoric acid
DMSO : Dimethyl sulfoxide
m.p. : Melting point
b.p. : Boiling point
M.W : Molecular weight
EtOH : Ethanol
G + : Gram positive bacteria
G - : Gram negative bacteria
nm : Nanometer
λ : Wavelength
PT : Proton transfer

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