Republic of Iraq
Ministry of Higher Education
And Scientific Research
University of Baghdad
College of Education for pure
science Ibn Al-Haitham
Department of Chemistry

Design, Synthesis, Characterization and Anti-Microbial Studies of New [Azobenzen-p,p'-di(3-Substituted 4(3H)Quinazolin-4-one, 4-Thion and 4-Substitued Quinazolin-2-yl] Derivatives From New Azobenzen-p,p-di(3,1-Benzoxazin-4-one-2-yl) Compounds

A Thesis

Submitted to the Council of College of Education for Pure Science, Ibn Al-Haitham, University of Baghdad, in Partial Fulfillment of the Requirements for the Degree of Doctor of Philosophy in Chemistry

By

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Supervisor

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2017 AC *1439AH*

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

﴿ فَفَهَّمْنَاهَا سُلَيْمَانَ ۚ وَكُلًّا آتَيْنَا حُكْمًا وَعِلْمًا ۚ ﴾

(صدق الله العظيم)

(سورة الانبياء/ الآية 79)

Supervisor Certification

I certified that this thesis was prepared under my supervision at Department of Chemistry, College of Education (Ibn Al–Haithem) at Baghdad University in partial requirements for the Degree of Doctor of Philosophy in Chemistry.

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Asst. Prof. Dr. Zakaria Hadi Aiube

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Asst. Prof. Dr. Najwa Issac Abdulla

Head of Chemistry Department

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We chairman and members of the examination committee, certify that we have studied this thesis presented by the student ***(Zainab Abdul Razzaq Abu Ragheef***)and examined her in its contents and that, we have found its worthy to be accepted for the Degree of Doctor of Philosophy in Chemistry Science **(Organic Chemistry)**.

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Dedication

To the Spirit of My Dear Father, and My Brothers the Martyrs of Iraq….

To My Soul, My Mother… with my great love

To My Brothers… Muath, Hassan & Saif…

And My Sister … (Sarab) with mercy…

To My Husband… Dr. Ahmed Al - Abadi…

To the light of My Eyes… my Son…

Hashem…

With my great love… and respect.

Zainab Abu Ragheef

Acknowledgment

Thanks to Allah the One, The Single for all this blessing during the pursuit of my academic and career goals.

I would like to express my sincere thanks and my appreciation to my supervisors Asst. Prof. Dr. Zakaria Hadi for their kindly interest, encouragement and guidance throughout the course of this work. Also my grateful thanks to the staff members of the college of Education Ibn Al–Hiatham and the Head of the Chemistry Department.

My deep grateful thanks to the staff members of the college of Agriculture and the head of basic science Division. And my deep thanks to my collogues Dr. Israa shkeeb and grateful thanks are due to all others who gave me help and sincere cooperation.

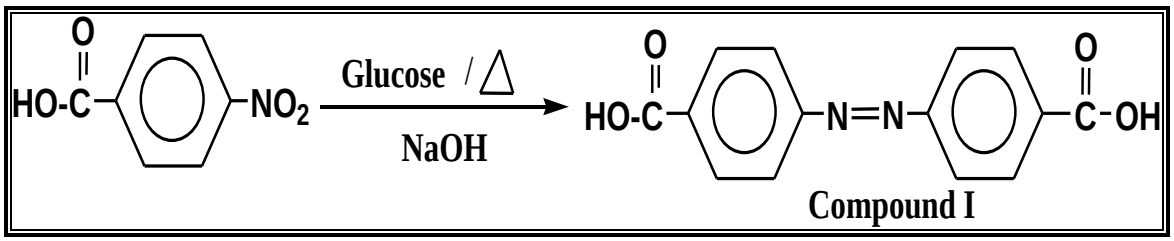
Finally, I am deeply indebted to my family for their support and patience during the years of my study.

The Researcher Zainab

Abstract

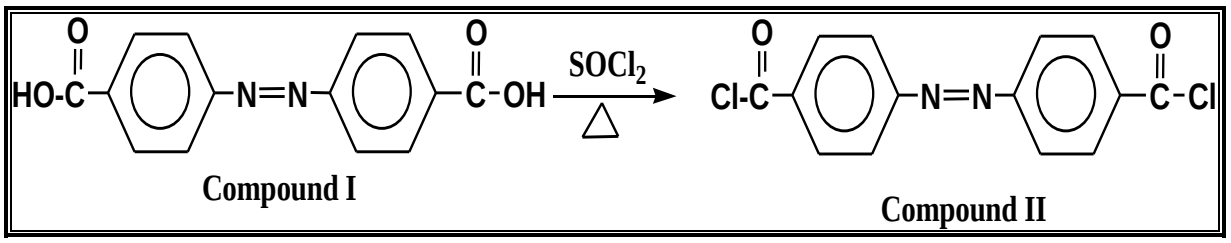
In the recent years many researches in the field of benzoxzine, quinazoline, quinazolinone and quinazoline-thione derivatives have much considerable attention, due to their effective biological and medicine of or/and pharmacological importance. for this reasons, we design anew synthetic routes of many compounds containing di[(3-substituted) quinazolin, quinzolinone and quinazoline thion-2-yl] moieties, substituted at (p,p'-position of bridged azobenzene molecule, via synthesized di(3,1-benzoxazin-4-one-2-yl) moiety, substituted at (p,p')-positions of bridged azobenzene molecule, according to the following synthetic routes:

1. Synthesis of azobenzen-p,p'-dicarboxylic acid [I] :



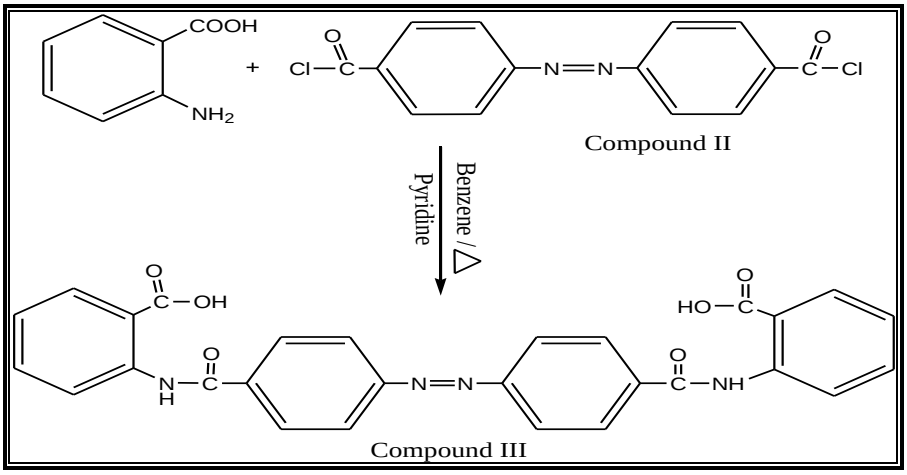
This compound was prepared in basic media, reductive-condensation reaction of p-nitrobenzoic acid in presence of glucose, which was characterized by C.H.N- analysis and FT-IR spectral analysis.

2. Synthesis of azobenzen-p,p'-diacid choride [II]:



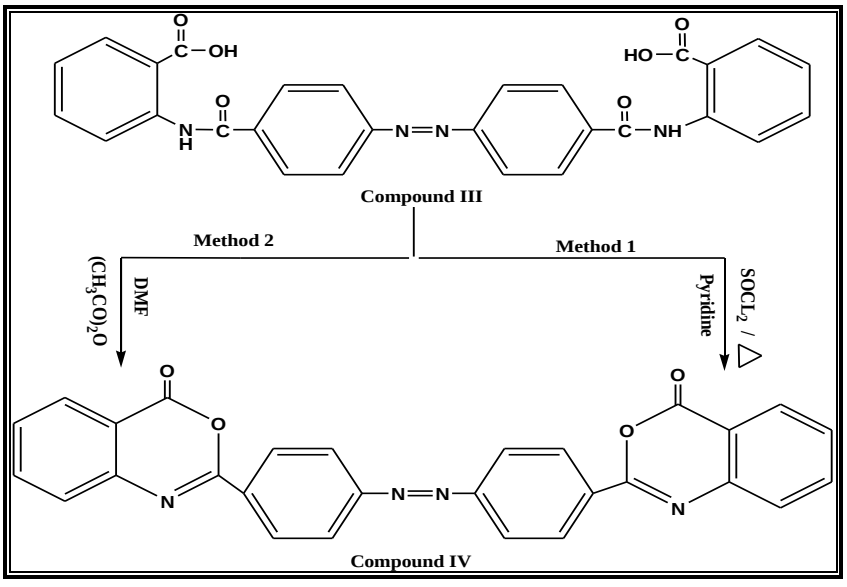
Treatment of compound [I], with excess of thionyl chloride in presence of pyridine give compound [II], which was characterized by C.H.N- analysis, FT-IR, ^{1}H-NMR, ^{13}C-NMR and mass spectral analysis.

3. Synthesis of azobenzen-p,p'- [(dibenzoic acid-2-yl)dicarboxamide] [III]:



Condensation of azobenzen-p,p'-diacid chloride [II], with anthranilic acid in molar ratio (1:2), in presence of pyridine give azobenzen-p,p'-[(dibenzoic acid-2-yl)dicarboxamide] [III], which was characterized by C.H.N- analysis, FT-IR, ^{1}H-NMR, ^{13}C-NMR and mass spectral analysis.

4. Synthesis of azobenzen-p,p'-di[3,1-benzoxazine-4-one-2-yl] [IV]:

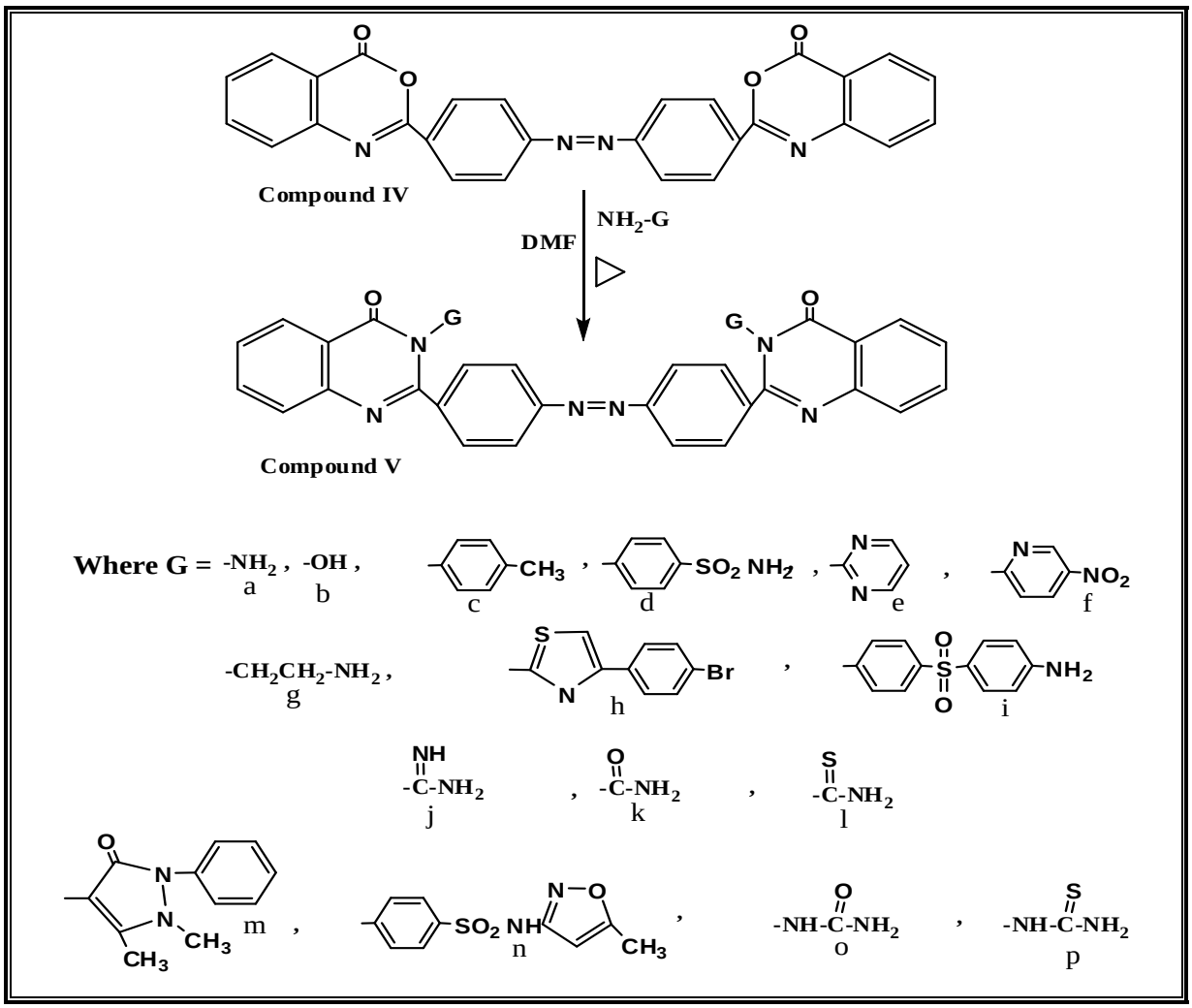


This compound [IV], was synthesized by two methods, either by heating azobenzene-p,p'-[(dibenzoic acid-2-yl)dicarboxyamide] [III], with excess of thionyl chloride in presence of pyridine, and or the second methods with excess of acetic anhydride in dimethyl formamide, which was identified by its melting point, and mixed melting point, of both products for two methods.

Compound [IV], was characterized by C.H.N- analysis, FT-IR, ^{1}H-NMR, ^{13}C-NMR and mass spectral analysis.

*** Series One:**

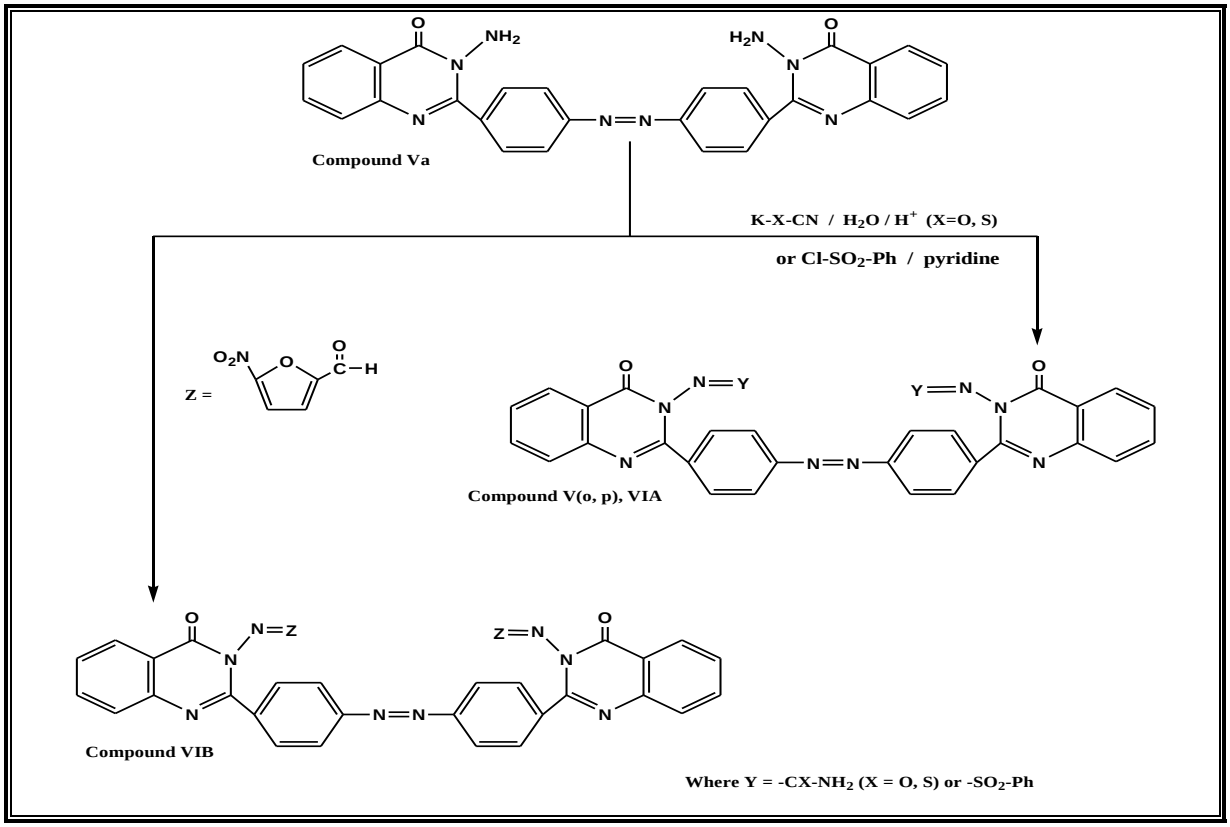
5. Synthesis of azobenzen-p,p'-di[3-substituted-4(3H)quinazolinone-2-yl] [Va- Vp]:



These compounds [Va - Vp], were synthesized by heating azobenzen-p,p'-di[3,1-benzoaxzin-4-one-2-yl] [IV], with amine moieties in molar ratio (1:2), like hydrazine hydrate, hydroxyl amine, quinidine, urea, thiourea, semicarbazide, thiosemicarbazide and aliphatic diamine. Azobenzen-p,p'-di[3-substituted-4(3H)quinazolinone-2-yl] compounds [Va- Vp], were characterized by FT-IR spectral analysis, many of them were characterized by ^{1}H-NMR, ^{13}C-NMR and some of them by mass spectrometry analysis.

*** Series Two:**

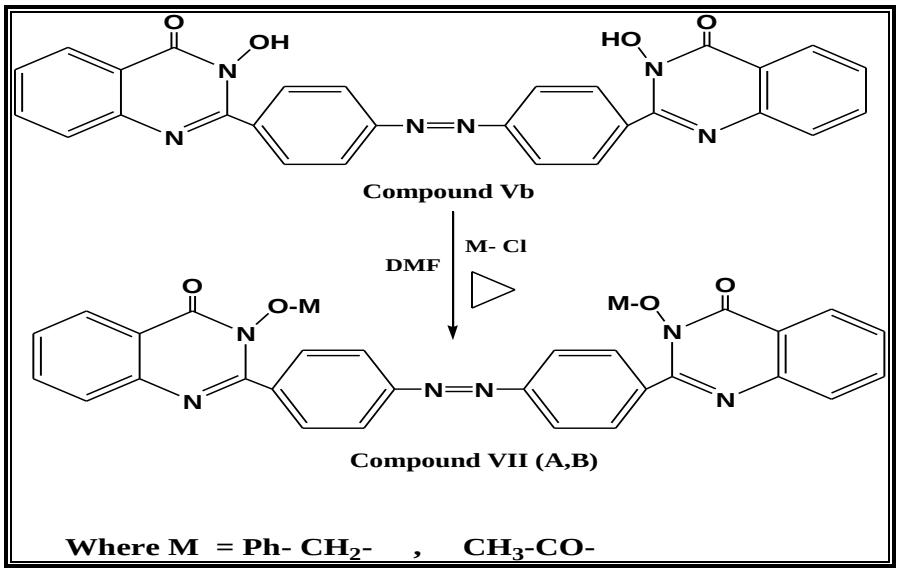
6. Synthesis of azobenzen-p,p'-di[3,N-substituted-4(3H) quinazolinone-2-yl] [V(o,p), VI(A,B)]:



Condensation of azobenzen-p,p'-[3-amino-4(3H)quinazolinone-2-yl] [Va], with potassium cyanite or thiocyanite, benzene sulphonyl chloride and 5-nitrofurfural in (1:2) molar ratio gave compounds [V(o,p) and VI(A,B)] respectively. Compounds [V(o,p)], characterized by melting points and mixed melting points, with these compounds prepared by condensation of azobenzen-p,p'-di[3,1-benzoxazine-4-one-2-yl] [IV], with semicarbazide and thiosemicarbazide in a molar ratio (1:2) respectively, and identity of these FT-IR spectrum. While compounds [VI(A,B)], were characterized by FT-IR spectrum and ^{1}H-NMR, ^{13}C-NMR spectrum for compound[VIA].

*** Series Three:**

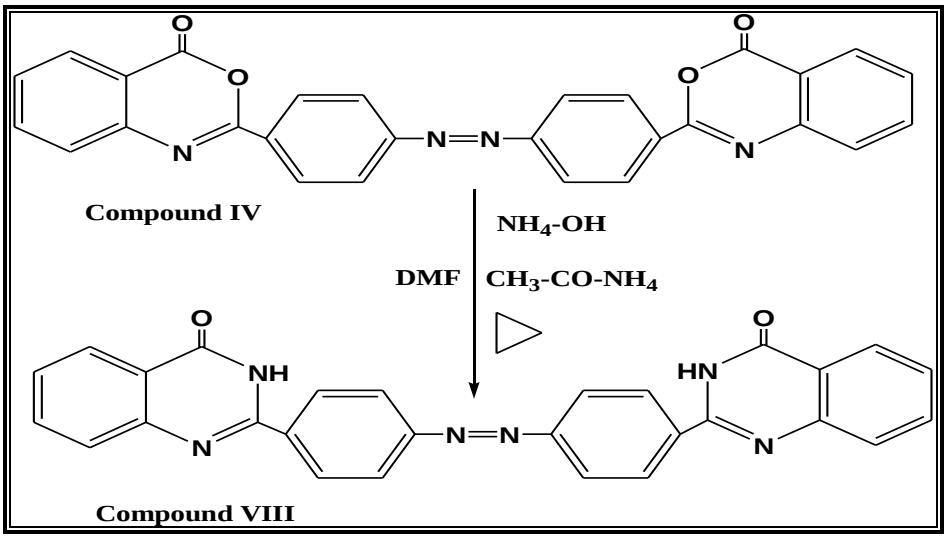
7. Synthesis of azobenzen-p,p'-di[3,O-subsitituted-4(3H)-quinazolinone-2-yl] [VII(A,B)]:



Condensation of azobenzen-p,p'-di[3-hydroxy-4(3H)-quinazolinone-2-yl] [Vb], with benzyl chloride or acetyl chloride in a molar ratio (1:2), gave compounds [VII(A,B)] respectively. These compounds were characterized by FT-IR, ^{1}H-NMR, ^{13}C-NMR spectral analysis.

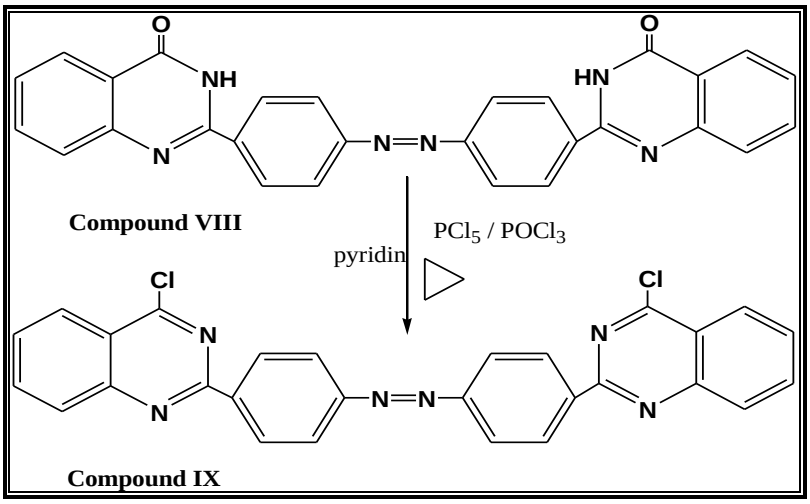
*** Series Four:**

8. Synthesis of azobenzen-p,p'-di[3-hydro-quinazolinone-2-yl] [VIII]:



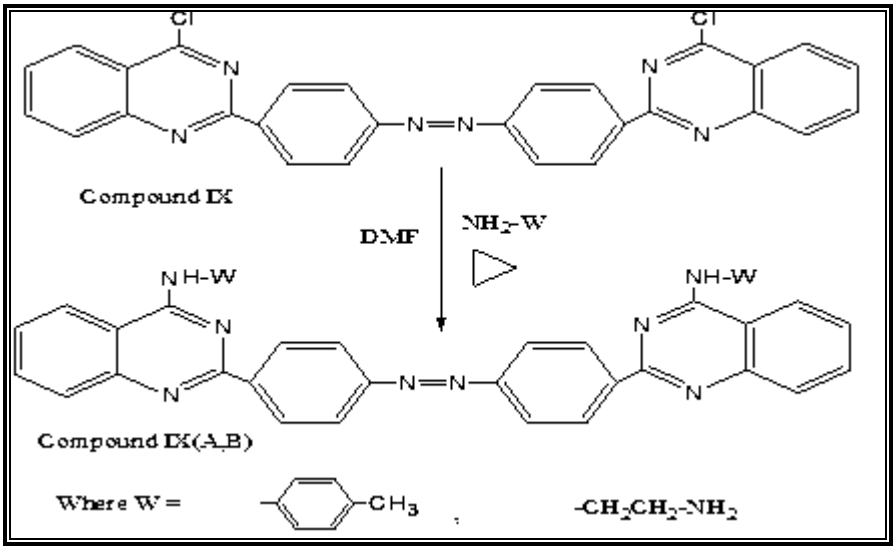
Condensation of azobenzen-p,p'-di[3,1-benzoxazin-4-one-2-yl] [IV], with excess of ammonia and ammonium acetate in DMF, in a molar ratio (1:2), gave azobenzen-p,p'-di[3-hydro-quinazolinone-2-yl] [VIII], which was characterized by FT-IR, ^{1}H-NMR, ^{13}C-NMR spectral analysis.

9- Synthesis of azobenzen-p,p'-di[4-chloro-quinazolin-2-yl] [IX]:



Treatment of azobenzen-p,p'-di[3-hydro-quinazolinone-2-yl] [VIII], with phosphorous-penta chloride / phosphorous-oxy chloride in a molar ratio (1:2), gave azobenzen-p,p'-di[4-chloro-quinazolin-2-yl] [IX], which was characterized by FT-IR, ^{1}H-NMR, ^{13}C-NMR spectrophotometry analysis.

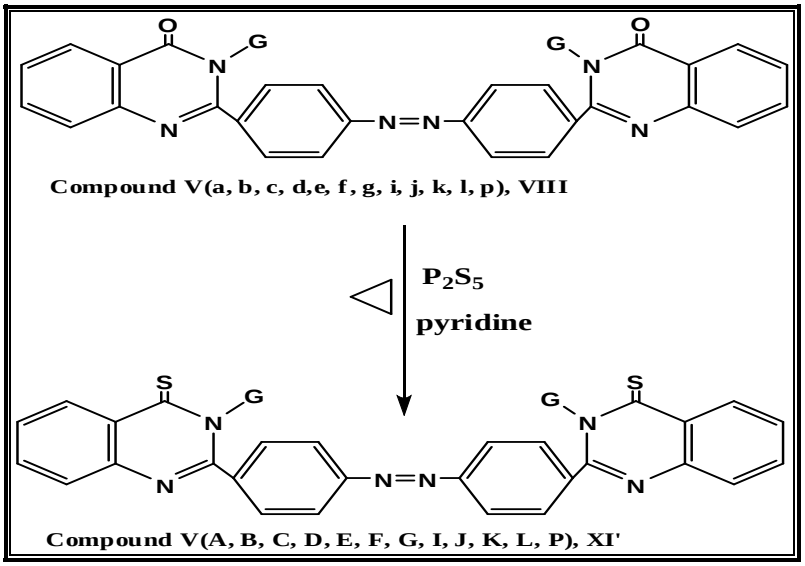
10- Synthesis of azobenzen-p,p'-di[4-substituted-quinazolin-2-yl] [IX(A,B)]:



Substitution of chlorin in azobenzen-p,p'-di[4-chloro-quinazolin-2-yl] [IX], with p-toluidine or ethylenediamine in molar ratio (1:2), gave azobenzen-p,p'-di[4,N-toludino-quinazolin-2-yl] [IXA], and azobenzene-p,p'-di[4,N-aminoethylamine-quinazolin-2-yl] [IXB]. These compounds were characterized by FT-IR, ^{1}H-NMR,^{13}C-NMR spectral analysises.

*** Series Five:**

11. Synthesis of azobenzen-p,p'-di[3-substituted-4-(3H)-quinazolinthion-2-yl] [X(A, B, C, D, E, G, F, I, K, L, P) and XI']:



Whenever heating some of azobenzene-p,p'-di[3-substituted-4(3H)quinazolinone-2-yl] [V(a,b,c,d,e,f,i,j,k,l,p), VIII], with excess of phosphorous penta sulphide in pyridine, give azobenzene-p,p'-di[3-substituted-4(3H)quinazolin-thion-2-yl] [X(A,B,C,D,E,F,I,J,K,L,P), XI]. These compounds were characterized by FT-IR spectral analysis, some of them were characterized by ^{1}H-NMR, ^{13}C-NMR and mass spectral analysis for compounds [X(A, B, E, F)].

12. Antimicrobial studies:

Awing to the importance of quinazoline derivatives in the pharmacological and biological fields, many types of di(3- and 4-substituted) quinazolin, quinazolinone and quinazolinthion-2-yl moieties, substituted at p,p'-position of azobenzene bridge. Antimicrobial activities behavior of these classes of compounds are examined against gram (+ve) *Staphylococcus aureus, Bacillus* bacteria, gram (-ve) *Escherichia coli, Klebsella pneumonia* bacteria and against *Aspergillus flavs, Peneicllium* fungi, in comparison with common pharmacological antibiotics Cephalexin, Amoxicillin, Tetracycline, Lincomycin and pharmacological antifungal agent Nystatin and Fluconazole.

In general most of the synthesized types of compounds are found to have a broad extended effect as antimicrobial effect against gram(+ve) *Staphylococcus aureus, Bacillus* bacteria, gram(-ve) *Escherichia coli, Klebsella pneumonia* bacteria and against *Aspergillus flavs, Peneicllium* fungi, as in following details:

First: Compounds, types azobenzen-p,p'-di[3-substituted-4(3H)quinazolinone-2-yl] [V(a, b, h, i), VIIA, VIIIB], azobenzen-p,p'-di[4-substituted-quinazolin-2-yl] [IXA, IXB], and azobenzen-p,p´-di[3-substituted-4(3H)quinazolinthione-2-yl] [X(A, P, I, K), XI'], have very broadening antibacterial effect on gram(+ve) *Bacillus* bacteria in comparison with effect of Cephalexin, Amoxicillin and Tetracycline antibiotics.

Second: Compounds, types azobenzen-p,p'-di[3,1-benzoaxazin-4-one] [IV] , azobenzen-p,p'-di[3-substituted-4(3H)quinazolinone-2-yl] [V(a, b, c, d)], and azobenzen-p,p'-di[3-hydro-4(3H)quinazolin-thione-2-yl] [XI], have a broadening antibacterial effect on gram (+ve) *Staphylococcus aures* bacteria, in comparison with effect of Cephalexin, Amoxicillin, and Tetracycline antibiotics.

Third: Compounds, types azobenzen-p,p'-di[3-substituted-4(3H)quinazolinone-2-yl] [VIA, VIB], have a broadening antibacterial effect

on *Escherichia coli* bacteria, in comparison with the effect of Tetracycline and Lincomycin antibiotics.

Fourth: Compounds, types azobenzen-p,p'-di[3-substituted-4(3H)quinazolinone-2-yl] [V(a, d, h, i)], azobenzen-p,p'-di[4-substituted-(3H)-quinazolin-2-yl] [IXB], and azobenzen-p,p'-di[3-substituted-4(3H)quinazolin-thione-2-yl] [XI, X(P, I)], have good antibacterial effect, on gram (-ve) *Klebsilla pneumonia* bacteria, in comparison with effect of Tetracycline antibiotics.

Fifth: Compounds, types azobenzen-p,p'-di[3,1-benzoxazin-4-one-2-yl] [IV], azobenzen-p,p'-di[3-substituted-(3H)quinazolinone-2-yl] [V(a, d, i, l, n, o, p), VIII], azobenzen- p, p'-di[4- substituted- quinazolin-2-yl] [IX, IXA, IXB], and azobenzen-p,p'-di[3-substituted-4(3H)quinazolin-thione-2-yl] [X(A, B, C, D, F, G, J, K, L)], have a moderate to excellent antifungal effect on *Aspergillus* fungi in comparison with the effect of Nystatin and Fluconazole antifungal treatments.

Sixth: Compounds, types azobenzen-p,p'-di[3-subsitituted-4(3H)quinazolinone-2-yl] [V(c, d, h, i), VIII], azobenzen-p,p'-di[4-substituted-quinazolin-2-yl] [IX], and azobenzen-p,p'-di[3-substituted-4(3H)quinazolin-thione-2-yl] [X(G, J, K, L)], have moderate to excellent antifungal effect on *penecillium* fungi in comparison with the effect of Nystatin and Fluconazole antifungal treatments.

Seventh: Compounds, types azobenzen-p,p'-dicarboxylic acid [I], azobenzen-p,p'-diacid chloride [II], and azobenzen-p,p'-[(dibenzoic acid-2-yl)-dicarbxamide] [III], have moderate to excellent effect gram (+ve), gram (–ve) antimicrobial result against *Staphylococcus aureus, Bacillus, Escherichia coli, Kelebsiella pneumonia* bacteria respectively, in comparison with the effect of Cephalexin, Amoxicillin, Tetracyclin and Lincomycin antibiotics. Also good effect on *Aspergillus flavs* and *Penecillium* fungi, in comparison with the effect of Fluconazole antifungal treatments.

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List of Abbreviations

Et_3N	Triethyl amine
Ac_2O	Acetic anhydride
Boc	T-Butyl oxy carbonyl
Mwt	Molecular weight
KBr	Potassium Bromide
Ph-	Benzene
Me	Methyl
mL	Milllileter
˚C	Degree Celsius
R.T	Room temperature
Conc.	Concentrated
gm	Gram
%	Percentage
Fig	Figure
No.	Number
Al.	Aliphatic
Ar.	Aromatic
DMF	N,N-Dimethyl formamide
DMSO	Dimethyl sulfoxide
m.p	Melting point
TLC	Thin layer chromatography
FT-IR	Fourier transform infrared
^{1}H-NMR	Proton nuclear magnetic resonans
^{13}C-NMR	Carbon nuclear magnetic resonans

m/z	Mass-to-charge ratio
$\bar{\upsilon}$	Wavenumber = frequency
δ	Chemical shift (in ppm)
σ	Sigma
AMPA	Amino-3-hydroxy-5-methyl-4-isoxazole propionic acid
HIV	Humman immunodefciancy virus
MIC	Minimum inhibition concentration
MeOH	Methanol
EtOH	Ethanol
CEPH	Cephaxlin
AMOX	Amoxicylin
TETRA	Tetracycline
LINCO	Lincomycin
NYST	Nystatin
FLUC	Fluconazole

Chapter One

Introduction

REVIEW OF LITERATURE

1. Heterocyclic Compounds

1.1. Oxazine:

Oxazines are six member ring heterocyclic compounds containing one nitrogen and one oxygen atoms, exist in three isomeric type on the relative position of the heteroatoms and the double bonds; 1,2; 1,3; and 1,4 oxazines (Fig. 1) [1].

