Synthesis, Characterization and Structural Optimization Using Density Functional Theory of Hydrazone Schiff Base Derivatives

by

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A thesis submitted in partial fulfillment of the requirements for the degree of Master of Science in Chemistry.

Khulna University of Engineering and Technology

Khulna-9203, Bangladesh

January, 2019

DEDICATED

TO MY BELOVED

PARENTS

Declaration

This is to certify that the thesis work entitled "Synthesis, Characterization and Structural Optimization Using Density functional Theory of Hydrazone Schiff Base Derivatives " has been carried out by Md. Zakaria Hossain in the department of Chemistry, Khulna University of Engineering & Technology Khulna-9203, Bangladesh. The above work has not been submitted anywhere for the award of any degree or diploma.

Signature of Supervisor

Md. Zakaria Hossain

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This is to certify that the thesis work submitted by Md. Zakaria Hossain entitled "Synthesis, Characterization and Structural Optimization using Density Functional Theory of Hydrazone Schiff Base Derivatives" has been approved by the board of examiners for the partial fulfillment of the requirements for the Degree of M.Sc in the Department of Chemistry, Khulna University of Engineering & Technology, Khulna, Bangladesh in January, 2019.

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Abstract

This thesis paper is related in an effective method for the addition of 2,4-dinitrophenyl hydrazine and various substituted 2,6-dibenzylidene cyclohexanone based bis-chalcones in the presence of hydrochloric acid to produce various hydrazone Schiffbase derivatives. First product, *N*-[2,6-bis-(4-chlorobenzylidene)-cyclohexylidene]-*N'*-(2,4-dinitrophenyl)-hydrazine has been synthesized by the reaction of 2,4-dinitrophenylhydrazine with 2,6-bis-(4-chlorobenzylidene)-cyclohexanone at reflux conditionat 2 hours. The isolated product was red in color and the melting point of the pure product was 185 °C. Second synthesized product, *N*-[2,6-bis-(4-methoxy-benzylidene)-cyclohexylidene]-*N'*-(2,4-dinitrophenyl)-hydrazine has been synthesized by the reaction of 2,4-dinitrophenyl hydrazine with 2,6-bis-(4-methoxybenzylidene)-cyclohexanone at the same condition. The pure product was coffee color and the melting point of the pure product was 225 °C. Final product, *N*-[2,6-bis-(4-dimethylamino-benzylidene)-cyclohexylidene]-*N'*-(2,4-dinitrophenyl)-hydrazine has been synthesized by the reaction of 2,4-dinitrophenylhydrazine with 2,6-bis-(4-dimethylbenzylidene)-cyclohexanone also at the same condition. The product of the color was black and the melting point of the pure product was 245 °C. The structures of the synthesized products were characterized by their physical, UV, FTIR, ^{1}H NMR & ^{13}C NMR spectra. Their optimized structures have been investigated by computational method, Gaussian 16 software Revision B.01. Their molecular geometry and vibrational frequencies were computed at density functional theory, DFT-B3LYP/6-311+G (2d, p) level of theory.

Chapter 1
Introduction

Chapter 1

Introduction

A compound in which the C=O is replaced by a C=N is known as an imine or Schiff base. Schiff bases are condensation products of primary amines and carbonyl compounds and they were discovered by a German chemist, Hugo Schiff [1].

Hydrazone is one kind of Schiff base. Because a Schiff base is a compound with the general structure $R_2C{=}NR_1$ and Hydrazones is a class of organic compounds having the basic structure $R^1R^2C{=}NNH_2$ [2]. They are related to aldehydes and ketones, by the replacement of the oxygen with the $-NNH_2$ group. They are derived by the condensation of substituted hydrazides with carbonyl compounds namely aldehydes and ketones. They are formed by the action of hydrazine on ketones or aldehydes. Hydrazones are azomethines characterized by the presence of the triatomic grouping >C=N-N< [3]. They are distinguished from other member of this class (imines, oximes etc.) by the presence of the two interlinked (-N=N-) nitrogen atoms [4]. According to the needs of a polydentate ligand, the group functionalities are increased by condensation and substitution [5]. Hydrazones are usually named after the carbonyl compounds from which they are obtained [6]. They are important intermediates in heterocyclic chemistry. Hydrazone moiety plays an important key role in heterocyclic chemistry [7]. Hydrazones have the general formula given below Figure-1 [8].

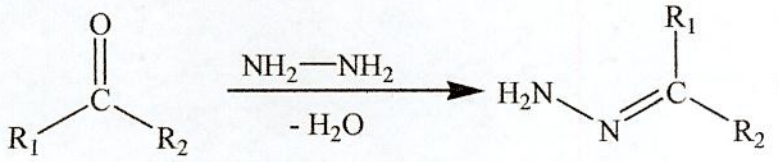
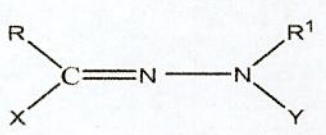


Figure-1 General formation and formula of hydrazone



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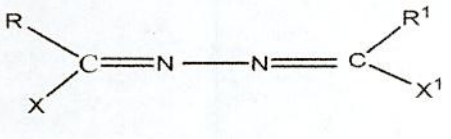


II

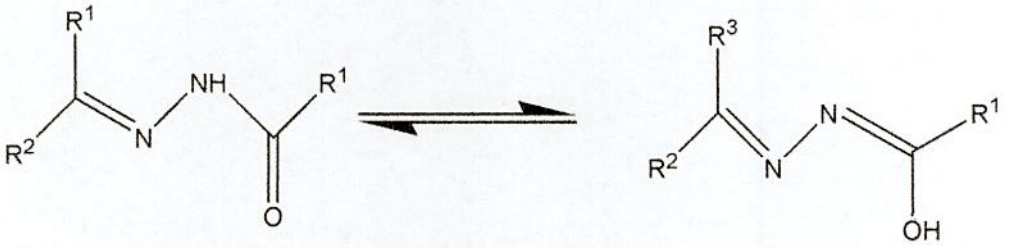
Where,

R and R^1 = H, Alkyl, Ar, RCO, Ht(Heterocyclic Group)

Y = H, Alkyl, Ar, Ht, RCOX and

X^1 = H, Alkyl, Ar, Ht, Halogens, OR, SR, CN, SO_2R, NO_2, $NHNRR^1$, N=NR, COOR, $CONRR^1$.

The functional grouping causes these compound to behave as bidentate ligands for metal ion and owing the availability of –NH–C=O group, acid hydrazones show ketoenol (amido-iminol) tautomerism Figure-2 [9]. In solid state they exist in keto form but in solution they exist as an equilibrium mixture keto and enol forms.



Keto Form Enol Form

Figure-2 Keto-enol tautomerism of substituted hydrazone

The most important property of hydrazones is their high physiologicalactivity[10].Hydrazones possessing an azomethine proton (–NHN=CH–) constitute an important class of compounds, contain two connected nitrogen atoms of different nature and a C=N double bond that is conjugated with a lone pair electron of the terminal nitrogen atom [11]. Extensive studies have revealed that the lone pair on trigonally hybridized nitrogen atom of the azomethine group is responsible for the chemical and biological activity [12]. It has been reported that metal complexes of hydrazones have diverse applications [13]. Many researchers have synthesized these compounds as well as their metal complexes as plasticizers, polymerization inhibitors and antioxidants [14]. They are used as fungicides and pesticides in biological and biochemical context [15]. The azomethine group H–N=N=CH– in hydrazones is highly reactive, in this two

nitrogen's have nucleophilic nature and carbon atom has both electrophonic and nucleophilic nature [16].

Due to the ability to react with electrophiles and nucleophiles hydrazones are widely used in synthesis of heterocyclic compounds.

A quick survey of the structure of a hydrazone Figure-3, reveals that it has nucleophilic imine and amino-type Nitrogens, an imine carbon that has both electrophilic and nucleophilic character, configurational isomerism stemming from the intrinsic nature of the C=N bond and in most cases an acidic N–H proton[17].

These structural motifs give the hydrazone group its physical and chemical properties, in addition to playing a crucial part in determining the range of applications it can be involved in.

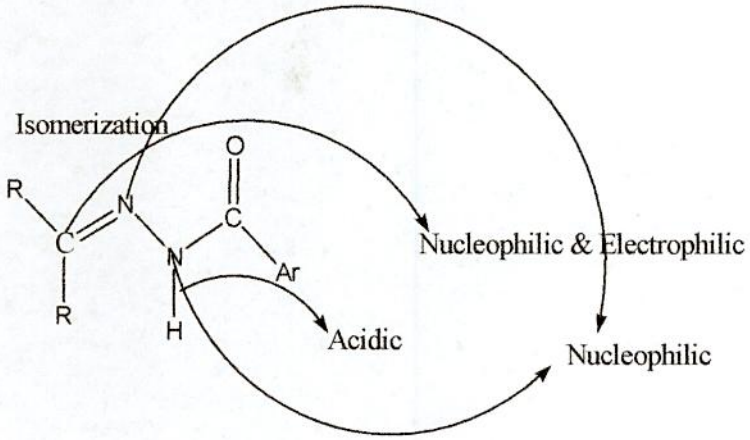


Figure-3 The Structural and functional diversity of the hrdrazone group

Hydrazones can be made by three main synthetic pathways:

i. Coupling between aryldiazonium salts and β-keto esters or acids, which is also known as the Japp–Klingemann reaction,[18]

ii. Coupling between hydrazines and ketones or aldehydes,[19]

iii. Coupling between aryl halides and non substituted hydrazones.[20]

Hydrazones can be synthesized in laboratory by heating the appropriate substituted hydrazines or hydrazides with aldehydes and ketones in various organic solvents like ethanol, methanol,

tetrahydrofuran, butanol and sometimes with glacial acetic acid or ethanol-glacial acetic acid. Also hydrazones can be synthesized by the coupling of aryldiazonium salts with compounds containing active hydrogen [21]. Hydrazones act as very important intermediates in the synthesis of various heterocyclic compounds but in addition to this property they are also very effective organic compounds with important biological activities. Many researchers have synthesized a number of new hydrazones because of their ease of synthesis. Hydrazones obtained by condensing substituted acid hydrazide with aromatic 2-hydroxyaldehyde, *p*-diketones, and keto-acids of the pyruvic type are most effective in complex formation.

When hydrazones are used as intermediates various coupling products can be synthesized by using the active hydrogen component of azomethine group(–CONHN=CH). Large number of biologically active compounds can be synthesized by researchers, for example: iproniazide and isocarboxazide are synthesized by hydrazones reduction. Iproniazide have structure similar to isoniazid that's why used in the treatment of tuberculosis. In some patients it also shows an antidepressant and mood changing effect [22].

Transition metals are particularly suitable for this purpose because they adopt a wide variety of coordination numbers, geometries and oxidation states in comparison with carbon and other main group elements [23] .The d-block metal ions have tendency to form the complexes. A series of transition metal complexes with Schiff bases, aromatic hydrazones have been quite extensively investigated [24-27]. The chemistry of hydrazone complexes involving O, N, S donor ligands has received special attention because of their coordination capability, their pharmacological activity and their uses in analytical chemistry as metal extracting agents [28-32]. It has recently been shown that the metal complexes are more potent and less toxic in many cases as compared to the parent compound.

Techniques for structural characterization

The composition and structure of the complexes are determined by the electronic structure of complex forming metal as well as preparation condition [33-34].They form coordination compounds through the oxygen atom of either carbonyl or the enol group and through the imine nitrogen atom, a five membered ring being produced [35-36].

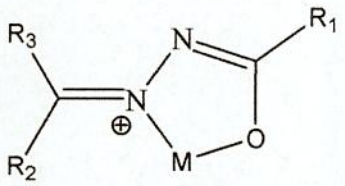


Figure-4 General mode of coordination of acid hydrazones

Many new complexes of transition metals with newly synthesized hydrazone derivatives and ligands have been synthesized and characterized by using different techniques viz., elemental analysis, molecular weight determination, magnetic susceptibility/moment measurements, conductivity, thermogravimetric, spectral studies (electronic, infra-red, mossbauer) etc. to investigate coordination behavior around metal ion thereby leading to the study of biological activities [37].

Diversity of coordination in the chelation of hydrazones tautomerisation

In solid state, hydrozones exist in keto form but in solution, they exist as an equilibrium mixture of keto and enol forms. These compounds are expected to exist in a trans form, but in such situation, they may act as a unidentate ligand, by bonding through enolate oxygen. It is well evident that stereochemistry of the ligand is much decided by the steric effects various substituents in the hydrazone moiety.

It was found that most of the hydrazones coordinate to the metal ion through cis form. This phenomenon is assumed to be due to better electron delocalization in the chelate ring system that increases the stability upon coordination with metal atoms. The"Synthesis and structural studies of some hydrazone derivatives and their vanadium complexes" composition and structure of the complexes are determined by the electronic structure of metal as well as preparation conditions. Hydrazones form coordination compounds through the oxygen atom of either carbonyl or the -enol group and through the imine nitrogen atom, a five member chelate ring is formed as shown below:

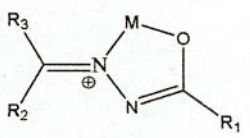


Figure-5 General bidentate coordination of acid hydrazones

In coordination chemistry, hydrazones find application as multidentate ligand forming chelates with metals, usually from the transition series. Studies have shown that theazomethine group having a lone pair of electrons in either a sp or sp^2 hybridized orbital on trigonally hybridized nitrogen has considerable biological importance. Hydrazones are versatile class of ligands which have been studied for a long time as potential multifunctional ligands with various coordination modes [38-39]. The coordination mode adopted by a hydrazone depends on different factors like tautomerism, reaction conditions, stability of the complex formed and number and nature of the substituents on hydrazone skeleton. The structural changes of the segment attached to the hydrazone will affect the metal binding of the ligand and exhibit interesting coordination modes with transition metal ions to form octahedral, square planar and tetrahedral complexes [40-42].

Applications of hydrazones

The modularity, straightforward synthesis and stability towards hydrolysis of hydrazones can be cited as reasons for their popularity. But in reality it is the functional diversity of this azomethine group which is characterized by the triatomic structure C=N–N, that enables its use in various fields.

In Analytical Chemistry

In the field of analytical chemistry, Hydrazones gives colour complexes with metal ions and used for determination of metal ions in different samples. Aruna bai et al. have reported hydrazones acts as a analytical reagents for spectrophotometric determination of Ni (II). Hydrazones are used in analytical chemistry as metal extracting agents [43]. Hydrazides also have been used for analytical chemistry as chelating agents [44].

Biscyclohexanone oxalyl dihydrazone is used for the determination of copper in paper pulp products, human serum, steel, plants, non-ferrous metals and alloys. Pyridine-2aldehyde 2-pyridyl hydrazone (PAPH) introduced by Lions and Martin has been used for the determination of copper in foodstuffs [45]. Hydrazones are extensively studied as reactants or reaction intermediates since they can readily undergo various ring closure reactions [46].

Hydrazones are also used as spot test reagents for the detection of metal ions. 2, 2′ bipyridyl-2-quinolyl hydrazone and 2, 2′ bipyridyl- 2-pyrimidyl hydrazone are used as spot test reagents for the detection of iron, cobalt and copper. *p*-dimethylamino benzaldehyde isonicotinoyl hydrazone forms an intensely orange-yellow precipitate with mercury (I or II) in slightly acidic, neutral or slightly alkaline medium [47].The complex of Co(III) with pyridine-2-aldehyde 2-pyridyl hydrazone (PAPH) has been used in the nephelometric determination of silver and mercury [48].

Many organic compounds react with metal ions and form colored precipitates or solutions. Hence, they are extensively used as analytical reagents; Yoe gave a list of more than twenty ways in which they are used [49]. It has been observed that the reactivity of organic reagents with metal ions in the use of the former as analytical reagents requires the presence of certain acidic or basic groupings and coordinating atoms [50]. The formation of aromatic hydrazone derivatives is used to measure the concentration of low molecular weight aldehydes and ketones in gas streams. For example dinitrophenylhydrazine coated on to silica sorbent is the basis of an adsorption cartridge. The hydrazones are then eluted and analyzed by HPLC using a UV detector.

The development of new strategies for the preparation of organic molecules in neat condition is a challenging area of organic synthesis. A large number of methods are available for the synthesis of organic compounds which are carried out under anhydrous condition using volatile organic solvents like benzene, which are the cause of environmental problems and are also potentially carcinogenic. Hence it is required to develop safe practical and environment friendly process. Here we synthesis hydrazone Schiff base derivatives by coupling between hydrazine (2, 4-dinitrophenylhydrazine) and ketone (substituted bis-chalcone).

Chapter 2
Literature Review

Chapter 2

Literature Review

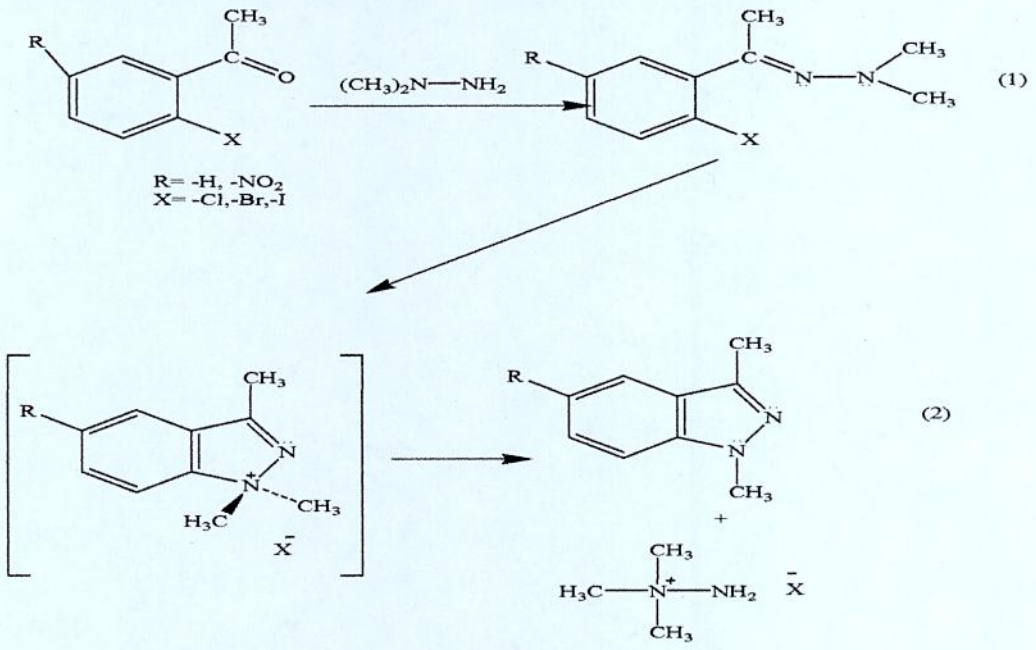
The finding from literature that hydrazones constitute an important class of biologically active drug molecules. A number of hydrazone derivatives have been reported to exert notably antimicrobial, antihypertensive, anticonvulsant, analgesic, anti-inflammatory, antituberculosis, antitumoral, antiproliferative and antimalarial activities which has attracted attention of medicinal chemists due to their wide range of pharmacological properties. These compounds are being synthesized as drugs by many researchers in order to combat diseases with minimal toxicity and maximal effects.

The common and traditional method for preparation of the hydrazone derivatives involves the treatment of substituted acid hydrazides and carbonyl compounds in the suitable solvents. All the reported approaches include organic classical synthetic methodologies and vary in the selectivity and reaction patterns. A wide variety of methodologies has been developed by the researchers in past decades. Some of the reported methods are described below.

G. R. Newkome and his co-workers, 1965, synthesized simple N-unsubstituted hydrazones of most aldehydes or ketones, usually difficult to obtain in good yields and high purity [51]. It was prepared from the corresponding N, N-dimethylhydrazones by exchange with anhydrous hydrazine. Since azine formation is nil under these conditions, the reaction can be followed by observing loss of color. The N, N-dimethylhydrazones used as reagents are prepared in high yields directly from aldehydes or ketones and unsym-dimethylhydrazine. Exceptions to this occur only if the carbonyl compound is steric hindered or possesses a labile group (toward nucleophilic substitution) ortho to the carbonyl function on an aromatic ring (scheme 1). Hydrazones prepared in this manner are stable for long periods when stored as crystalline solids. Hydrazones prepared in this manner are stable for long periods when stored as crystalline solids.

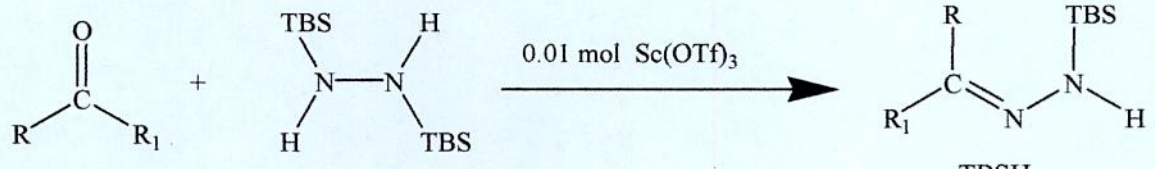
Michael E. Furrow and his coworkers, 2004, synthesized N -tert -butyldimethylsilylhydrazone (TBSH) (scheme 2) derivatives from carbonyl-containing compounds and shown that these products serve as superior alternatives to simple hydrazones in Wolff-Kishner-type reduction

reactions, in the Barton vinyl iodide preparation, in the synthesis of vinyl bromides, and in the synthesis of gem -diiodides, gem -dibromides, and gem -dichlorides. .



Scheme -1

Wolff-Kishner-type reduction reactions, in the Barton vinyl iodide preparation, in the synthesis of vinyl bromides, and in the synthesis of gem-diiodides, gem-dibromides, and gem –dichlorides [52].



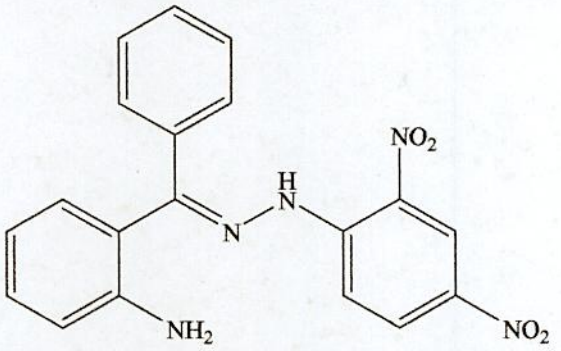
carbonyl compound N tert-butyldimethylsilylhydrazine

Scheme -2

In their new procedure for silyl hydrazone synthesis, aliphatic and aromatic ketones and aldehydes are shown to undergo highly efficient coupling (typically >95% yield) to form the corresponding TBSH derivatives when combined with equimolar amounts of 1,2-bis (tert - butyldimethylsilyl)hydrazine (BTBSH) and a catalytic quantity of scandium trifluoromethanesulfonate (typically, 0.01 mol %), neat, or in solvent. Optimized procedures are

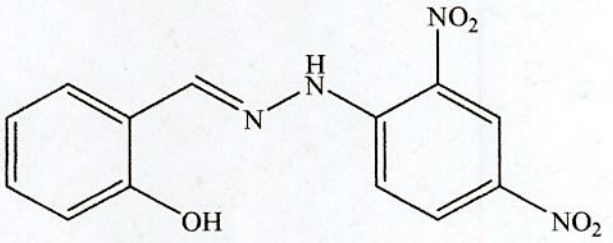
provided for the use of TBSH derivatives in a Wolff-Kishnertype reduction protocol that proceeds at low temperature (23-100 °C) and in a single reaction flask. Similarly, protocols for the use of TBSH derivatives as precursors to vinyl halides and gem -dihalides are described in detail [52].

Hassan et al., 2006 prepared a series of hydrazone derivatives by treating the salicylaldehyde with 2,4-dinitrophenyl hydrazine in methanol as per the below mentioned scheme [53].



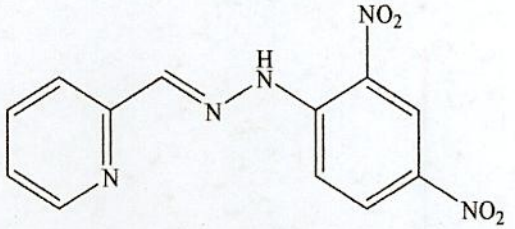
2-{[(2, 4-dinitrophenyl)-hydrazono]-phenylmethyl}-phenylamine

Scheme-3(a)



2-[(2, 4-dinitrophenyl)-hydrazonomethyl]-phenol

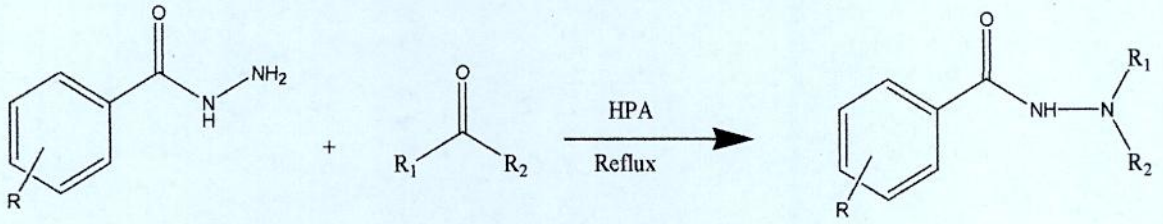
Scheme -3(b)



N-(2, 4-dinitrophenyl)-N'-pyridin-2-ylmethylene-hydrazine

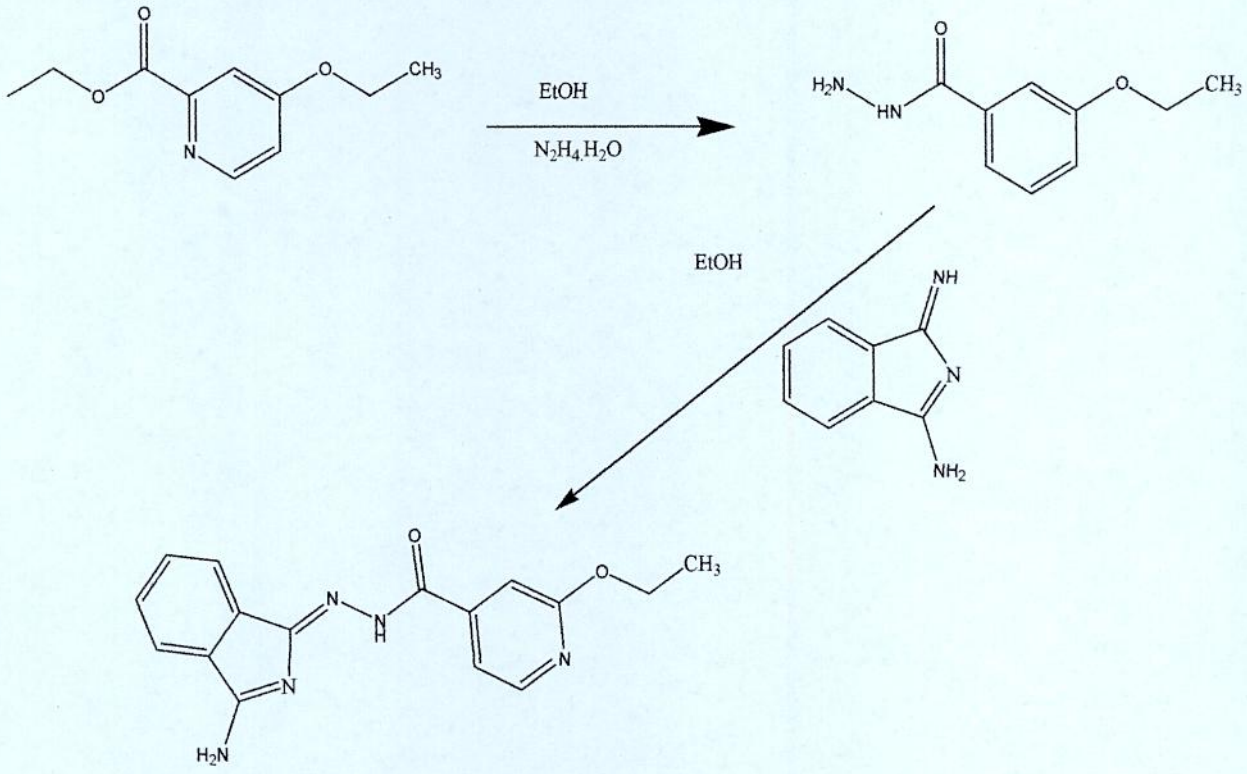
Scheme –3(c)

S. Sadjadi et al., 2009 reported the preparation of N-acyl-benzoyl hydrazone and benzoyl hydrazone derivatives in the presence of different types keg in type of heteropolyacids like $H_3[PMo_{12}O_{40}]$, $H_4[PMo_{11}VO_{40}]$, $H_5[PMo_{10}V_2O_{40}]$, and $H_6[PMo_9V_3O_{40}]$ as catalyst in the acetonitrile solvent(Scheme-4). Reaction mixture was filtered to recycle the catalyst [54].



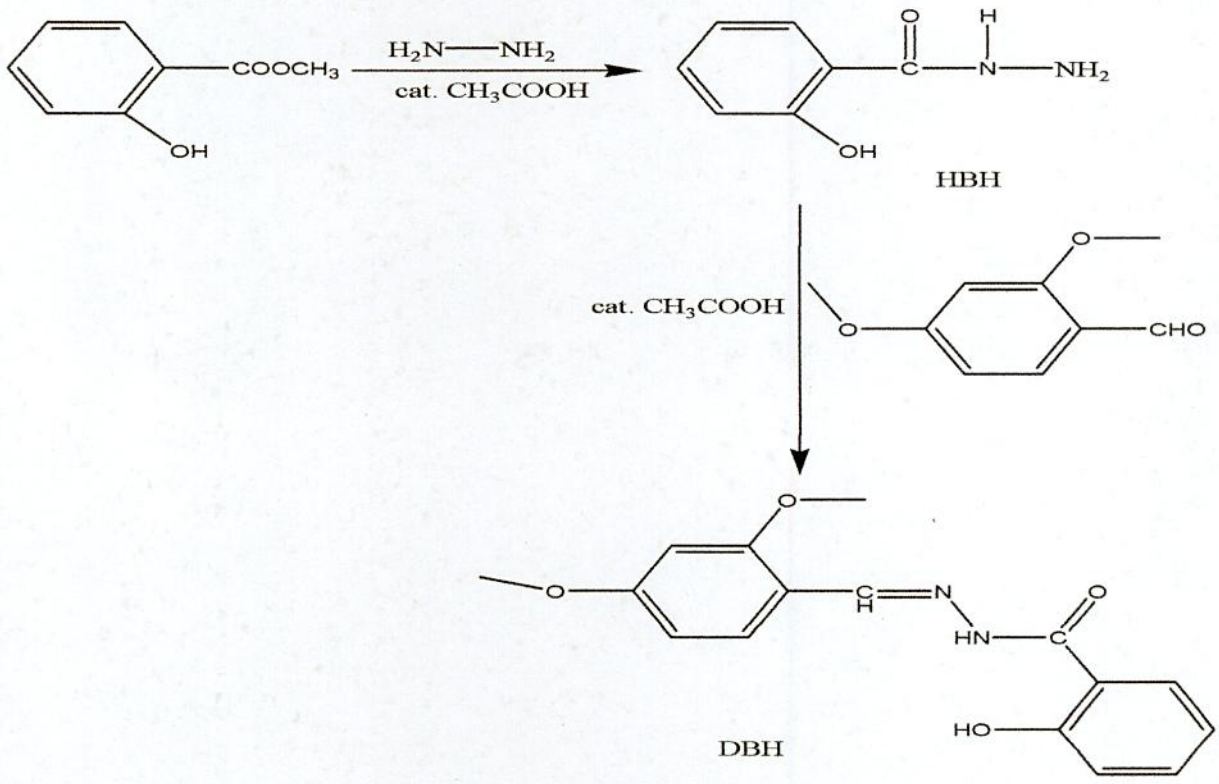
Scheme - 4

C. Witschel et al., 2014, prepared a series of 1,3-diiminoisoindoline carbohydrazides by treating the ethyl ester with hydrazine and the corresponding hydrazide derivatives to synthesized isoindoline in ethanol as per the below mentioned scheme and the obtained compounds were found to be potent inhibitors of *P.* falciparum proliferation in red blood cells [55].