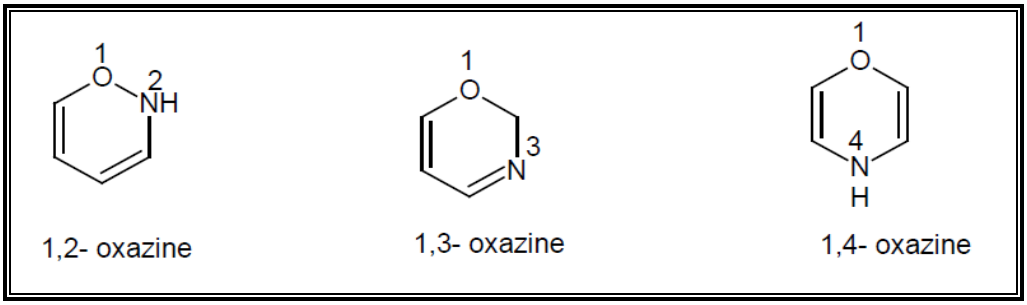


Fig. (1-1): Types of oxazines

Oxazines have been the object of interest for past three decades, due to increases of importance in pharmaceutical and biological fields[2] . Oxazine derivatives are an important class of heterocycles, which has attracted much synthetic interest due to their wide range of biological activities like sedative[3] , analgesic[4] , antipyretic[5] , anticonvulsant[6] , antitubercular[7] , antitumour[8] , antimalarial[9] and antimicrobial [10].

1.2. Benzoxazine:

Benzoxazinones are 1,3-oxazine fused with benzene ring, and the most important types of these compounds are 3,1-benzoxazin-4-one derivatives with substituents at position-2 [11-22].

1.3. Synthesis of 3,1-benzoxazin-4-ones:

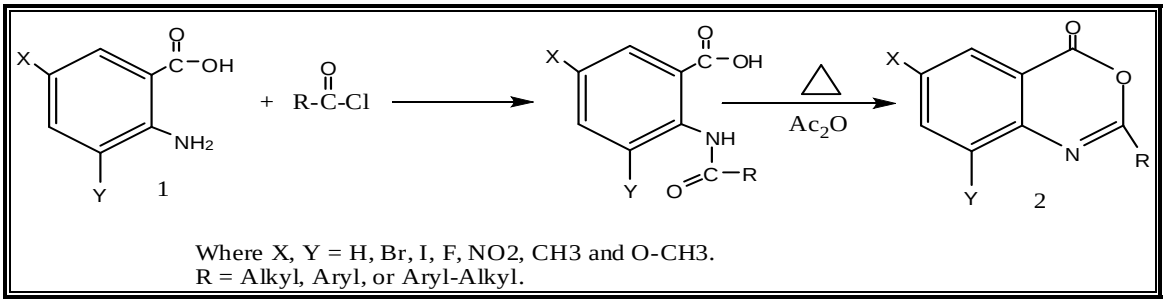
3,1-benzoxazinones are a versatile substances to synthesize many pharmaceutical fields, as following routes [14-17, 22].

1.3.1. From anthranilic acids:

Anthranlic acid or its derivatives are a convenient starting material for a versatile routes to synthesize 3,1-benzoxazinones.

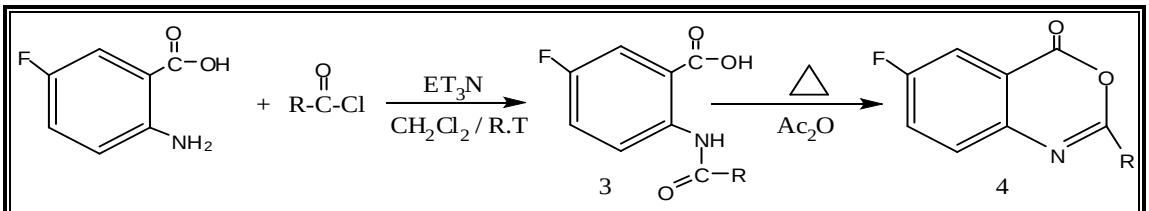
1.3.1.1. Reaction of anthranilic acid with acid chloride:

2-substituted -3,1-benzoxazinones have been obtained by heating anthranilic acid or substituted anthranilic acid with alkyl, aryl, or aryl alkyl acid chlorides[23].



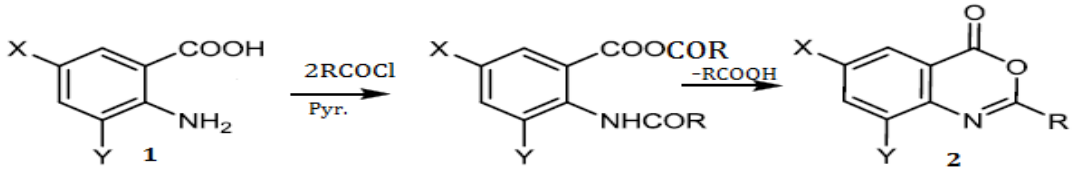
Where X, Y = H, Br, I, F, NO2, CH3 and O-CH3.
R = Alkyl, Aryl, or Aryl-Alkyl.

5-fluoroanthranilic acid reacts with acid chloride in the presence of triethylamine and methylene chloride at room temperature to afford compound (3), which on heating with acetic acid anhydride for 1-hour produces 6-fluoro-2-substituted benzoxazinones(4)[24].



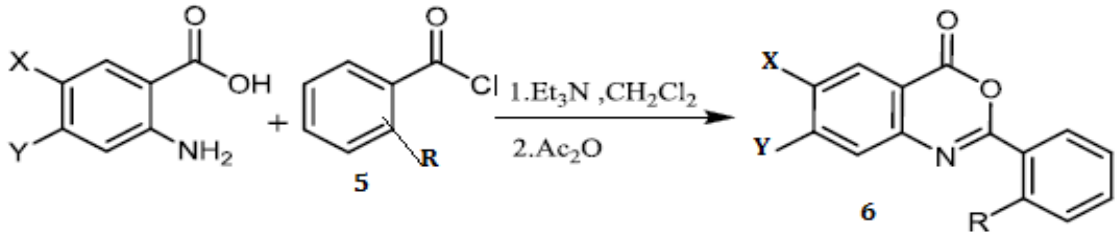
Where R = C_4H_9, C_6H_5, -CH_2CH_2Ph, $C_4H_3S.CH_2$-

Also a modification was obtained by reaction of anthranilic acid with two equivalents of acid chloride in presence of pyridine[25-27].



Where X, Y = H, Cl, Br, NO_2, CH_3, O-CH_3, F, CF_3. And R = Alkyl, Aryl, or Aryl-Alkyl.

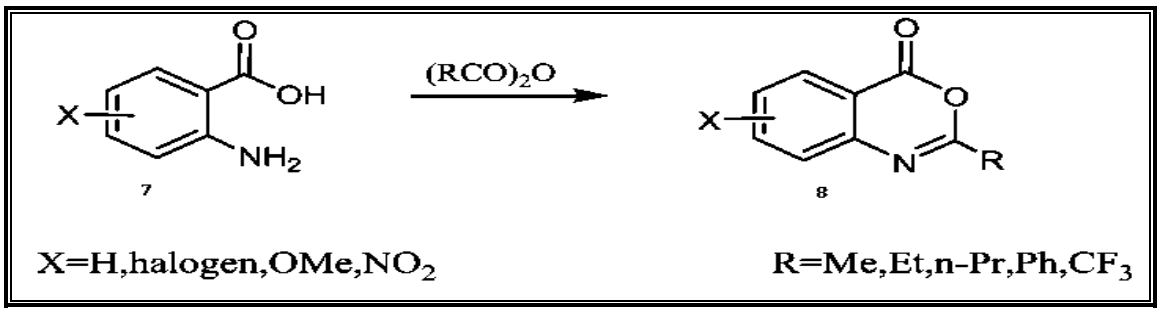
One-pot reaction of substitute anthranilic acid with to 2-substituted benzoyl chlorides (5) in presence of Et_3N and CH_2C1_2 followed by addition of acetic anhydride affords di-substituted benzoxazinones (6) [26].



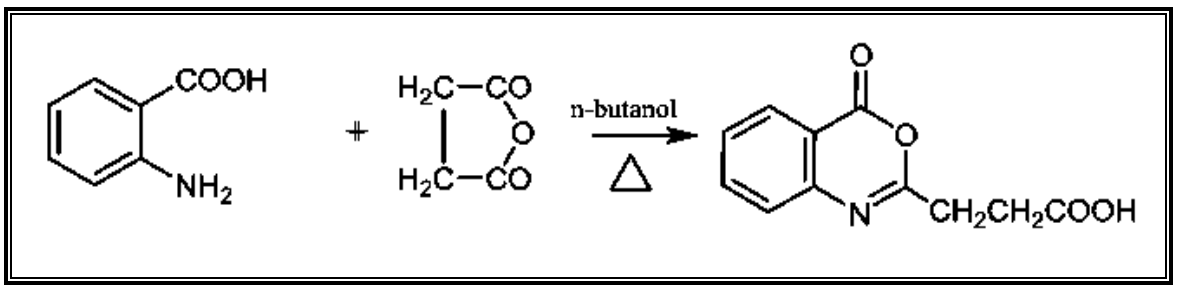
Where X, Y = H, Br, O-CH_3. And R = H, CH_3, O-CH_3, O-CF_3.

1.3.1.2. Reaction of anthranilic acid with acid anhydried:

2-substituted 3,1-benzoxazinones (8) are best prepared by heating an anthranilic acid or its derivative (7) with an appropriate lower molecular weight acid anhydrides are usually employed as the solvents [28-29].

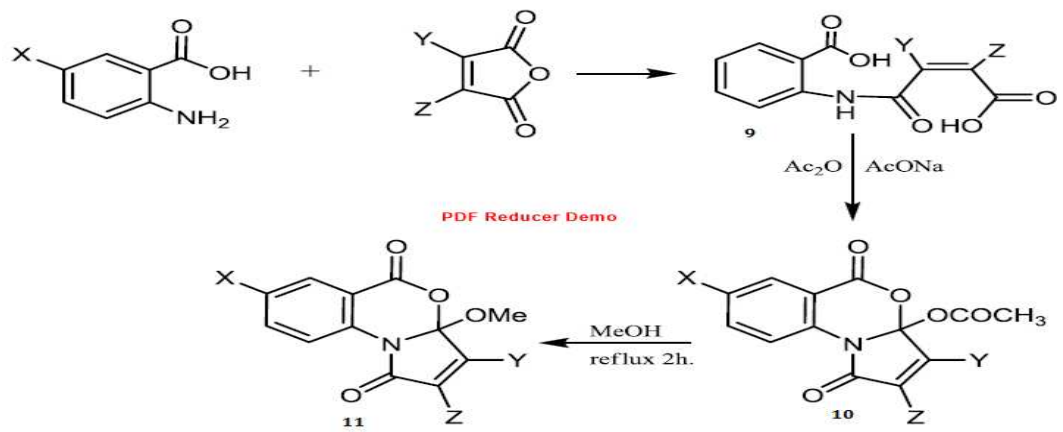


Similarly, 2-(β-carboxyethyl)-3,1-benzoxazin-4-one has been obtained by heating anthranilic acid with succinic anhydride in n-butanol [30].



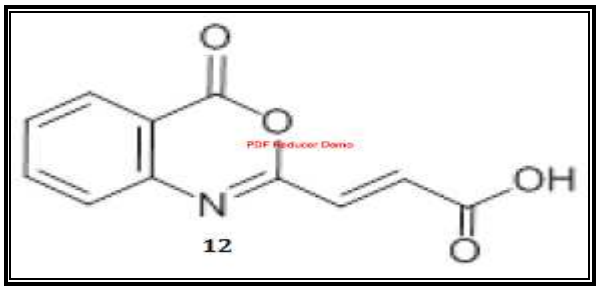
Also co-solvents as chloroform, dioxane, toluene, and orthoesters are used successfully as cyclizing agents [31]. A series of o-carboxymaleanilic acids (9)

are prepared by reacting anthranilic acid with maleic anhydride, methylmaleic anhydride, or phenylmaleic anhydride, which intermolecularly dehydrated to afford pyrolobenzoxazinones (10), which undergo solvolysis via refluxing with anhydrous methanol furnishes (11) [32].



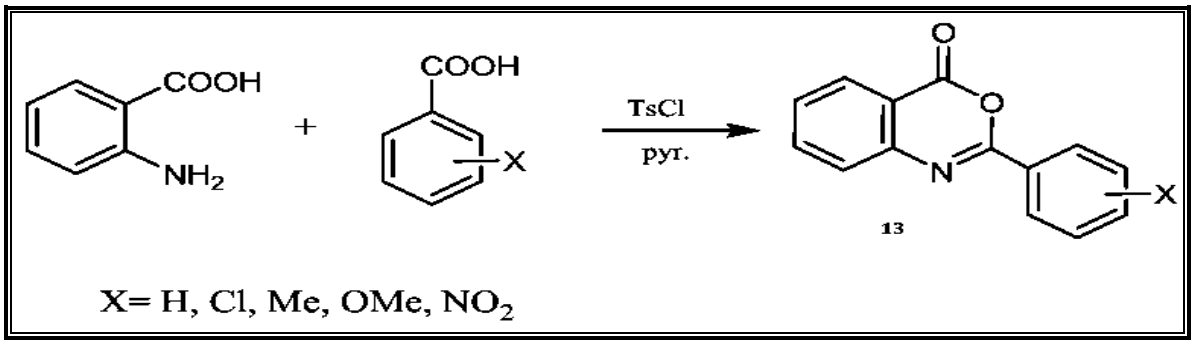
Where X= H, Cl, Br, I. And Y,Z = H, CH_3, Ph-, O-C_4H_4.

Under identical conditions,o-carboxyfumaranilic acid afforded 2-carboxyvinylbenzoxazinone which does not cyclized due to its trans-geometry (12) [33].

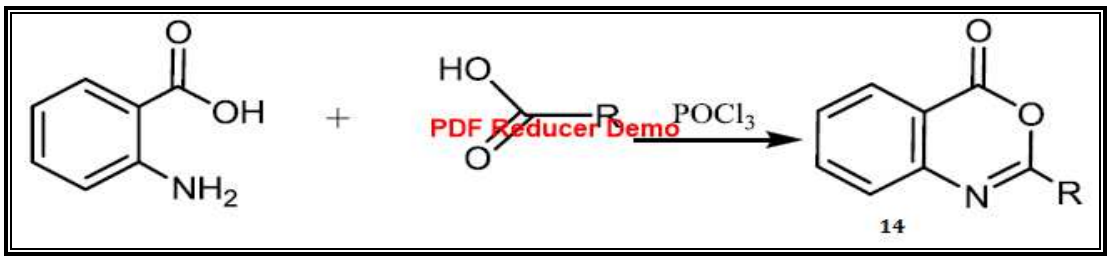


1.3.1.3. Reaction of anthranilic acid with aromatic carboxylic acid:

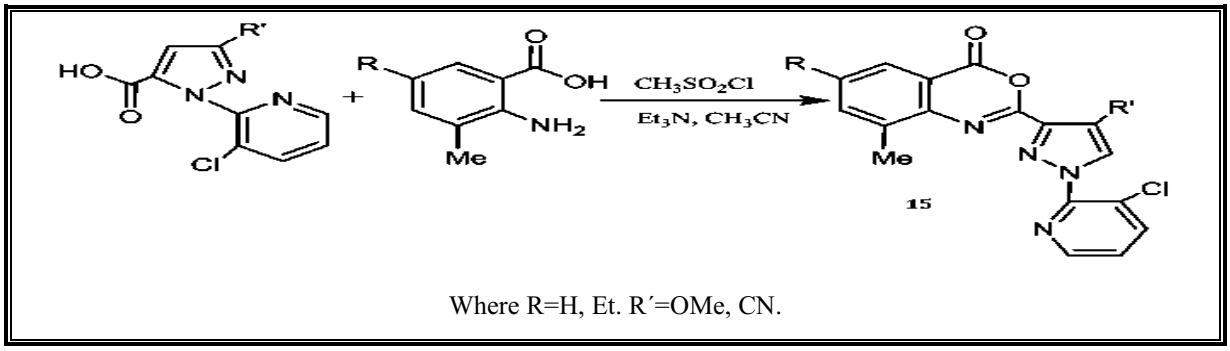
2-ortho or para substituted phenyl-3,1-benzoxazin-4-ones (13), are obtained when anthranilic acid reacts with two equivalents of ortho or para substituted benzoic acid in the presence of tosyl chloride [34].



Also anthranilic acid reacts with two equivalents of aromatic or heteroaromatic carboxylic acids in presence of phosphorous oxychloride as a chlorinating agent which furnishes the acid chloride to give compound (14) [35].



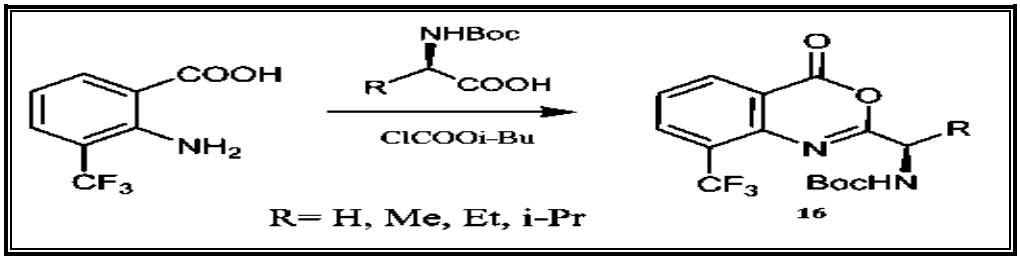
2-substituted heteroaromatic 3,1-benzoxazinone (15), are obtained upon reaction of substituted anthranilic acid with heteroaromatic carboxylic acid in acetonitril and triethylamine in presence of methanesulphonyl chloride[36-37].



1.3.1.4. Reaction of substituted anthranilic acid with Boc-protected amino acids:

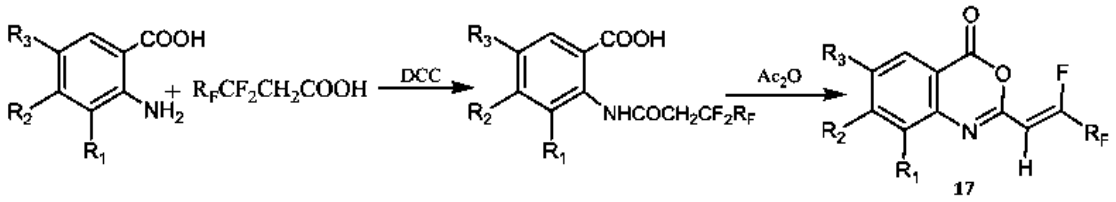
Amino benzoxazinione derivative (16), was readily prepared from the reaction of equimolar quantities of 3-trifluoromethyl anthranilic acid and Boc-

protected amino acid with two equivalents of isobutylchloroformate in the presence of N-methyl morpholine as a solvent[38].



1.3.1.5.Reaction of substituted anthranilic acid with 2,2-dihydro fluoroalkanoic acid:

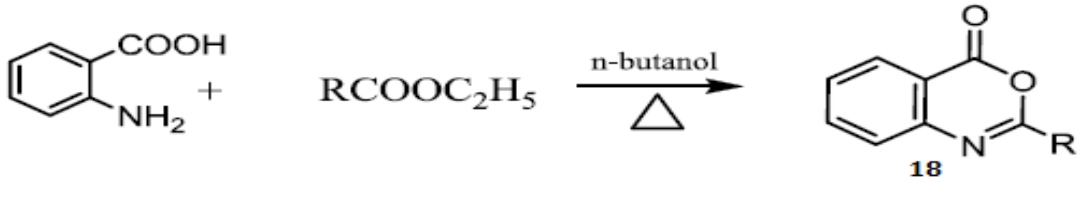
2-[(z)-1′-hydrofluoro-1′-alkenyl]-3,1-benzoxazin-4-ones (17), are obtained via condensation of 2,2-dihydropolyfluoroalkanoic acid with anthranilic acid or its derivatives in the presence of N,N′-di cyclohexyl carbodimide (DCC) in CH_2C1_2[39].



Where R_1= H, Br. R_2= H, Cl. R_3= H, OMe, Br. And R_F= C_5F_{11}, CF_2C1, CF_3, CF_2Br.

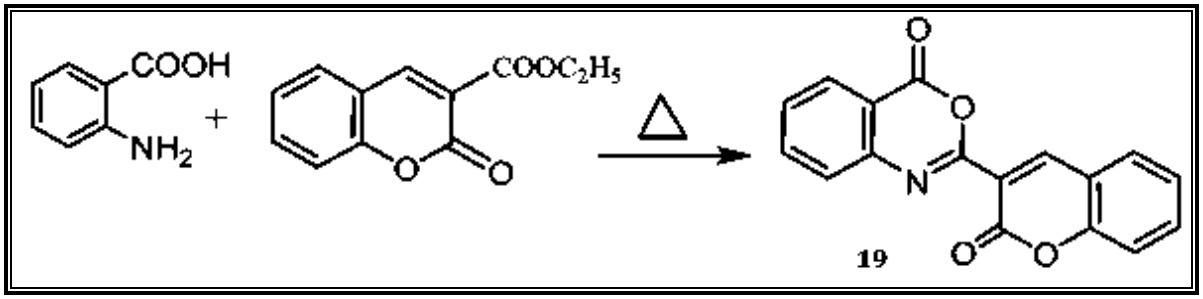
1.3.1.6. Reaction of substituted anthranilic acid with esters:

2-cyanomethyl, acetonyl and or ethoxycarbonyl-4H-3,1-benzoxazin-4-one (18) was obtained via interaction of ethylcyanoacetate, ethylacetoacetate and diethyloxalate with anthranilic acid in boiling n-butanol[40-41].

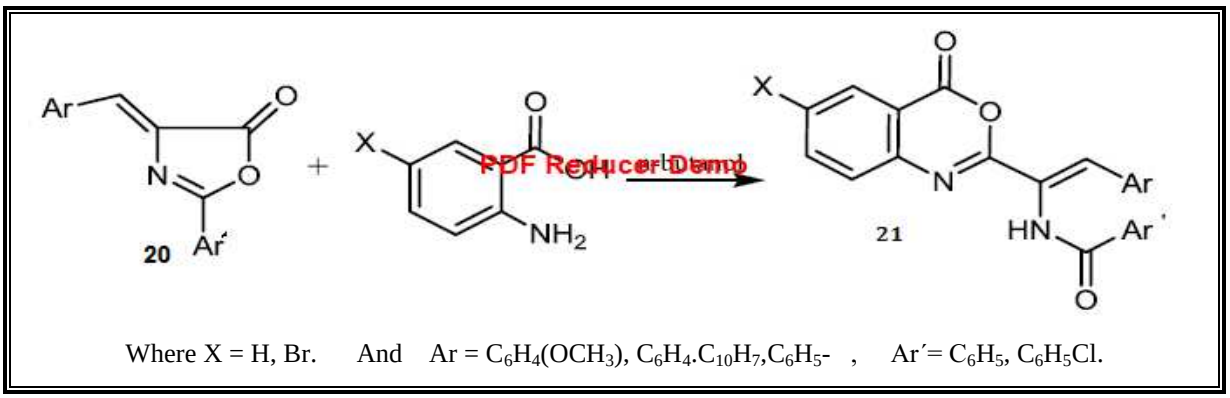


Where R = CH_2CN, $-CH_2COCH_3$, $-CO_2C_2H_5$.

3,1-Benzoxazin-4-one bearing coumarin-3-yl moiety at position-2 (19), was obtained via interaction of 3-ethoxycarbonyl coumarin with anthranilic acid by fusion at 150 °C or refluxing in n-butanol[42].

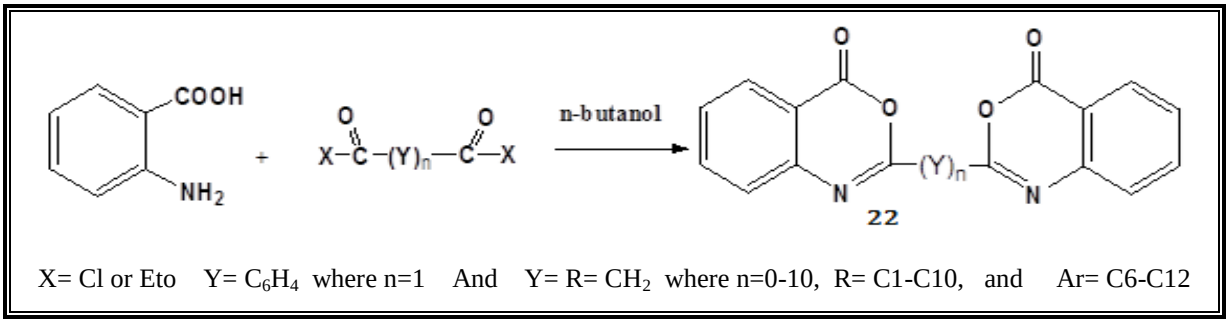


2-substituted 3,1-benzoxazin-4-ones (21), are obtained via interaction of 4-arylidene-2-aryl- oxazolin-5-one(20), with anthranilic acid in boiling n-butanol[43].



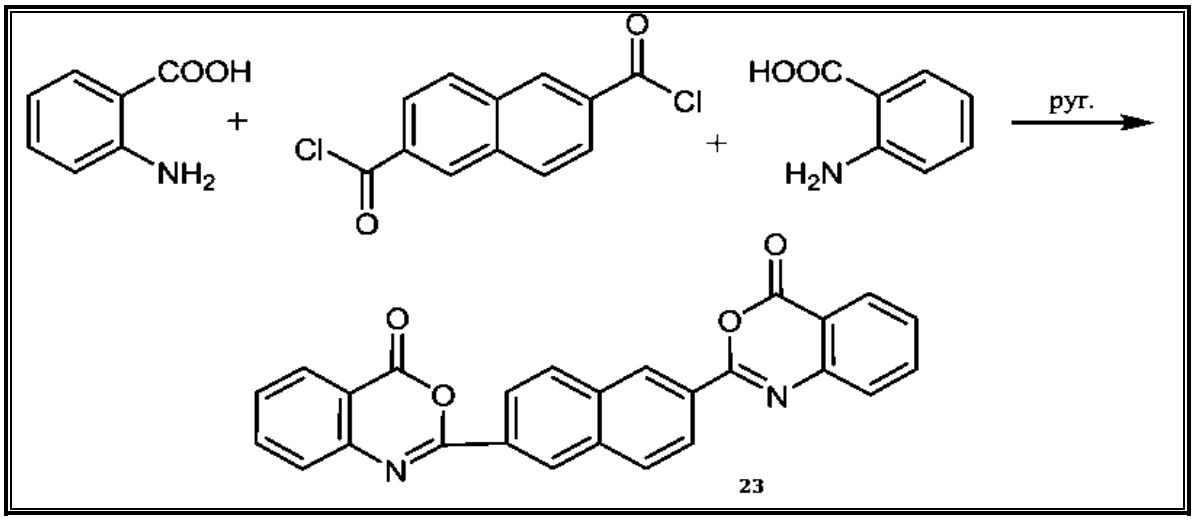
Where X = H, Br. And Ar = $C_6H_4(OCH_3)$, $C_6H_4.C_{10}H_7$,C_6H_5- , Ar′= C_6H_5, C_6H_5Cl.

Bis 3,1-benzoxazin-4-one derivatives (22), are obtained from interaction of terephthaloyl chloride or diethyloxalate with anthranilic acid in boiling n-butanol [44-45]. In case of terephthaloyl chloride which gave p-phenylen-bis-2,2′[3,1-benzoxazin-4-one] (22), and used as light stabilizer for polyester fibers [46].



X= Cl or Eto Y= C_6H_4 where n=1 And Y= R= CH_2 where n=0-10, R= C1-C10, and Ar= C6-C12

A bis benzoxazine (23), as a UV absorbent, has been obtained via interaction of 2,6-naphthalene dicarboxylic acid chloride with anthranilic acid in pyridine [47]. It is resistant to water, not readily soluble in organic solvents, fats, oils, and nonirritating to the skin. It prevents skin rash and acts as skin conditioner.



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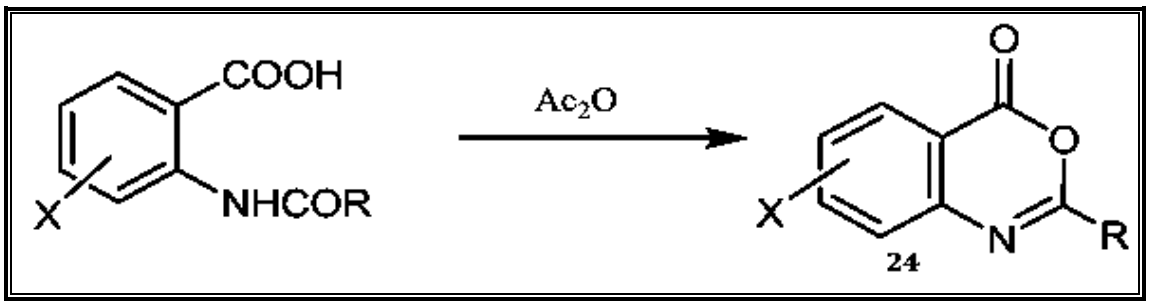
1.3.2. From N-acylanthranilic acid:

2-subsititued 1,3-benzoxazin-4-one were synthesized by cyclodehydration of N-acylanthranilic acid with various cyclizing agents.

1.3.2.1. Acetic anhydride as cyclizing agent:

Acetic anhydride is the most widely used reagent for cyclodehydration can accommodate a wide variety of acyl groups (R = alkyl, substituted phenyl, CH_2Cl,$CH(CH_3)Cl$, styryl , trifluoromethyl, phthalimidomethyl , COOEt , 2-thienylpyridyl or thiadiazole), and X = electron with drawing and donating group)(24) [48].



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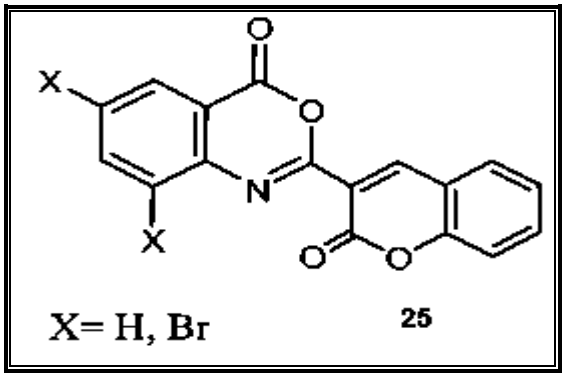
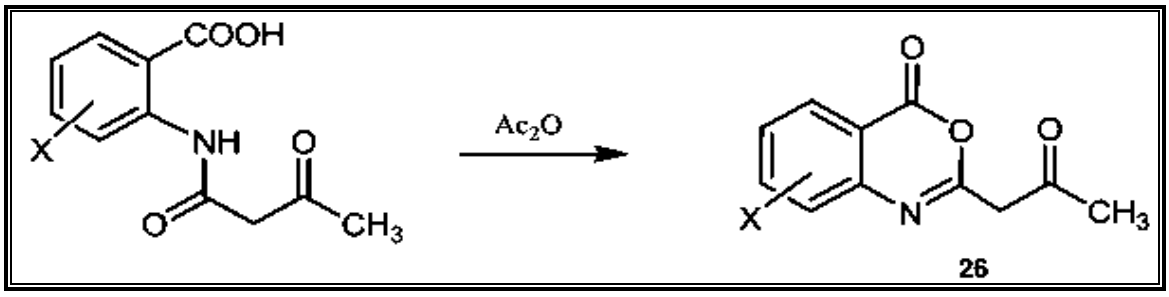
More complex heterocyclic systems such as a coumarin can be introduced into the position-2 of the benzoxazinone affording (25)[49].

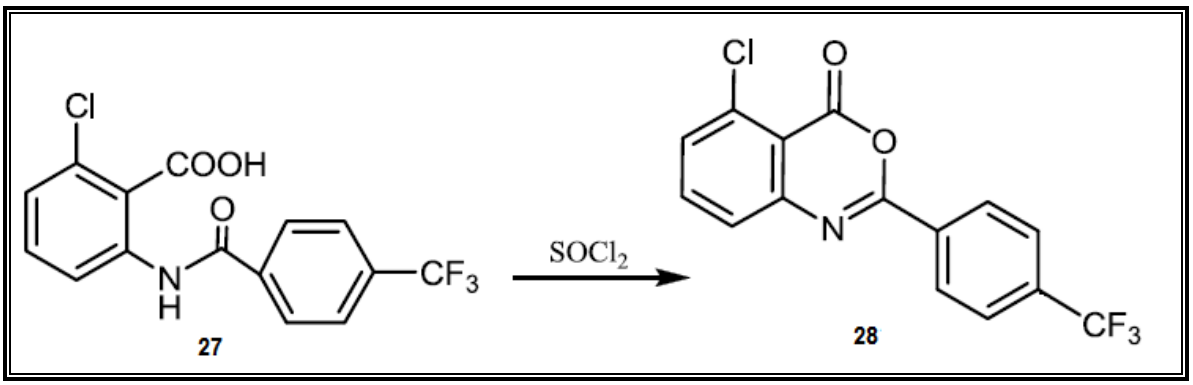


Anthranilic acid can also be acylated under nitrogen with either diketene [45] or 2,2,6-trimethyl-4H-1,3-dioxin-4-one (ketene acetone adduct) to give (26), which when exposed to acetic anhydride cyclized to the 2-acetonyl derivative[50-51].



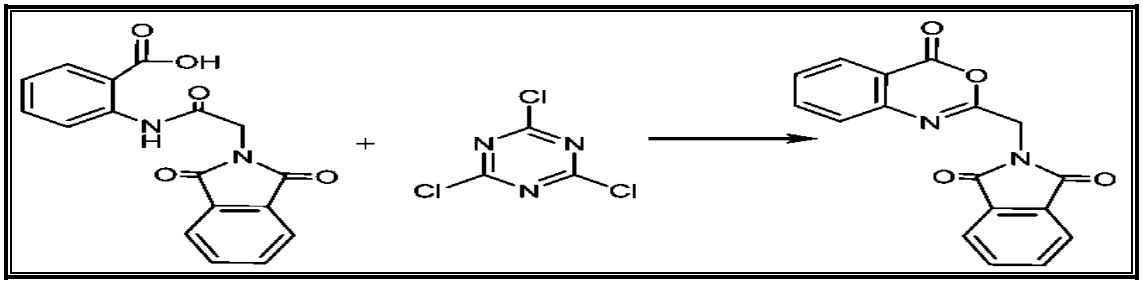
1.3.2.2. N-acyl or N-benzoyl anthranilic acid:

Refluxing a solution of substituted N-acylanthranilic acid (27), with a small excess of thionyl chloride in 1,2-dichloroethane produces the benzoxazin-4-one derivative (28) [52].