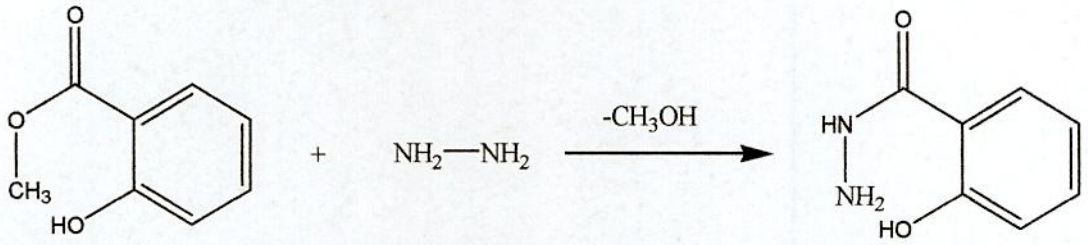
Scheme -5

A novel hydrazone, N′-(2,4-dimethoxybenzylidene)-2-hydroxybenzohydrazide (DBH), has been synthesized and characterized by Fang-Fang Tian and his coworkers [56]. The interactions between DBH and bovine serum albumin (BSA) have been investigated systematically by fluorescence, molecular docking, circular dichroism (CD), UV-VIS absorption, and electrochemical impedance spectroscopy (EIS) methods under physiological conditions (Scheme-6). The fluorescence quenching observed is attributed to the formation of a complex between BSA and DBH, and the reverse temperature effect of the fluorescence quenching has been found and discussed. The primary binding pattern is determined by hydrophobic interaction occurring in Sudlow's site I of BSA. DBH could slightly change the secondary structure and induce unfolding of the polypeptides of protein. An average binding distance of~4.0 nm has been determined on the basis of the Forster resonance energy theory (FRET). The effects of iron on the system of DBH-BSA have also been investigated. It is found that iron could compete against BSA to bind DBH. All of these results are supported by a docking study using a BSA crystal model. It is shown that DBH can efficiently bind with BSA and be transported to the focuses needed. Subsequent antitumor test and detailed anticancer mechanism are undergoing in lab.



Scheme-6

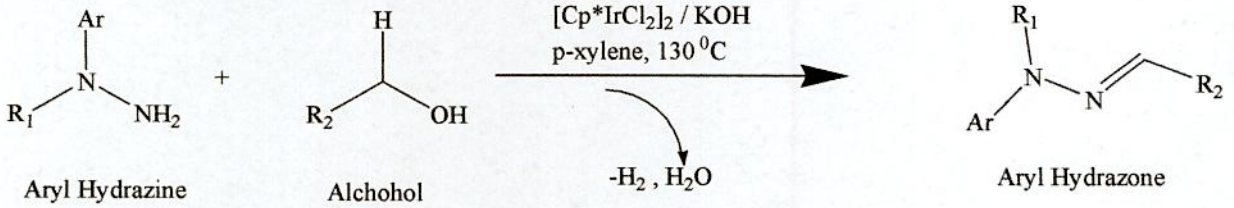
P. V. Hemalatha et al., 2017, synthesized salicyl hydrazide from esters by reaction with hydrazine hydrate (Scheme-7). It was confirmed by IR analysis. The melting point determination confirmed its purity [57].



Methyl-2-hydroxy benzoate hydrazine 2-Hydroxy benzohydrazide

Scheme -7

Feng Li, et al., 2017, synthesized the direct synthesis of arylhydrazones via catalytic acceptorless dehydrogenative coupling of arylhydrazines and alcohols has been accomplished. More importantly, complete selectivity for arylhydrazones and none of the N-alkylated byproducts were generated in this process, which exhibit new potential and provide a new horizon for the development of catalytic acceptorless dehydrogenative coupling reactions (Scheme-8) [58].



Aryl Hydrazine Alchohol Aryl Hydrazone

Scheme -8

Chapter 3
Experimental

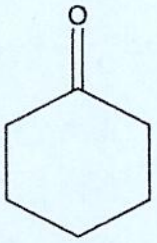
Chapter 3

Experimental

3.1 Reagent

Cyclohexanone:

Cyclohexanone is a six-carbon cyclic molecule with a ketone functional group. It is a colorless, oily liquid (less dense than water) with an acetone-like smell.



It also known as oxo cyclohexane, pimelic ketone, ketohexamethylene, cyclohexyl ketone or ketocyclohexane.

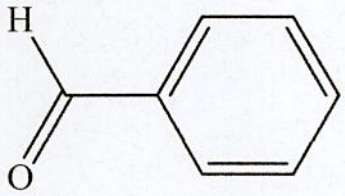
Cyclohexanone is occasionally found as a volatile component of human urine. Biological fluids such as blood and urine have been shown to contain a large number of components; some of them are volatiles (low boiling point) apparently present in all individuals, while others such are much more variable.

There is a strong correlation between the concentration of cyclohexanone in the working environment and its concentration in urine. Cyclohexanone is obtained through oxidation of cyclohexane or dehydrogenation of phenol. It is used in a large scale for the production of nylon.

Benzaldehyde:

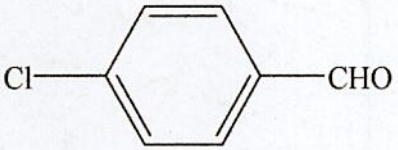
Benzaldehyde (C_6H_5CHO) is an organic compound consisting of a benzene ring with a formyl substituent. It is the simplest aromatic aldehyde .

It is a colorless liquid with a characteristic almond-like odor. Benzaldehyde is the primary component of bitter almond oil and can be extracted from a number of other natural sources. Synthetic benzaldehyde is the flavoring agent in imitation almond extract, which is used to flavor cakes and other baked goods.



p-Chlorobenzaldehyde:

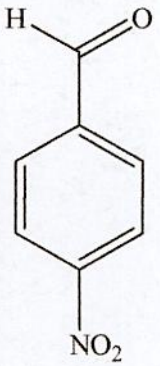
p-chlorobenzaldehyde is a substituted aromatic benzaldehyde. It is a white to pale yellow powder which melts at 46□ and stable in normal condition but it is air and light sensitive. It is insoluble in water, easily soluble in alcohol, ether and benzene and soluble in acetone. It can be evaporated together with the steam.



p-chlorobenzaldehyde is used as the intermediates of medicine and dyes, for the manufacturing of chlormezanone, dapsone aminobutyric acid and so on. It can be used for producing the plant growth regulator paclobutrazol. 4-Chlorobenzaldehyde is also used as an intermediate for the manufacture of dyestuffs, optical brighteners, pharmaceuticals, agricultural chemicals and metal finishing products.

***p*-Nitrobenzaldehyde**

4-Nitrobenzaldehyde is an organic aromatic compound containing a nitro group *p*-substituted to an aldehyde. Its chemical formula is $C_7H_5NO_3$ and melting point is 103 to106 °C.



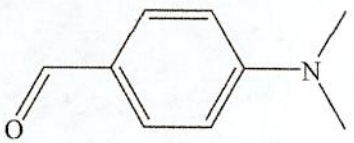
p-Methoxybenzaldehyde

p-Anisaldehyde also known as anisic aldehyde or anisealdehyde is an organic compound that is commonly encountered in fragrances, both synthetic and natural. It is also known as *p*-methoxybenzaldehyde or *p*-methoxybenzaldehyde. The compound consists of a benzene ring with an aldehyde and a methoxy group. It is a clear liquid with a strong aroma.

p-methoxybenzaldehyde or *p*-anisaldehyde is an interesting compound which is used in the field of medicine. It plays an important role in preparation of various drugs.

***N, N*-dimethylaminobenzaldehyde**

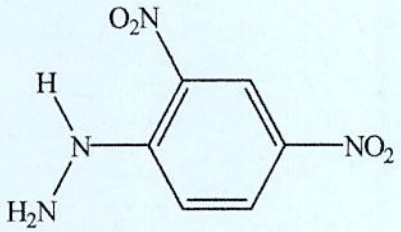
N, N-dimethylaminobenzaldehyde is an organic compound containing amine and aldehyde moieties which is used in Ehrlich's reagent and Kovac's reagent to test for indoles. Ehrlich's reagent acts as a strong electrophile which reacts with the electron-rich α-carbon (2-position) of indole rings to form a blue-colored adduct. The carbonyl group typically reacts with the electron rich 2-position of the indole but may also react at the C-3 or N-1 positions. It may also be used for determination of hydrazine as same as indole by forming azo dye which show yellow color.



2, 4-dinitrophenylhydrazine

2, 4-dinitrophenylhydrazine is an organic compound consisting of a benzene ring which contains two nitro groups and one hydrazine group. Its chemical formula is $C_6H_6N_4O_4$. It is a red to orange solid powder which melts as 198-202 °C. It is often used to qualitatively test for carbonyl groups associated with aldehydes and ketones. The hydrazone derivatives can also be used as evidence toward the identity of the original compound. The melting point of the derivative is

often used, with reference to a database of values, to determine the identity of a specific carbonyl compound.



3.2 Experimental Techniques

Chromatographic Technique (Thin layer chromatography):

Chromatography is a separation process, which depend on the differential distributions of the component of a mixture between a mobile bulk phase and an essentially thin film stationary phase according to their polarity.

When this stationary phase remain in the form of a thin layer adhering to a suitable from of backing material over which the mobile phase is allow to ascent by capillary action, the technique is called thin layer chromatography (TLC).

The most commonly used stationary phases, which are available in different grades specially prepared for TLC use, include silica gel, alumina, kieselguhr and cellulose powders.

Preparation of plates

In this technique the glass plates were cleaned by detergent to remove the greasy material and then dried. The plates were coated with silica gel. The TLC plates (2.5 cm× 6.0 cm) were prepared by dipping the plates into slurry made of UV active silica gel.

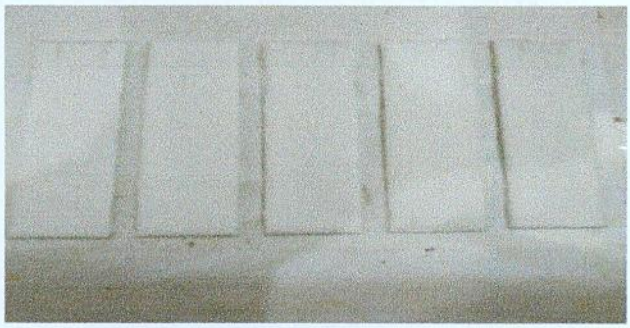


Fig 3.1 Prepared TLC Plate

The plates were activated by heating at 150 °C for 10-12 hours in an oven to remove moisture.

Cylindrical glass chamber (TLC tank) was used for the development of chromatoplates. The selected solvent system was poured in sufficient quantity into the tank. A smooth sheet of filter paper was introduced into the tank and allowed to soak in the solvent. The tank was then made airtight and kept for few minutes to saturate the internal atmosphere with the solvent vapor.

A small amount of dried extract was dissolved in a suitable solvent to get a solution (approximately 1%). A small spot of the solution was applied on the activated silica plate with a capillary tube just 1 cm above the lower edge of the plate (base line). The spot was dried with a hot air blower and a straight line was drawn 2 cm below the upper edge of the activated plate which marks the upper limit (solvent front) of the solvent flow. The spotted plate was then placed in the tank (n-hexane: ethyl acetate = 60:40) in such a way as to keep the applied spot above the surface of the solvent system and the cap was placed again. The plate was left for development.

When the solvent front reaches up to the given mark, the plate was taken out and air-dried. The properly developed plates were kept in an iodine chamber for 10-15 minutes and viewed the spot travelled by the compound. By measuring the distance travelled by the solute and solvent the R_f value was calculated.

Application of sample on the plate:

Sample was applied to thin layer by capillary tube. But considerably more skill and care are needed so that a hole was not produced on the film.

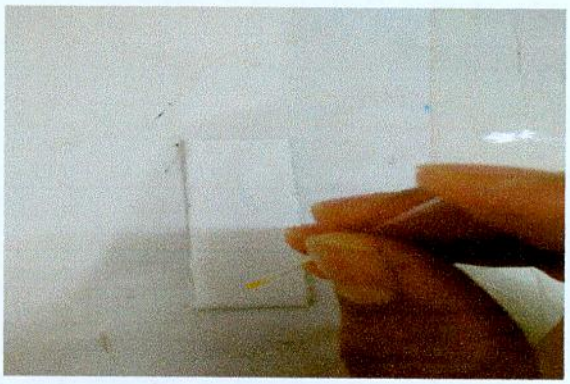


Fig 3.2 process of spotting

Solvent Systems

The solvents of different polarity used for TLC are given below:

a. n-Hexane

b. n-Hexane : Ethyl acetate (in different ratio)

c. Ethanol (EtOH)

Development of plates:

When the sample was spotted on the film of plates, it was developed in ascending process. Usually plates were placed in a tank. The plates were put in such a way that they were inclined and the lower edge immersed in the selected mobile phase, but the solvent barrier was somewhat below than the starting line (base line).

Location of Spots:

Detection of compounds in TLC plates was a very important topic in analyzing extractives to isolate pure compounds. The following technique was used for detecting the compounds in TLC plates.

Iodine chamber

The developed chromatogram was placed in a closed chamber containing crystals of iodine and kept for few minutes. The compounds that appeared as yellow spots were marked. Unsaturated compounds absorb iodine. Bound iodine is removed from the plate by air blowing

The R_f value:

The retarding factor (R_f value) of any compound seen on a TLC plate was calculated according to the following equation

$$R_f = \frac{\text{Distance (cm) traveled by solute}}{\text{Distance (cm) traveled by solvent}}$$

Recrystallization

Crystallization was employed as a final purification process. The solvent in which the compound was dissolved in a minimum volume of solvent in normal condition and was left undisturbed for crystallization. Sometimes mixtures of solvents were used.

The compound was dissolved in a suitable solvent and then a solvent in which the compound was insoluble. The solvent with comparatively lower polarity was gradually added until cloudiness developed in the solution.

3.3 Spectroscopic Techniques

Ultraviolet and visible spectra:

Ultra violet and visible spectra of the sample were recorded on UV-1800 SHIMADZU Spectrophotometer, ultraviolet spectrometer with a scanning range of 800-220 nm. The spectra were run by using ethanol, ethyl acetate and DCM as solvents.