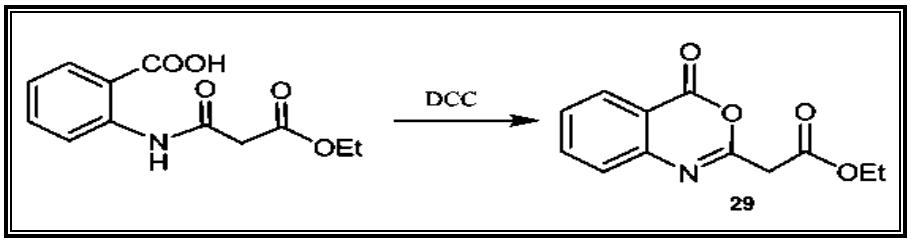
1.3.2.3. Cyanuric chloride as cyclizing agent:

2-(N-phthaloylmethyl)-3,1-benzoxazin-4-one, are prepared via reaction of the acyl chloride derivative (N-phthaloyl glycine) with anthranilic acid in chloroform and N-phthaloyl anthranilic acid is generated. It reacted with cyanuric chloride to form the final product [53].

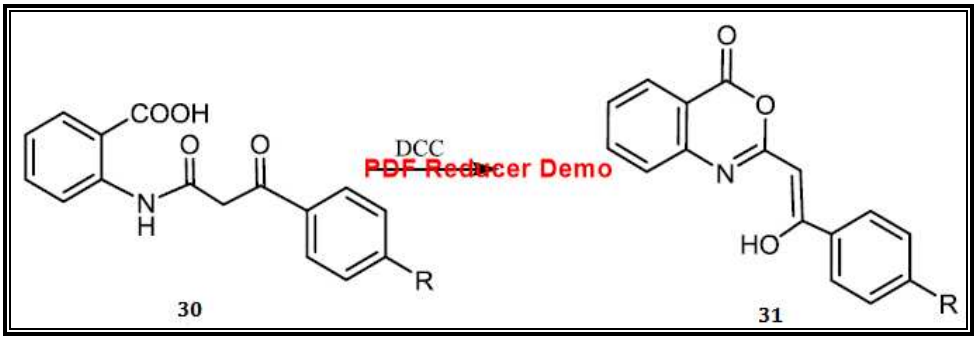


1.3.2.4. Dicyclohexylcarbodiimide as cyclizing agent:

N,N'-dicyclohexylcarbodiimide (DCC), is used for cyclodehydration of N-acyl anthranilic acid to obtain 2-ethoxy-3,1-benzoxazin-4-one (29). Where, N-acyl anthranilic acid was obtained via reaction of anthranilic acid with diethyl malonate[54].

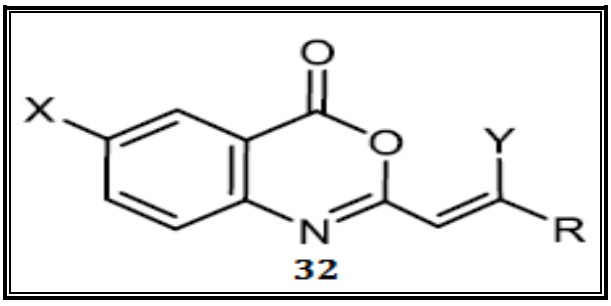


Dehydration of N-acylanthranilic acid (30), to benzoxazinone (31), using DCC is achieved in higher yield and shorter reaction time (R=H, Br, Me), as compared to the conversion with acetic anhydride as dehydrating agent [55].



1.3.2.5. From 2-methyl-3,1-benzoxazin-4-one:

2-styryl or substituted styryl-3,1-benzoxazin-4-ones (32), have been obtained, via interaction of 2-methyl-3,1-benzoxazin-4-one with aromatic aldehydes and or ketones in the presence of anhydrous zinc chloride at 170 °C [56-57].



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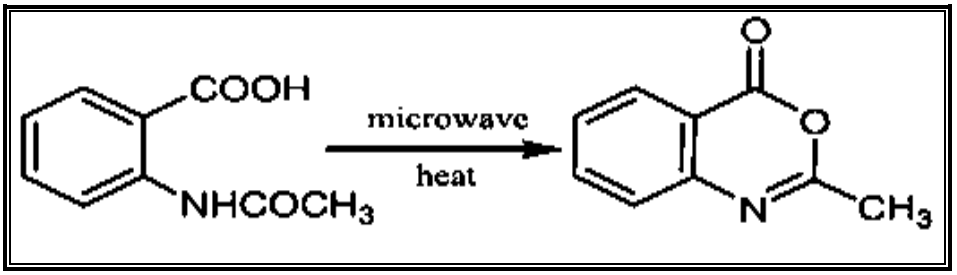
1.3.2.6. From heating of N-acetylanthranilic acid by microwave:

2-methyl-3,1-benzoxazinone, was obtained via heating of N-acetyl anthranilic acid under microwave conditions [58].

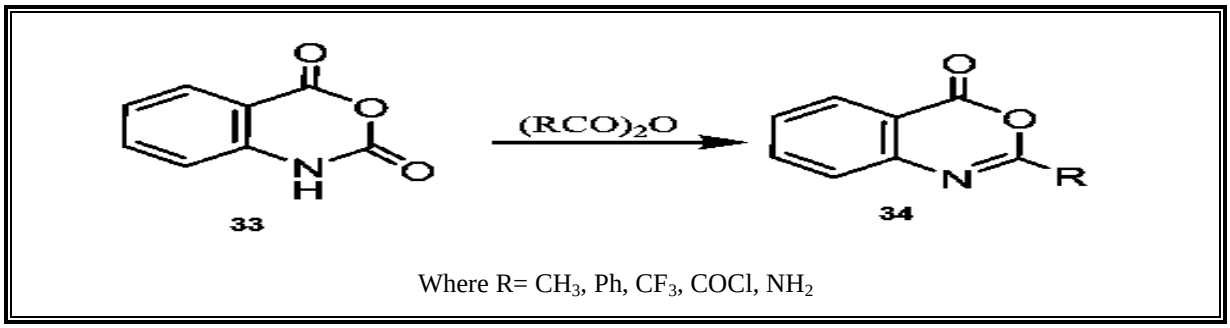


1.3.3. From isatoic anhydrides:

Isatoic anhydride is versatile molecule in heterocyclic syntheses, so that 3,1-benzoxazin-4-one heterocycle can be obtained from the closely related 3,1-benzoxazin-2,4-dione (33) system.

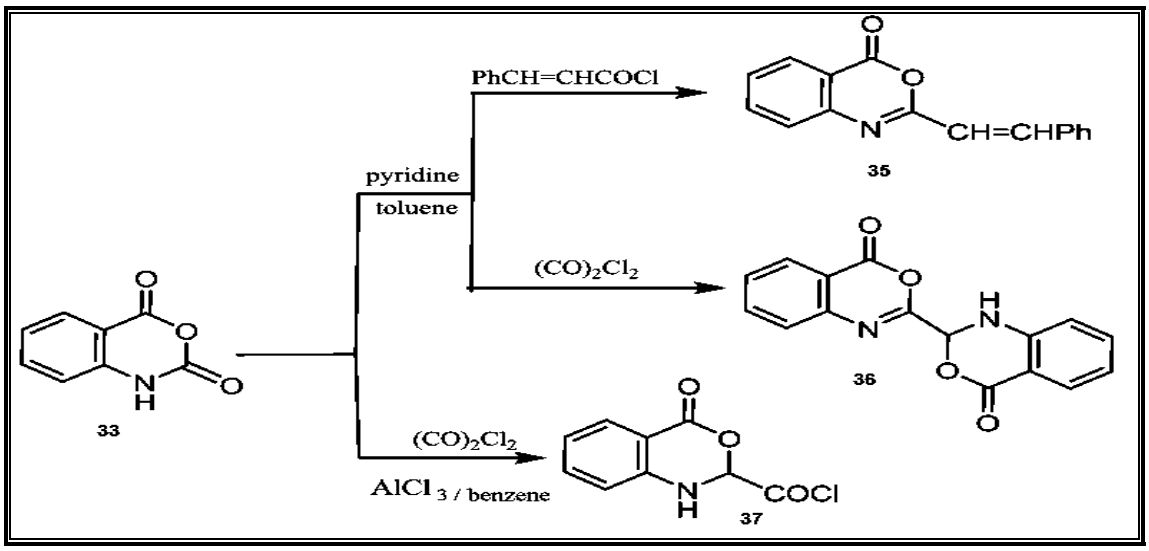
1.3.3.1. Reaction of isatoic anhydride with acid anhydrides:

When isatoic anhydride is refluxed in acetic anhydride [59], acetic anhydride / pyridine or stirred with trifluoro acetic anhydride / pyridine at room temperature [60], the corresponding benzoxazinone (34) is isolated in high yield.

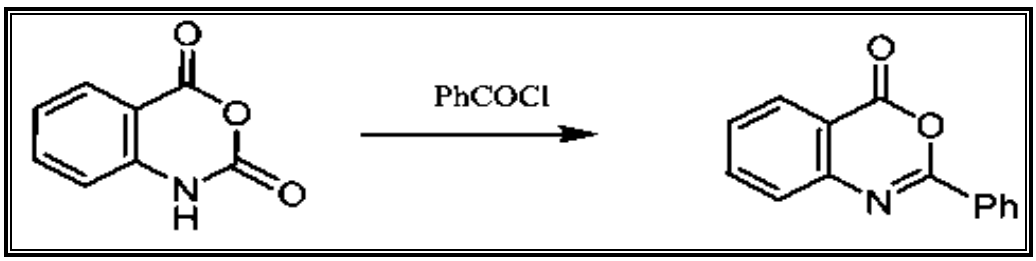


1.3.3.2. Reaction of isatoic anhydride with acid chlorides:

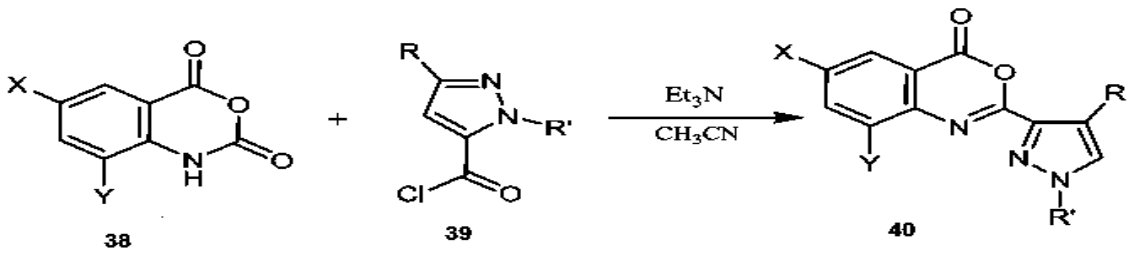
Heating a mixture of isatoic anhydride (33), and either cinnamoyl chloride or oxalyl chloride in pyridine/toluene solvent produces the 2-styryl analog (35) or the bis-3,1-benzoxazin-4-one (36) [61]. If the reaction with oxalyl chloride carried out in benzene using anhydrous aluminum chloride, 2-chloroformyl derivative (37) is isolated [62].



Isatoic anhydride also reacts with acid chlorides at elevated temperature to give 3,1-bezoxazin-4-one. Thus, heating compound (33) and benzoyl chloride give 2- phenylbenzoxazinone [63].



Coupling of trifluoromethyl-substituted isatoic anhydride (38), with pyrazoly acid chlorides (39) affords benzoxazinones (40) in modest yield [64].

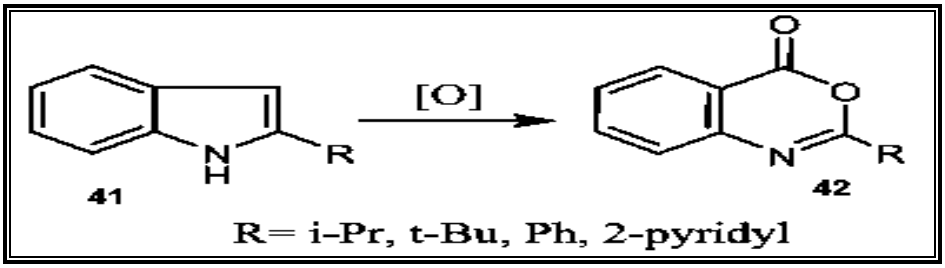


Where X= CF_3, H. Y = CH_3, H. R = OCH_3, CF_3, Cl, OCF_2H.

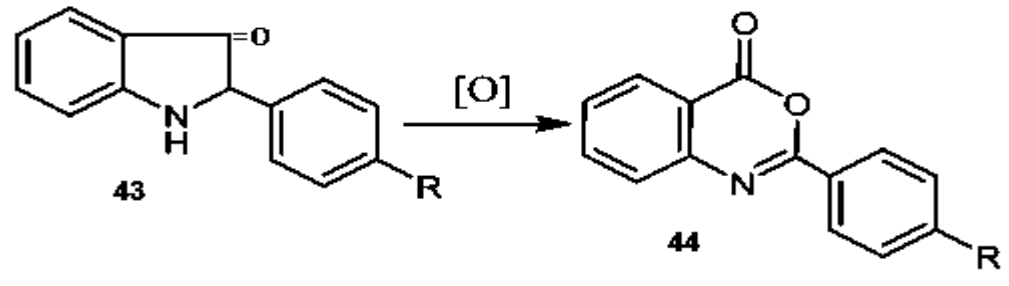
R´= C_5H_3Cl, C_6H_5

1.3.4. Oxidation of Indoles:

2-substituted indoles (41), were readily oxidized with m-chloro peroxy benzoic acid or p-chloro peroxy benzoic acid [65-66] and the corresponding benzoxazinone (42) are produced.



Oxidation of 2-phenylindolen-3-one (43), with m-chloroperoxybenzoic acid in chloroform affords 2-phenyl benzoaxzin-4-one (44). Whereas oxidation of 4-dimethylamino phenyl analog with hydrogen peroxide in N,N-dimethylformamide furnishes 2-(p-N,Ndimethylamino)phenylbenzoaxzin-4-one [67].

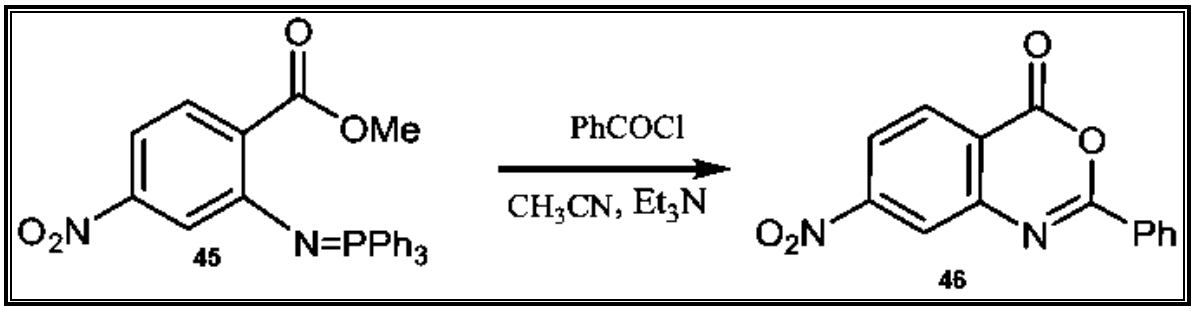


Where R= H, NMe_2

1.3.5. Miscellaneous:

1.3.5.1.From iminophosphorane:

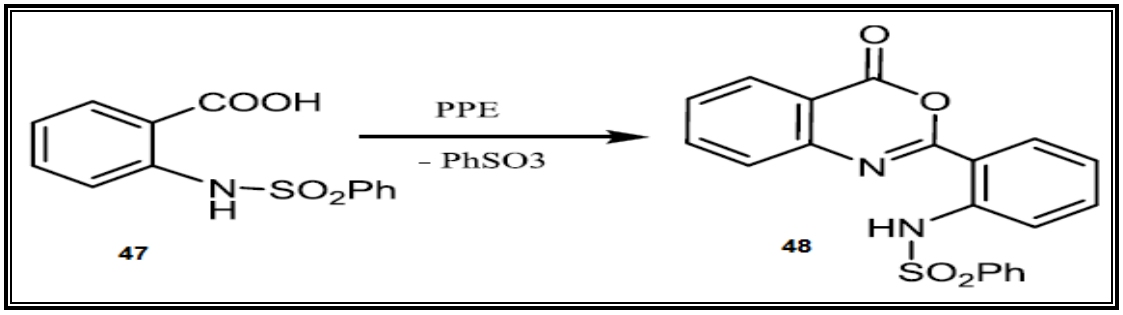
Similarly, treatment of iminophosphorane (45), with benzoyl chloride in acetonitrile in the presence of amount of triethyl amine yielded 7-nitro-2-phenyl-3,1-benzoxazin-4-one(46) [68].



This reaction is used for the production of hetroannulated 3,1-benzoxazin-4-ones, where the benzene ring is replaced with thiophene, thiazole, and pyridazine [68].

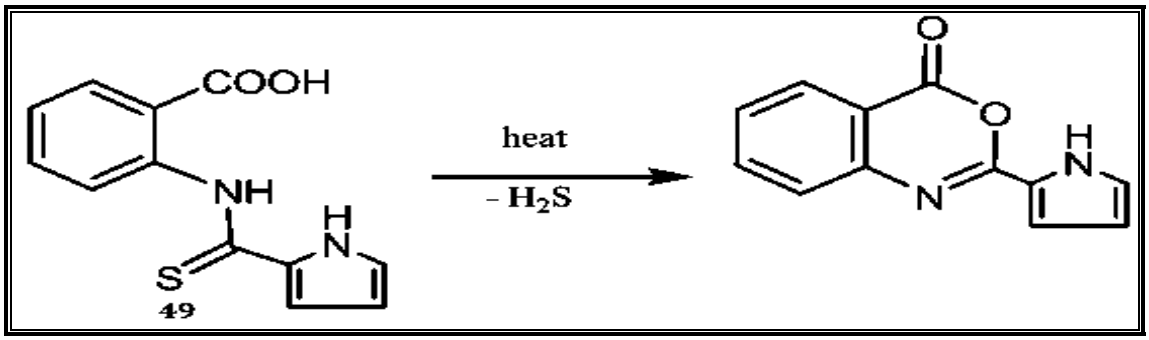
1.3.5.2. From N-benzenesulphonylanthranilic acid:

The self-condensation of 2-molecules of N-benzenesulphonyl anthranilic acid (47), in polyphosphate ester (PPE), results in the formation of 2-(p-benzensulphon amido)phenyl-3,1-benzoxazin-4-one(48) [69].



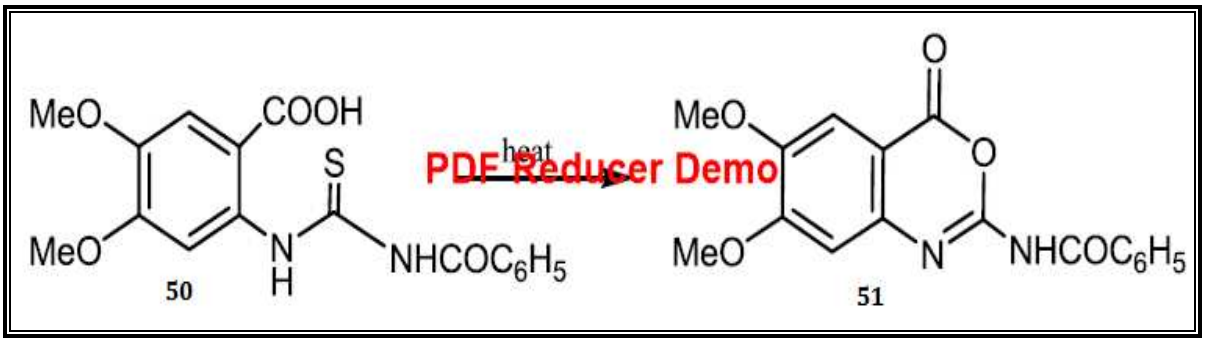
1.3.5.3. From thioamide derivatives:

Heating thioamide derivative (49), in refluxing t-butylbenzene causes cyclization to occur with loss of hydrogen sulphide and produces 2-pyrrolyl-3,1-benzoxazin-4-one [70].



1.3.5.4. Thermolysis of 2-(3-benzoylthioureido)-4,5-dimethoxy benzoic acid:

2-benzoylamino-6,7-dimethoxy-3,1-benzoxazin-4-one (51), is prepared by thermal treatment of benzoic acid derivative (50) [71].

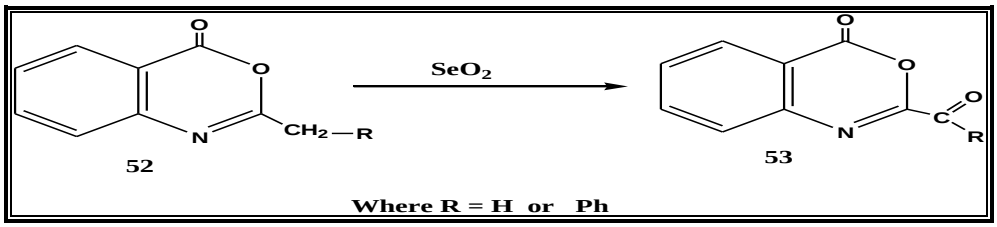


1.4. Reactions of 3,1-benzoxazin-4-ones:

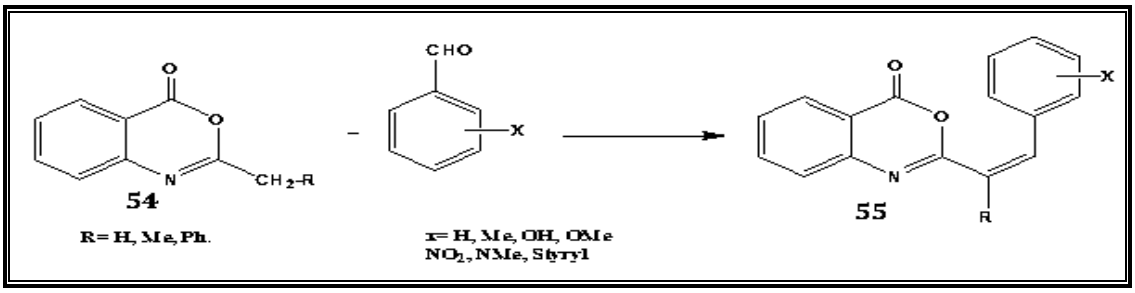
Electrophilic reactions on the benzene ring of the benzoxazinone nucleus are rare and are probably unnecessary due to the plethora of diversely substituted anthranilic acids which are available. We will concern on the remaining reactive sites and feature the reactions at the C-4 and C-2 carbons of our heterocyclic, as well as the substituent attached to position-2 [14].

1.4.1. Reactions at the 2-substituent:

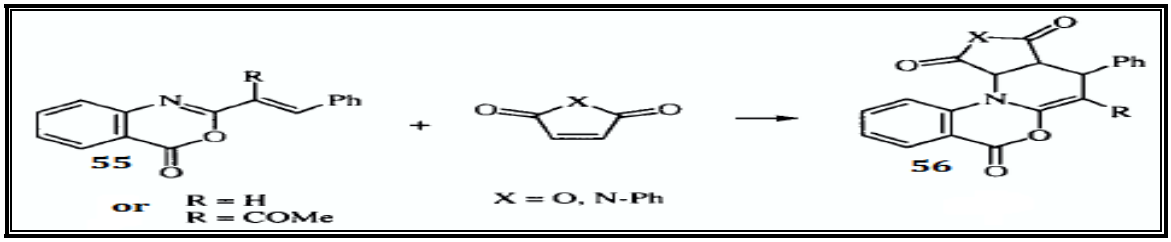
Alkyl substituent at postion-2 of 3,1-benzaxazin-4-one (52), are oxidized at methylene adjacent to heterocyclic ring. Oxidant of methyl or benzyl substituent with selenium dioxide in ethanol or acetic anhydride gives 2-carboxaldehyde or 2-benzoyl derivative (53) [14,71].



2-alkyl-3,1-benzoaxzin-4-ones (54), are readily condensed with aromatic aldehydes to give 2-styryl-3,1-benzoaxzin-4-ones(55) [14].

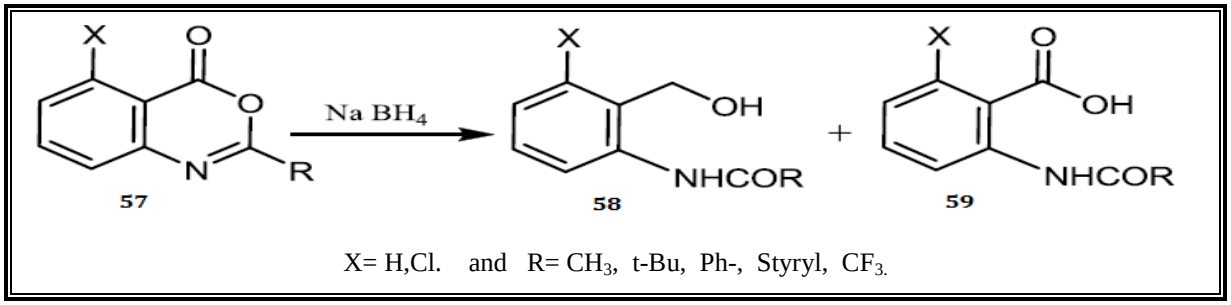


2-styryl-3,1-benzoaxzin-4-ones (55), behave as dienes in Diels-Alder reaction, upon heating with either maleic anhydride or N-phenylmaleimid in refluxing xylene, afforded the [4+2] adducts (56) [14].

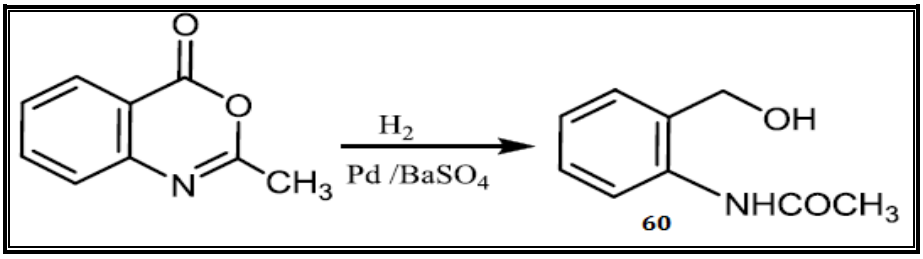


1.4.2. Reactions with hydrogen nucleophiles:

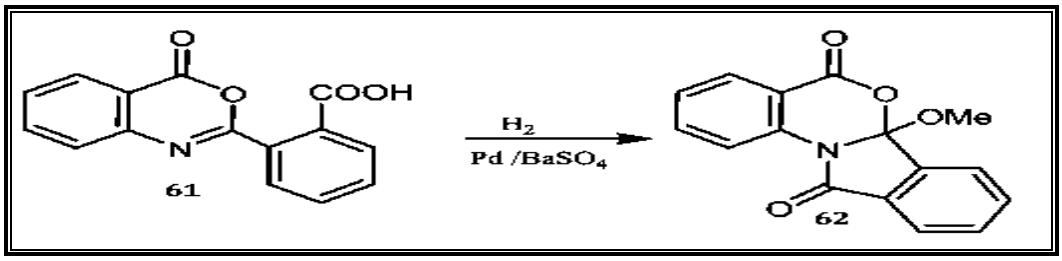
Hydride reagents such as sodium borohydreid, attack benzoaxzine nucleus (57), to give mixture of 2-acylaminobenzyl alcohols (58), and N-alkylanthranilic acid (59) [73].



While, catalytic hydrogenation of 2-methyl-3,1-benzoxazin-4-one, in acetic acid affords only N-acetyl aminobenzyl alcohol (60) [74].

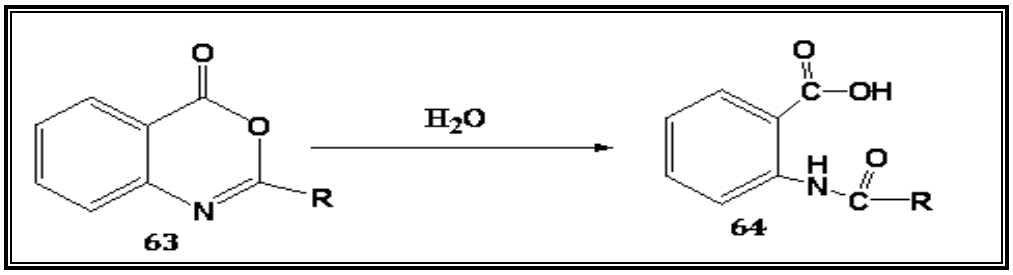


Similary, hydrogenation of benzoxazinone (61), under neutral conditions resulted in the initial reduction of C=N bond then cyclization with o-carboxylic acid group and furnished the tetracycle (62) [75].

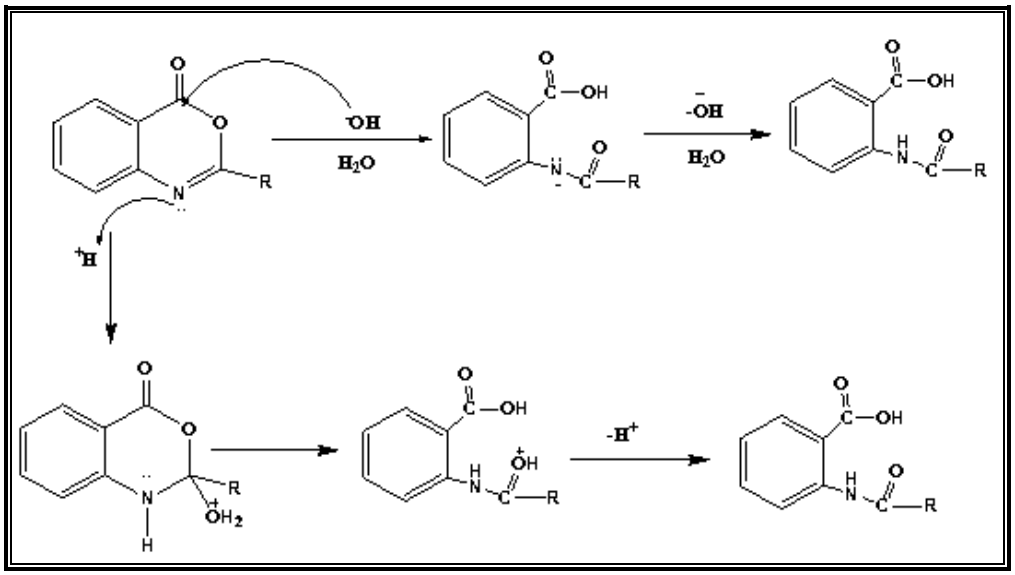


1.4.3. Reactions with oxygen nucleophiles:

Some 2-substituted 3,1-benzoaxzin-4-one (63), with substituent like R = (H, CH_3, Et, n-pr, Ph, CF_3), is sensitive to moisture and extremely hydroscopic [14]. But 2-alkylsubstituted are more sensitive to hydrolysis than 2-arylsubstituted (64).



2-methyl substituent is hydrolyzed under either acidic or basic condition, under basic condition, nucleophilic attack (C4) carbon, whereas under acidic condition protonation of (N1) activated (C2) carbon to attack [76].



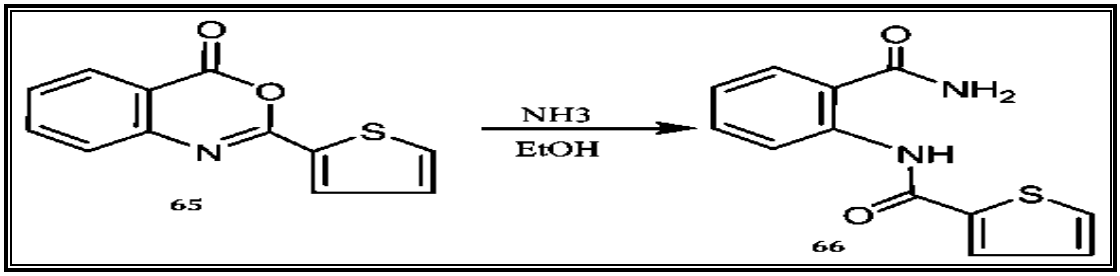
Scheme (1-1): Mechanism of hydrolysis reaction of benzoxazine.

1.4.4. Reactions with nitrogen nucleophiles:

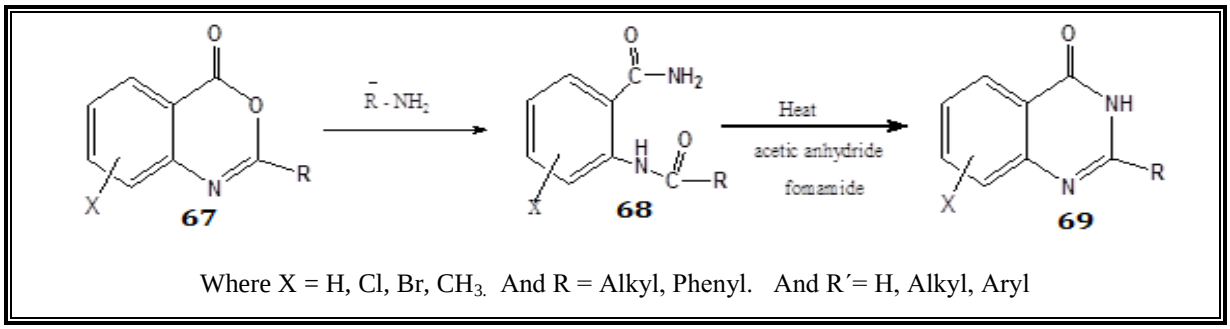
Reaction of 3,1-benzoxazin-4-ones with amines is the most interesting because of the wide range of heterocycles that can be produced either directly or through further transformations of the initially formed products[14].

1.4.4.1. Reaction with ammonia:

The interaction of 3,1-benzoxazin-4-one derivative (65), with ammonia in ethanol produces compound (66) [77].

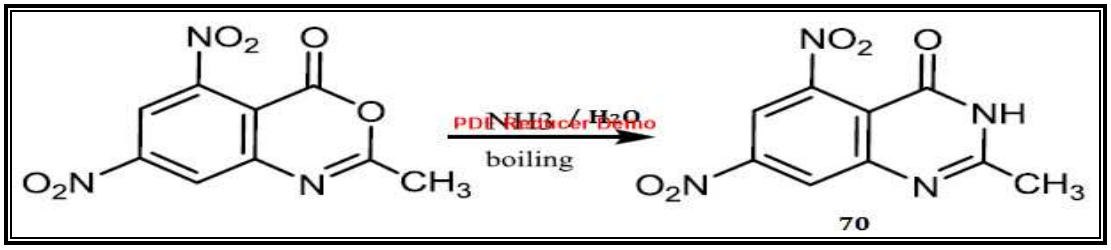


2-substituted-3,1-benzoaxzin-4-one derivatives (67), react with ammonia in ethanol to give anthranilamide (68) in a good yield. It can be cyclized under thermal (240-280℃) or with acetic anhydride or by heating with formamide, to 3-unsubstituted-4-quinazoline (69) [78].