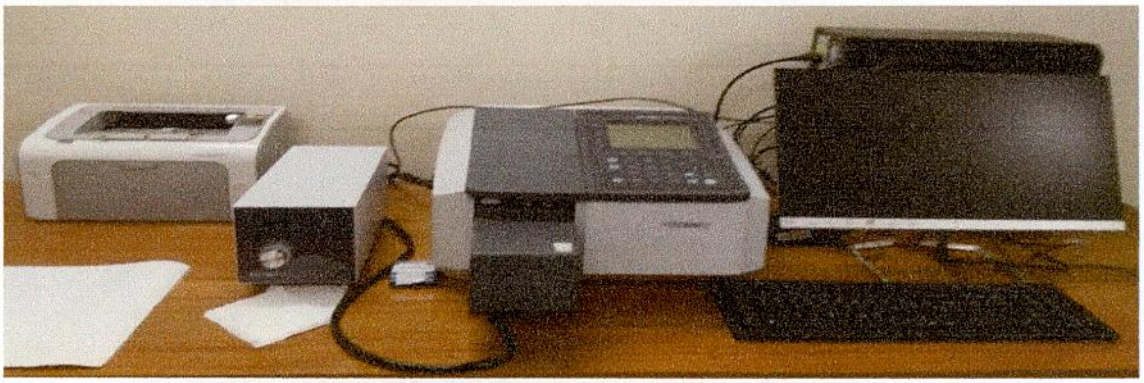


Fig 3.3 UV-Vis spectrophotometer

Infra-red-spectra: Infra-red spectra of the samples were recorded on the IRTracer-100 (FOURIER TRANSFORM INFRARED SPECTROPHOTOMETER) SHIMADZU. The spectra for solid samples were recorded as KBr pellets.

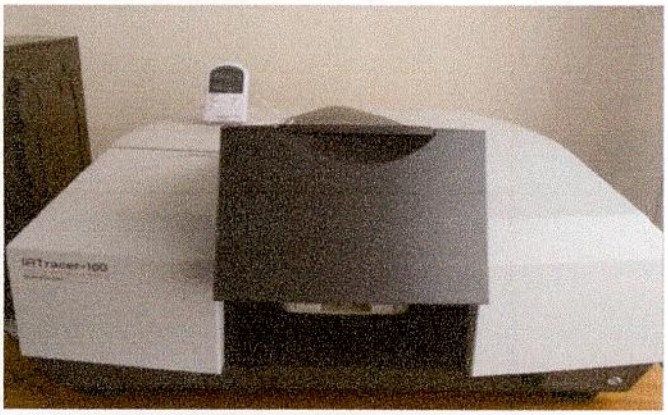


Fig 3.4 IR spectrophotometer

^{1}H NMR spectra:

^{1}H NMR spectra of the sample were recorded on a 400 MHz NMR spectra. The solvent used was $CDCl_3$ and DMSO-d_6. TMS was used as an internal standard.

Abbreviation Used

UV	Ultraviolet
IR	Infra-red
NMR	Nuclear magnetic resonance
S	Singlet
d	Doublet
m	Multiplet
J	Coupling constant
TLC	Thin Layer Chromatography
R_f	Retarding factor
Bp	Boiling point
Hz	Hertz
δ	Chemical shift
TMS	Tetra methyl Silane
DMSO-d_6	Deuterated Dimethylsulfoxide

Evaporation

All evaporations were carried under reduced pressure using rotary vacuum evaporator; the bath temperature was not exceeding 40 -50 °C.

Melting point apparatus

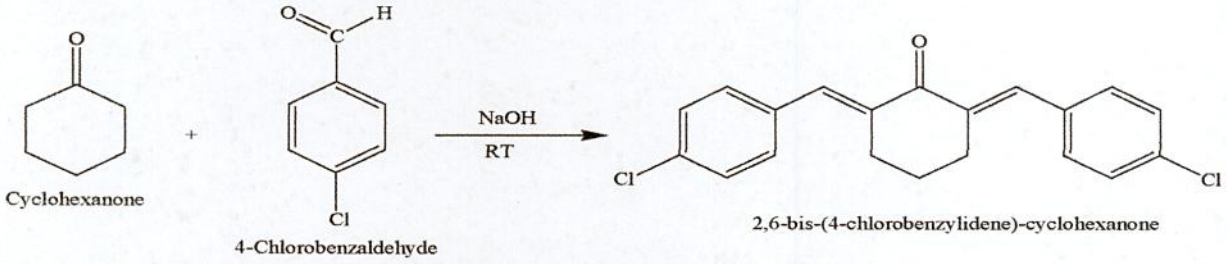
Melting point (m.p) was determined by using an electro thermal melting point apparatus (Stuart, Melting point SPM 30).

Fig 3.5 Melting point apparatus

3.4 Preparation of substituted bis-chalcones

3.4.1 Preparation of 2, 6-bis-(4-chlorobenzylidene)-cyclohexanone

A mixture of 1.0 equivalent of cyclohexanone, 0.52 ml, 2 equivalent of 4-chlorobenzaldehyde, 1.41 g and 2.20 equivalent of solid NaOH, 0.44g was grind in a mortar and pestle for 20 minutes at RT and then dilute hydrochloric acid was poured in the reaction mixture. The separated solid product was filtered and dried. The solid obtained was purified by recrystallization from ethanol and ethyl acetate mixture. The R_f value of this compound is 0.55 (n-hexane: ethyl acetate = 3: 2). The percentage of yield of the product was 85%.



Characterization and structure determination of the product

The product of the color was yellowish green and the melting point of the pure product was 144 °C.

Spectral properties

UV-Visible spectrum

The UV spectrum of the product in EtOH exhibited λ_{max} at 336 nm.

IR Spectrum:

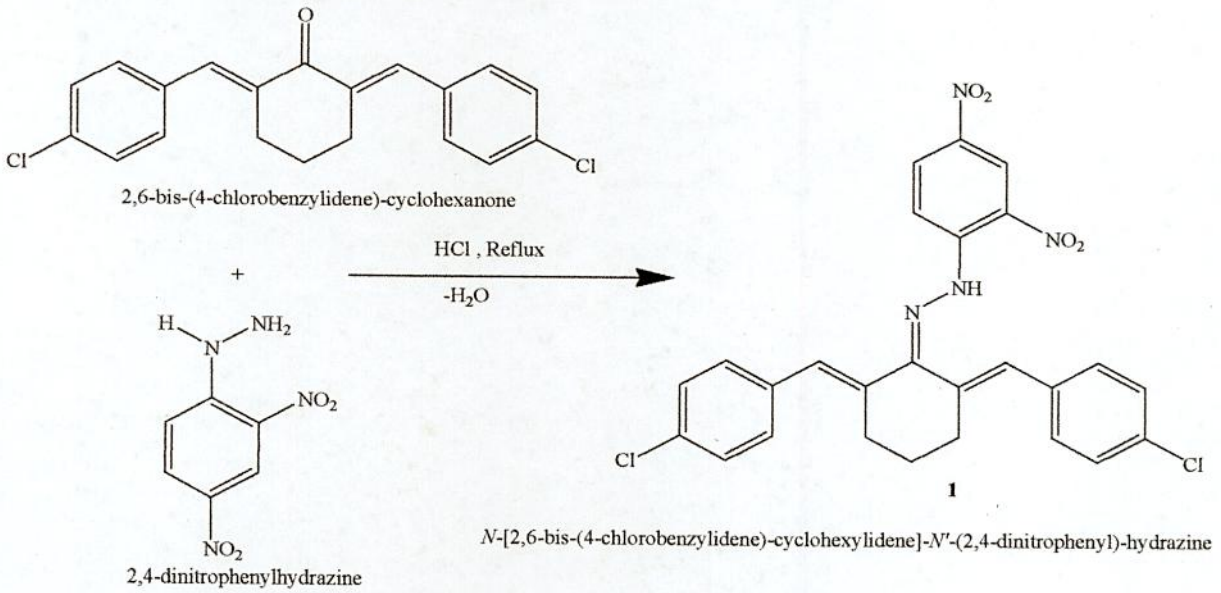
The IR spectrum of the product run as KBR pellet asserted absorption band ν in cm^{-1} which was assigned as: 2929.87, 1666.50, 1575.84, 1576, 1489.05, 1263.37, 1159.22, 819.75, 798.53ν.

^{1}H NMR

The ^{1}H NMR spectrum of the compound in $CDCl_3$ gave the following signals (δ value) using TMS as an internal standard. ^{1}H NMR (400MHz, $CDCl_3$) δ: =7.73 (s, 2H, Allylic), 7.38-7.25 (m, 8H, Ar), 2.91-2.87 (m,4H,2×CH_2), 1.84-1.77 (m,2H,CH_2) [59].

3.4.2 Preparation of N-[2, 6-bis-(4-chlorobenzylidene)-cyclohexylidene]-N'-(2, 4-dinitrophenyl)-hydrazine

To make a solution of (0.198 g, 1.0 mmol) of 2, 4-dinitrophenyl hydrazine in 20 ml of methanol. Then added 1.0 ml of hydrochloric acid to this solution .Now to the clear solution, 2, 6-bis-(4-chlorobenzylidine)-cyclohexanone (0.343 g, 1.0 mmol) was added. The reaction mixture was reflux about 2 hour and allowed to stand for overnight . The product precipitated as red crystal, was separated by filtration washed with ethanol and air dried .The product was recrystalized from ethanol and dimethylsulfoxide. The R_f value of this compound was 0.51 (n-hexane: ethyl acetate =3:2). The percentage of yield of the product was 50%.



2,6-bis-(4-chlorobenzylidene)-cyclohexanone

2,4-dinitrophenylhydrazine

1

N-[2,6-bis-(4-chlorobenzylidene)-cyclohexylidene]-*N'*-(2,4-dinitrophenyl)-hydrazine

Characterization and structure determination of the product

The product **1** of the color was red and the melting point of the pure product was 185 °C.

Spectral properties

UV-Visible spectrum

The UV spectrum of the product **1** in EtOH exhibited λ_{max} at 342 nm.

IR Spectrum:

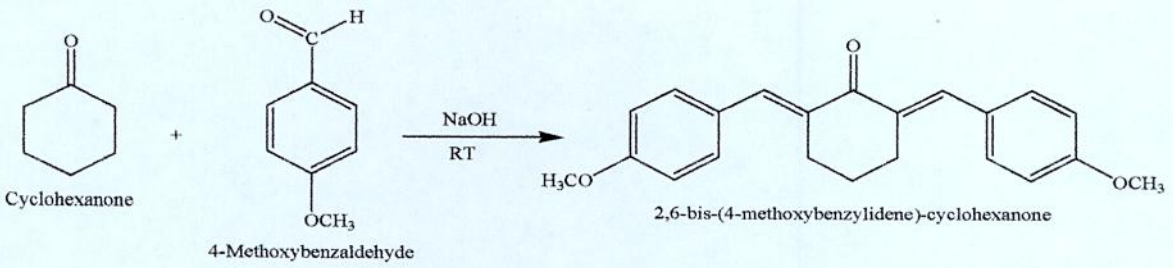
The IR spectrum of the product **1** run as KBR pellet asserted absorption band ν in cm^{-1} which was assigned as: 3263, 3095, 2941, 2916, 1612, 1508, 1490, 1585, 1332, 1082, 827.

^{1}H NMR

The ^{1}H NMR spectrum of the compound **1** in DMSO-d_6 gave the following signals (δ value) using TMS as an internal standard. ^{1}H NMR (400MHz, DMSO-d_6) δ: =12.0 (s, 1H, N-H), 8.9 (d, 1H, Ar), 8.5 (d, 1H, Ar), 8.2 (d, 1H, Ar) ,7.5 (m, 4H Ar)-7.4 (m, 4H, Ar), 7.2(m, 2H, allylic), 2.6-2.8 (m, 4H, cyclic),1.7 (m, 2H, cyclic).

3.4.3 Preparation of 2, 6-bis-(*p*-methoxybenzylidene)-cycloexanone

A mixture of 1.0 equivalent of cyclohexanone, 0.52 ml, 2.0 equivalent of *p*-methoxybenzaldehyde,1.21 ml and 2.20 equvalent of solid NaOH, 0.44 g was grind in a mortar (where the basic NaOH is act as a catalyst) and pestle for 20 minutes at RT and then dilute hydrochloric acid was poured in the reaction mixture. The separated solid product was filtered and dried. The solid obtained was purified by re-crystallization from ethanol and ethyl acetate. The R_f value of this compound was 0.75 (n-hexane: ethyl acetate = 3: 2). The percentage of yield of the product was 80%.



Cyclohexanone

4-Methoxybenzaldehyde

2,6-bis-(4-methoxybenzylidene)-cyclohexanone

Characterization and structure determination of the product

The product of the color was pale yellow and the melting point of the pure product was 150 °C.

Spectral properties

UV-Visible spectrum

The UV spectrum of the product in EtOH exhibited λ_{max} at 360 nm.

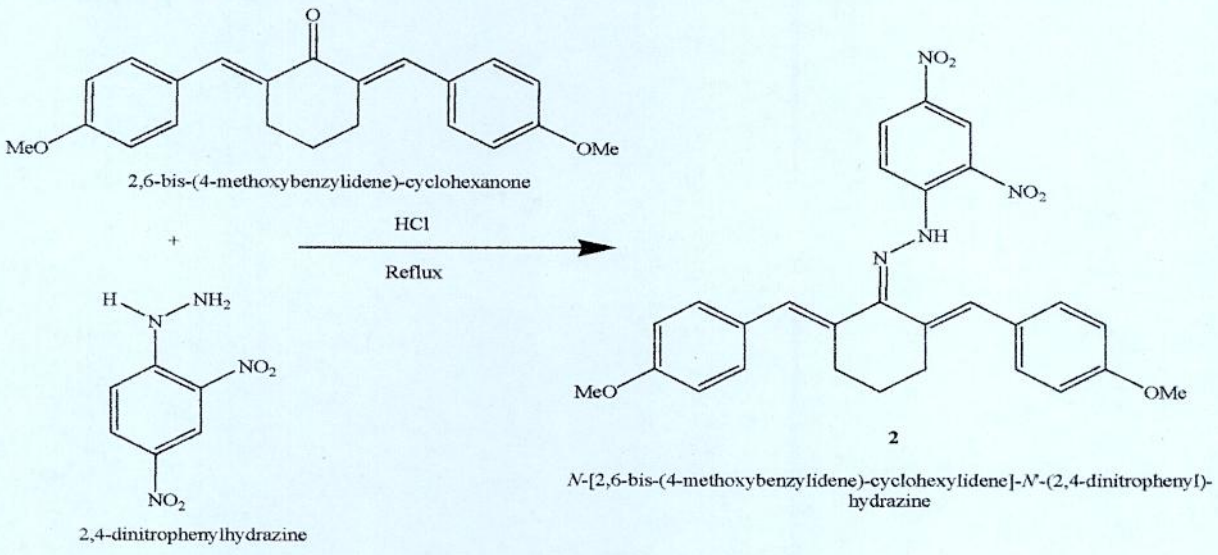
IR Spectrum

The IR spectrum of the product run as KBR pellet asserted absorption band ν in cm^{-1} which was assigned as: 2937, 1656, 1593, 1161, 1184, 833

^{1}H NMR

The ^{1}H NMR spectrum of the compound in DMSO gave the following signals (δ value) using TMS as an internal standard. ^{1}H NMR (400MHz $CDCl_3$) δ: =7.76 (s, 2H, allylic), 7.45 (d, J = 8.7 Hz, 4H, Ar), 6.93 (d, J = 8.7 Hz, 4H, Ar), 3.85 (s, 6H, 2×CH_3O), 2.92 (t, J = 14.2, 4H, 2 × CH_2), 1.84-1.78 (m, 2H, CH_2) [59].

3.4.4 Prepartion of *N*-[2, 6-bis-(4-methoxybenzylidene)-cyclohexanone]-*N'*-(2, 4-dinitrophenyl)-hydrazine



To make a solution of (0.198 g, 1.0 mmol) of 2, 4-dinitrophenyl hydrazine in 20 ml of methanol. Then added 1.0 ml of hydrochloric acid to this solution. Now to the clear solution, 2, 6-bis-(4-methoxybenzylidine)-cyclohexanone (0.334 g, 1.0 mmol) was added. The reaction mixture was reflux about 1hour and allowed to stand for overnight. The crude product precipitated as coffee crystal, was separated by filtration washed with ethanol and air dried. The product was recrystalized from ethanol and dimethylsulfoxide. The R_f value of this compound was 0.60 (n-hexane: ethyl acetate =3:2). The percentage of yield of the product was 55%.

Characterization and structure determination of the product

The product **2** of the color was coffee and the melting point of the pure product was 225 °C.

Spectral properties

UV-Visible spectrum

The UV spectrum of the product **2** in EtOH exhibited λ_{max} at 384 nm.

IR Spectrum:

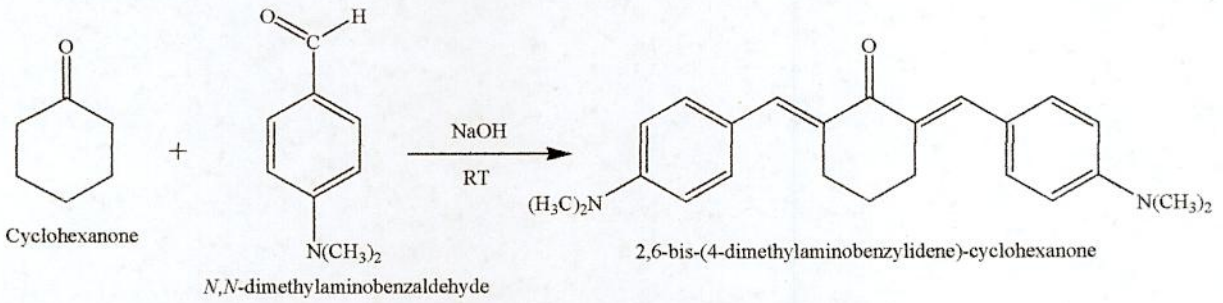
The IR spectrum of the product **2** run as KBR pellet asserted absorption band ν in cm^{-1} which was assigned as: 3269, 3107, 2931, 2835, 1612, 1585, 1506, 1475, 1249, 1170, 1130.

^{1}H NMR

The ^{1}H NMR spectrum of the compound **2** in DMSO-d_6 gave the following signals(δ value) using TMS as an internal standard. ^{1}H NMR (400MHz, DMSO- d_6) δ:= 8.7 (s, 1H, N-H), 8.4 (d, 1H, Ar), 8.0-8.01(m,4H,Ar), 7.7 (s, 1H, Ar), 7.2 (s, 1H, Ar) 7.0-7.1 (m, 4H, Ar), 6.9-7.0 (m, 2H, allylic), 3.8-3.9 (d, 6H, 2×CH_3), 1.6- 1.8 (d, 4H, cyclic), 1.2 (m, 2H, cyclic).

3.4.5 Preparation of 2, 6-bis-(4-dimethylaminobenzylidene)- cyclohexanone

A mixture of 1.0 equivalent of cyclohexanone, 0.32 ml, 2 equivalent of *N*, *N*-dimethyl amino benzaldehyde 0.98 g and 2.2 equivalent of solid NaOH, 0.29 g was grind in a mortar and pestle for 20 minutes at RT and then dilute Hydrochloric acid was poured in the reaction mixture. The separated solid material was filtered and dried. The solid obtained was purified by re-crystallization from ethanol and ethyl acetate mixture. The R_f value of this compound was 0.58 (n-hexane: ethyl acetate = 3: 2). The percentage of yield of the product was 80%.



Cyclohexanone

N,N-dimethylaminobenzaldehyde

2,6-bis-(4-dimethylaminobenzylidene)-cyclohexanone

Characterization and structure determination of the product

The product of the color was yellow and the melting point of the pure product was 70 °C.

Spectral properties

UV-Visible spectrum

The UV spectrum of the product in EtOH exhibited λ_{max} at 450 nm.

IR Spectrum

The IR spectrum of the product run as KBR pellet showed absorption band ν_{max} in cm^{-1} which was assigned as: 2900, 1658, 1591, 1367, 1302, 1159, 823 .

^{1}H NMR

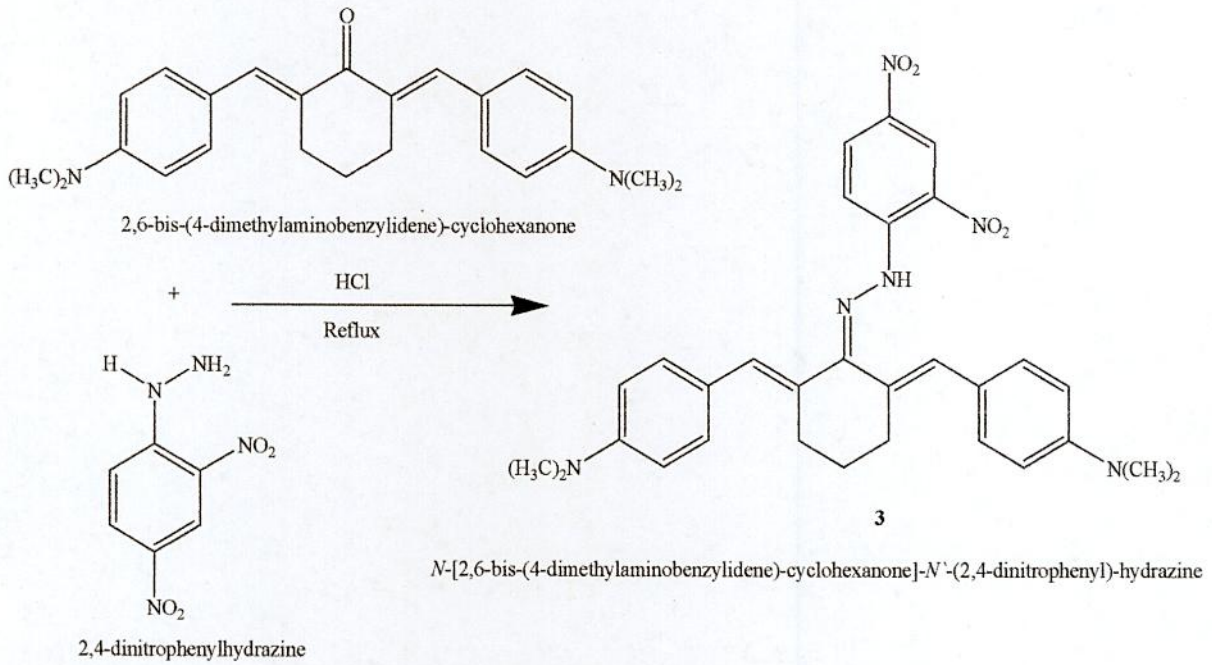
The ^{1}H NMR spectrum of the compound in DMSO gave the following signals (δ value) using TMS as an internal standard.

^{1}H NMR (400MHz $CDCl_3$) δ : = 7.76 (s, 2H, allylic), 7.45 (d, *J* = 8.70 Hz, 4H, Ar), 6.71 (d, *J* = 8.8 Hz, 4H, Ar), 3.01 (s, 12H, 2×N $(CH_3)_2$), 2.94 (t, *J* = 14.1, 4H, 2 × CH_2), 1.83 -1.79 (m, 2H, CH_2) [59].

3.4.6 Prepartion of *N*-[2, 6-bis-(4-dimethylaminobenzylidene)-cyclohexanone]-*N'*-(2, 4-dinitrophenyl)-hydrazine

To make a solution of (0.198 g, 1.0 mmol) of 2, 4-dinitrophenyl hydrazine in 20 ml of methanol. Then added 1.0 ml of hydrochloric acid to this solution. Now to the clear solution, 2, 6-bis-(4-dimethylamino-benzylidine)- cyclohexanone (0.364 g, 1.0 mmol) was added. The reaction mixture was reflux about 1 hour and allowed to stand for overnight . The product precipitated as

black crystal, was separated by filtration washed with ethanol and air dried. The product was recrystalized from ethanol and dimethylsulfoxide. The R_f value of this compound was 0.38 (n-hexane: ethyl acetate =3:2). The percentage of yield of the product was 60%.



Characterization and structure determination of the product

The product **3** of the color was black and the melting point of the pure product was 245 °C.

Spectral properties

UV-Visible spectrum

The UV spectrum of the product **3** in EtOH exhibited λ_{max} at 439 nm.

IR Spectrum: The IR spectrum of the product **3** run as KBR pellet asserted absorption band ν in cm^{-1} which was assigned as: 3271, 3091, 2931, 2835, 1612, 1602, 1502, 1413, 1327 and 1305.

^{1}H NMR

The ^{1}H NMR spectrum of the compound **3** in DMSO- d_6 gave the following signals (δ value) using TMS as an internal standard. ^{1}H NMR (400MHz, DMSO-d_6): δ = 8.9 (m, 1H, N-H), 8.6 (s,

1H, Ar), 8.3 (m, 1H, Ar), 8.0- 8.01 (m, 1H,Ar), 7.6 (d, 4H, Ar), 6.8 (d, 4H, allylic), 3.5 (s, 2H, allylic), 3 (s, 12H, 4×CH_3), 2 (s, 4H, cyclic),1.27 (s, 2H, cyclic).

Theoretical Calculation

Theoretical Calculations were carried out using the Gaussain 16 program suite [60]. The geometries were fully optimized at the DFT-B3LYP/6-311+G(2d,p) level of theory. Vibrational normal-mode analyses were performed at the same level to ensure that each optimized structure was a true minimum on the potential energy surface. Unscaled B3LYP/6-311+G(2d, p) frequencies were used to obtain thermochemical quantities, the thermal enthalpy and free energy corrections.

Chapter 4
Results and discussion

Chapter 4

Results and discussion

4.1Reaction of 2, 4-dinitrophenylhydrazinewith 2, 6-bis-(4-chlorobenzylidene)-cyclohexanone

The reaction of 2, 6-bis-(4-chlorobenzylidene)-cyclohexanone with 2, 4-dinitrophenylhydrazine in presence of hydrochloric acid at reflux condition gave a red crystalline solid 1 m.p 185 °C. The R_f value of this compound was 0.51 (n-hexane : ethyl acetate =60 : 40). The percentage of yield of the product was 50%.

Spectral Properties

UV-Visible spectrum

The UV spectrum of the compound 1in EtOH

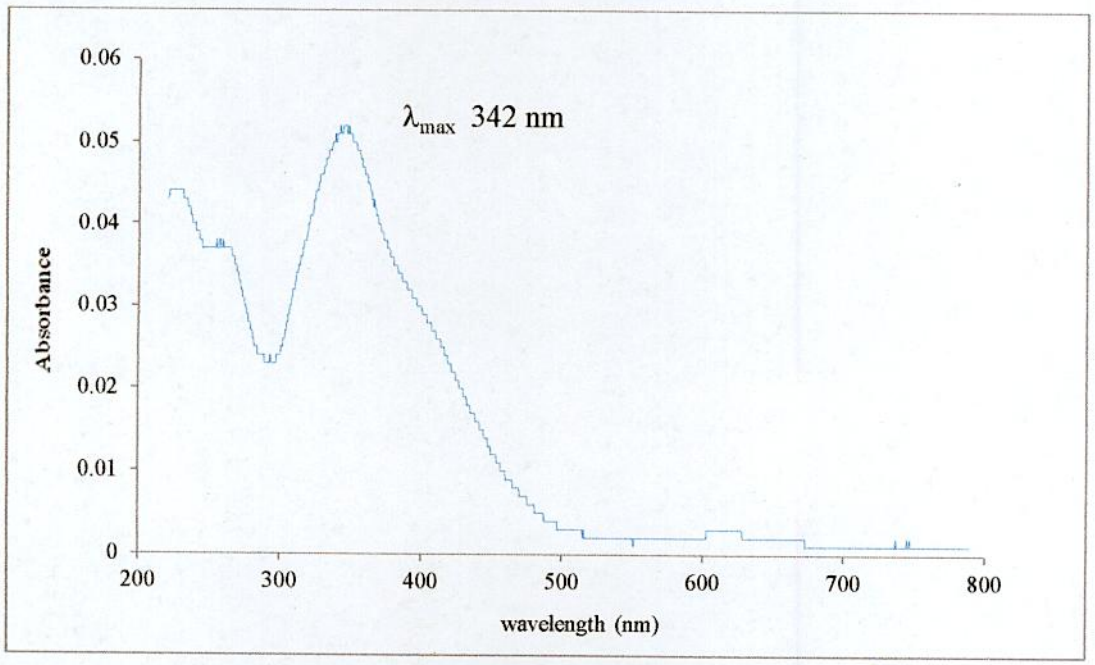


Figure: 4.1 UV spectrum of compound 1 in EtOH

IR spectrum

Table 4.1 : IR value of compound 1

Absorption bands , ν in cm^{-1}	**Group present**
3263	N-H stretching .
3095	C-H stretching in aromatic.
2941, 2916	C-H stretching in aliphatic.
1612	C=N in conjugation with C=C
1508, 1490	N=O stretching in phenyl.
1585	C=C in conjugation with C=N and C=C stretching of phenyl.
1332, 1082	C-N stretching
827	C- Cl stretching in aromatic.

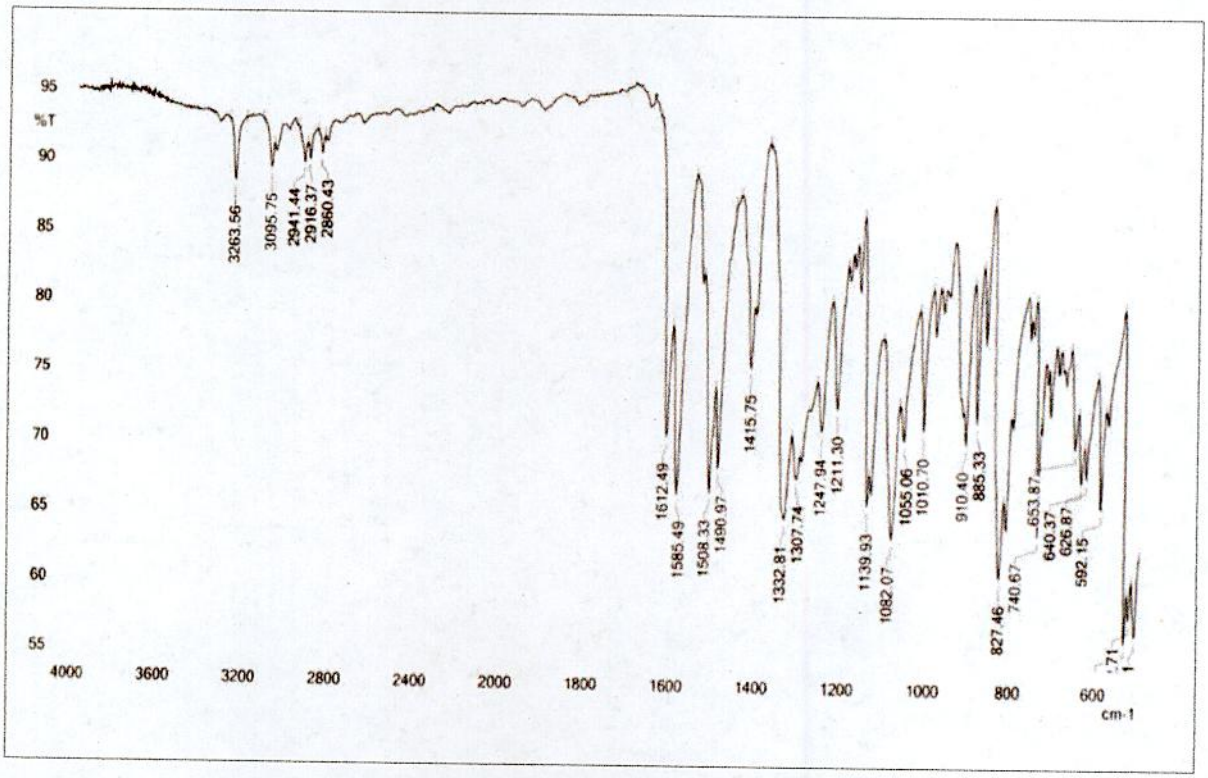


Figure: 4.2 IR spectrum of compound 1

^{1}H NMR spectrum

The ^{1}H NMR spectrum of the compound 1 in DMSO-d_6 gave the following signals (δvalue) using TMS as an internal standard. ^{1}H NMR (400 MHZ DMSO-d_6) : δ=12.0 (s, 1H, N-H), 8.9 (d, 1H, Ar), 8.5 (d, 1H, Ar), 8.2 (d, 1H, Ar) ,7.5 (m, 4H Ar)-7.4 (m, 4H, Ar), 7.2(m, 2H, allylic), 2.6-2.8 (m, 4H, cyclic),1.7 (m, 2H, cyclic)