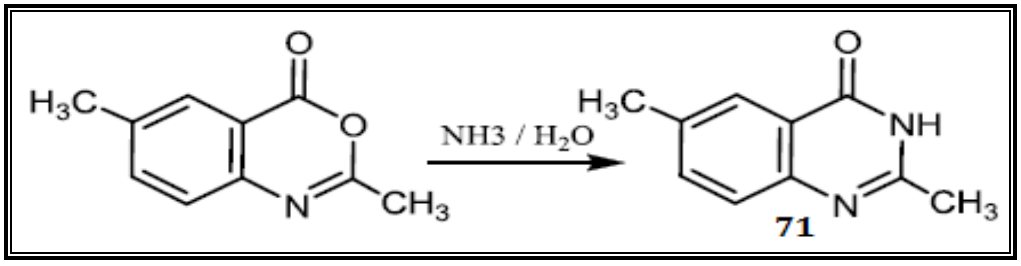


Where X = H, Cl, Br, CH_3. And R = Alkyl, Phenyl. And R´= H, Alkyl, Aryl

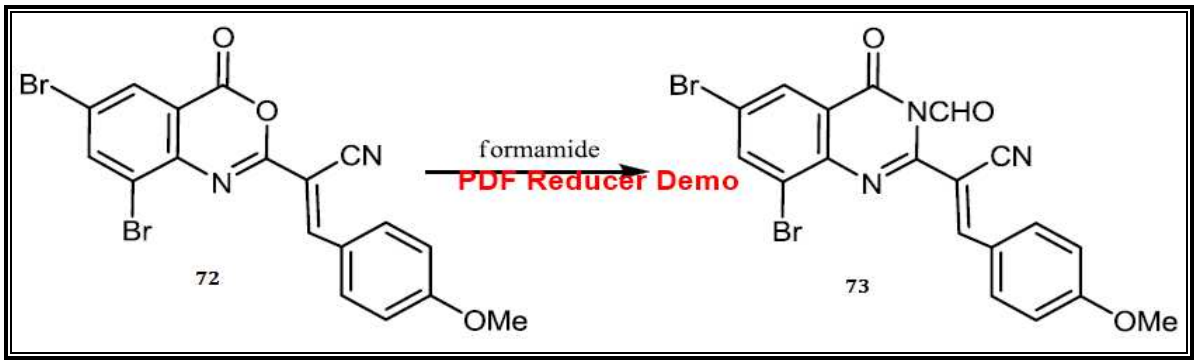
Boiling 5,7-dinitro-2-methyl-3,1-benzoxazin-4-one, with aqueous ammonia; suffered recyclization into the corresponding quinazolone derivative (70) [79].



2,6-Dimethyl-4(3H)-quinazolinone (71) is produced via interaction of 2,6-dimethyl-benzoaxinone, with 25% aqueous ammonia in ethanol at room temperature for 48 hours [80].

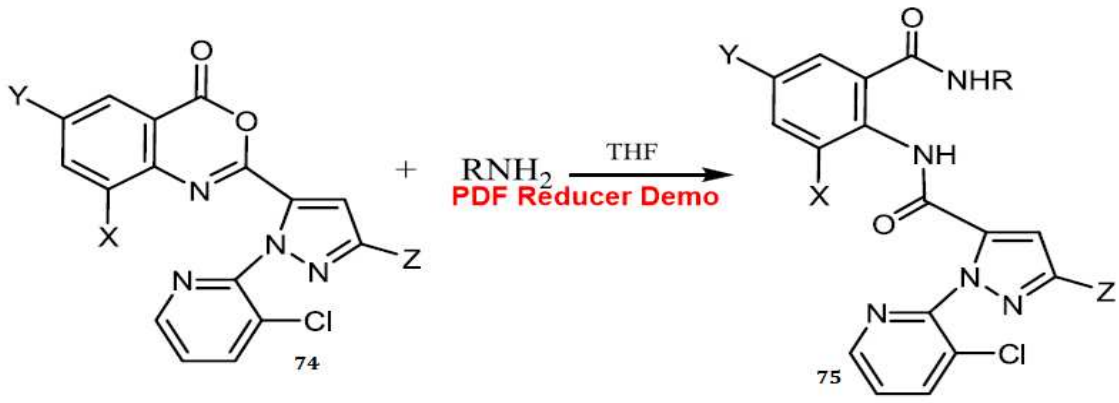


In contrast, 3,1-benzoxazin-4-one derivative (72), is formylated on treatment with excess of formamide to give N-formyl-quinazolinone derivative (73) [81].



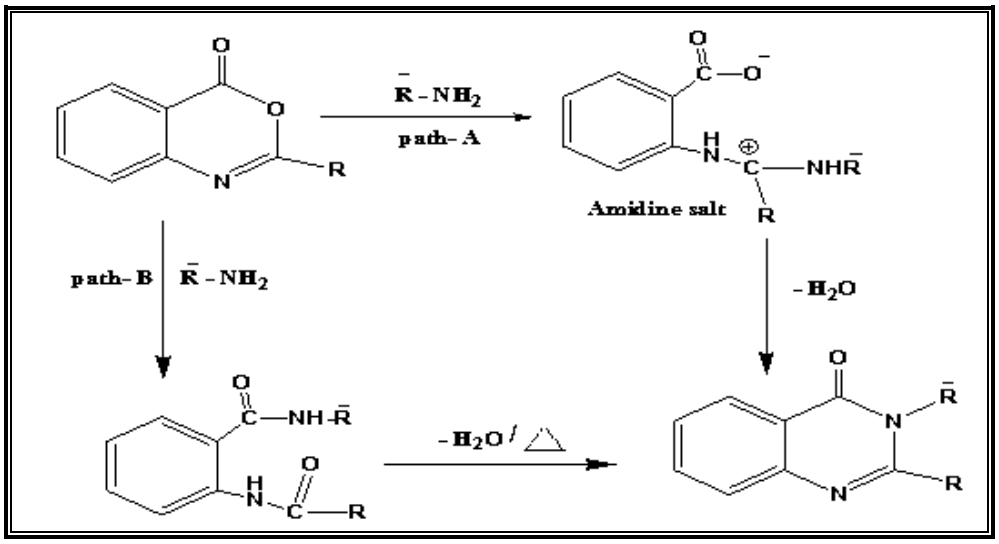
1.4.4.2. Reaction with primary amines:

In many cases, acylanthranilamides are the products of the interaction of benzoxazin-4-ones with primary amines (due to the weak nucleophilicity of primary amines in comparison with aromatic amines and consequently depend on the mode of attacking the benzoxazinone moiety). Reaction of 3,1-benzoxazinone (74), with isopropyl amine and / or methylamine in THF produced the corresponding pyridylpyrazole anthranilic diamides (75). Compounds have insecticidal potency and a Calcium Mobilization Threshold (CMT) [82-83].



Where X,Y = H, Cl, CH_3, CF_3. And Z= H, CH_3.

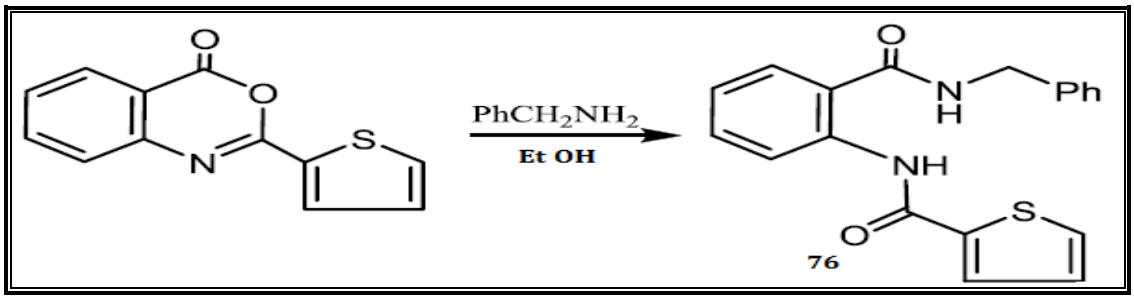
Mechanisticaly conversion of benzoaxzine to quinazoline can obtained by either path-A, where ammonia or primary amine hydrogen bonded to nitrogen atom of benzoaxzinone, then undergo nucleophlic addition to C2-carbon to form amidine salt [14], which subsequently dehydrated to quinazolinone. Or path-B, where ammonia or amine nuclophlic attack C4-carbon to form N-acylanthranilamide, which subsequently dehydrated to qunazolinone as in following scheme.



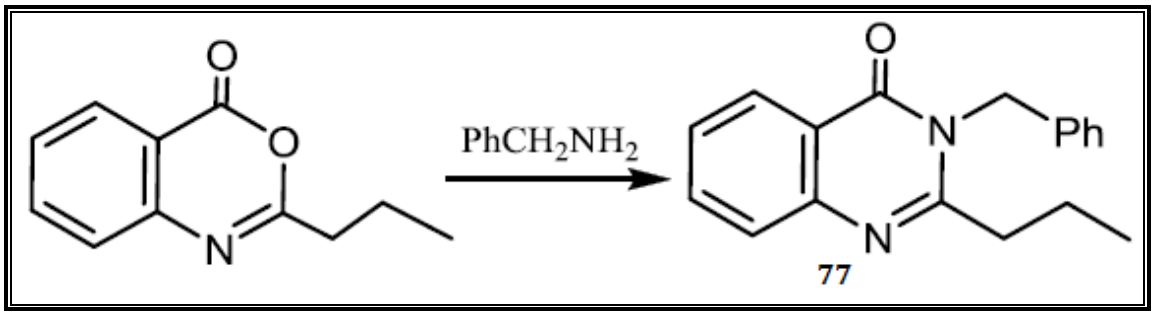
Scheme(1-2): Mechanism of reaction primary amine with benzoxazin

With primary aromatic amine, amidine salt can be isolated, and it has been converted to quanzolinone at room temperature. Path-B mechanistically precludes because N-acylanthranilamide require temperature above 200℃ to affect cyclization to quinazolinone [84].

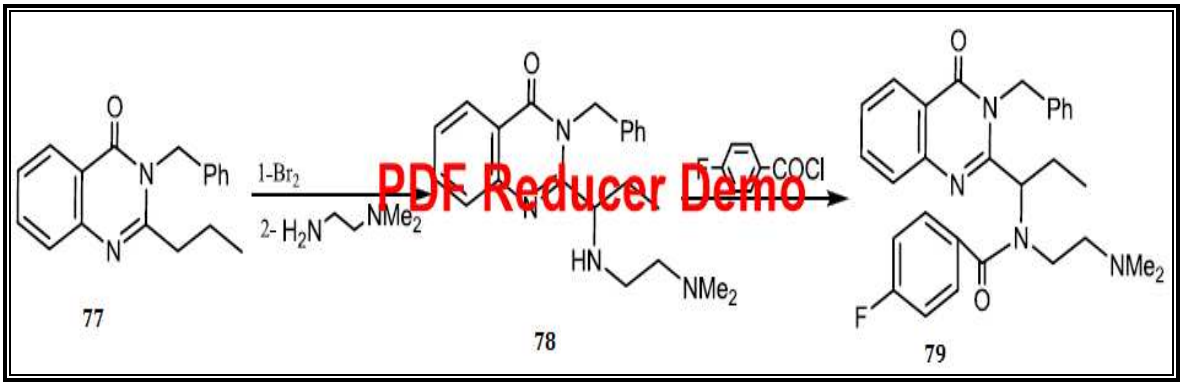
Treatment of 2-thinylbenzoxazinone with benzylamine in ethanol affords N-acylanthranilamides (76) [85].



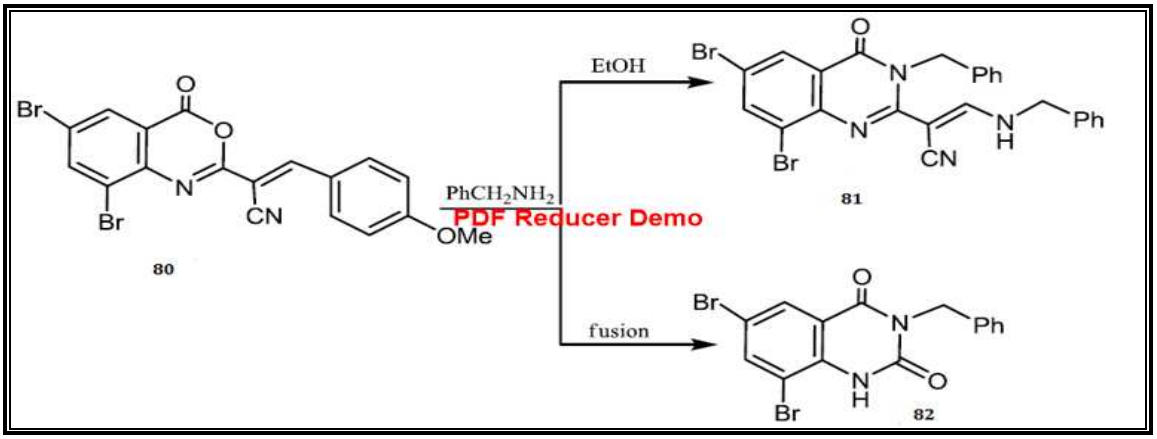
On the other hand, treatment of 2-propyl-3,1-benzoxazin-4-one, with benzylamine yields 3-benzyl quinazolinone (77) [86].



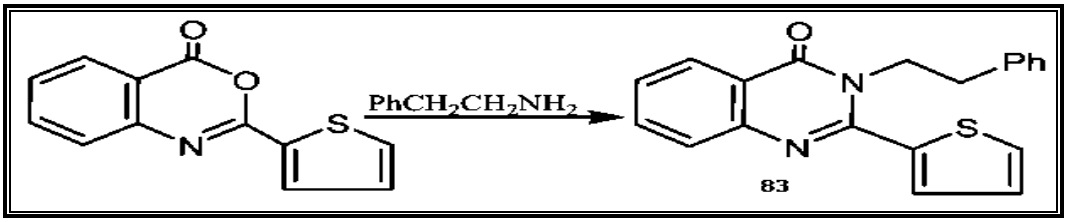
Bromination of quinazolinone (77), followed by addition of N,N-dimethyl ethylene diamine produces (78). The latter quinazolinone (78) reacts with 4-fluorobenzoyl chloride to give (79), compound (79) is a biologically active compound and useful in treatment of Cancer, Hyperplasmia, Restenosis immune disorders and inflammation [86].



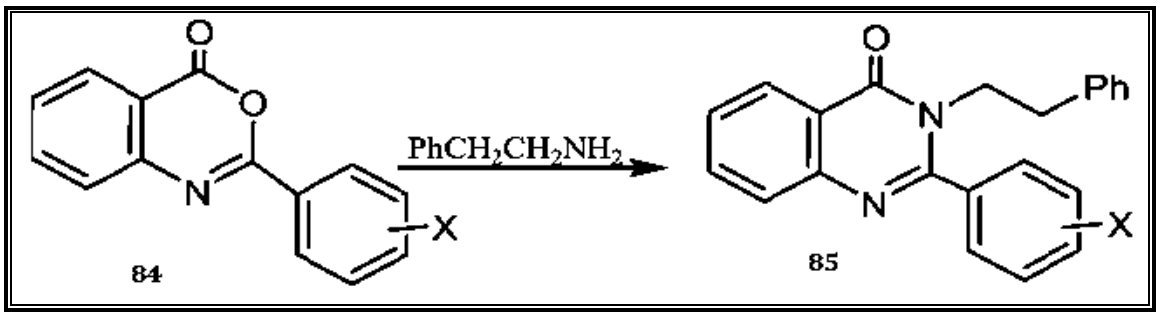
2-Substituted acrylonitril-3,1-benzoxazin-4-one(80), reacts with benzylamine under different reaction conditions, in order to give a mixture of N-benzylquinazolinone derivative (81) and quinazolin-2,4-dione (82) [87].



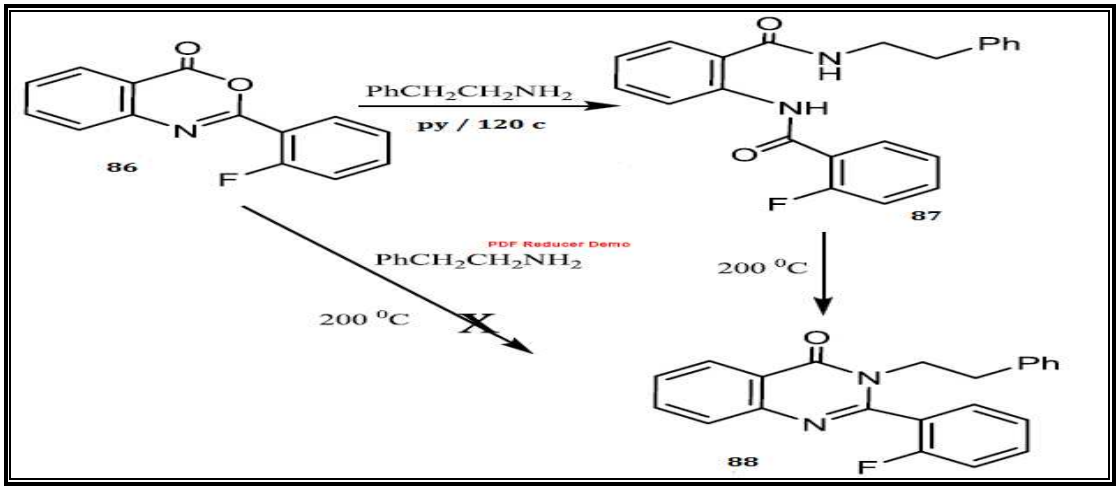
A new quinazolinone derivative, formed via heating 2-thinyl-3,1-benzoxazin-4-one, with phenylethylamine to give compound (83) [88].



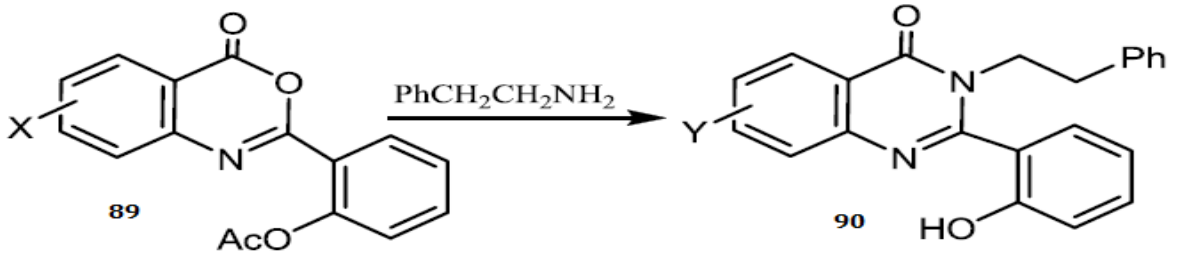
Refluxing 2-phenyl (or substituted phenyl)-3,1-benzoaxzin-4-one (84), with a 10 fold excess of phenylethylamine for 2-3 hours at 200 °C produce the corresponding 4(3H)-quinazolin-4-one derivatives (85) [89].



Fusion of 2-(2-fluorophenyl)-substituted benzoxazinone (86), and phenylethylamine at 200 °C, resulted in the dominant nucleophilic displacement of fluorine substituent with the amino moiety. For preservation of the 2-(2-fluorophenyl) fragment, synthesis of the intermediate bisamide (87), was carried out in pyridine at 120 °C followed by thermal cyclization to 2-(2-fluorophenylphenethyl-3H-quinazolin-4-one (88) [90].

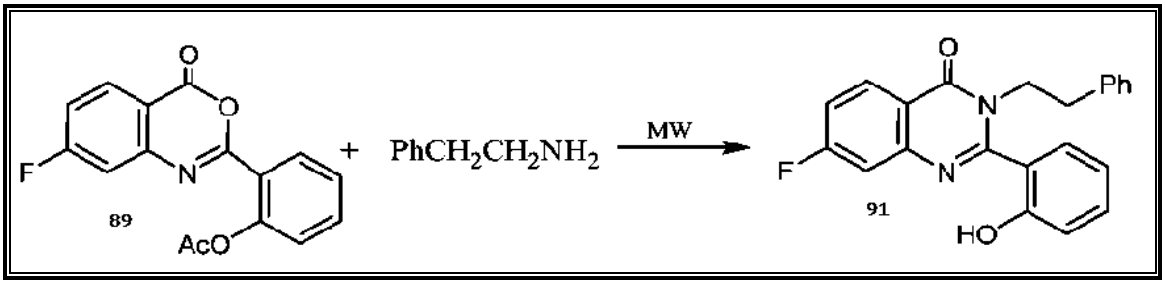


Benzoxazinones (89), bearing fluorine at 5, 7, or 8- position are submitted to the latter reaction with phenethylamine lead to amino-substituted quinazolinone (90), (where undesired nucleophilic displacement of the fluorine by the amine occurs), probably due to the reaction conditions (elevated temperature and absence of solvent) [91].



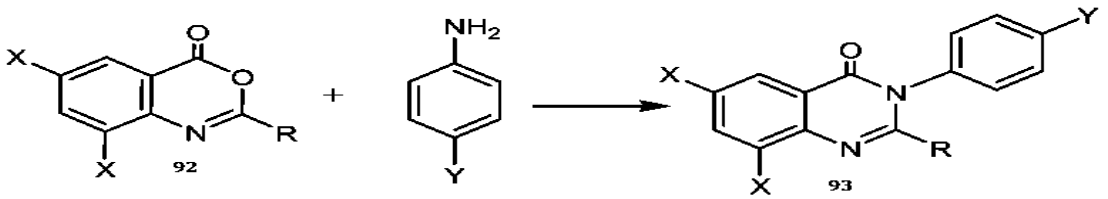
Where X= 5-F, 7-F. Y= 5-Ph-CH_2CH_2NH, 7-Ph-CH_2CH_2NH-

Applying microwave irradiation to the above benzoxazinone (89), results 7-fluoro-substituted quinazolinone (91), whereas 5- and 8-fluoro-substituted benzoxazinones (89), still produce products of nucleophile displacement [91].



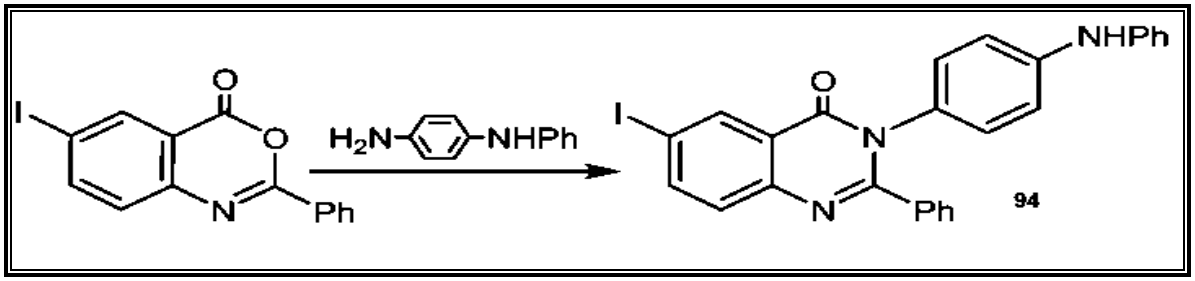
1.4.4.3. Reactions with anilines:

Reaction of anilines with 3,1-benzoxazin-4-ones either, reactants can be combined neat at room temperature, at elevated temperature ranging from 150- 220°C, or at 150-180°C in the presence of zinc chloride [92]. Alternatively, the reaction can be performed in solvents such as pyridine, dioxane, acetic acid, dimethylformamide or ethanol [93]. Substituted anilines, afforded quinazolinones (93), when reacted with substituted benzoxazinones (92).

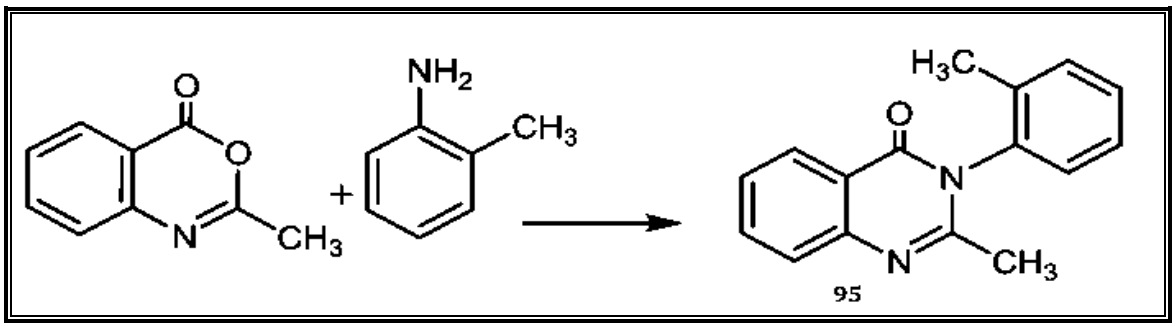


Where Y= halied, CH_3, OCH_3, PhO, NO_2, SO_2NH_2, CO_2Et. X= H, halied. And R= CH_3, CH_2Cl, Ph, CH_2Ph, CO_2Et.

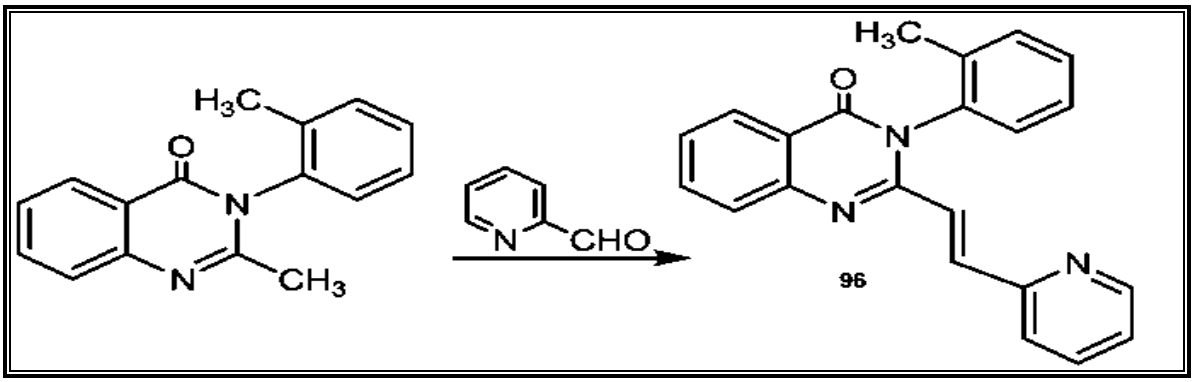
In similar fashion, interaction of 2-phenyl-6-iodo-3,1-benzoxazin-4-one, with p-aminodiphenyl amine yields 6-iodo-2-phenyl-3-(4'-phenylaminophenyl)-quinazolin-4-one(94) [95-96].



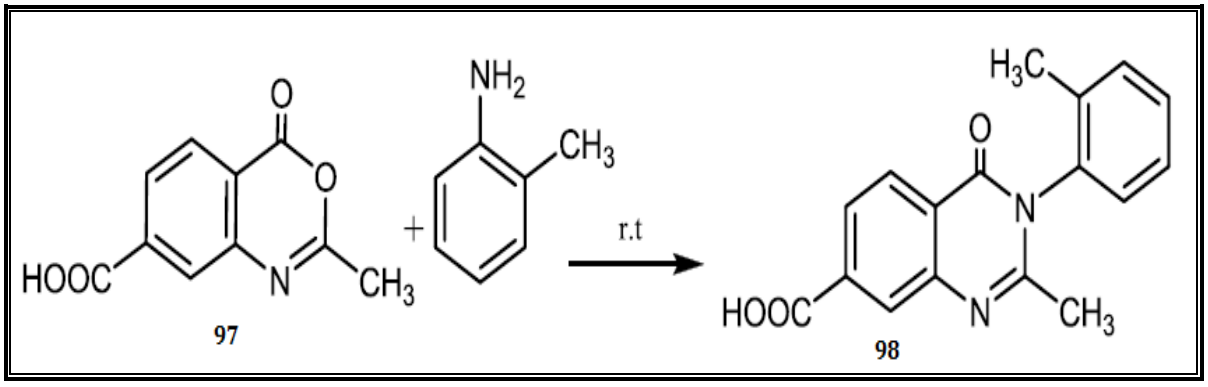
Refluxing a mixture of 2-methyl-3,1-benzoxazin-4-one, and o-toluidine in toluene under azeotropic conditions furnishes the CNS agent Methaqualone (95) [97].



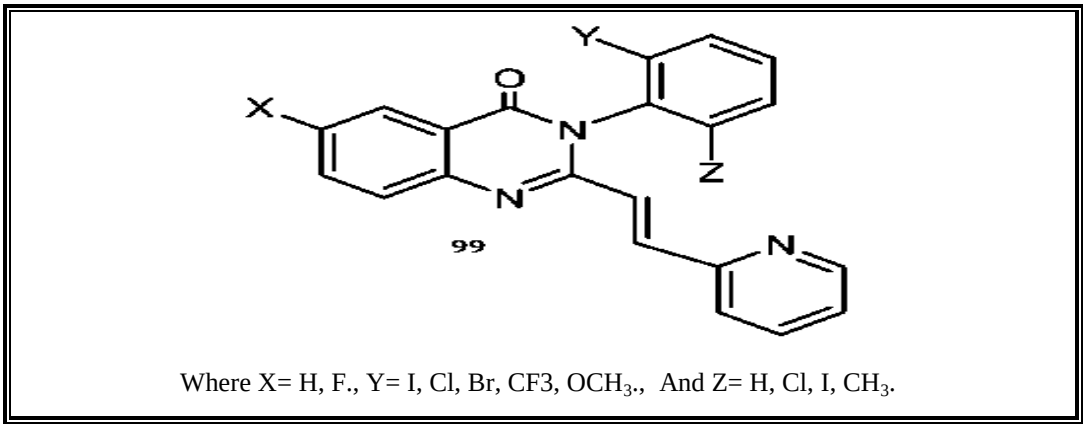
The above reaction also can be conducted in acetic acid followed by condensation of the produced quinazolinone (95), with 2-pyridine carboxaldehyde in the presence of zinc chloride and provided 2-[(pyridine-2-yI)vinyl]-3-(2methylphenyl)-quinazolin-one (96), which is known as Piriqualone and it was tested as anticonvulsant agent [98].



7-Carboxyquinazolone (98), is synthesized by mixing benzoxazinone (97), and o-toluidine at room temperature for 3-4 hours [98].

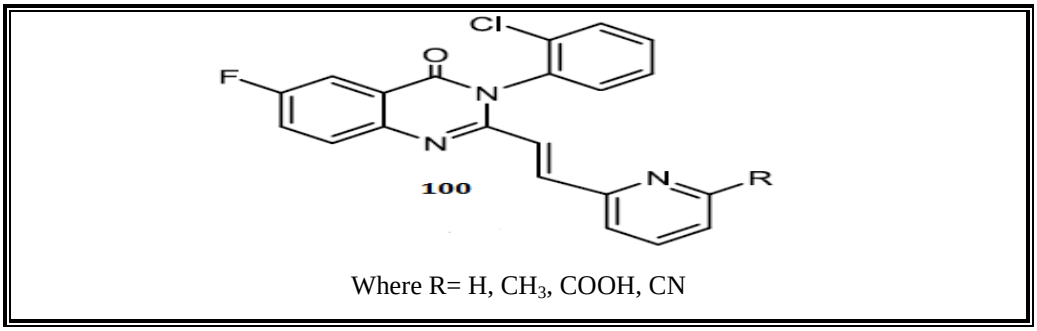


A variety of 2-substituted and / or 2,6-disubstituted anilines, interact with substituted 3,1-benzoxazin-4-ones, to produce quinazolinone derivatives (99) [98].



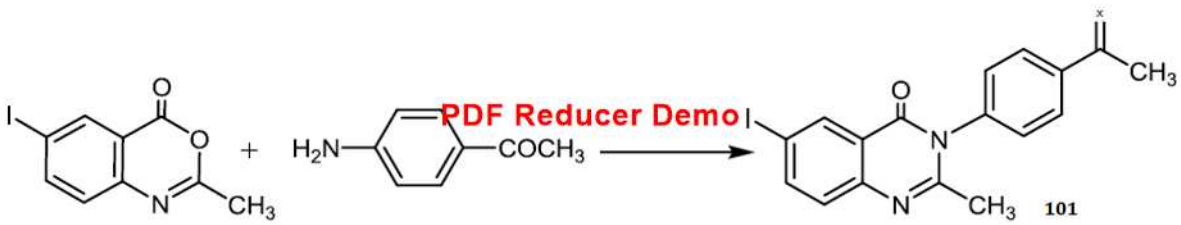
Where X= H, F., Y= I, Cl, Br, CF3, OCH_3., And Z= H, Cl, I, CH_3.

A series of 3-(2'-chlorophenyl)-2-substituted quinazolones (100), is prepared and their biological activity are tested. They are identified as antagonist template for AMPA receptors (play an important role in pharmacological studies of glutamate receptors) [99].



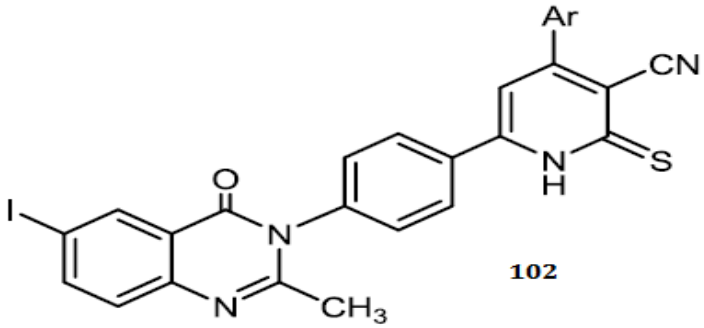
Where R= H, CH_3, COOH, CN

Condenzation of 6-iodo-2-methyl-3,1-benzoxazin-4-one, with 4-amino acetophenone in n-butanol gives 2-methyl-6-iodo-3-(4'-acetylphenyl)-quinazolin-4-one (101) [100].



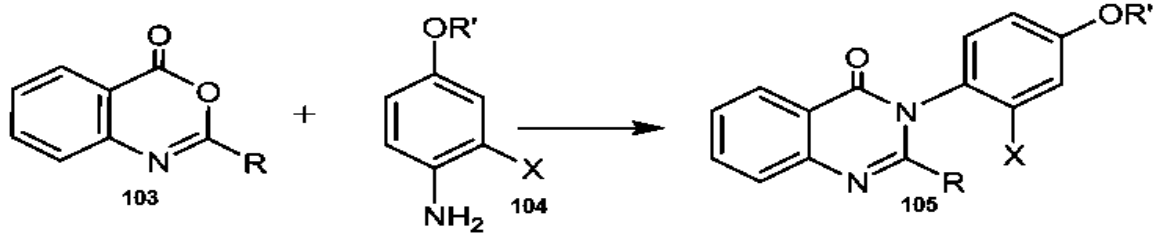
Semicarbazone derivatives, were obtained from refluxing benzoxazine (101), by refluxing with an equimolar amount of semicarbazide hydrochloride in ethanol [101].

Cyanopyridin-2-(1H)-thione derivatives (102), were obtained via the reaction of arylmethylene–cyanothioacetamide ($ArCH=C-(CN)CSNH_2$), with the active methylene carbonyl quinazolone. An assay for Antitumor activity showed that compound (102) (Ar= $4\text{-}OCH_3C_6H_4$), has a significant activity against Ehrlich. A cites Carcinoma tumor cells (in vitro) and displayed a significant percent of the nonviable tumor cells to about 40% and 80% at concentration of 10 and 100mg, respectively [101].