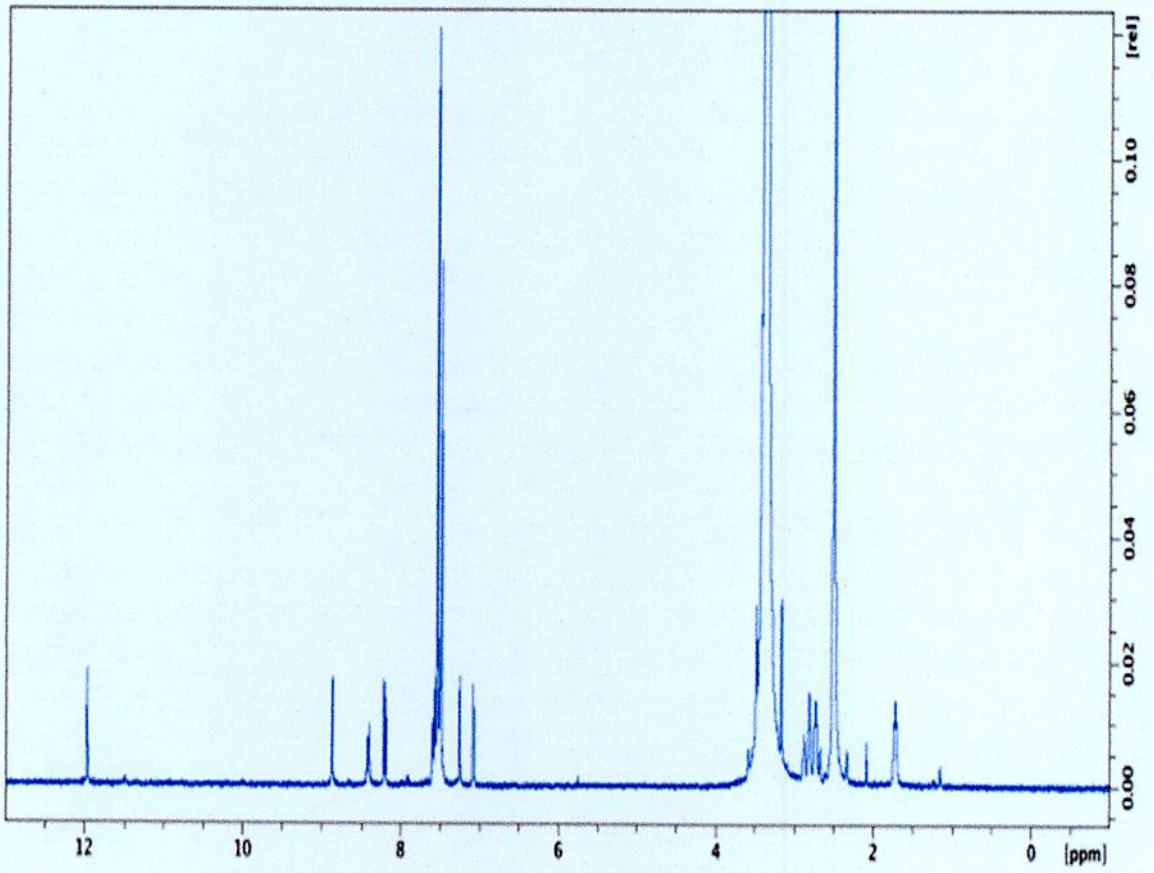


Figure: 4.3 ^{1}H NMR spectrum of compound 1

^{13}C NMR spectrum

The ^{13}C NMR spectrum of the compound 1 in DMSO-d_6 gave the following signals ((δ value) using TMS as an internal standard.

^{13}C NMR(125MHZ DMSO-d_6) : δ= 185, 137, 134, 134, 133.5, 132, 129, 28, 22

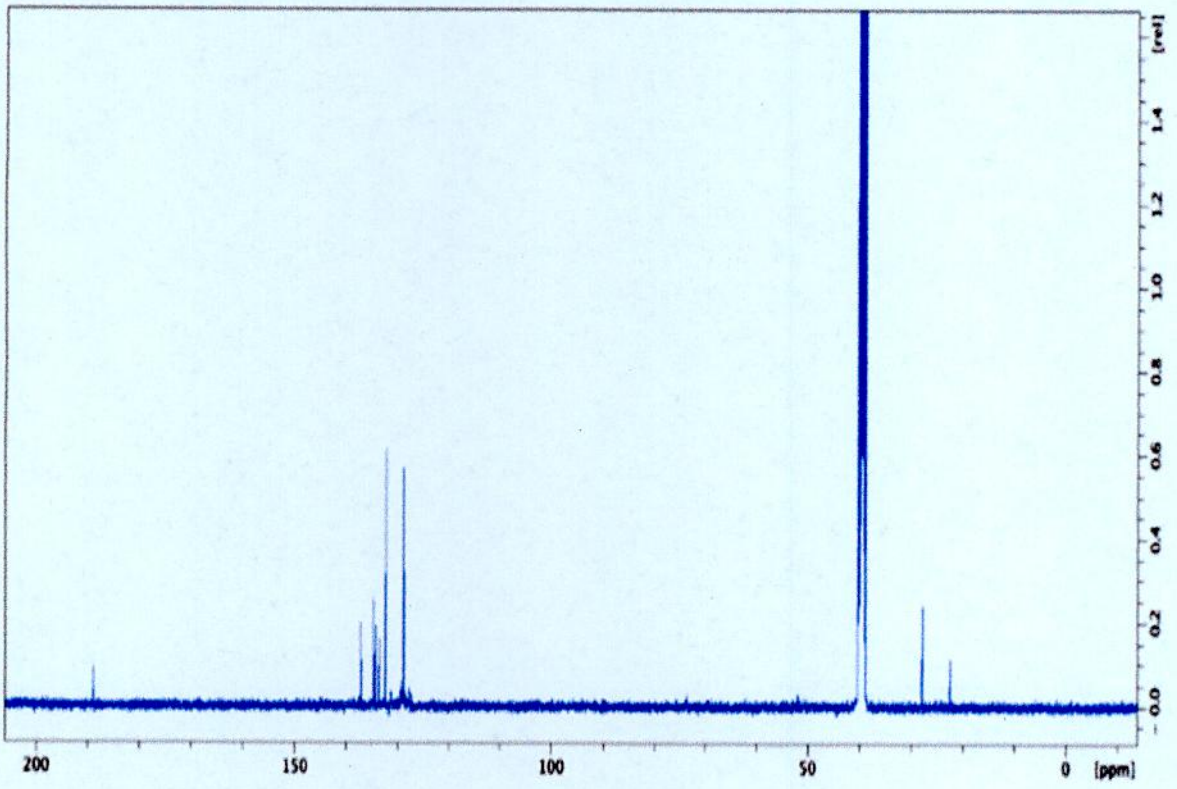
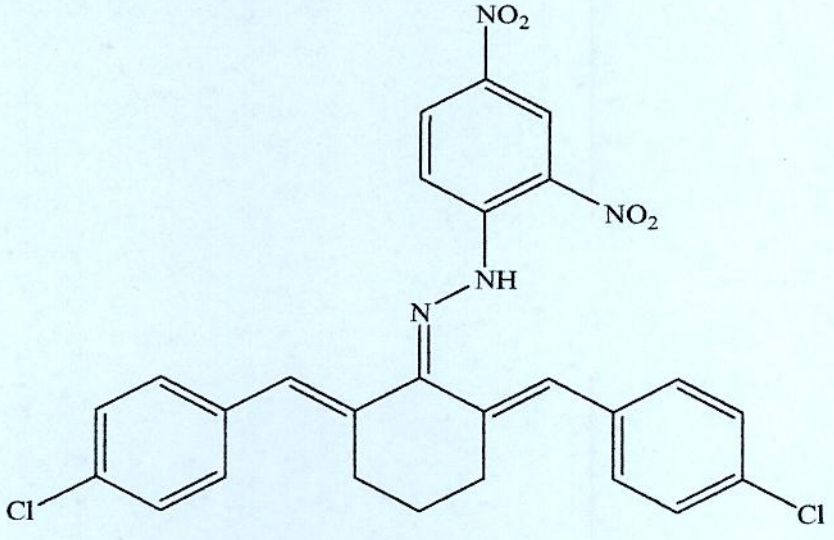


Figure: 4.4 ^{13}C NMR spectrum of compound 1

On the basis of the spectral properties (UV, IR, ^{1}H NMR & ^{13}C NMR) the following structure has been assigned to the obtained product.



N-[2, 6-bis-(4-chlorobenzylidene)-cyclohexylidene]-*N'*-(2,4-dinitrophenyl)-hydrazine

4.2 Reaction of 2, 4-dinitrophenylhydrazine with 2, 6-bis-(*p*-methoxybenzylidene)-cycloexanone

The reaction of 2, 6-bis-(*p*-methoxybenzylidene)-cycloexanone with 2, 4-dinitrophenylhydrazine in presence of hydrochloric acid at reflux condition gave a coffee color crystalline solid m.p 225 °C. The R_f value of this compound was 0.60 (n-hexane: ethyl acetate =60: 40). The percentage of yield of the product was 55%.

Spectral Properties

UV-Visible spectrum

The UV spectrum of the compound 2 in EtOH

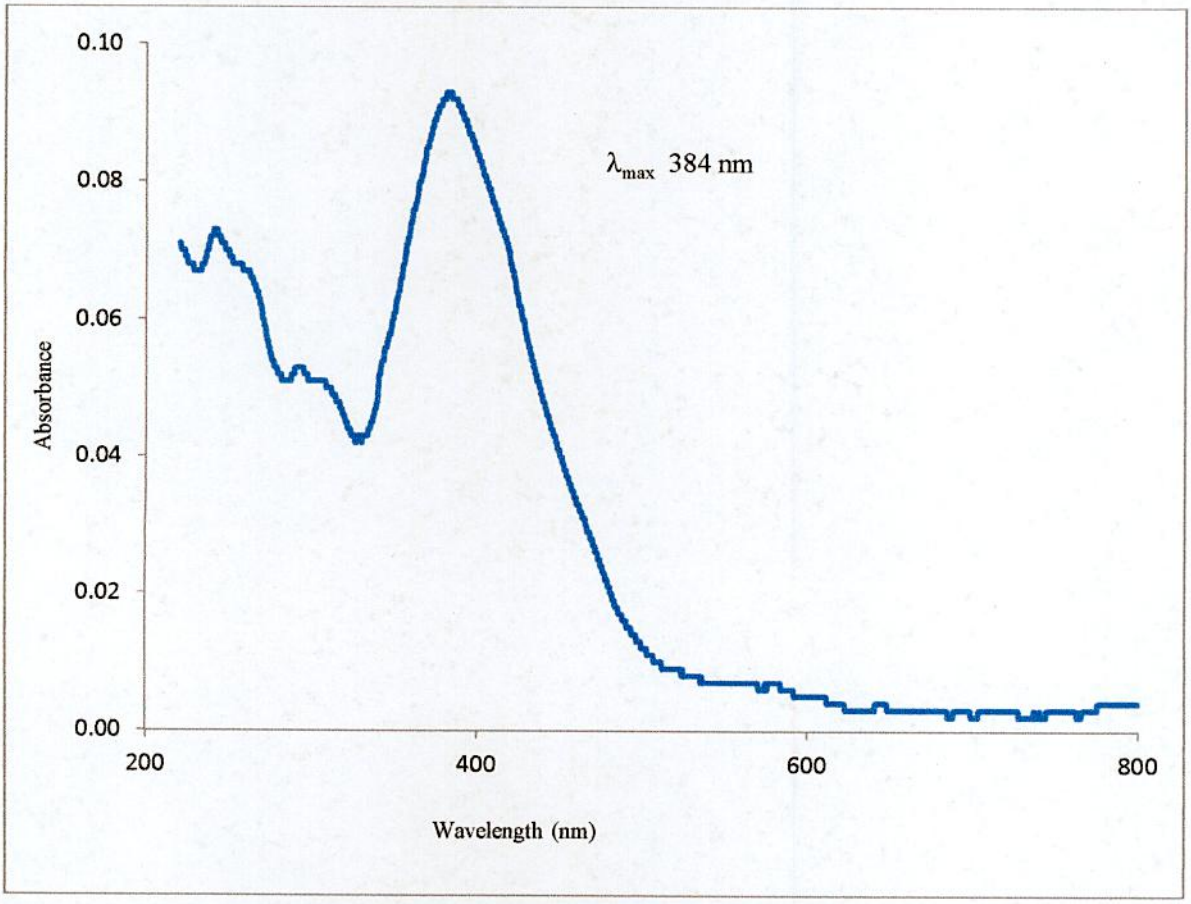


Fig 4.5 UV spectrum of compound 2 in EtOH

IR spectrum

Table 4.2 : IR value of compound 2

Absorption bands , ν in cm^{-1}	**Group present**
3269	N-H stretching
3107	C-H stretching in aromatic
2931, 2835	C-H stretching in aliphatic
1612	C=N in conjugation with C=C
1585	C=C in conjugation with C=N and C=C stretching of phenyl
1506, 1475	N=O stretching
1249, 1130	C-N stretching
1170	C-O stretching

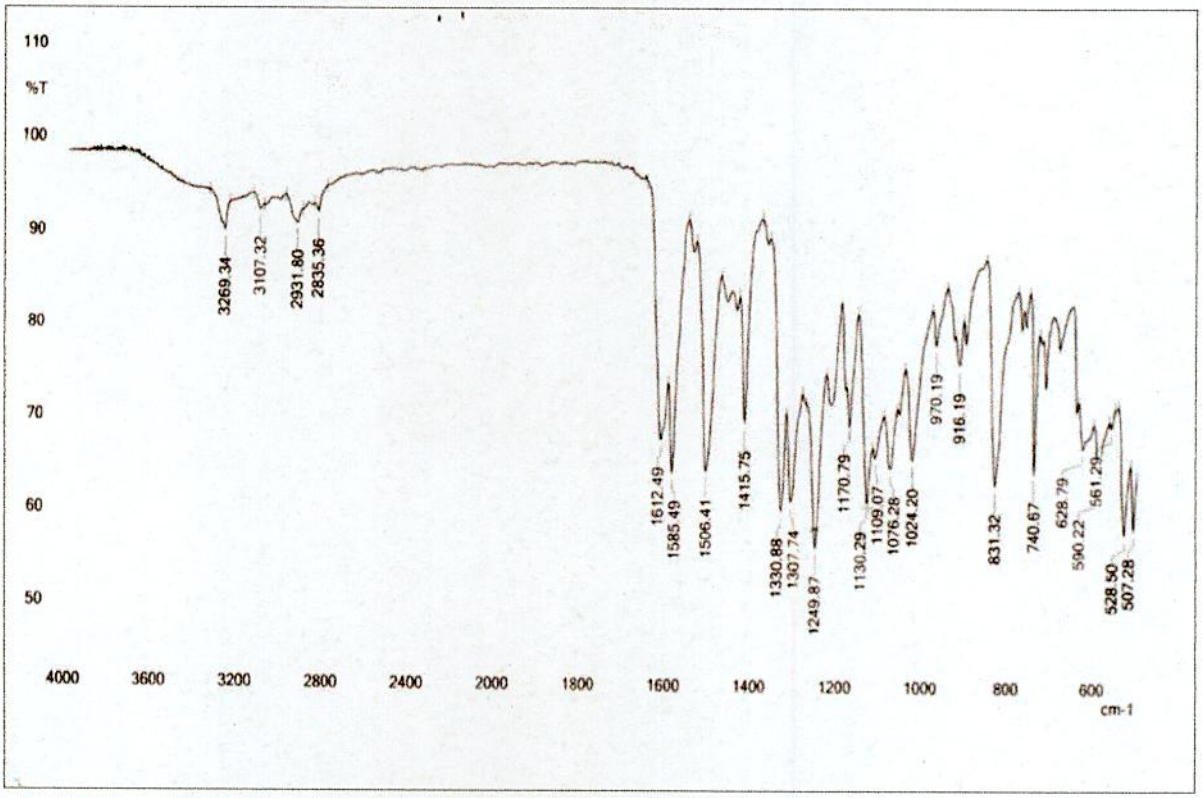


Figure: 4.6 IR spectrum of compound 2

^{1}H NMR spectrum

The ^{1}H NMR spectrum of the compound 2 in DMSO- d_6 gave the following signals (δvalue) using TMS as an internal standard.