Where Ar = Ph, 4-pyridyl, 2-thienyl

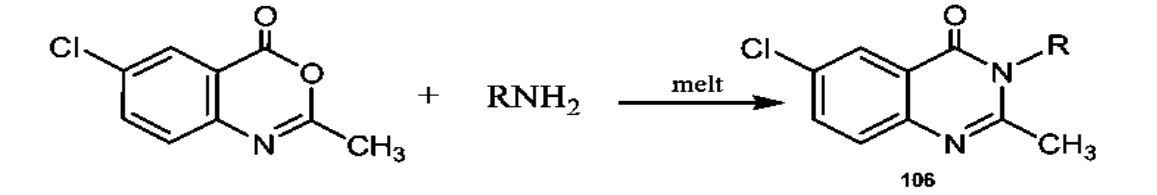
Treatment of 3,1-benzoxazin-4-ones (103) with 4-hydroxyl or 4-alkoxyanilines (104) yield the corresponding quinazolone (105) [102].



Where R= CH_3, Ph, CH_2Cl, CH_2Ph. X= H, NO_2, and R´= CH_3, ,H.

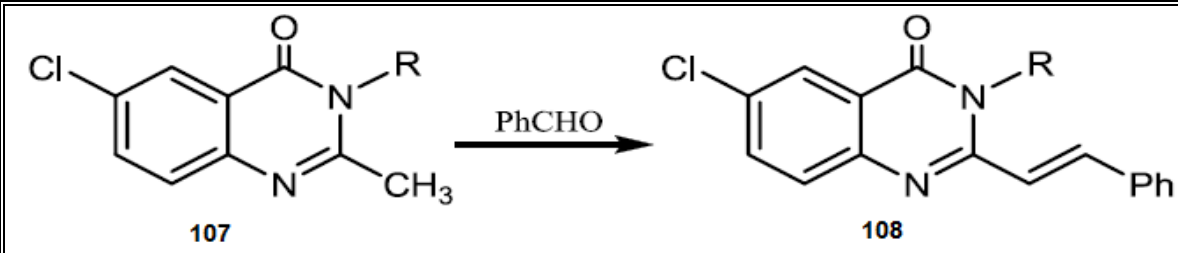
1.4.4.4. Reactions with amino heterocyclic compounds:

Amino heterocyclic, such as amino (pyridine, pyrimidine, pyrazole, thiazole, or 1,3,4-thiadiazole), have been successfully useful to prepare 3-heterosubstituted quinazolone (106), with high biological activity [103].



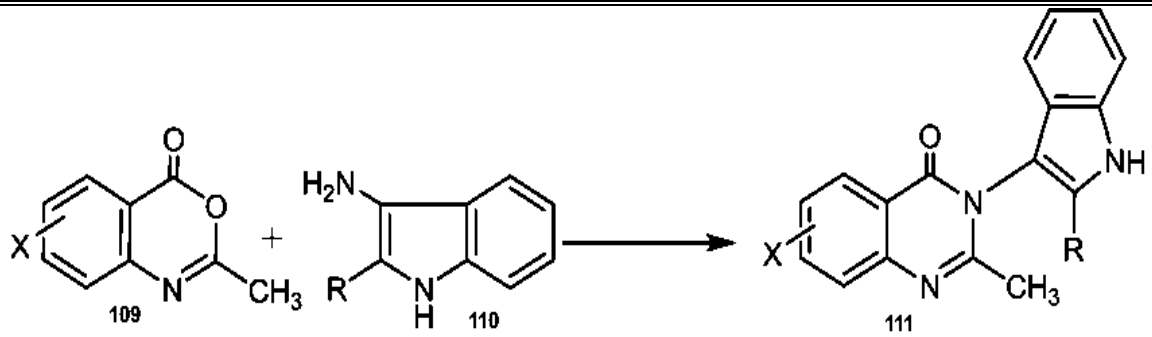
Where R= 5-indazolyl, 1-ethyl-5-pyrazolyl.

Refluxing equimolar amounts of 2-methyl quinazolone (107), and benzaldehyde in glacial acetic acid; the 3-heterocyclo-2-styrylquinazolinones (108), are generated [104].



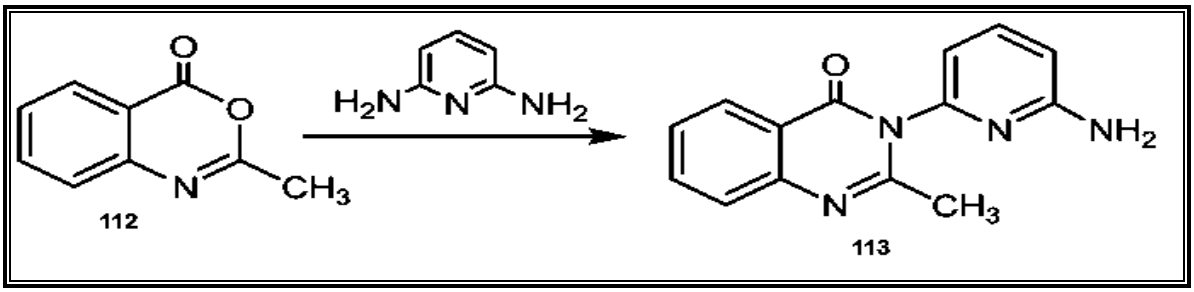
Where R= 5-indazolyl, 1-ethyl-5-pyrazolyl

Reaction of 2-methyl-3,1-benzoxazin-4-ones (109), with 2- substituted-3-aminoindoles (110), in dry pyridine produce 2-methyl-3-(2'-substituted indol-3-yl)-4(3H)-quinazolinone (111) [105].

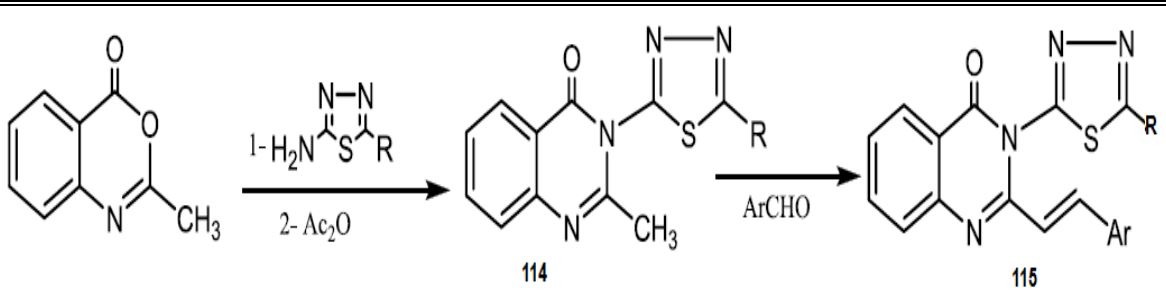


Where X= H, I, Br. And R= H, CH_3.

Also 2-methyl-3,1-benzoxazin-4-one (112), reacts with 2,6-diamino pyridine, to give 3-substituted quinazolone (113) [106].



Synthesis of 3-(1',3',4'-thiadiazolyl)-2-styrylquinazolin-4(3H)-one (115), is accomplished by a three-step procedure, the intermediate 3-(1',3',4'-thiadiazoloIyl)-2-methyl quinazolinones (114), is obtained by refluxing 2-methy-3,1-benzoxazin-4-one, with 2-amino-1',3',4'-thiadiazol derivatives, in acetic anhydride [119]. Then condensed with aromatic aldehyde to give (116) [105].

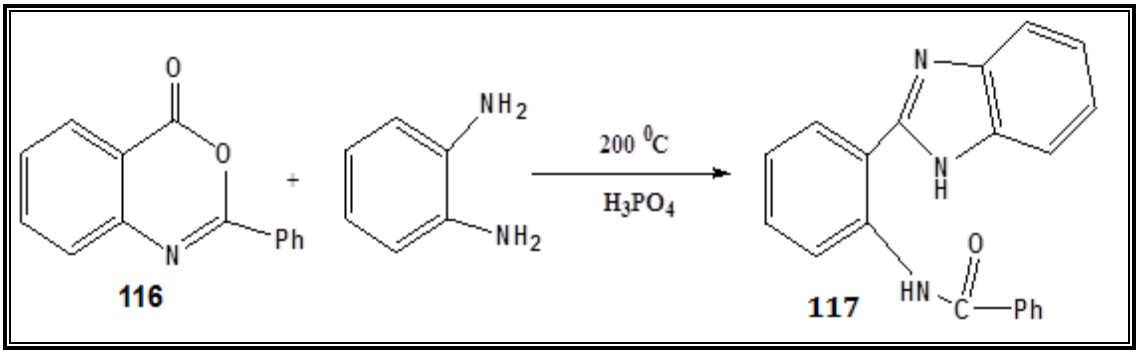


Where R = Ph, 3-ClC_6H_4, -CH=CH-Ph. And Ar = 4-ClC_6H_4, 3-ClC_6H_4, 4-pyridyl.

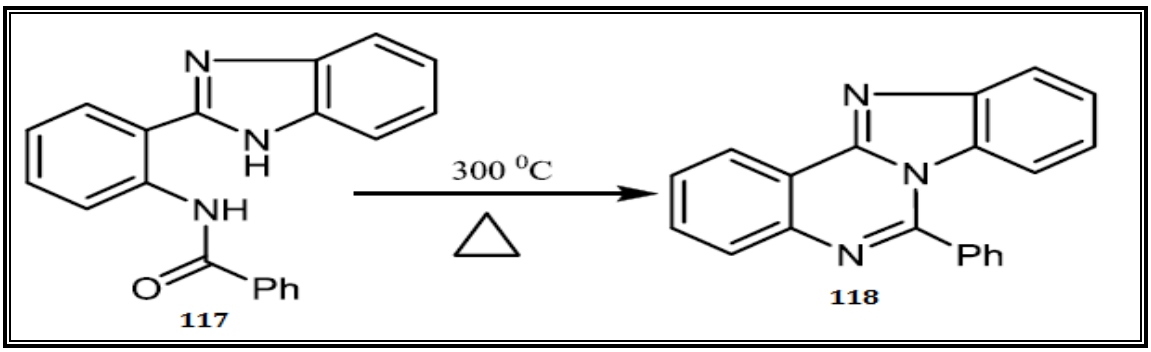
1.4.4.5. Reactions with diamines:

A. Reactions with o-phenylenediamine:

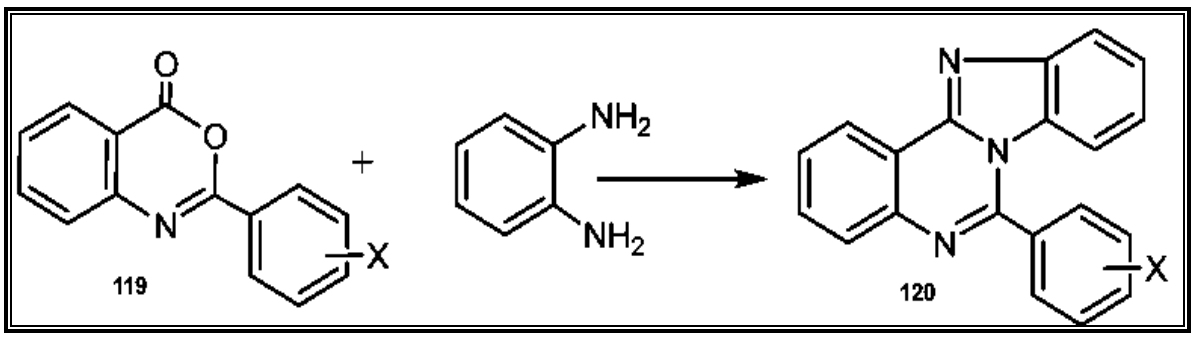
Heating 2-phyenylbenzoxazinone derivative(116), with o-phenylene diamine with poly phosphoric acid at 200 °C provided (117) [106].



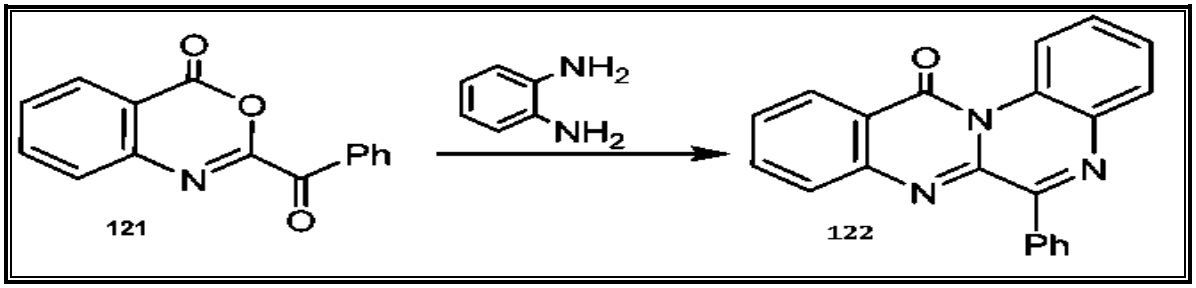
Upon sublimation of (117), at 300℃, cyclodehydration leads to the formation of benzimidazoquinazoline (118) [107].



Cyclocondensation of 2-aryl benzoxazinones (119), with o-phenylene diamine catalyzed by orthophosphoric acid yield analgos benzoimidazo quinazolinone (120) [108].

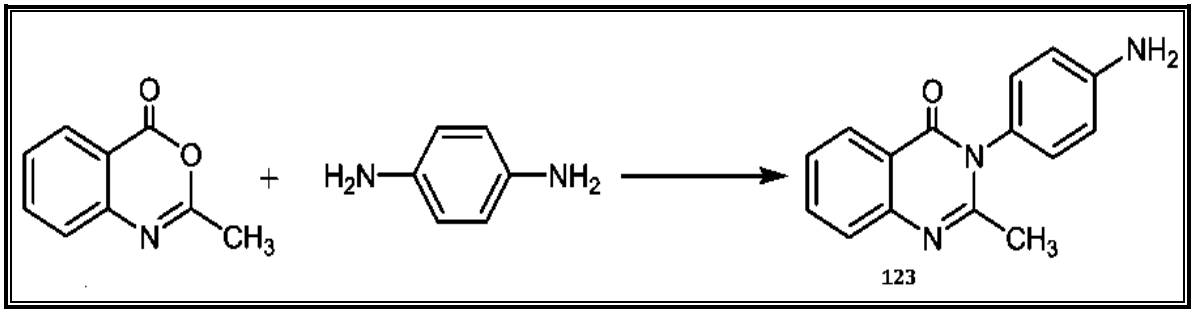


2-benzyol-3,1-benzoxazin-4-ones(121), reacts with o-phenylenediamine to afford (122) [108].

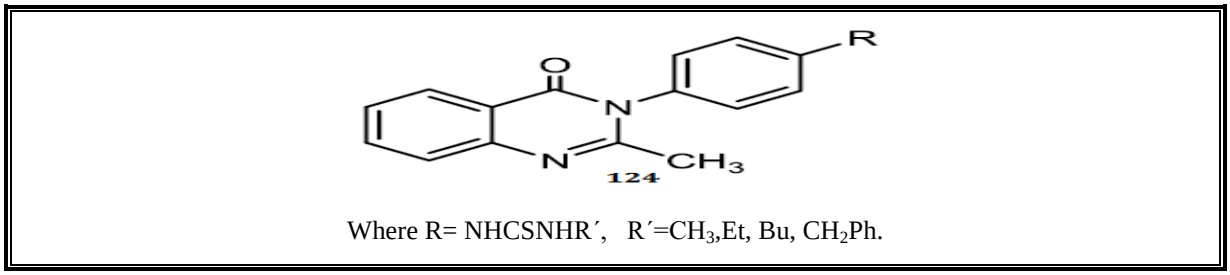


B. Reactions with p-phenylenediamine:

Interaction of 2-methyl-3,1-benzoxazin-4-one, with p-phenylenediamine and give quinazolinone (123) [109].



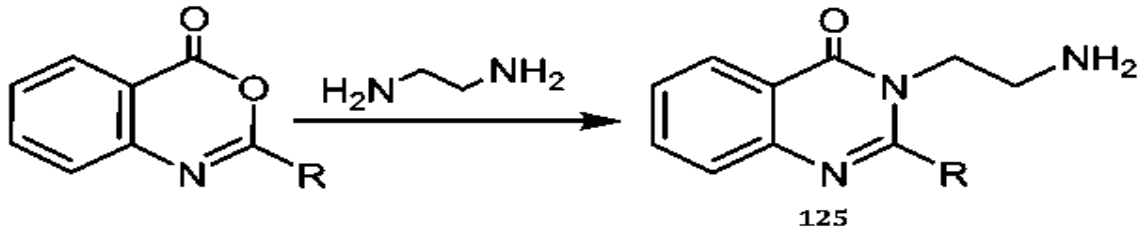
Treatment of quinazolinone (123), with alkyl isothiocyanates (R'-N=C=S) give quinazolinones (124), bearing heterocyclic moieties with high biological activities [109].



Where R= NHCSNHR´, R´=CH_3,Et, Bu, CH_2Ph.

C. Reactions with ethylenediamine:

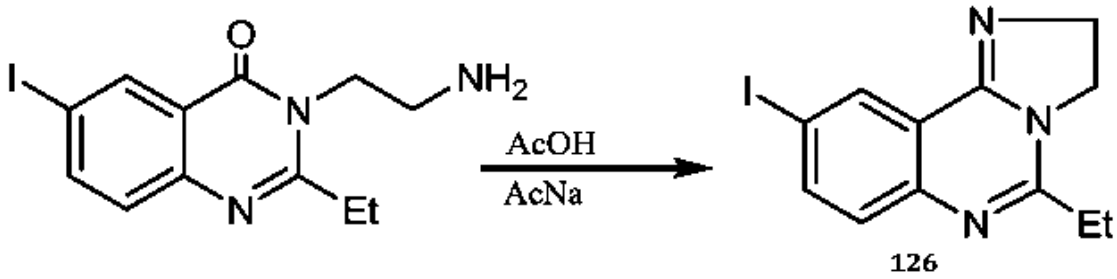
2-Methyl-3,1-benzoxazin-4-one as well as 2- phenyl analog, are reacting with ethylenediamine and produce the conesponding 3-functionalized quinazolones (125) [110].



125

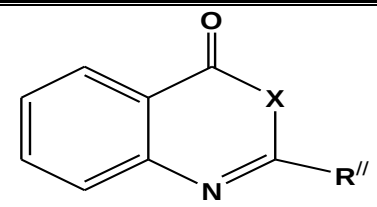
Where R= CH_3, Ph.

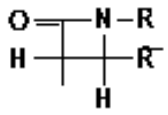
Heating quinazolinone in acetic acid in presence of fused sodium acetate, cyclodehydration occurred and the imidazole quinazoline (126), is generated [110].



126

Treatment of 2-substituted-3,1-benzoaxzin-4-one, with amino acid (H_2NCH_2COOH), gives quinazoline 3-acetic acid (A), which is converted to acid chloride upon reaction with thionyl chloride (B), then quinazolin-3-acid chloride (B) is converted to ketene (C) is formed in situ, upon treatment (B) with triethyl amine, and Schiff base RN=CHR', gave quinazoline-3(3'-azetidinone) (D) [111].



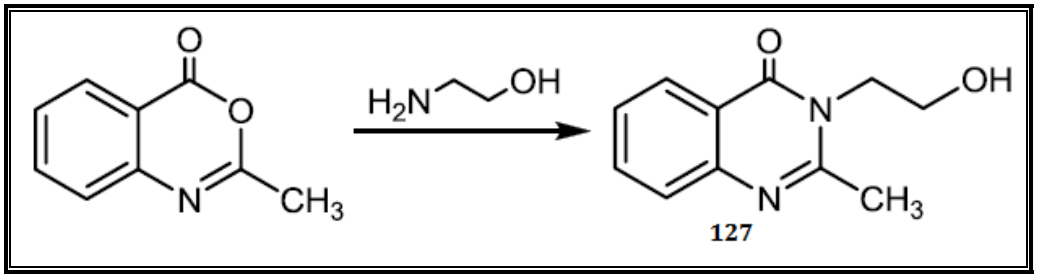


Where X=A= N-CH_2COOH, B=X=N-CH_2COCl, C=X= N-CH=C=O, D=X=

R= R´= Ph or Substituted phenyl.

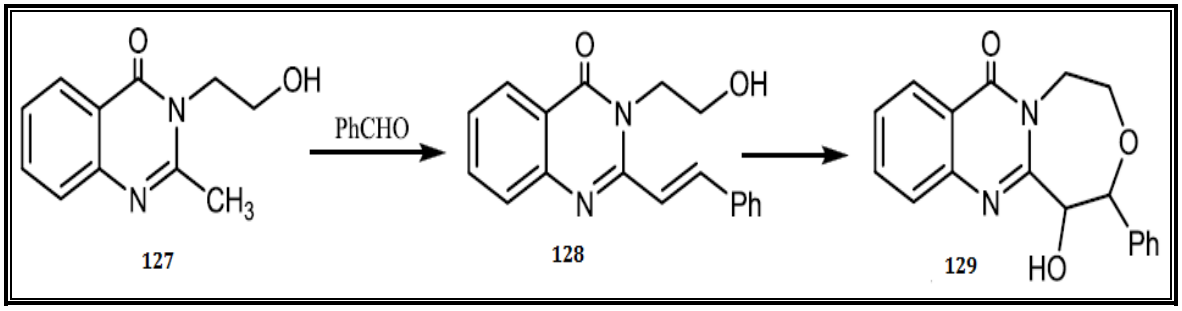
1.4.4.6. Reactions with aminoalcohols:

2-Methyl-3,1-benzoxazin-4-one, reacts with ethanolamine to produce the corresponding 3-hydroxyethyl quinazolone (127) [112].



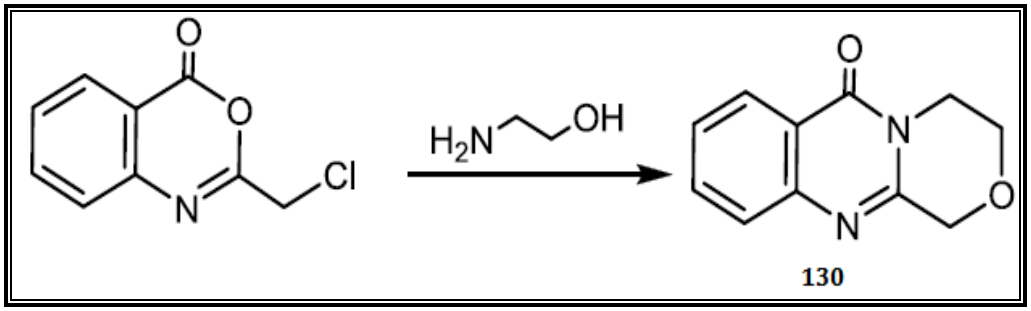
127

Heating quinazolinone (127), with benzaldehyde yields the styryl derivative (128). Epoxidation of the double bond, then treatment of the product with sodium methoxide afforded (129), as a result of intermolecular attack of ethanol group on the epoxide [112].



127 128 129

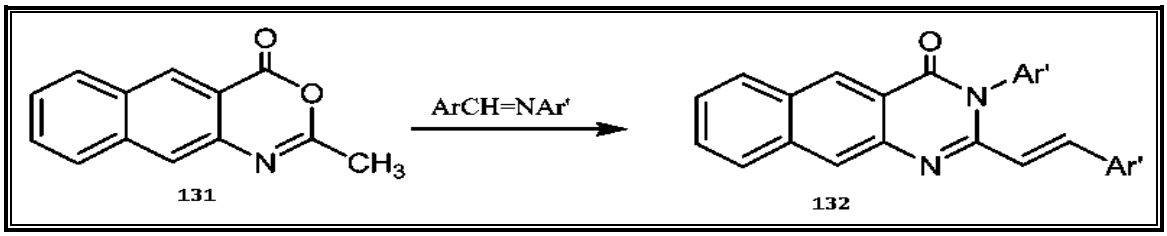
Heterocondensed quinazolones 1,4-oxazino-[3-4-b]quinazolin-5-one (130), has been obtained by treatment of 2-(chloromethyl)-3,1-benzoxazin-4-one, with ethanol amine followed by base-catalyzed cyclization [113].



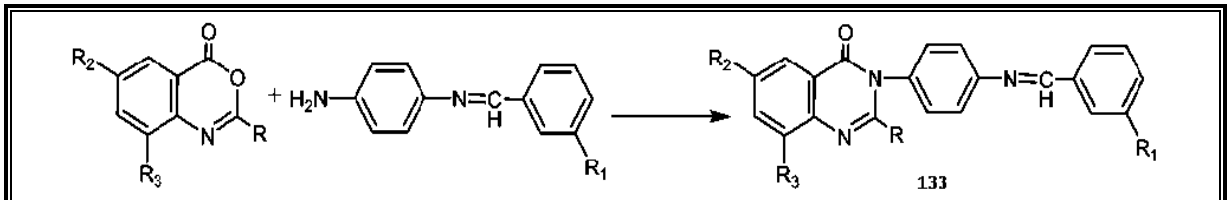
130

1.4.4.7. Reactions with Schiff's bases:

Condensation of 2-methylnaphthoxazinone (131), with Ar-CH=N-Ar′ where (Ar and Ar′= substituted phenyl) in acetic acid yield benzoquinazolones (132) [114].

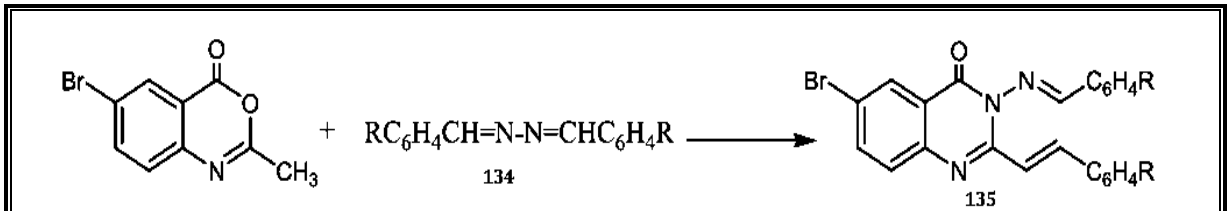


Compounds (133) are prepared by reaction of 3,1-benzoxazin-4-one derivatives, with Schiff's base. Compounds (133) are tested for Anthelmintic, Virucidal and Bactericidal activity [115].



Where R= CH_3, Ph. R1= 3-NO_2, 4-OH, 4-NMe_2, 2-OH, 4-Cl. R2= H, Br. And R3= H, Br.

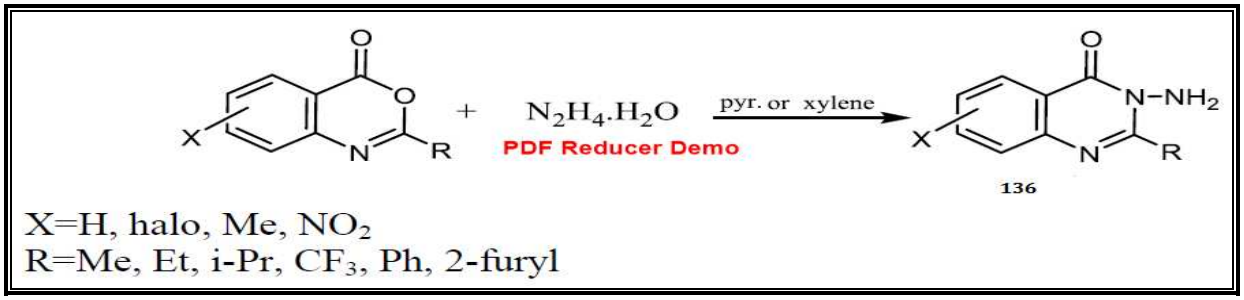
6-Bromo-2-methyl-3,1-benzoxazin-4-one undergoes hetero-ring opening followed by recyclization and condensation when treated with azines (134) and yielded substituted-3-arylideneamino-quinazolin-4-(3H)one (135). The reaction involves a cleavage of the azine into its amine and arylidene moieties which are smoothly incorporated into 6-Bromo-2-methyl-3,1-benzoxazin-4-one via nucleophilic attack of the amine at position-4 and condensation of the aldehyde with a reactive methyl group at position-2 respectively [115].



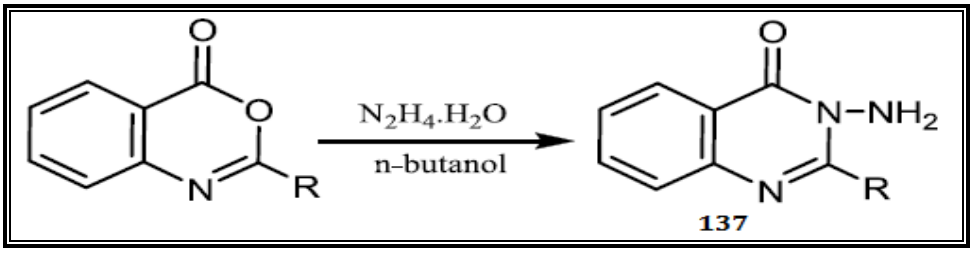
Where R= H, 4-OMe

1.4.4.8. Reactions with hydrazine hydrate:

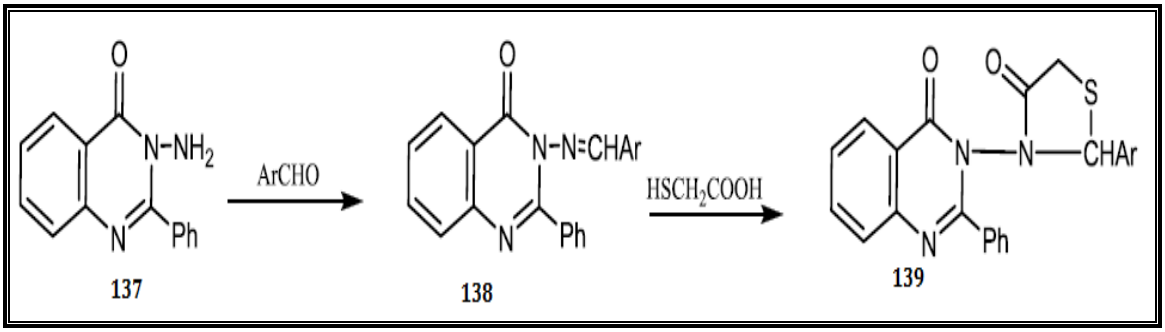
Heating 3,1-benzoxazin-4-ones, with neat hydrazine hydrate in pyridine or xylene solutions, produces the 3-amino-4-quinazolones (136) [116].



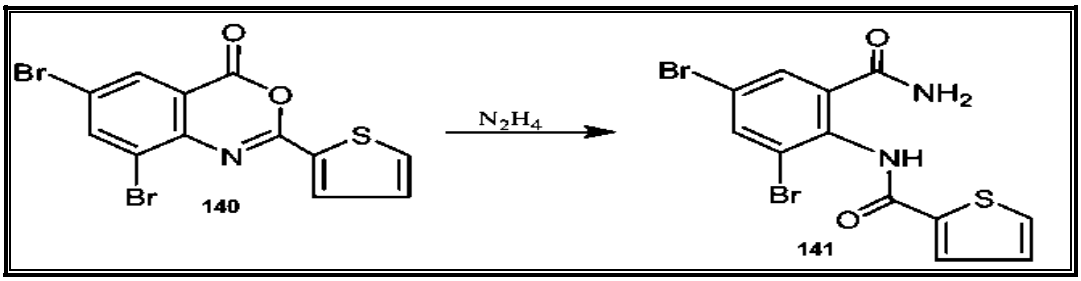
Also, heating benzoxazinone derivatives with hydrazine hydrate in n-butanol afford 3-aminoquinazolone derivatives (137) [147].



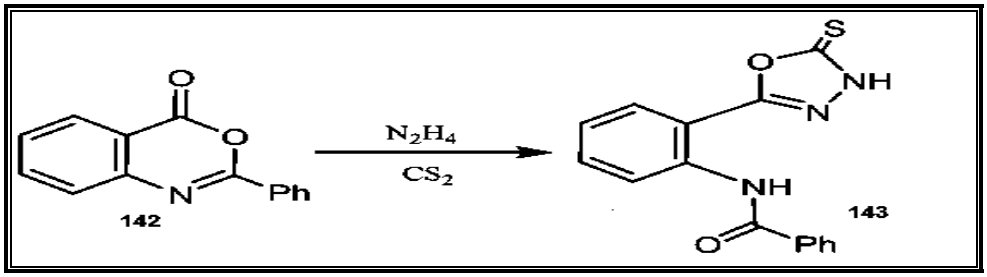
3-amino quinazolone (137), is reacted with aromatic aldehydes and produces the corresponding benzylidene aminoquinazolinone derivatives (138), which in turn cyclized to thiazolone derivative (139), by its interaction with thioglycolic acid [117].



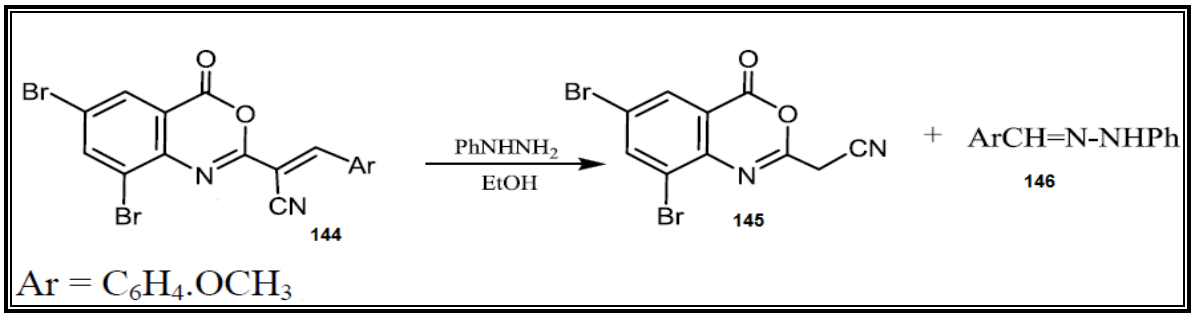
On the other hand, treatment of the benzoxazinone derivative (140), with hydrazine hydrate in ethanol affords the (thienoylamino) dibromobenzamide (141) [117].



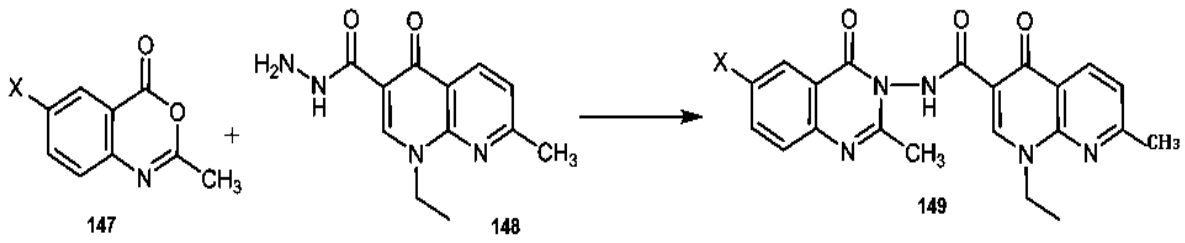
When the reaction of 3,1-benzoxazin-4-one (142), with hydrazine hydrate is conducted in the presence of carbon disulphide in alcoholic potassium hydroxide, the 1,3,4-oxadiazolin-5-thione(143) is produced directly [118].



3,1-benzoxazin-4-one (144) is reacted with phenyl hydrazine in the same manner like reaction with hydrazine hydrate, it gives a mixture of carbonitrile (145) and hydrazine derivative (146)[119].