^{1}H NMR (400 MHZ DMSO-d_6) : δ = 8.7 (s, 1H, N-H), 8.4 (d, 1H, Ar), 8.0-8.01(m, 4H, Ar), 7.7 (s, 1H, Ar), 7.2 (s, 1H, Ar) 7.0-7.1 (m, 4H, Ar), 6.9-7.0 (m, 2H, allylic), 3.8-3.9 (d, 6H, 2×CH_3), 1.6- 1.8 (d, 4H, cyclic), 1.2 (m, 2H, cyclic).

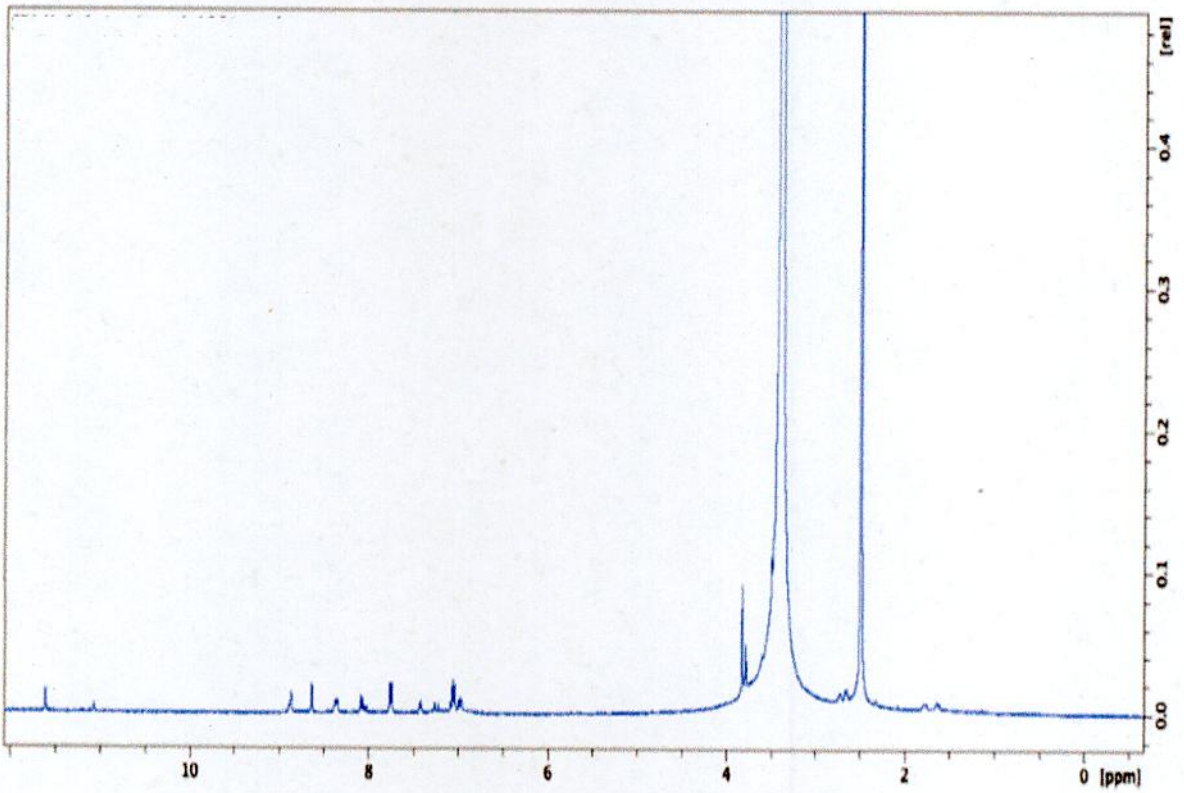


Figure: 4.7 ^{1}H NMR spectrum of compound 2

^{13}C NMR spectrum

The ^{13} C NMR spectrum of the compound 2 in DMSO-d_6 gave the following signals (δ value) using TMS as an internal standard.

^{13} C NMR(125MHZ DMSO-d_6) : δ= 150,145,137,131.5,130,129,127,123,117,114, 57.

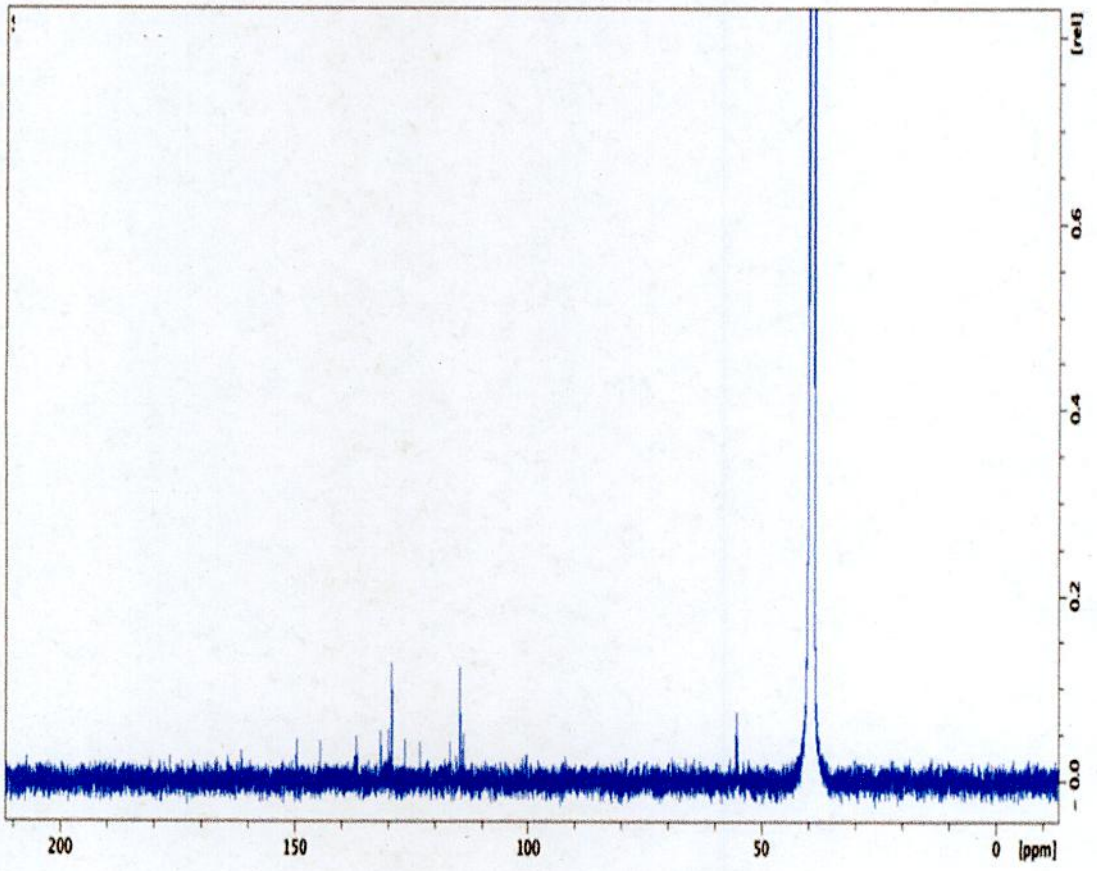
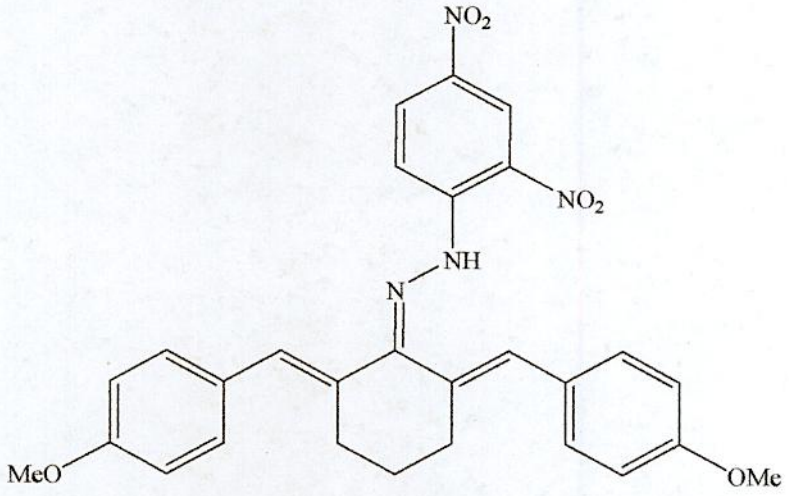


Figure: 4.8 ^{13}C NMR spectrum of compound 2

On the basis of the spectral properties (UV, IR & ^{1}H NMR) the following structure has been assigned to the obtained product .



N-[2, 6-bis-(4-methoxybenzylidene)-cyclohexylidene]-*N'*-(2,4-dinitrophenyl)-hydrazine

4.3 Reaction of 2, 4-dinitrophenylhydrazine with 2, 6-bis-(4-dimethylaminobenzylidene)-cyclohexanone

The reaction of 2, 6-bis-(4-dimethylamino-benzylidene)-cyclohexanone with 2, 4-dinitrophenylhydrazine in presence of hydrochloric acid at reflux condition gave a black crystalline solid 3 m.p 245 °C. The R_f value of this compound was .38 (n-hexane: ethyl acetate =60: 40). The percentage of yield of the product was 60%.

Spectral Properties

UV-Visible spectrum

The UV spectrum of the compound 3 in EtOH

Fig 4.9 UV spectrum of compound 3 in EtOH

IR spectrum

Table 4.3 : IR value of compound 3

Absorption bands , ν in cm^{-1}	**Group present**
3271	N-H stretching
3091	C-H stretching in aromatic
2931, 2835	C-H stretching in aliphatic
1612	C=N in conjugation with C=C
1602	C=C in conjugation with C=N and C=C stretching of phenyl
1502, 1413	N=O stretching
1327, 1305	C-N stretching in aromatic

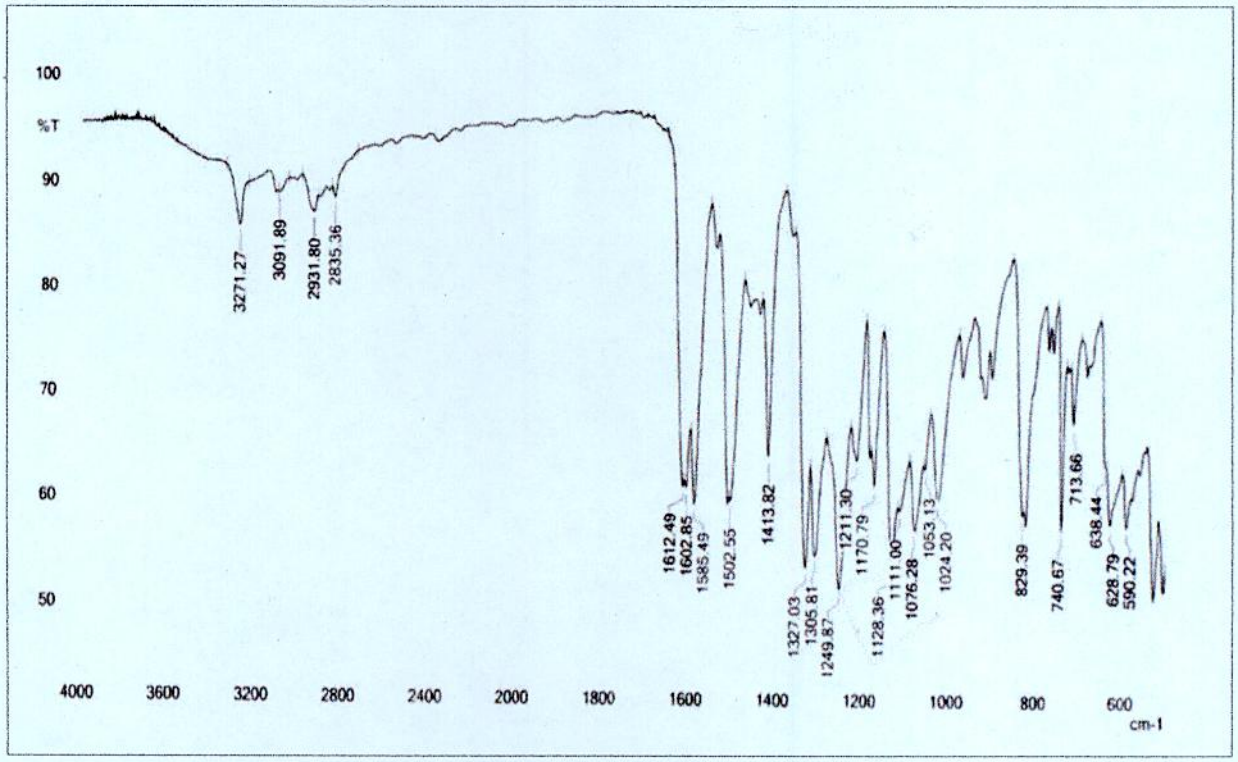


Figure: 4.10 IR spectrum of compound 3

^{1}H NMR spectrum

The ^{1}H NMR spectrum of the compound 3 in DMSO- d_6 gave the following signals (δvalue) using TMS as an internal standard.

^{1}H NMR (400 MHZ DMSO-d_6) : δ = 8.9 (m, 1H, N-H), 8.6 (s, 1H, Ar), 8.3 (m, 1H, Ar), 8.0-8.01 (m, 1H,Ar), 7.6 (d, 4H, Ar), 6.8 (d, 4H, allylic), 3.5 (s, 2H, allylic), 3 (s, 12H, 4×CH_3), 2 (s, 4H, cyclic),1.27 (s, 2H, cyclic).