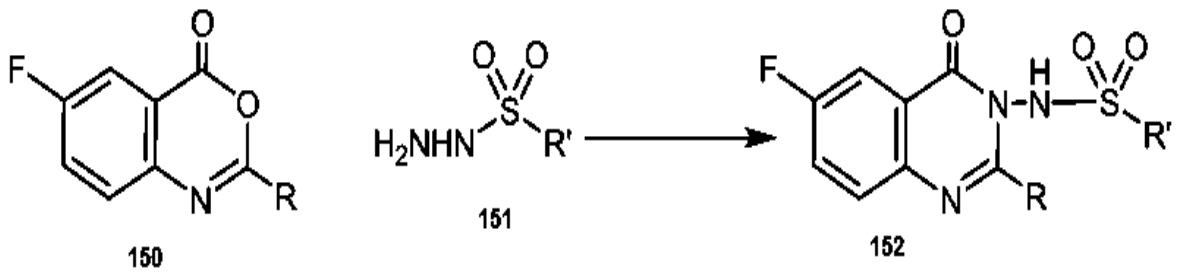


Interaction of 2-methyl-3,1-benzoxazin-4-one derivatives(147), with nalidixic acid hydrazide (148), yield substituted 3,1-quinazolin-4-one derivatives of nalidixic acid (149), which exhibited inhibitory activity against A. hydrophila [120].



Where X= H, I, NO_2.

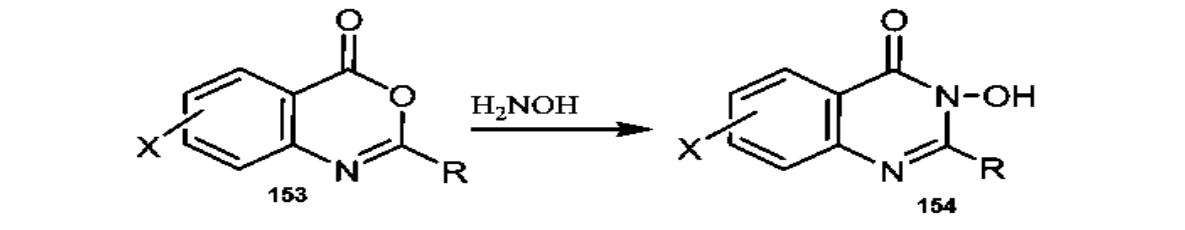
Combining 2-Substituted 6-fluro-3,1-benzoxazin-4-ones (150), with acid substituted sulphonyl hydrazides (151), devoid of solvents, followed by heating at 160 °C (oil bath) gave compounds (152) as the major products [120-122].



Where R´= phenethyl, Ph, thiophene-methylene. And R = 4-COOH-Ph, 4-CN-Ph, 4-t.Bu.

1.4.4.9. Reactions with hydroxylamine hydrochloride:

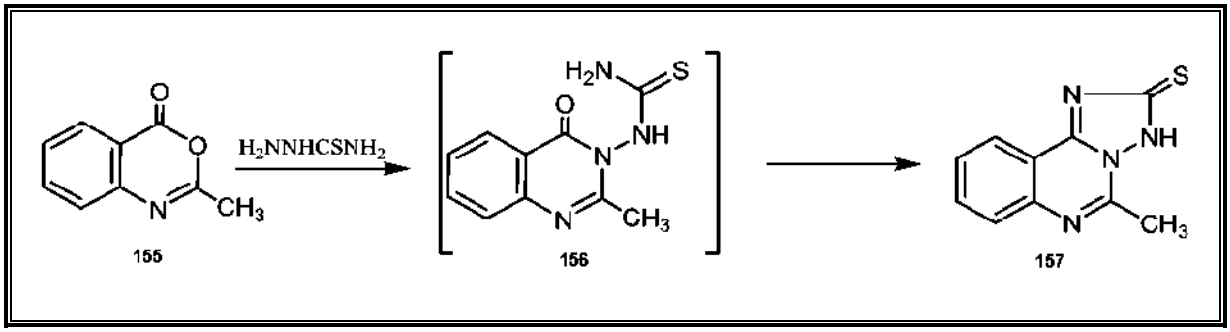
Reflexing 3,1-benzoxazine-4-one derivatives (153), with hydroxylamine hydrochloride in pyridine afford 3-hydroxy-4-quinazolinone derivatives (154) [123].



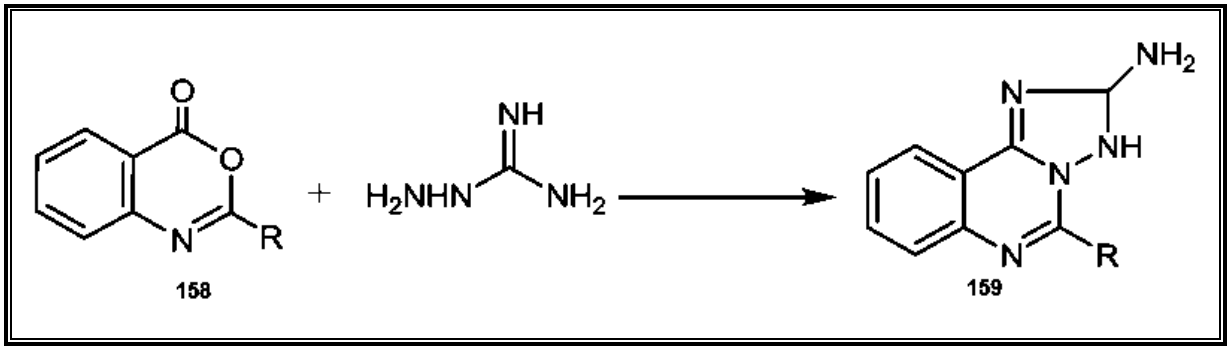
Where R= Me, Et, ph. And X= H, Halo, Me

1.4.4.10. Reactions with thiosemicarbazide and aminoguanidines:

If heating 2-methyl-3,1-benzoxazin-4-one (155), with thiosemicarbazide in acetic acid in the presence of fused sodium acetate, the thiocarbamide intermediate (156), which undergo cyclodehydrate to give (157) [124].



Also, refluxing 2-phenyl (or methyl)-3,1-benzoxazin-4-ones (158), with amino guanidine in pyridine to afford the amino derivatives (159) [125].



1.5. Importance of 3,1-benzoxazin-4-ones:

1.5.1. Pharmaceutical importance of 3,1-benzoxazin-4-ones:

Many 2-substitutant-3,1-benzoaxzin-4-one derivatives, have been biological activities propose, so it had led to member of drugs[126-129].

3,1-benzoaxzin-4-one have considerable attention, as inhibitions of serine protease, particularly, 2-aryl derivatives acts as Clr serine protease inhibitors [163]. Also it was converted into quinazolin-4-one, upon interaction with amino antipyrine, which act as Non-steroidal anti-inflammatory agents [130].

Chiral-2-alkylamino-3,1-benzoaxzin-4-one derivative, were reported as inhibitors of the chymotrypsin superfamily [131].

A series of 2-amino substituted-3,1-benzoxazin-4-one derivatives, as well as was reported as human protease inhibitors, some of them demonstrate Anti-Viral activity in cell culture [132].

Also a combination of 3,1-benzoxazin-4-one with 2-aminothiadiazole, gives substituted quinazolinone which act as Anticonvulsants and Enzyme inhibitors [133].

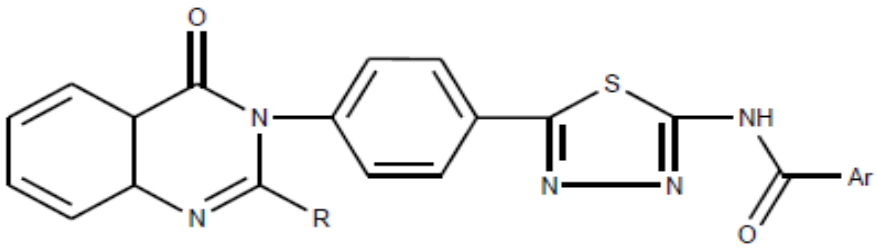
5-Methyl-3,1-benzoxazin-4-one derivatives, showed strong and highly specific inhibition of Human Sputum Elastase (HSE), which is equivalent to human Leukocyte Elastase (HLE) [134].

Also, 2-substituted-3,1-benzoxazin-4-one derivatives, showed good Cytotoxic activity [168], Herbicidal properties [135].

Also, some 2-substituted 4H-3,1-benzoxazin-4-ones, have the ability to lower the levels of cholesterol and triglycerides in plasma [136]

Moreover, the importance of these 3,1-benzoxazin-4-one, also resides in that, these compounds are useful precursors for the preparation of other pharmaceutically quinazoline derivatives [137].

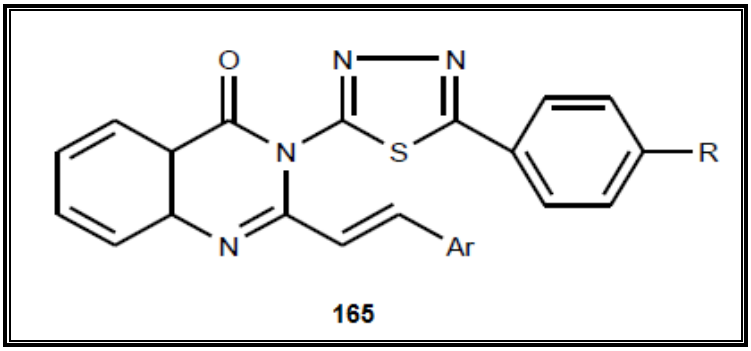
Many 2-subsitituted quinazoline derivatives, act as a new class of Anti-Microbial, Anti-Cancer agents which inhibited Tubulin polymerization [138]. Abroad spectrum of Anti-tumor activity and Anti- HIV-1 potency [139]. Synthesis and characterization of new quinazolines (164), as potential antimicrobial[140].



R = 2- chlorophenyl, Ar = Different aryl groups

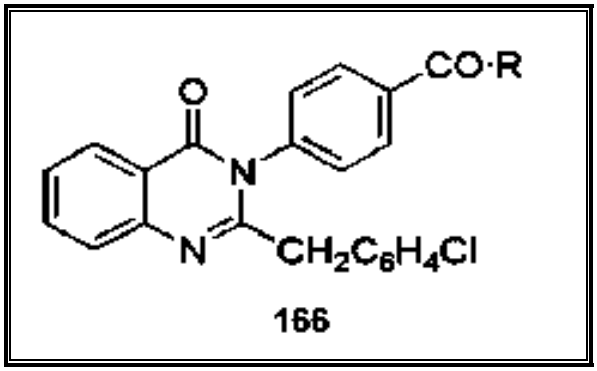
164

Synthesized substituted 3-[5-(4-sustituted-phenyl)-1,3,4-thiadiazole-2-yl]-2-styrylquinazoline4(3H)-ones(165) and reported their antibacterial and antifungal activity[141].



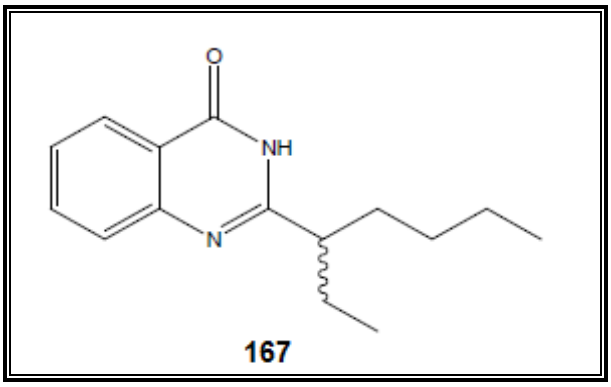
165

Synthesis of 4-[2-(4'-chlorobenzyl)-3-(acetophenon-4"yl)-quinazolin-4-one] derivatives (166), as in Vitro Anti-Tumor Activity[142].



166

Synthesis of an Antifungal quinazolinone (167) of Marine Source [143].



167

1.5.2.Industrial applications:

Many 2-subsitituted-3,1-benzoxazin-4-ones are additives comprising surfactants, of carboxy polymers, polysaccharides or polyalicylene glycols in 5-7 % of these compounds. It has good storage stability in detergent components containing peroxygen bleach [144-149].

Also, 2-Alkyl and 2-aryl-3,1-benzoxazin-4-ones, are widely used in the synthesis of polymeric materials and optical bleaching agents [150-151]. Recently 2-aryl or vinyl-3,1-benzoaxzin-4-one derivatives, were reported as useful U.V. absorber [152].

Aim of this work:

The aim of this work involves:

First: Design to synthesize many of di (3-substituted quinazolin, quinazolin-4-one and quinazolin-4-thion-2-yl) moiety, substituted at (p,p´)-position of bridged azobenzenes molecule, via p,p'-(3,1-benzoxazine-4-one-2-yl) moiety, substituted at (p,p')-position of bridge azobenzene molecule.

Second: Examination of antimicrobial activities of synthesized quinazolin, quinazolinone and quinazolin-thion derivatives, as antibacterial and antifungal agents, in comparison with the effect of common pharmacological antibiotic and antifungal treatments.

Chapter Two

Experimental Part

2.1. Supplied chemicals companies:

All chemicals used in this work, and their suppliers are listed in Table (2-1), and used as received without further purification.

Table (2-1) : Chemicals used in this work and their suppliers.

Materials	Supplied from	Purity (%)
P-Nitro benzoic acid	Riedal-dehaën	99
Glucose	Pharmaceutical drug Samara PDS	99
Dimethylsulphoxide (DMSO)	BDH	95
N,N-dimethylformamide (DMF)	BDH	95
Anhydrous potassium carbonate	Merck	99
Thionyl chloride	CDH	99.9
Anthranilic acid	SCL	98
Diethylether	BDH	99
Pyridine	BDH	95
Acetic anhydride	BDH	98
Sulphuric acid	Merck	98
Hydrochloric acid	BDH	99.9
Sodium hydroxide	Merck	98
Potassium thiocyanate	Riedal-dehaën	98.5
Potassium cyanate	Riedal-dehaën	98.5
Acetic acid (glacial)	Riedal-dehaën	99
Urea	Merck	99
Thiourea	Merck	99
Quinidine hydrochloride	Merck	99
Benzenesulphonyl chloride	Riedal-dehaën	99

Ethanol	Scharlau	99
Methanol	Scharlau	99
Acetone	Scharlau	99
n-Hexane	Aldrich	99
Chloroform	Scharlau	99
Benzene	Scharlau	99
Petroleum ether	BDH	b.p.(60-80)
Ethyl acetate	Aldrich	99
Hydrazine hydrate	Scharlau	98
Thiosemicarbazide	Aldrich	99
Semicarbazide hydrochloride	BDH	99
p- Toluidine	Riedal-dehaën	99
4-Amino-N-(5-methyl-3-isoxaloly)benzenesulphonamide	Pharmaceutical drug Samara PDS	99
2-Amino-5(p-bromo)phenyl-1.3-thiazole	Fluka	98
2-Amino pyrimidine	Merck	99
4-Amine-1,5-dimethyl-2-phenyl-3-pyrazolin-5-one	Fluka	98
2-Amino-5-nitro pyridine	BDH	99
p-Aminobenzenesulphone amide	Merck	99
4,4´-Diaminodiphyenyl sulphone	Fluka	99
1,2-Diaminoethane di hydrochloride	Aldrich	99
Ammonium acetate	Romil	>98
5-Nitro-2-furaldehyde	Aldrich	99
Iodine	BDH	99.9

Acetyl chloride	CDH	98
Phosphorousoxychloride	CDH	98
Di phosphoruspentasulphide	Merck specification	98
Hydroxylammonium chloride	Merck	99
Ammonium hydroxide solution	Aldrich	28%

2.2. Identification and Instruments:

The following measurements were used to characterise the synthesised organic compounds.

2.2.1. Thin layer chromatography (TLC)

The (TLC) was performed, using alumina plates coated with (0.25mm) layer of silica gel F_{254} (Fluka), spots were detected by iodine vapour.

2.2.2. Melting point measurements:

Melting points were recorded by Dig melt MPA 161 (MSRS) electronic up to 300℃. And repeated by Stuart Scientific Melting point SMPL UK up to 360℃ was in corrected, at College of Education for pure science (Ibn- Al Haitham).

2.2.3. Fourier Transform Infrared Spectra (FT-IR):

Infrared spectra **(FT-IR)** were recorded using KBr discs on Shimadzu FT-IR (8300) spectrophotometer in the range (4000 – 400) cm^{-1}, at Ibn Saina State Company **(ISSC).**

2.2.4. Nuclear Magnetic Resonance (^{1}H-NMR) and (^{13}C-NMR):

These spectra were carried out by: Ultra Shield 300 MHz, Bruker, Switzerland at University of Al al-Bayt (Jordan), and are reported in ppm (δ), DMSO-d^6 was used as a solvent with TMS as an internal standard. And some of samples measured in Institute of Organic and Pharmaceutical Chemistry (IOPC), National Hellenic Research Foundation, 48 Vassileos Constantinou Ave., 11635 Athens, Greece.

2.2.5. Mass spectroscopy:

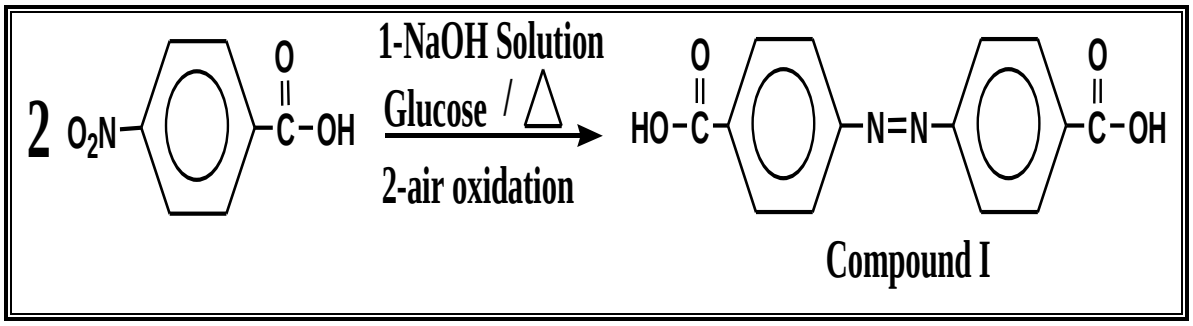
The mass spectra were determined using Varian Saturn 2000 GC-MS-MS system, electron impact (EI), chemical ionisation (CI) modes, Molecular mass range 45- 650 Dalton. Spectrometer at electron ionizing energy 70ev. The mass spectra recorded at Institute of Organic and Pharmaceutical Chemistry (IOPC) National Hellenic Research Foundation, 48 Vassileos Constantinou Ave., 11635 Athens, Greece.

2.2.6. Element microanalysis:

Elemental microanalyses were recorded by microanalysis (C.H.N) analyser, Euro vector EA 3000A at Al-Bayt University, Jordan.

2.3. Synthesis of azobenzen-p,p'-dicarboxylic acid [I]:[153-154]

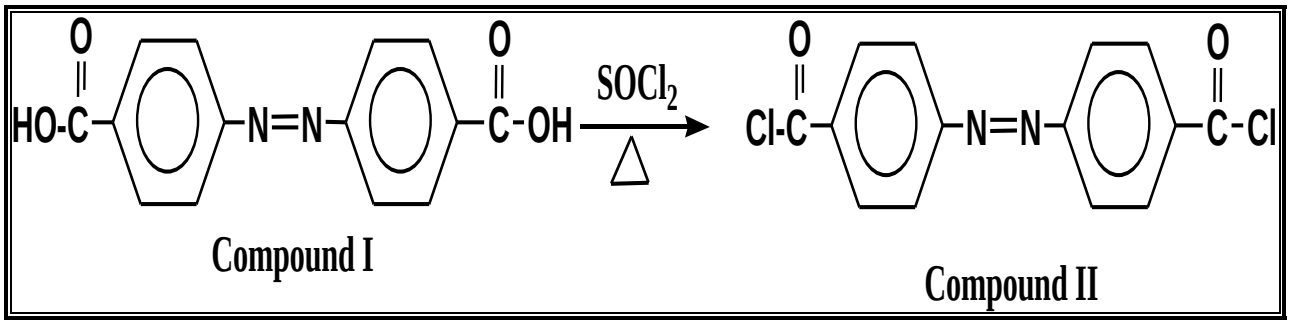
Compound [I] was obtained by reductive-condensation of P-nitrobenzoic acid with itself under the effect of reducing agents like glucose, then upon air oxidation give azobenzen-p,p'-dicarboxylic acid, yield: 70%, m.p.302℃, lit. > 300℃.



Equation (2-1): Synthesis of compound [I]

2.4. Synthesis of azobenzen-p,p'-diacid chloride [II]:

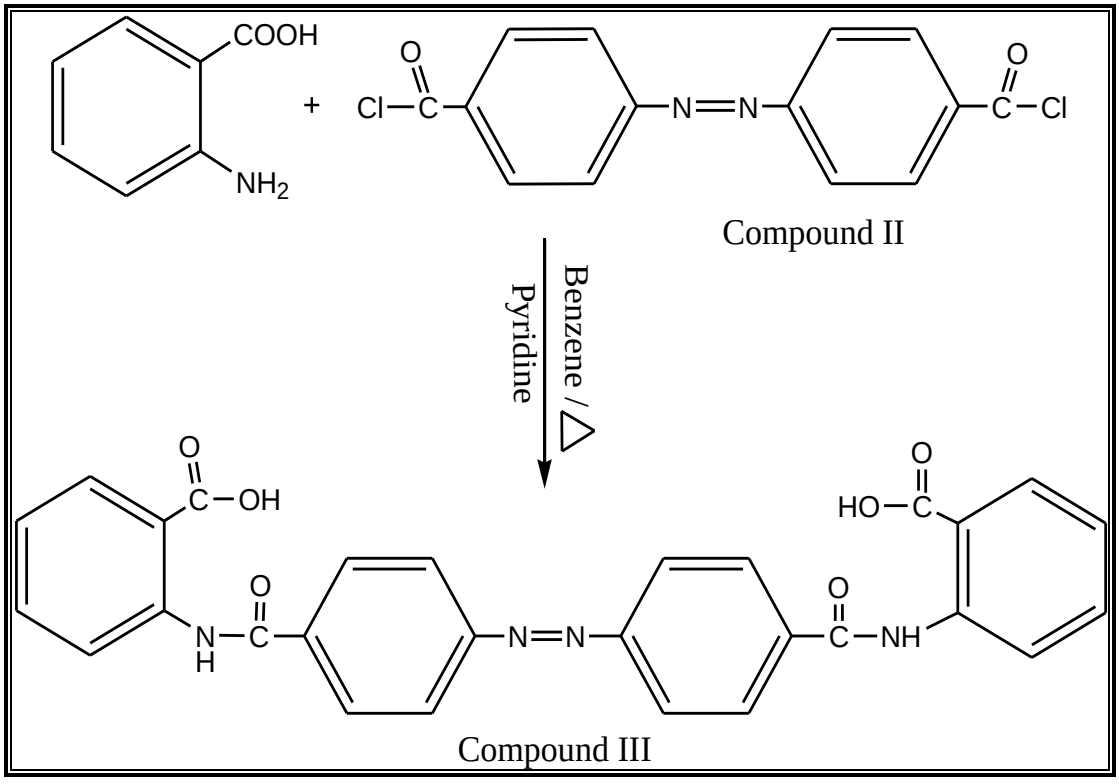
A mixture of azobenzen-p,p'-dicarboxylic acid (0.27gm, 0.001mol), excess of thionyl chloride (10ml), and dry pyridine (3ml), was refluxed for 2hrs. The reaction mixture was extracted several times with n-hexane, and then rotary evaporated. Resulted residue was washed with dry diethyl ether, recrystallized from petroleum ether to give compound [II]. 0.28gm, yield 91.2%, m.p.154℃.



Equation (2-2): Synthesis of compound [II]

2.5. Synthesis of azobenzen-p,p'-[(dibenzoic acid-2-yl)di carboxamide] [III]:

To a clear stirred solution of azobenzen-p,p'-diacid chloride (0.307gm, 0.001mol) in dry benzene (50ml) containing dry pyridine (5ml), anthranilic acid (0.274gm, 0.002mol) was added. Reaction mixture was stirred for further 5hrs, until completion of reaction which was monitored by TLC, using ethyl acetate : ethanol [2:3] eluent. A precipitate was formed, filtered, washed with distilled water, recrystallized from benzene, to give compound [III]. 0.4gm, yield 80.7%, m.p. 288-290°C.



Equation (2-3): Synthesis of compound [III]

2.6. Synthesis of azobenzen-p,p'-di[3,1-benzoxazine-4-one-2-yl] [IV]:

This compound [IV] was synthesized by two methods:

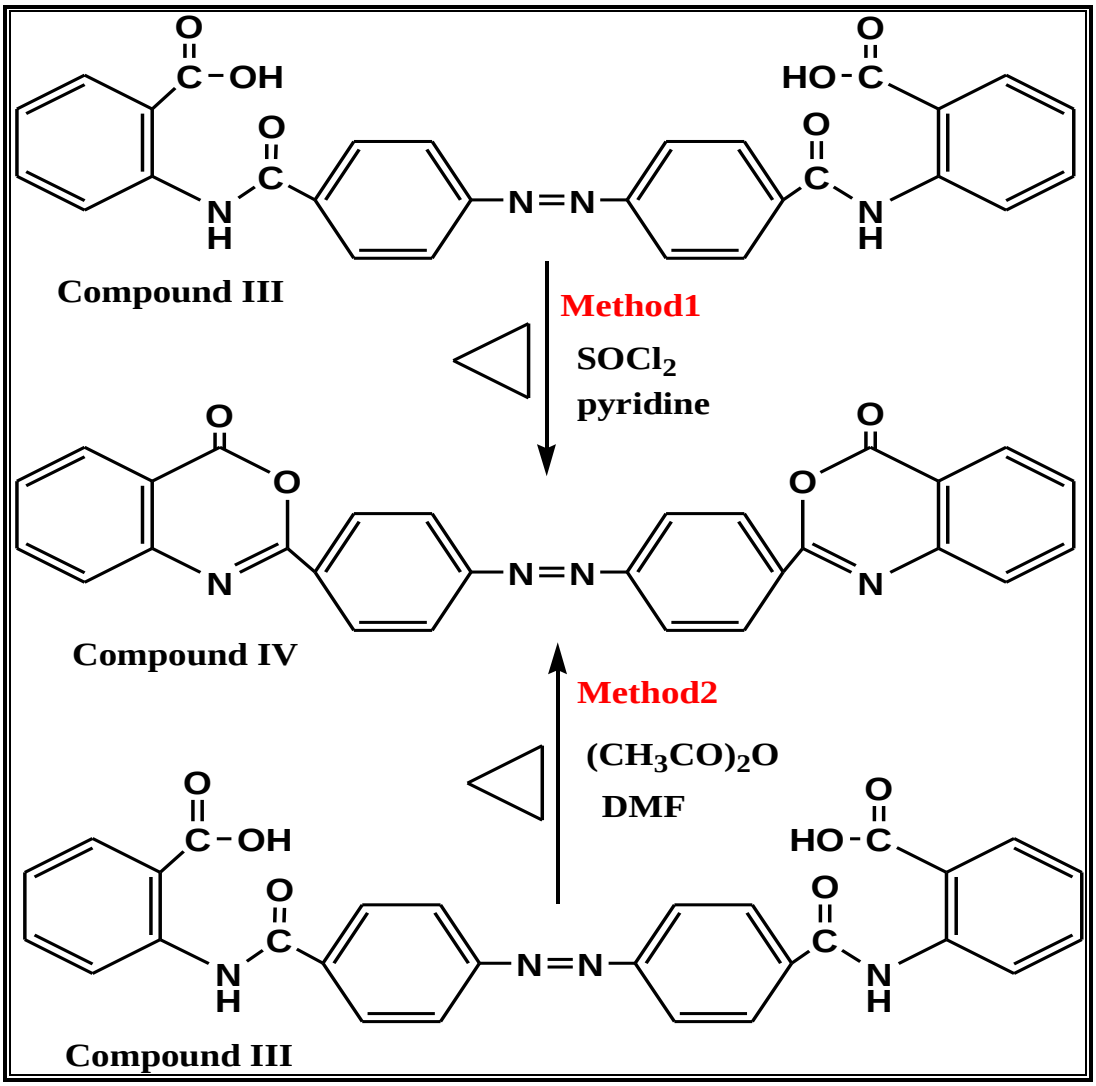
- **Method- A:**

To a clear solution of azobenzen-p,p'-[(dibenzoic acid-2-yl)dicarboxamide] (0.508 gm, 0.001 mol) in DMF (25ml), containing dry pyridine (5ml), excess of acetic anhydride (7ml) was added. Reaction mixture was refluxed for 6hrs, until completion of reaction which was monitored by TLC, using ethyl acetate : ethanol [2:3] eluent. A solid began to formed. Reaction mixture was cooled, filtered and precipitate was washed with chloroform, recrystallized from DMF, to give compound [IV], 0.42gm; yield 89%, m.p. 320 °C.

- **Method- B:**

To a clear solution of azobenzen-p,p'-[(dibenzoic acid-2-yl)dicarboxamide] (0.508gm, 0.001mol), in excess of thionyl chloride (10ml), dry pyridine (5ml), was added. Reaction mixture was stirred under reflux for 2hrs, until completion of reaction which was monitored by TLC, using ethyl acetate : ethanol [2:3] eluent. A solid was formed. Reaction mixture was cooled, filtered and precipitate was washed with dry diethyl ether, recrystallized from DMF, to give compound [IV]. 0.4gm, yield 84.74%, m.p. 320℃.

Undepressed melting point upon mixing equals quantities of products for both methods.

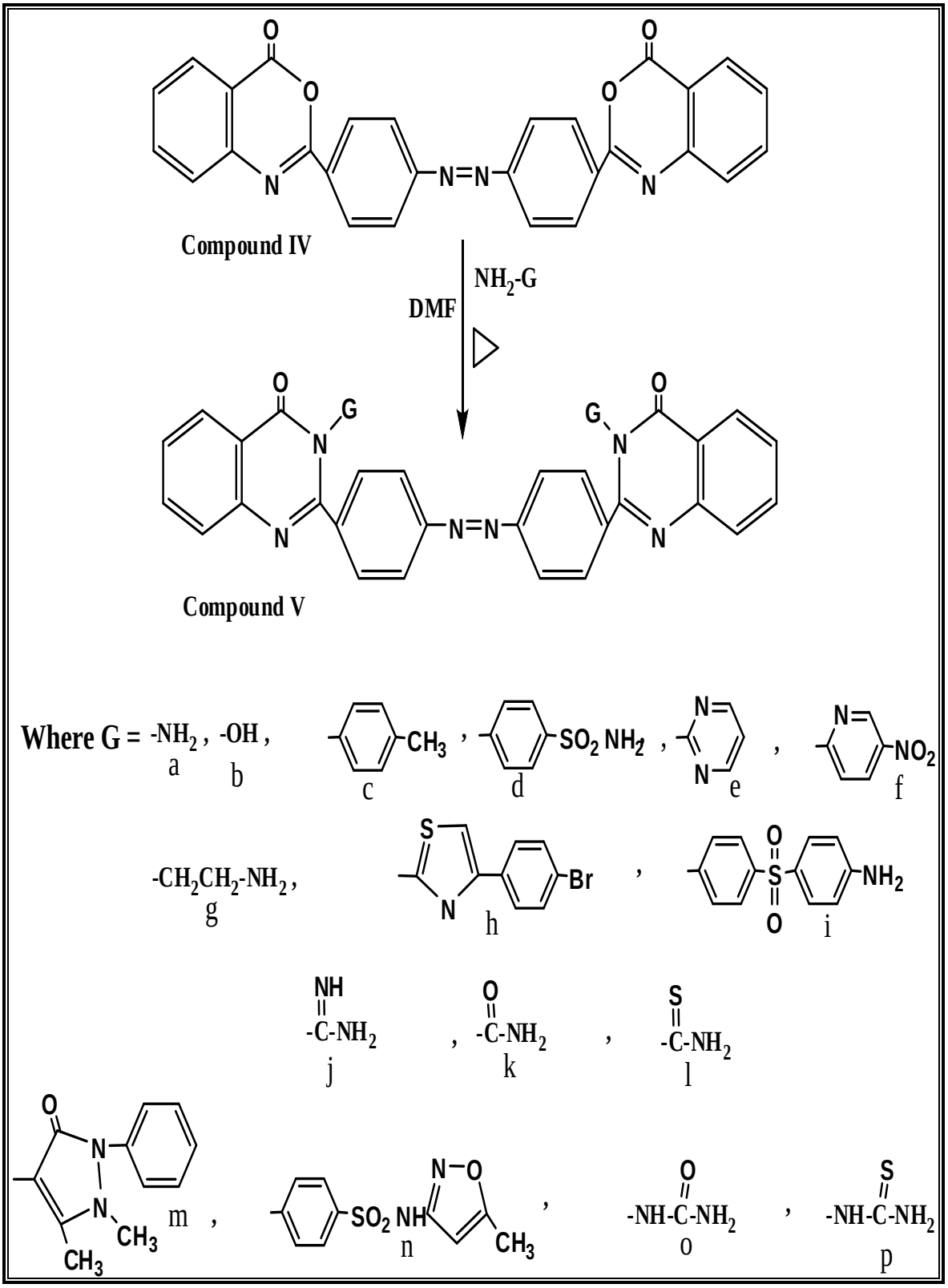


Scheme (2-4): Synthesis of compound [IV].

- **Series One.**

2.7. Syntheses of azobenzen-p,p'-di[3-substituted-4(3H)quinazolinone-2-yl] [Va-Vp]:

A mixture of azobenzen-p,p'-di[3,1-benzoxazine-4-one-2-yl] (0.472gm: 0.001 mol), and amino-moieties compounds, like hydrazine hydrate, hydroxylamine hydrochloride, quinidine hydrochloride, urea, thiourea, semicarbazide, thiosemicarbazide, aromatic, hetro-aromatic or aliphatic amines (0.002 mol), as mentioned in table (2-2) in DMF (25ml), which was heated under refluxed for a time, as mentioned in table (2-2), until completion of reactions which was monitored by TLC using petroleum ether : ethyl acetate [3:2] eluent. Separated solid, was filtered and purified by crystallization from DMF or DMSO solvents, which was mentioned in table (2-3) to give azobenzen-p,p'-di[3-substituted-4(3H)-quinazolinone-2-yl] [Va-Vp] derivatives, Table (2-3).

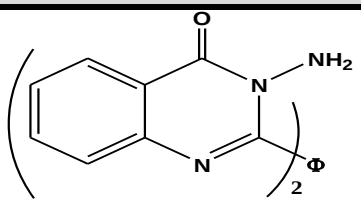
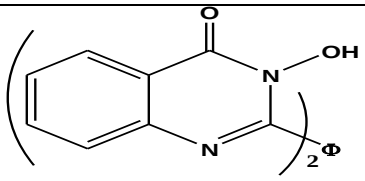
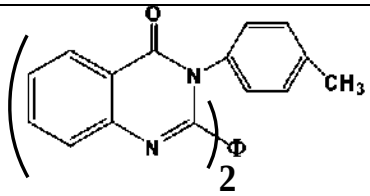
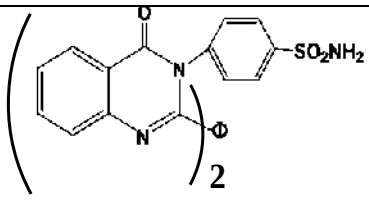
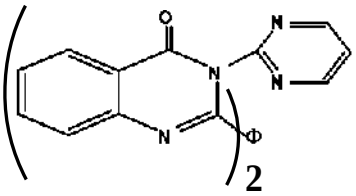


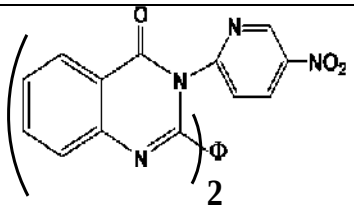
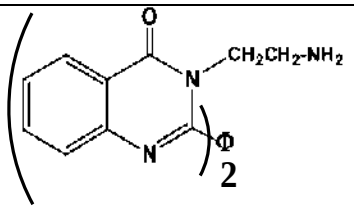
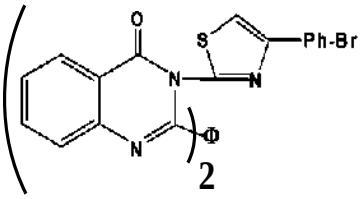
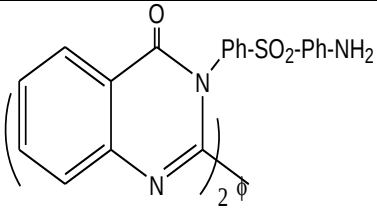
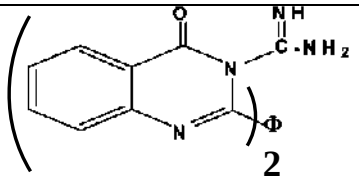
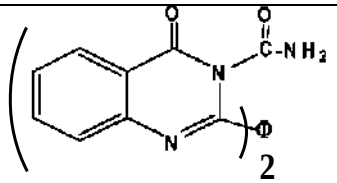
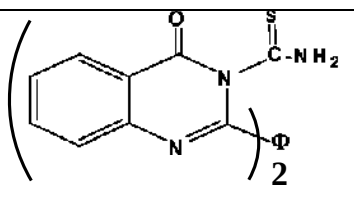
Scheme (2-5): Syntheses of azobenzen-p,p'-di[3-substituted-4(3H)-quinazolinone-2-yl] derivatives [Va-Vp].

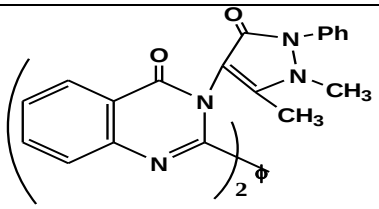
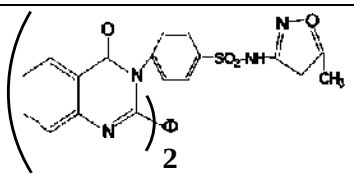
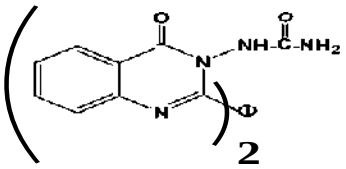
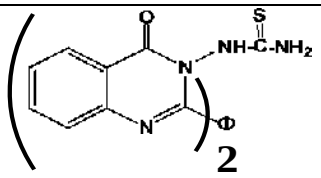
Table (2-2) : Details of using, amino-moieties compounds, aromatic, weight and refluxing time, for syntheses of azobenzen-p,p'-di[3-substituted-4(3H)-quinazolinone-2-yl] derivatives [Va-Vp]

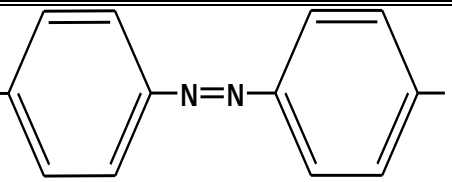
No.	Amino – moieties compounds	Wt.	Reflexed time
1	Hydrazine hydrate	0.12 ml	8hrs
2	Hydroxylammonium chloride	0.69 gm	6hrs
3	p-toluidine	0.214 gm	7hrs
4	p-Aminobenzenesulphoneamide	0.344 gm	8hrs
5	2-aminopyrimidine	0.166 gm	6hrs
6	2-amino-5-nitropyridine	0.278 gm	8hrs
7	1,2-diaminoethanedihydrochloride	0.266 gm	6hrs
8	2-Amino-5(p-bromo)phenyl-1,3-thiazole	0.51 gm	7hrs
9	4,4´-diaminodiphenylsulphone	0.496 gm	8hrs
10	Quinidine hydrochloride	0.118gm	5hrs
11	Urea	0.12 gm	5hrs
12	Thiourea	0.152 gm	5hrs
13	4-amin-1,5-dimethyl-2-phenyl-3-pyrazolin-5-one(amino antipyrine)	0.406 gm	10hrs
14	4-amino-N(5-methyl-3-isoxaly)benzenesulphonamide	0.482 gm	10hrs
15	Semicarbazide	0.15 gm	8hrs
16	Thiosemicarbazide	0.182 gm	8hrs

Table (2-3) : Physical properties of synthesized azobenzen-p,p'-di[3-substituted-4(3H)-quinazolinone-2-yl] derivatives [Va-Vp]

No.	Name of compounds	Structure formula and Molecular formula	M.wt	Weight of product	Yield %	color	m.p ℃	Crystal solvent
Va	Azobenzen-p,p'-di[3-amino-4(3H)qunazolinone-2-yl]	 $C_{28}H_{20}N_8O_2$	500	0.53	88.33	yellow	340 - 343	DMF
Vb	Azobenzen-p,p'-di[3-hydroxy-4(3H)qunazolinone-2-yl]	 $C_{28}H_{18}N_6O_4$	502	0.4	79.68	Pale orange	272 - 273	DMF
Vc	Azobenzen-p,p'-di[3,p-touldino-4(3H)qunazolinone-2-yl]	 $C_{42}H_{30}N_6O_2$	650	0.3	46.15	pale orange	307 - 308	DMSO
Vd	Azobenzen-p,p'-di[3,p-benzenesulfoneamido-4(3H)qunazolinone-2-yl]	 $C_{40}H_{28}N_8S_2O_6$	780	0.4	51.12	light orang	210 - 212	DMF
Ve	Azobenzen-p,p'-di[3,2'-pyrimidino-4(3H)qunazolinone-2-yl]	 $C_{38}H_{22}N_{10}O_2$	626	0.48	76.67	red	190 - 192	DMF

Vf	Azobenzen-p,p'-di[3,5'-nitro-2'-pyridin-2'yl-4(3H)qunazolinone-2-yl]	 $C_{36}H_{22}N_{10}O_6$	714	0.44	61.62	orang	288 - 290	DMF
Vg	Azobenzen-p,p'-di[3,2'-ethylamino-4(3H)qunazolinone-2-yl]	 $C_{32}H_{28}N_8O_2$	556	0.45	80.93	yellow	333 - 335	DMSO
Vh	Azobenzene-p,p'-di[3,4'-p-bromophenyl-2'-(1',3'-thiozolyl)-4(3H)qunazolinone-2-yl]	 $C_{46}H_{28}N_8S_2O_2Br_2$	859	0.42	48.89	orang	170 - 171	DMSO
Vi	Azobenzen-p,p'-di[3(p,4'-aminodiphenylsulfone)-4(3H)-qunazolinone-2yl]	 $C_{52}H_{36}N_8O_6$	868	0.45	51.84	grey	185 - 187	DMSO
Vj	Azobenzen-p,p'-di[3-imidino-4(3H)qunazolinone-2-yl]	 $C_{30}H_{22}N_{10}O_2$	554	0.47	84.83	yellow	350 - 351	DMF
Vk	Azobenzen-p,p'-di[3-carbomido-4(3H)qunazolinone-2-yl]	 $C_{30}H_{20}N_8O_4$	556	0.43	77.33	orang	253 - 255	DMF
Vl	Azobenzen-p,p'-di[3-thiocarbomido-4(3H)qunazolinone-2-yl]	 $C_{30}H_{20}N_8S_2O_2$	588	0.42	71.42	grey	280 - 283	DMF

Vm	Azobenzen-p,p'-di[3-(1',5'-dimetyl-2´-phenyl-3'-pyrazolinone)-4(3H)-qunazolinone-2-yl]	 $C_{50}H_{40}N_{10}O_4$	820	0.38	46.34	orang	302 - 305	DMF
Vn	Azobenzen-p,p'-di[3-(5'-methyl-3'-isoxazolyl)benzenesulfoneamido-4(3H)qunazolinone-2-yl]	 $C_{48}H_{36}N_{10}S_2O_8$	946	0.41	43.34	yellow	311 - 313	DMF
Vo	Azobenzen-p,p'-di[3,N-ureido-4(3H)quinazolinone-2-yl]	 $C_{30}H_{22}N_{10}O_4$	566	0.4	71	Yellow	220 - 222	DMF
Vp	Azobenzen-p,p'-di[3,N-thioureido-4(3H)quinazolinone-2-yl]	 $C_{30}H_{22}N_{10}S_2O_2$	598	0.4	69	brown	240 - 241	DMSO

Where ϕ = 

- **Series Two:**

2.8. Syntheses of azobenzen-p,p'-di[3,N-substituted-4(3H)quinazolinone-2-yl]

2.8.1. Synthesis of azobenzen-p,p'-di[3-ureido-4(3H)quinazolinone-2-yl][Vo] :

This compound was synthesized by method - 1, as well as to method - 2.

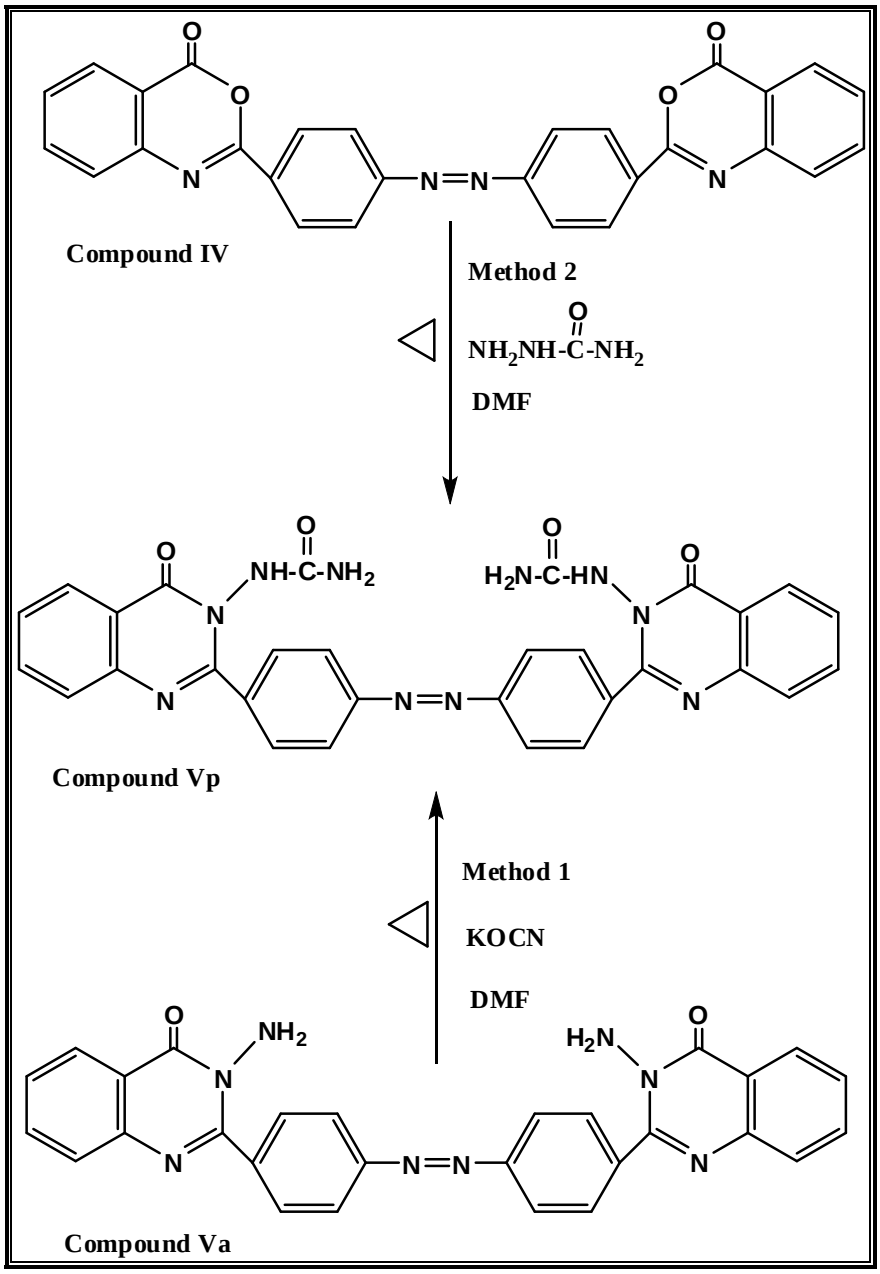
- **Method – 1:**

To a stirred solution of azobenzen-p,p'-di[3-amino-4(3H)quinazolinone-2-yl] [Va] (0.5gm, 0.001mol), in DMF (20ml), glacial aceticacid (5ml), a solution of potassium cyanate (1.64gm, 0.002mol), in distilled water (5ml), was added slowly. Reaction mixture was stirred for 10hrs, until completion reaction mixture which was monitored by TLC using [3:2] petroleum ether : ethyl acetate eluent. Precipitate was formed, filtered and washed with distilled water, recrystallized from DMF. To give compound [Vo]. 0.4gm, yield; 71%, m.p. 220-222℃.

- **Method – 2:**

Compound [Vo] was prepared by condensation of azobenzen-p,p'-di[(3,1-benzoaxzin-4-one)-2yl] [IV], with semicarbazide in DMF. (c.f. page 51).

Undepressed melting point, upon mixing equal quantities of products for both methods.



Scheme (2-6): Synthesis of compound [Vo].

2.8.2. Synthesis of azobenzen-p,p'-di[3,N-thioureido-4(3H)-quinazolinone-2-yl] [Vp] :

This compound was synthesized by method- 1, as well as to method- 2.

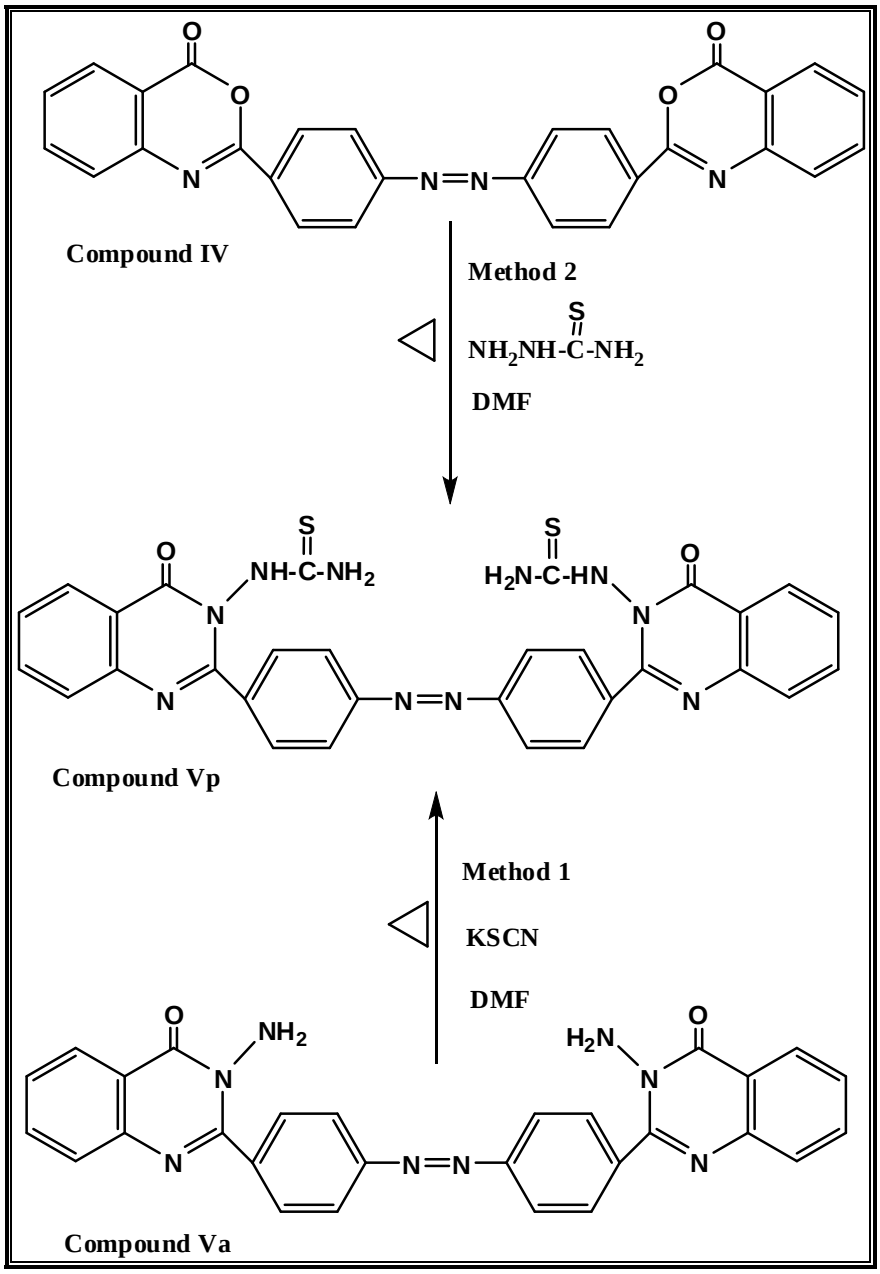
- **Method – 1:**

To a stirred solution of azobenzen-p,p'-di[3-amino-4(3H)quinazolinone-2-yl] [Va] (0.5gm, 0.001mol), in DMF (20mL), and glacial acetic acid (5mL), a solution of potassium thiocyanate (0.18gm, 0.002mol) in distilled water (5mL) was added slowly. Reaction mixture was stirred for 10hrs, until completion of reaction which was monitored by TLC using petroleum ether : ethyl acetate [3:2] eluent. Precipitate was formed, filtered and washed with distilled water, recrystallized from DMF. To give compound [Vp]. 0.4gm, yield; 69%, m.p. 240-241℃.

- **Method – 2:**

Compound [Vp] was prepared by condensation of azobenzen-p,p'-di[3,1-benzoaxzin-4-one-2-yl] [IV], with thiosemicarbazide in DMF. (c.f. page 51).

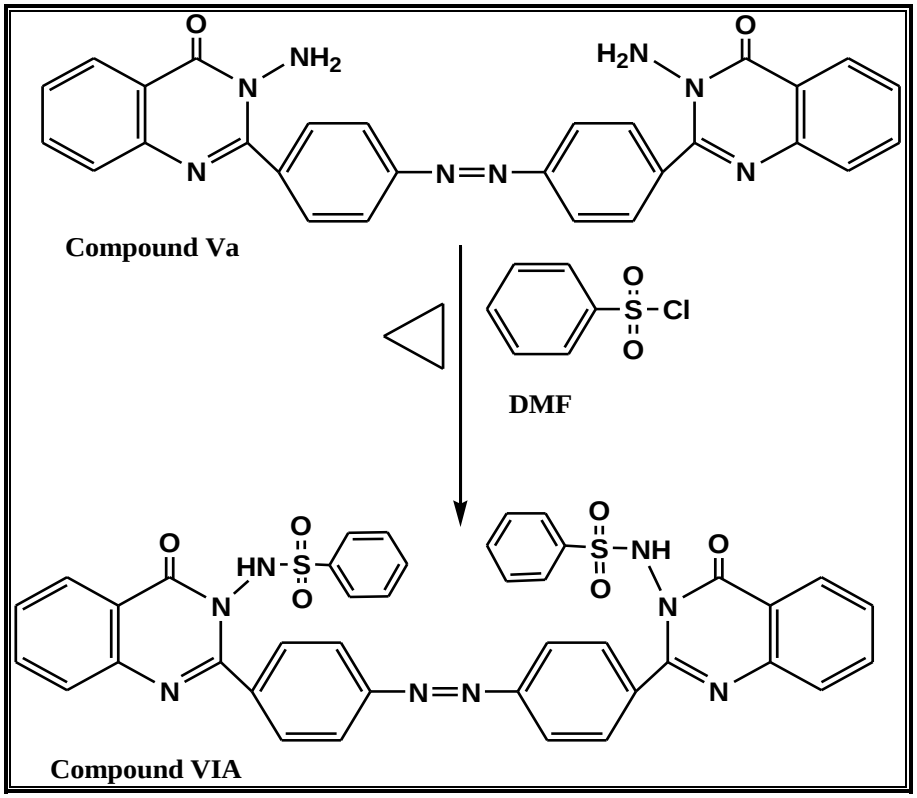
Undepressed melting point, upon mixing equal quantities of products for both methods.



Scheme (2-7): Synthesis of compound [Vp].

2.8.3. Synthesis of azobenzen-p,p'-di[3,N-benzenesulphonamido-4(3H)quinazolinone-2-yl] [VIA] :

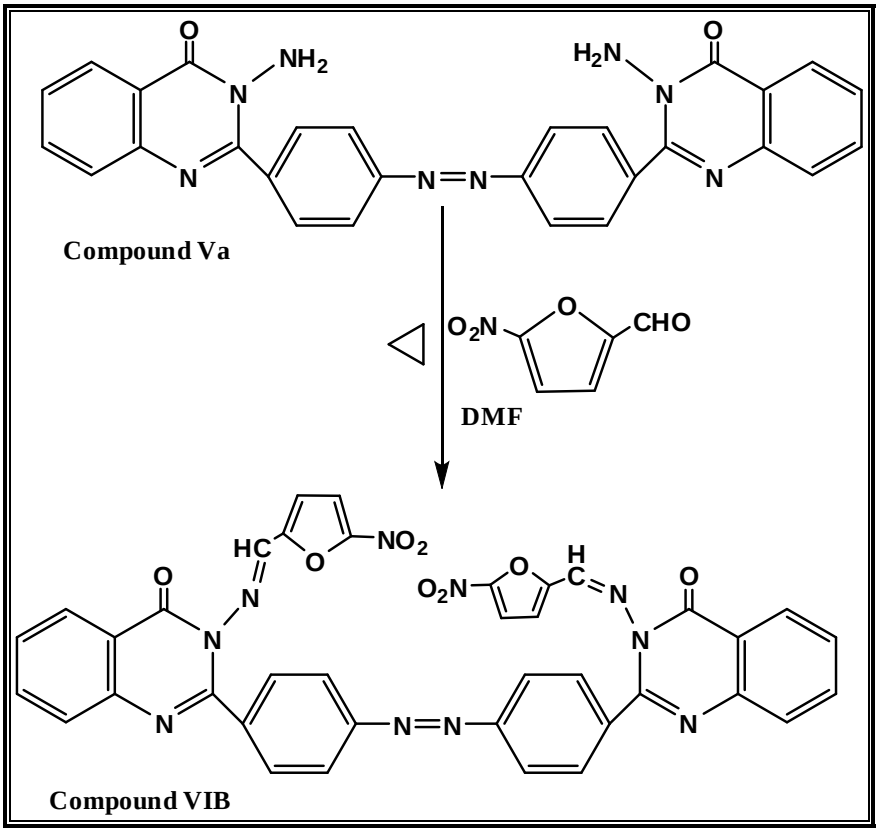
To a solution of azobenzen-p,p'-di[3-amino-4(3H)quinazolinone-2-yl] [Va] (0.5 gm, 0.001 mol), in DMF (10 mL), containing dry pyridine (3 mL), benzenesulfonyl chloride (0.2 ml, 0.002 mol), was added in small portions, reaction mixture was reflexed for 6hrs, until completion of reaction which was monitored by TLC using petroleum ether : ethyl acetate [3:2] eluent. Reaction mixture was cooled, poured slowly into stirred ice-cold water, and kept in refrigerator for 1/2h. The precipitate formed was filtered, washed with distilled water and dried. Then recrystallized from DMF, to give compound [VIA]. 0.32 gm, yield; 42 %, m.p. 301-303℃.



Equation (2-8): Synthesis of compound [VIA].

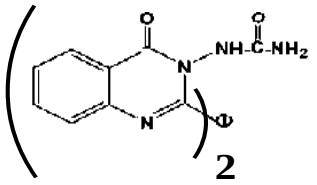
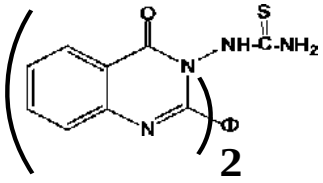
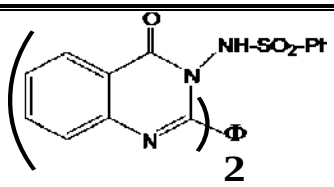
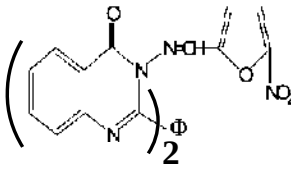
2.8.4. Synthesis of azobenzen-p,p'-di[3,N-imino-5´-nitrofurfurylidino-2'-yl-4(3H)-quinazolinone-2-yl] [VIB] :

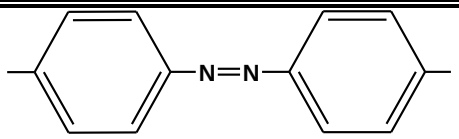
To a stirred solution of azobenzen-p,p'-di[3-amino-4(3H)quinazolinone-2-yl] [Va] (0.5gm, 0.001mol), in DMF (20mL), glacial acetic acid (3drops). A solution of 5-nitro-2-furaldehyde (0.274 gm, 0.002 mol) in ethanol (10mL), was added slowly. Reaction mixture was stirred for 8hrs, until completion of reaction which was monitored by TLC using petroleum ether : ethyl acetate [3:2] eluent. Precipitate was formed, filtered and washed with distilled water, recrystallized from DMSO, to give compound [VIB]. 0.38 gm, yield; 52 %, m.p. 211-213℃.



Equation (2-9): Synthesis of compound [VIB].

Table (2-4) : Physical properties of azobenzen-p,p'-di[3-N-substituted-4(3H)-quinazolinone-2-yl] derivatives (Vo, Vp, VIA-VIB)

No.	Name of compound	Structure formula and Molecular formula	M.wt	Wight of product	Yield %	Color	m.p ℃	Crystal solvent
Vo	Azobenzen-p,p'-di[3,N-ureido-4(3H)quinazolinone-2-yl]	 $C_{30}H_{22}N_{10}O_4$	566	0.33	50	yellow	220-222	DMF
Vp	Azobenzen-p,p'-di[3,N-thioureido-4(3H)quinazolinone-2-yl]	 $C_{30}H_{22}N_{10}S_2O_2$	598	0.38	63	brown	240-241	DMSO
VIA	Azobenzen-p,p'-di[3,N-benzene sulphonamido-4(3H)quinazolinone-2-yl]	 $C_{40}H_{28}N_8S_2O_6$	770	0.35	45	brown	301-303	DMSO
VIB	Azobenzen-p,p'-di[3,N-imino-5'-nitrofurfuryldino-2'yl-4(3H)quinazolinone-2-yl]	 **$C_{38}H_{22}N_{10}O_8$**	726	0.44	55	Light red	211-213	DMF

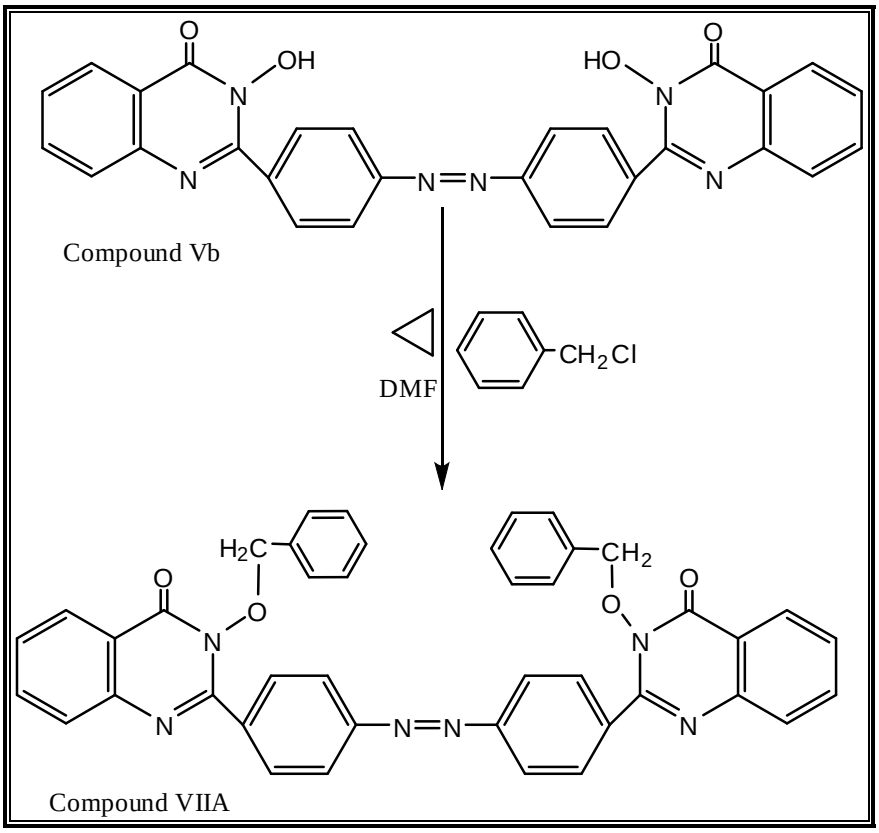
Where ϕ = 

- **Series Three:**

2.9. Syntheses of azobenzen-p,p'-di[3-O-substituted-4(3H)quinazolin-4-one-2-yl]

2.9.1. Preparation of azobenzen-p,p'-[3-benzyloxy-4(3H)-quinazolinone-2-yl] [VIIA]:

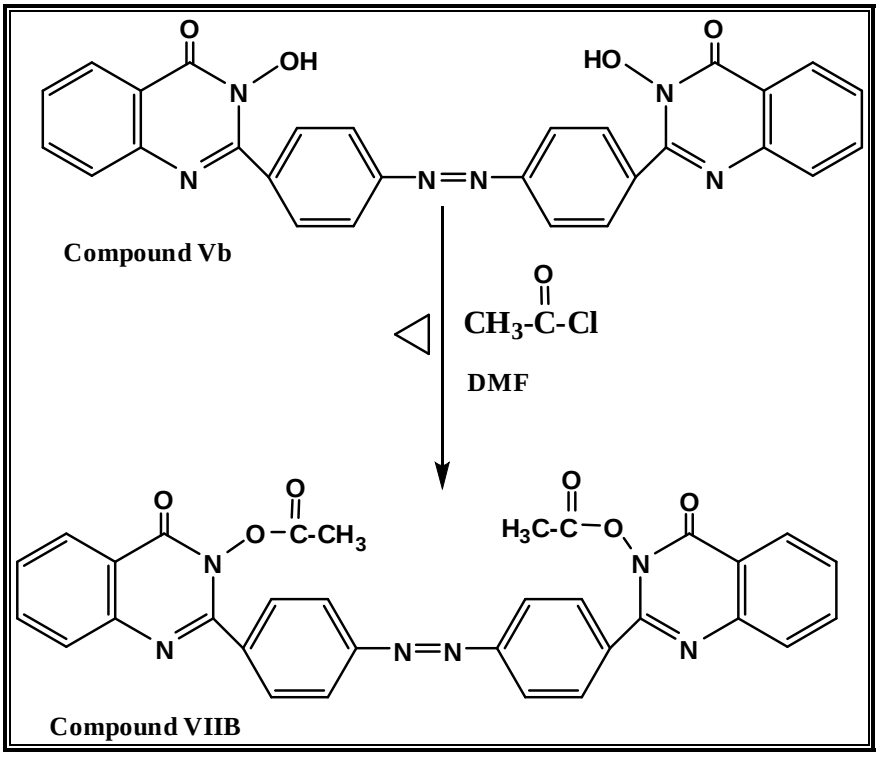
To a solution of azobenzen-p,p'-[3-hydroxy-4(3H)-quinazolinone-2-yl] [Vb] (0.5gm, 0.001mol), in DMF (20mL), freshly distilled benzyl chloride (0.25ml, 0.002mol), and sodium hydroxide (0.1gm), were added was added . Reaction mixture was refluxed for 6hrs, until completion of reaction which was monitored by TLC using petroleum ether : ethyl acetate [3:2] eluent. Precipitate was formed, filtered and washed with distilled water, recrystallized from DMF, to give compound [VIIA]. 0.38gm, yield; 55.71%, m.p. 249-251℃.



Equation (2-10): Synthesis of compound [VIIA].

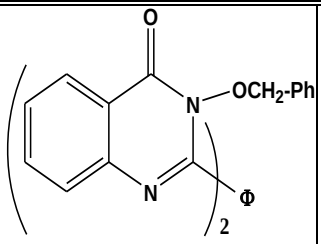
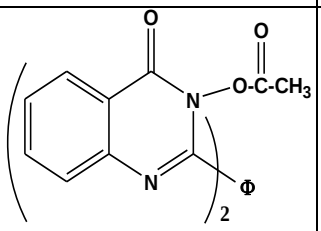
2.9.2. Synthesis of azobenzen-p,p'-[3,O-acetoxy-4(3H)-quinazolinone-2-yl] [VIIB]:

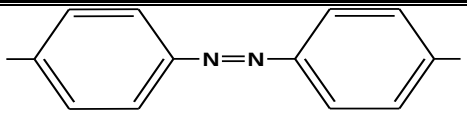
To a solution of azobenzen-p,p'-[3-hydroxy-4(3H)-quinazolinone-2-yl] [Vb] (0.5 gm, 0.001 mol), in DMF (20mL), freshly distilled Acetyl chloride (1.56mL, 0.002mol), and sodium hydroxide (0.1gm), were added. Reaction mixture was refluxed for 3hrs, until completion of reaction which was monitored by TLC using petroleum ether :ethyl acetate [3:2] eluent. Precipitate was formed, filtered and washed with distilled water, recrystallized from DMF, to give compound [VIIB]. 0.41gm, yield; 60%, m.p. 218-220℃.



Equation (2-11) : Synthesis of compound [VIIB].