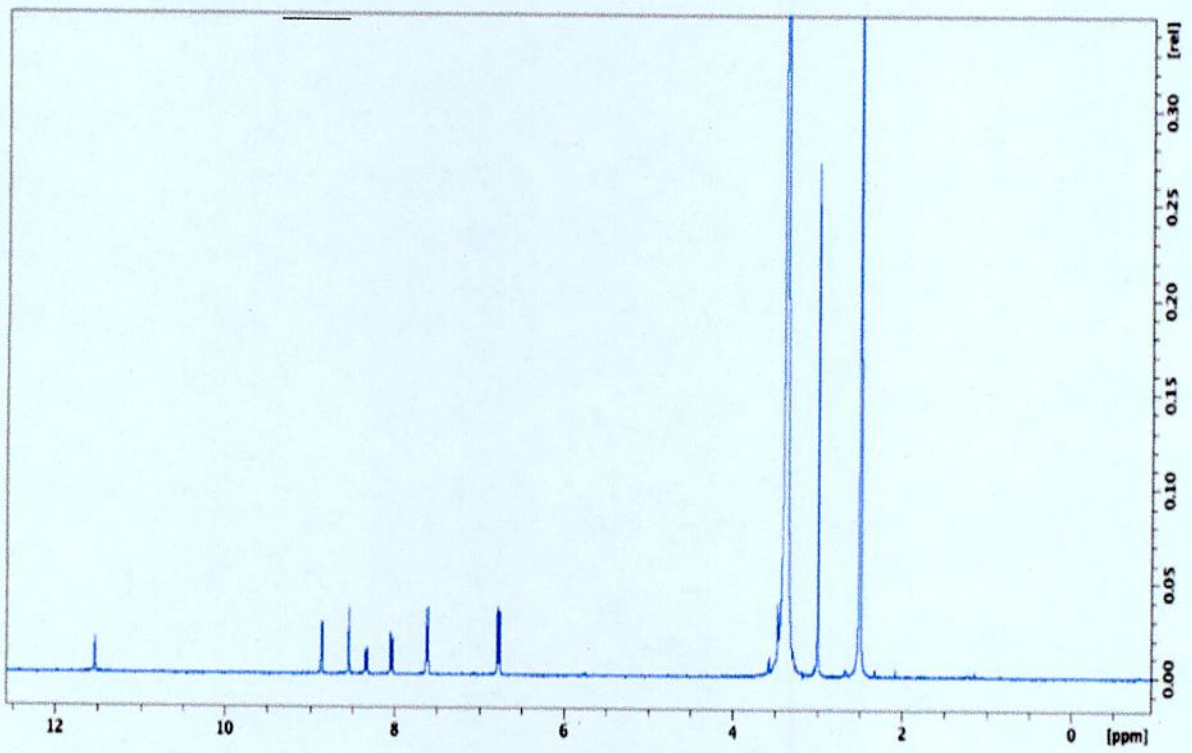


Figure: 4.11 ^{1}H NMR spectrum of compound 3

^{13}C NMR spectrum

The ^{13} C NMR spectrum of the compound 3 in DMSO-d_6 gave the following signals (δ value) using TMS as an internal standard.

^{13} C NMR(125MHZ DMSO-d_6) : δ=152,151,144,136,5,130,129,128.5,123.5,121,116.5,112

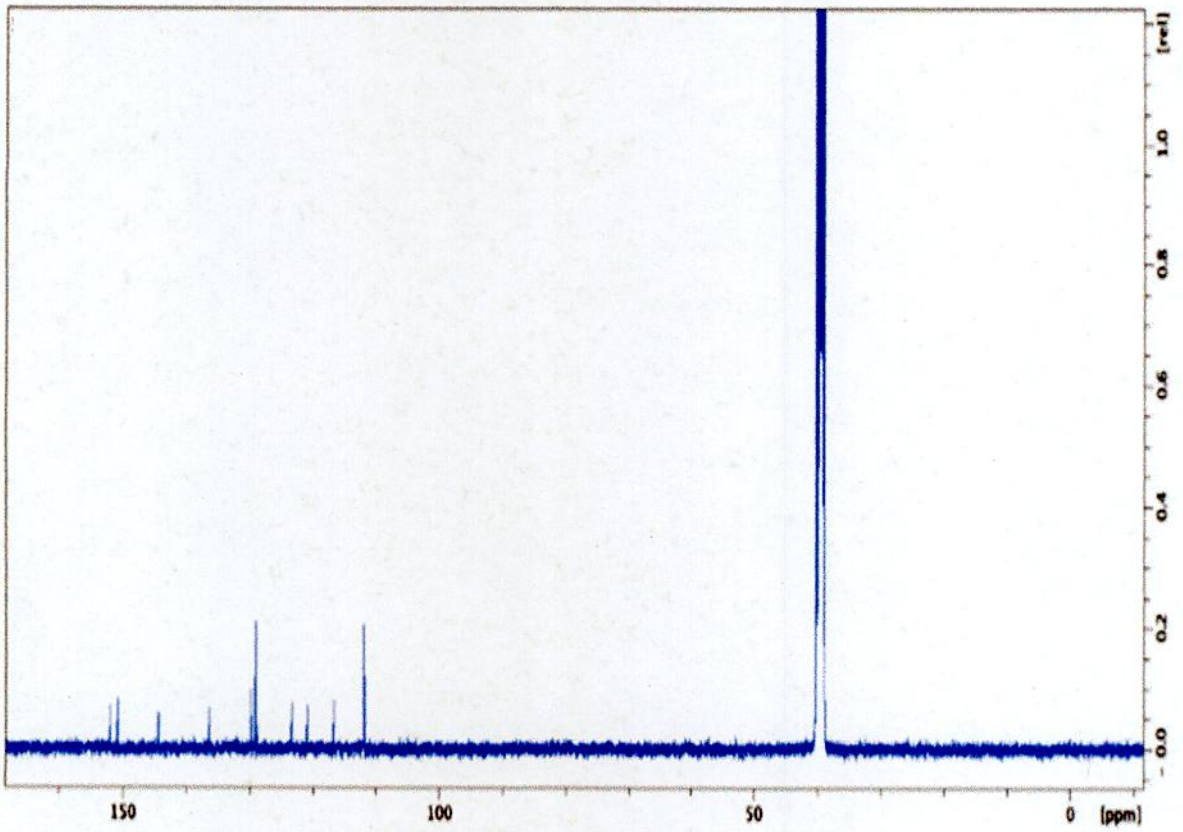
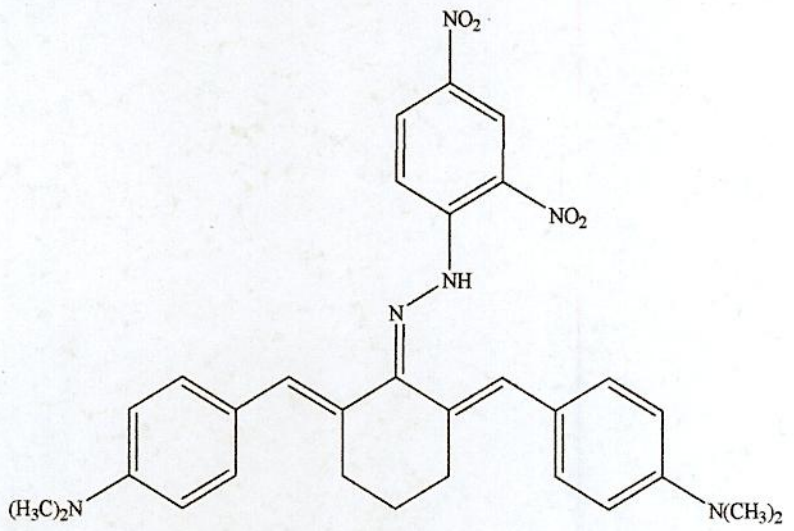


Figure: 4.12 ^{13}C NMR spectrum of compound 3

On the basis of the spectral properties (UV, IR & ^{1}H NMR) the following structure has been assigned to the obtained product .



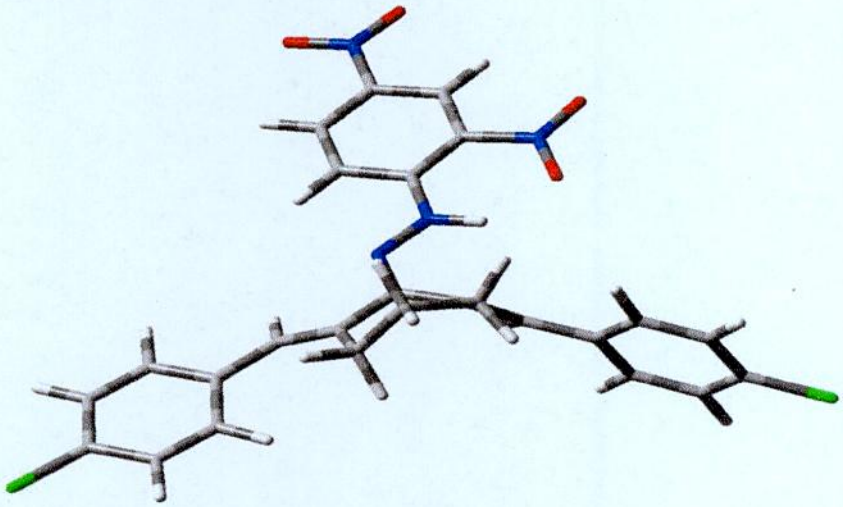
N-[2, 6-bis-(4-dimethylamino-benzylidene)-cyclohexanone]-*N'*-(2, 4-dinitrophenyl)-hydrazine

Computational study

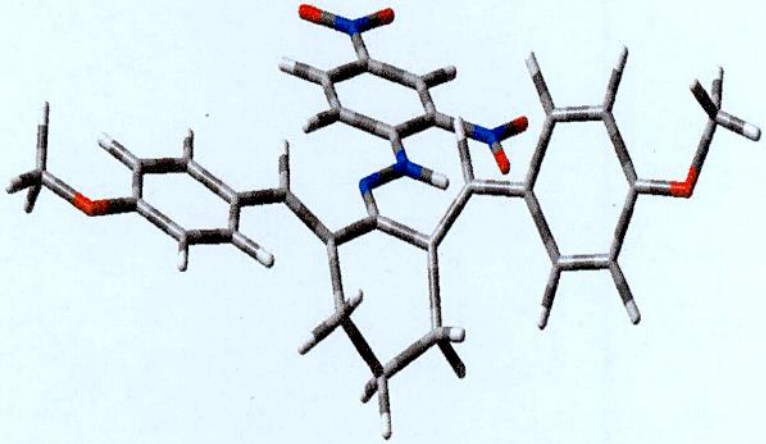
The geometries were fully optimized at the DFT-B3LYP/6-311+G(2d,p) level of theory. Vibrational normal-mode analyses were performed at the same level to ensure that each optimized structure was a true minimum on the potential energy surface. Unscaled B3LYP/6-311+G(2d,p) frequencies were used to obtain thermochemical quantities, the thermal enthalpy and free energy corrections.

The optimized structure of the substituted hydrazone Schiff base derivatives and there thermochemical quantities are given below.

***p*-Cl Substituted hydrazone schiff base derivative**



***p*-methoxy Substituted hydrazone Schiff base derivative**



***p*-*N*,*N*-dimethylamino Substituted hydrazone Schiff base derivative**

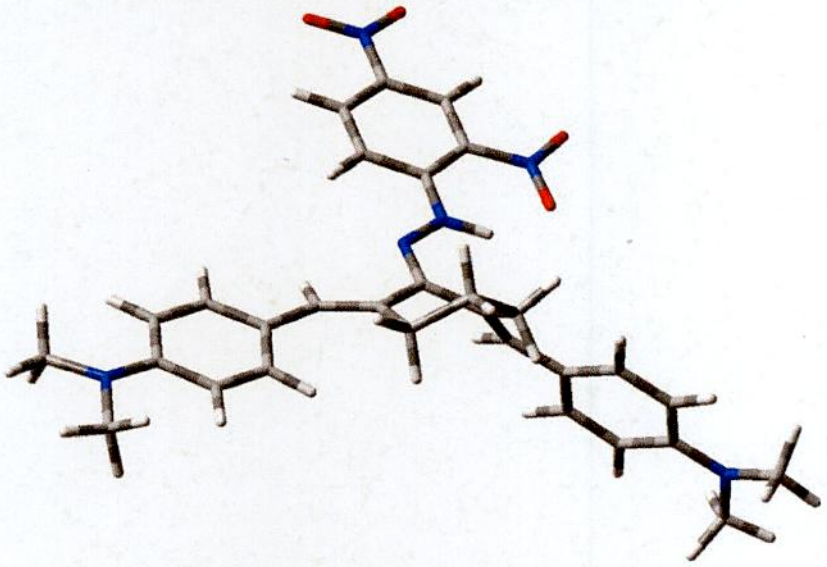


Table 4.4: Thermochemical properties among the substituted hydrazone Schiff base derivatives

	p-$N(CH_3)_2$	*p*-$O(CH_3)_2$	*p*-Cl
Calculation Method	RB3LYP	RB3LYP	RHF
Basis Set	6-311+G(2d,p)	6-311+G(2d,p)	3-21G
Spin	Singlet	Singlet	Singlet
Imaginary Freq	0	0	0
Dipole Moment	13.308864 Debye	9.783643 Debye	9.6291902 Debye
Electronic Energy (EE)	-1792.143341 Hartree	-1753.248256 Hartree	-2419.2381 Hartree
EE + Thermal Free Energy Correction	1791.638715 Hartree	1752.818742 Hartree	-2418.8531 Hartree
Entropy (S)	241.167 cal/mol-kelvin	222.379 cal/mol-Kelvin	201.16 cal/mol-kelvin

Table 4.5: Bond length and dihedral angel among the substituted hydrazone Schiff base derivatives

Substitute	*p*-OMe	*p*-NMe2	*p*-Cl
Bond	Bond lengths	Bond lengths	Bond lengths
C14-N37	1.29561	1.29767	1.30552
N37-N38	1.36239	1.36353	1.39234
C14-C16	1.49003	1.48138	1.47844
C16-C25	1.35004	1.35142	1.34351
C14-C13	1.48274	1.48847	1.47652
C13-C11	1.34948	1.35235	1.34050
C25-C16-C14-N37	57.44	27.45	54.88
C11-C13-C14-N37	-28.10	-56.07	-46.53

Chapter 5
Conclusion

Chapter 5

Conclusion

Hydrazone Schiff base derivatives were synthesized a general method for the addition of 2,4-dinitrophenyl hydrazine and various substituted 2,6-dibenzylidene cyclohexanone based bis-chalcones in the presence of hydrochloric acid. The product, *N*-[2, 6-bis-(4-chlorobenzylidene)-cyclohexylidene]-*N'*-(2, 4-dinitrophenyl)-hydrazine has been synthesized by the reaction of 2,4-dinitrophenylhydrazine with 2,6-bis-(4-chlorobenzylidene)-cyclohexanone at reflux condition at 2 hours. After recrystalization, the pure product was red in color and the melting point of the product was 185 °C. The other product, *N*-[2, 6-bis-(4-methoxybenzylidene)-cyclohexylidene]-*N'*-(2,4-dinitrophenyl)-hydrazine has been synthesized by the reaction of 2,4-dinitrophenyl hydrazine with 2,6-bis-(4-methoxybenzylidene)-cyclohexanone at the same condition. The pure product was coffee color and the melting point of the product was 225 °C. Final product, *N*-[2,6-bis-(4-dimethylaminobenzylidene)-cyclohexylidene]-*N'*-(2,4-dinitrophenyl)-hydrazine has been synthesized by the reaction of 2,4-dinitrophenyl hydrazine with 2,6-bis-(4-dimethylamino benzylidene)-cyclohexanone also at the same condition. The product of the color was black and the melting point of the pure product was 245 °C. The structures of the synthesized products were characterized by their physical, UV, FTIR, ^{1}H NMR & ^{13}C NMR spectra. Their optimized structures have been investigated by computational method, Gaussian 16 software Revision B.01. Their molecular geometry and vibrational frequencies were computed at density functional theory, DFT-B3LYP/6-311+G(2d, p) level of theory. Bond length and dihedral angles are consistent with experimental results.

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