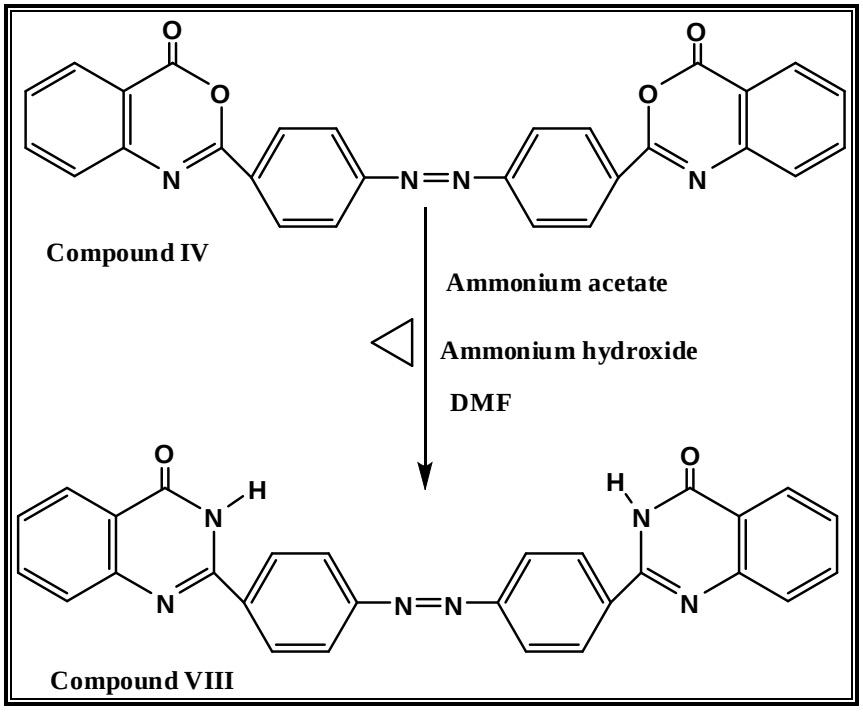
Table (2.5): Physical properties of azobenzen-p,p'-di[3-O-substituted-4(3H)-quinazolinone-2-yl] derivatives (Series Three)

No.	Name of compound	Structure formula and molecular formula	M.wt	Wight of product	Yield %	Color	m.p℃	Solvent crystal
VIIA	Azobenzen-p,p'-[3,O-benzyloxy-4(3H)-quinazolinone-2-yl]	 **$C_{42}H_{30}N_6O_4$**	682	0.38	55.7	brown	249-251	DMF
VIIB	Azobenzen-p,p'-[3,O-acetoxy-4(3H)-quinazolinone-2-yl]	 **$C_{32}H_{22}N_6O_6$**	634	0.41	60	yellow	218-220	DMF

Where ϕ = 

2.10. Synthesis of azobenzen-p,p'-di[3-hyrdo-4-quinazolinone-2-yl] [VIII]:

A mixture azobenzen-p,p'-di[3,1-benzoxazine-4-one-2-yl] (0.472 gm, 0.001 mol) in DMF (20ml), ammonium acetate (0.154 gm, 0.002 mol), ammonium hydroxide (28%), (4mL) and 10% sodium hydroxide (5mL), pyridine (15 mL), was heated under reflux for 8hrs, until completion of reaction which was monitored by TLC using petroleum ether : ethyl acetate [3:2] eluent, and then left to cold. The reaction mixture was then triturated with cold distilled water (100 mL), and neutralized with 1N HCl (5 mL), resulting precipitate was collected by filtration, washed with water, dried and recrystallized from DMF, to give compound [VIII]. 0.36 gm, yield; 76%, m.p. 190-192℃.



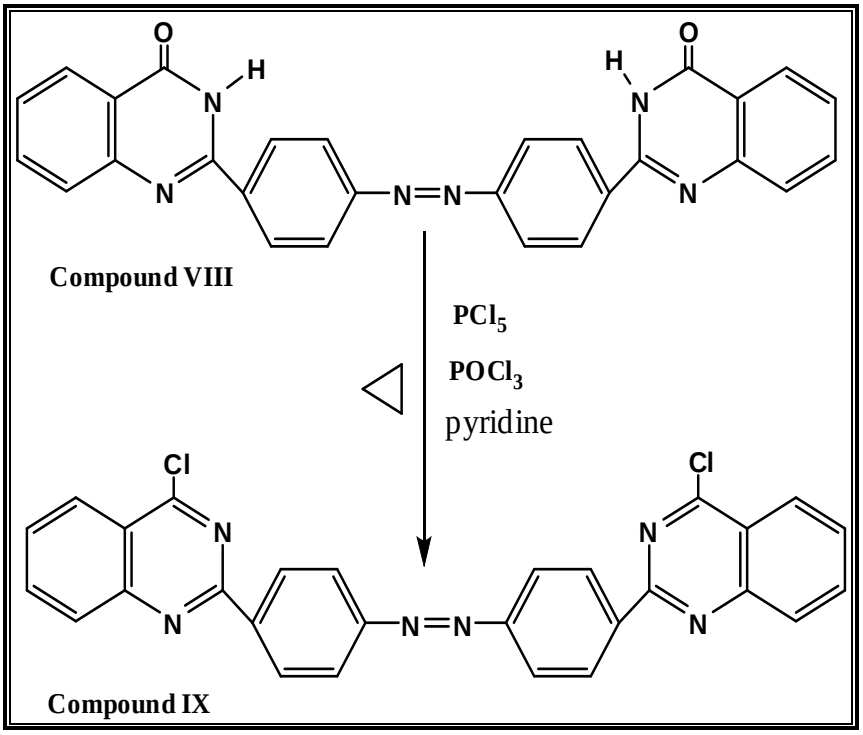
Equation (2-12): Synthesis of compound [VIII].

- **Series Four:**

2.11. Synthesis of azobenzen-p,p'-di[4-substituted-quinazoline-2-yl]

2.11.1. Synthesis of azobenzen-p,p'-di[4-chloro-quinazoline-2-yl] [IX]:

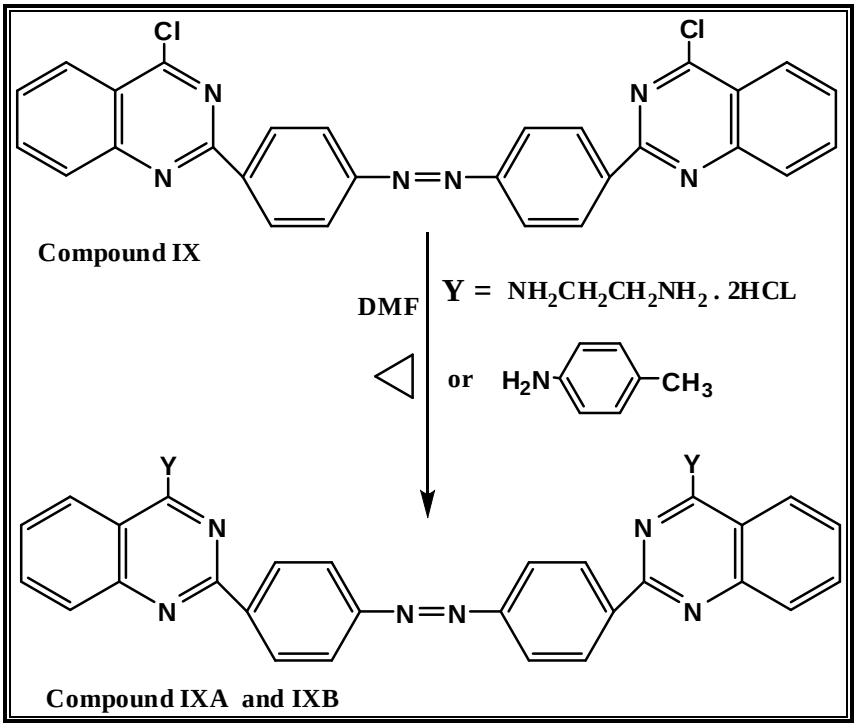
A mixture of azobenzen-p,p'-di[3-hydro-4H-quinazolinone-2-yl] [VIII] (0.47gm, 0.001mol), phosphorouspenta chloride (0.416gm, 0.002mol), phosphorousoxy chloride (20mL), containing dry pyridine (5mL), was heated on a water bath for 6hrs, until completion of reaction which was monitored by TLC using petroleum ether : ethyl acetate [3:2] eluent. Reaction mixture was poured gradually on crashed ice. The separated solid was filtered off, dried then recrystallized from DMF to give compound [IX]. 0.35gm, yield; 69%, m.p. 236℃.



Equation (2-13): Synthesis of compound [IX].

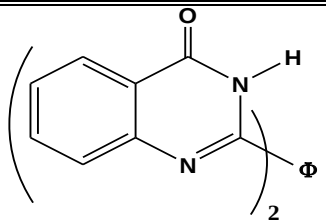
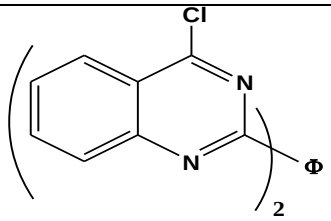
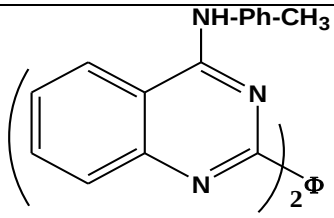
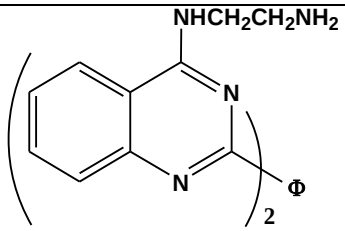
2.11.2. Synthesis of azobenzen-p,p'-di[4,N-subsitituted-quinazolin-2-yl] [IXA and IXB]:

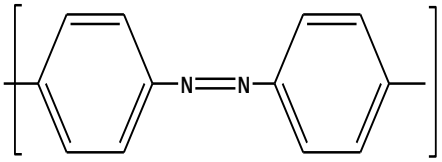
A mixture of azobenzen-p,p'-di[4-chloro-quinazoline-2-yl] [IX] (0.507gm,0.001mol), and amino-moieties like [p-toluidine (2.1gm) or 1,2-diaminoethanedihydrochloride (0.27gm) equivalent to (0.002mol) respectively], in DMF (20mL) was reflexed for 6hrs, until completion of reaction which was monitored by TLC using petroleum ether : ethyl acetate [3:2] eluent. Separated solid was filtered off, dried then recrystallized from DMF to give compounds [IXA and IXB] respectively. yield and m.p. are given in table (2-6).



Equation (2-14): Synthesis of compounds [IXA and IXB].

Table (2-6): Physical properties azobenzen-p,p'-di[4,N-subsitituted-quinazolin-2-yl] compounds Series Four.

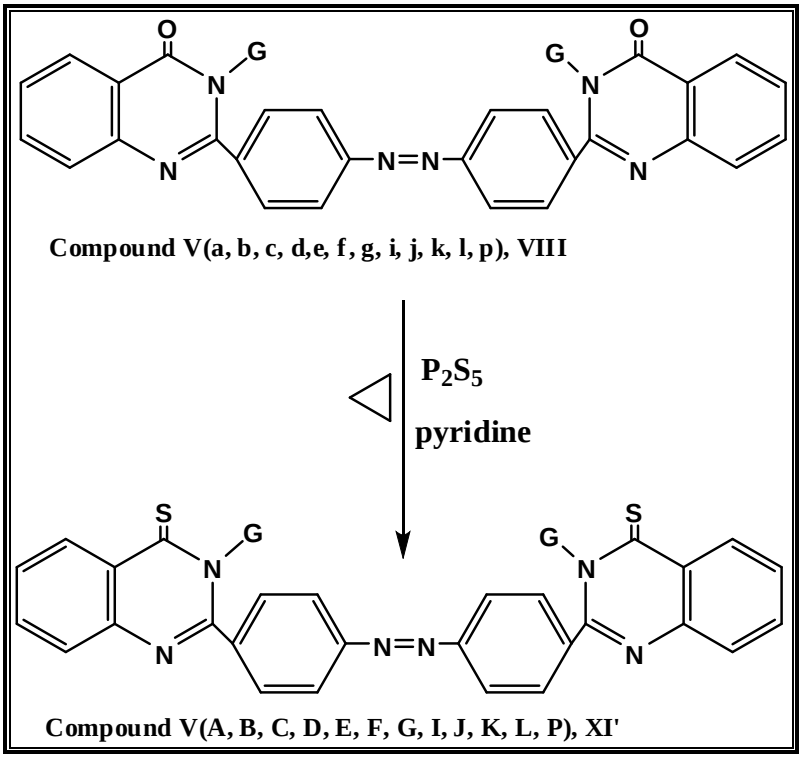
No.	Name of compound	Structure formula and molecular formula	M.wt	Wight of product	Yield %	Color	m.p ° C	Solvent crystal
VIII	Azobenzen-p,p'-di[3-hydro-4-qunazolinone-2-yl]	 $C_{28}H_{18}N_6O_2$	470	0.36	76.5	dark Yellow	190-192	DMF
IX	Azobenzen-p,p'-di[4-chloro-qunazolin-2-yl]	 $C_{28}H_{16}N_6Cl_2$	507	0.35	69.0	Pale yellow	236-237	DMSO
IXA	Azobenzen-p,p'-di[4,N-toluidino-qunazolin-2-yl]	 $C_{42}H_{32}N_8$	648	0.4	61.7	White orange	285-287	DMF
IXB	Azobenzen-p,p'-di[4-N-ethylamino-qunazolin-2-yl]	 $C_{32}H_{24}N_{10}$	548	0.38	69.4	brown	307-309	DMF

when the Φ = 

- **Series Five.**

2.12. Synthesis of azobenzen-p,p'-di[3-substituted-4(3H)-quinazolinthion-2-yl] [X(A, B, C, D, E, F, G, I, J, K, L, P) and XI']:

To a solution of azobenzen-p,p'di[3-substituted-4(3H)quinazolinone-2-yl] [V(a, b, c, d, e, f, g, i, j, k, l, p), VIII] (0.001mol), mentioned in Table (2-7), dry pyridine (20mL), Phosphorous penta sulphide (0.3gm, 0.002mol) was added. Reaction mixture was refluxed for times mentioned in Table (2-7), until completion of reaction which was monitored by TLC using petroleum ether : ethyl acetate [3:2] eluent. Solvent was evaporated under reduced pressure. Residues were poured in to an ice-cold water. Precipitate was formed, filtered, and washed with distilled water, dried and crystallized from proper solvent, as mentioned in Table (2-8), to give compounds [X(A, B, C, D, E, F, G, I, J, K, L, P), XI'].

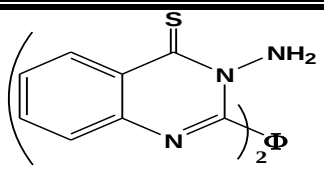
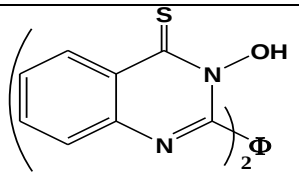
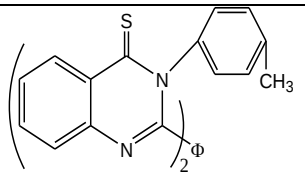
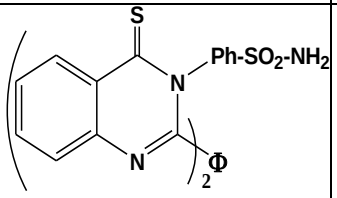
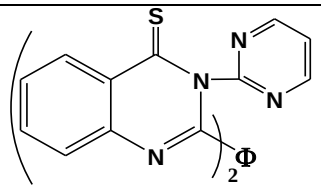
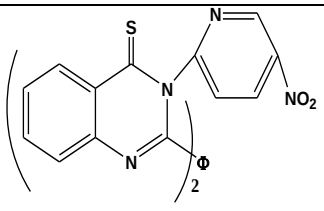


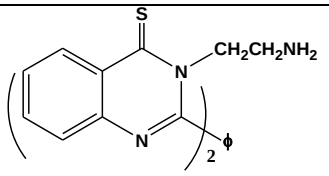
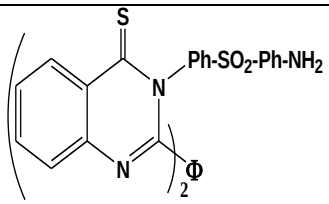
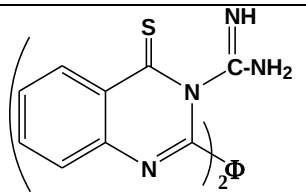
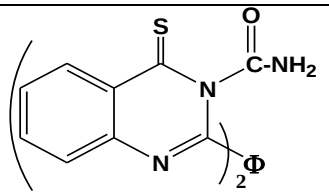
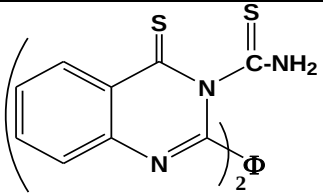
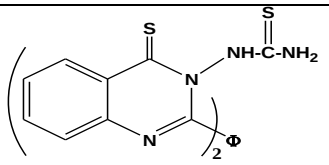
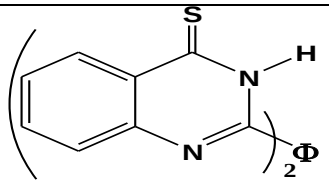
Scheme (2-15): Syntheses of compound [X(A, B, C, D, E, F, G, I, J, K, L, P), XI']

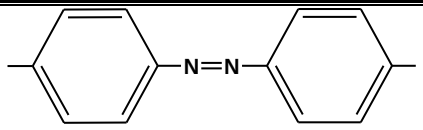
Table (2-7): Details of reaction azobenzen-p,p'di[3-substituted-4(3H)-quinazolinthione-2yl] [V(a, b, c, d, e, f, g, j, k, l, p),VIII], as a reactant weight and refluxing time with phosphorous panta chloride

No.	Azobenzen-p,p´di[3-substituted-4(3H)quinazolinone-2yl] derivatives	Equivalent to (0.001mol) azobenzen-p,p'di[3-substituted-4(3H)quinazolin-2yl] (gm)	Reflex time
Va	Azobenzene-p,p'-di[3-amino-4(3H)-qunazolinone-2-yl]	0.500	6hrs
Vb	Azobenzene-p,p'-di[3-hydroxy-4(3H)-qunazolinone-2-yl]	0.502	6hrs
Vc	Azobenzene-p,p'-di[3,p-toludino-4(3H)-qunazolinone-2-yl]	0.650	6hrs
Vd	Azobenzene-p,p'-di[3,p-benzenesulphonamido-4(3H)-qunazolinone-2-yl]	0.780	5hrs
Ve	Azobenzene-p,p'-di[3,2'-pyrimidine-4(3H)-qunazolinone-2-yl]	0.626	8hrs
Vf	Azobenzene-p,p'-di[3,5'-nitropyrimdino-2´yl-4(3H)qunazolinone-2-yl]	0.714	7hrs
VG	Azobenzen-p,p'-di[3-2'-ethylamino-4(3H)qunazolinone-2-yl]	0.556	6hrs
Vi	Azobenzene-p,p'-di[3,4'-aminodiphenylsulphone)-4(3H)-qunazolinone-2-yl]	0.868	10hrs
Vj	Azobenzene-p,p'-di[3-imidino-4(3H)-qunazolinone-2-yl]	0.554	5hrs
Vk	Azobenzene-p,p'-di[3-carbomido-4(3H)-qunazolinone-2-yl]	0.556	5hrs
Vl	Azobenzene-p,p'-di[3-thiocarbomido-4(3H)-qunazolinone-2-yl]	0.588	5hrs
Vp	Azobenzene-p,p'-di[3,N-thioureido-4H-qunazolinone-2-yl]	0.650	6hrs
VIII	Azobenzene-p,p'-di[3-hydro-4H-qunazolinone-2-yl]	0.598	7hrs

Table (2-8): Physical properties for synthesized azobenzen-p,p'-di[3-substituted-4(3H)-quinazolin-thion-2yl] [X(A, B, C, D, E, F, G, I, J, K, L, P) and XI']

No.	Name of compounds	Structure formula and molecular formula	M.wt	Wight of product	Yield %	color	m.p˚C	Crystal solvent
XA	Azobenzene-p,p'-di[3'-amino-4(3H)-qunazolin-thion-2-yl]	 **$C_{28}H_{20}N_8S_2$**	532	0.41	77.6	yellow	320-322	DMF
XB	Azobenzene-p,p´-di[3-hydroxy-4(3H)-qunazolin-thion-2-yl]	 **$C_{30}H_{22}N_{10}S_2O_2$**	534	0.36	67.4	Pale brown	210-212	DMSO
XC	Azobenzene-p,p'-di[3,p-toluidino-4(3H)-qunazolin-thion-2-yl]	 **$C_{42}H_{30}N_6S_2$**	682	0.42	61.58	white orange	340-343	DMF
XD	Azobenzene-p,p'-di[3,p-benzene sulfonamido-4(3H)qunazolinthion-2-yl]	 **$C_{40}H_{28}N_8S_4O_2$**	780	0.36	46.1	Dark brown	320-323	DMF
XE	Azobenzene-p,p'-di[3,2'-pyrmidino-4(3H)-qunazolin-thion-2-yl]	 **$C_{36}H_{22}N_{10}S_2$**	658	0.35	53.1	Light orange	255-258	DMF
XF	Azobenzene-p,p'-di[3,5'-nitro-pyrimdin-2'-yl)-4(3H)qunazolin-thion-2-yl]	 **$C_{38}H_{22}N_{10}S_2O_4$**	810	0.37	45.67	yellow	311-313	DMSO

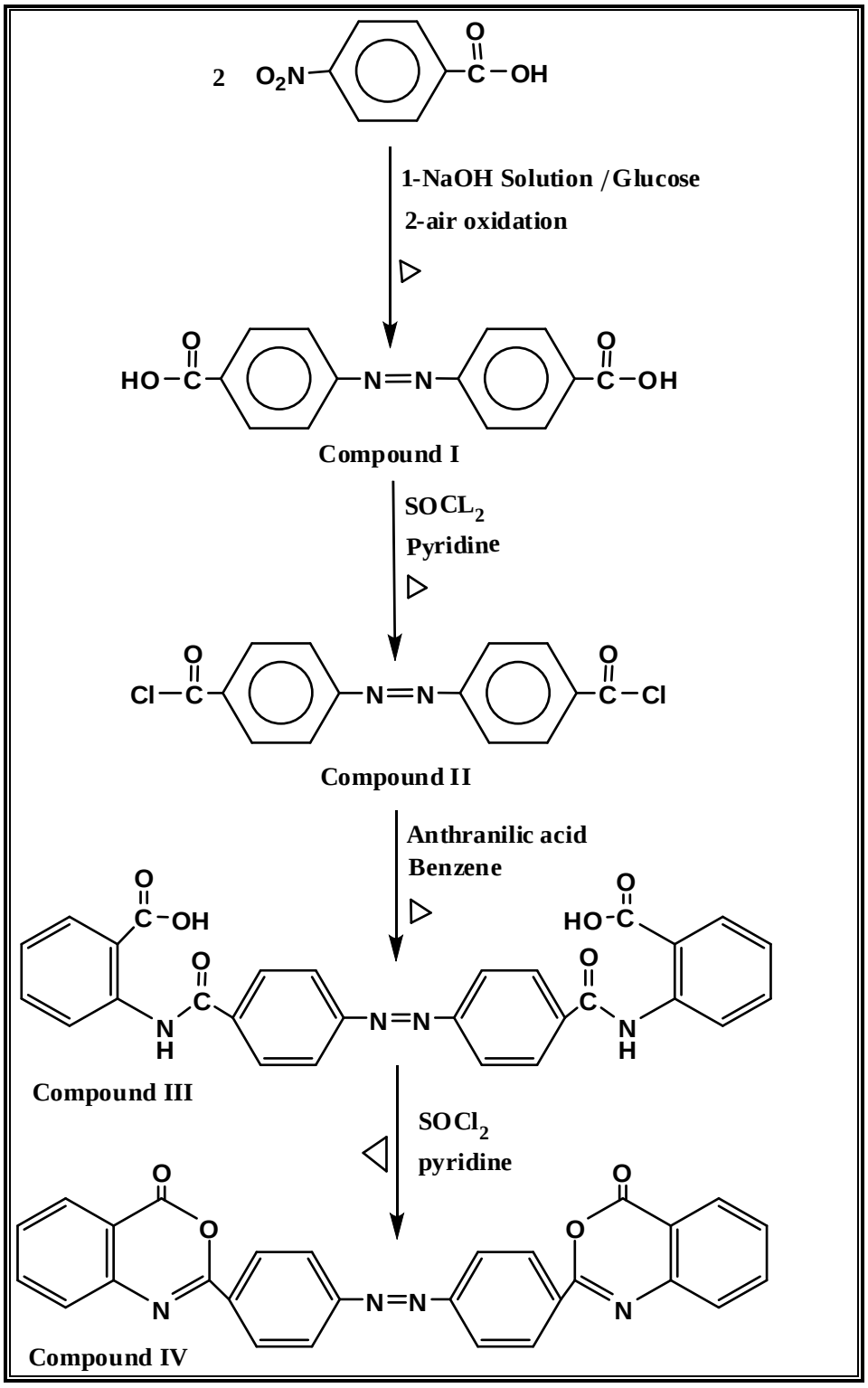
XG	Azobenzene-p,p'-di[3,2'-ethylamine-4(3H)-qunazolin-thion-2-yl]	 **$C_{32}H_{24}N_8S_2$**	582	0.4	68	red	296-297	DMF
XI	Azobenzene-p,p'-di[3,4'-aminodiphenyl sulfone-4(3H)-qunazolin-thion-2-yl]	 **$C_{52}H_{32}N_8S_4O_4$**	848	0.35	41.2	yellow	314-317	DMSO
XJ	Azobenzene-p,p'-di[3-imidino-4(3H)-qunazolin-thion-2-yl]	 **$C_{30}H_{22}N_{10}S_2$**	586	0.38	64.8	brown	237-238	DMF
XK	Azobenzene-p,p'-di[3-carbomido-4(3H)-qunazolin-thion-2-yl]	 **$C_{30}H_{20}N_8S_2O_2$**	588	0.38	64.6	Light yellow	268-270	DMF
XL	Azobenzene-p,p'-di[3,N-thio carbomido-4(3H)-qunazolin-thion-2-yl]	 **$C_{30}H_{20}N_8S_4$**	620	0.39	62.9	Pale yellow	290-291	DMF
XP	Azobenzene-p,p'-di[3,N-thiourido-(3H)-qunazolin-thion-2-yl]	 **$C_{30}H_{22}N_{10}S_4$**	650	0.36	55.38	yellow	276-277	DMF
XI'	Azobenzene-p,p'-di[3-hydro-3(4H)-qunazolin-thion-2-yl]	 **$C_{28}H_{18}N_6S_2$**	504	0.33	65.7	brown	290-293	DMSO

Where ϕ = 

Chapter Three
Results & Discussion

3. Synthesis and characterization:

In the recent years chemistry of oxazines and quinazoline and their derivatives have much considerable attention due to their effective biological importance and pharmaceutical application[155-165]. Awing to their many reasons much attention is being paid for synthesis of new quinazoline derivatives. In continuation to our interest in synthesis and antimicrobial studies, we design to synthesize of many derivatives of di(3-substituted quinazolin, and quinazolin-4-one and quinazolin-4-thion-2-yl) moiety substituted at (p,p')-position of bridged azobenzenes molecule via p,p'-(3,1-benzoxazine-4-one-2-yl) moiety substituted at (p,p')-position of bridge azobenzene molecule scheme (1), according to the following synthetic routs:-



Scheme (3-1): Main scheme of synthetic compounds

3.1. Synthesis of azobenzen-p,p'-dicarboxylic acid [I]:

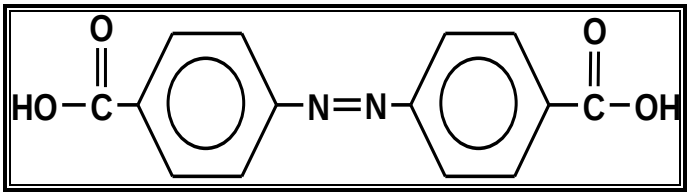
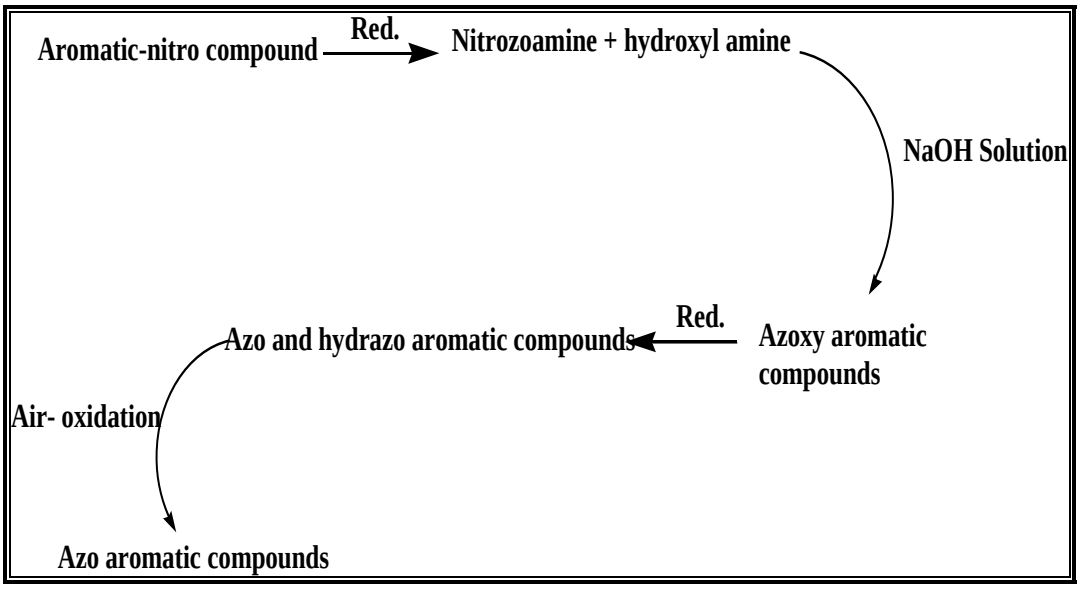


Figure (3-1): Structure of compound [I]

Azobenzen-p,p'-dicarboxylic acid [I], azobenzen-4,4'-dicarboxyic acid or 4(4'-carboxy phenyl)diaza-yl benzoic acid as IUPAC-name, was prepared by multistep reaction of nitro-aromatic compounds as in the following mechanistic-steps [166].



Scheme (3-2): Mechanism of compound [I]

Azobenzen-p,p'-dicarboxylic acid [I], was prepared in a good yield, characterized by its melting point, C.H.N- analysis, and FT-IR spectral analysis. C.H.N- analysis data formed agree with theoretical data Table (3-4). FT-IR spectrum[167], of compound [I] fig (3-1), showed (OH) stretching vibration of carbonyl group as a broad band at (3437-2544 cm^{-1}) and (C=O) stretching vibration at 1693 cm^{-1}, (N=N) azo group stretching vibration at 1575 cm^{-1}, beside to (CH) stretching vibration of aromatic rings at 3088 cm^{-1}. All these data are given in Table (3-1).

3.2. Synthesis of azobenzen-p,p'-diacidchloride [II]:

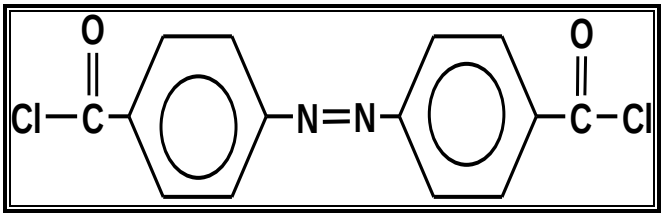
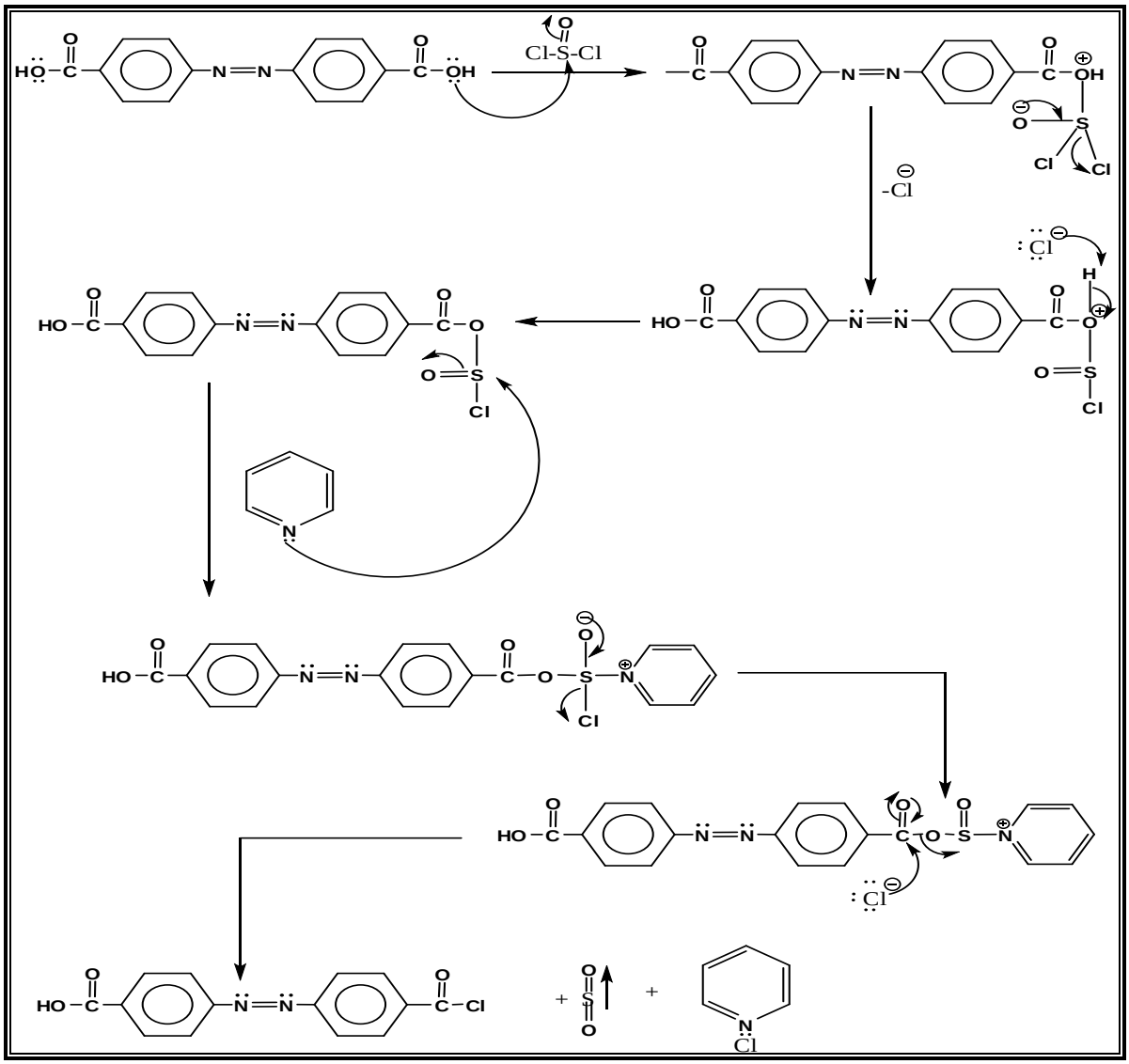


Figure (3-2): Structure of compound [II]

Treatment of compound [I], with excess of thionyl chloride in presence of pyridine, give good yield of compound [II], according to the following mechanistic-steps [168].



Scheme (3-3) : Mechanism of formation azobenzen-p,p'-diacidchloride [II]

Compound [II] was characterized by C.H.N- analysis, FT-IR, ^{1}H-NMR, ^{13}C-NMR and mass spectral analysis.

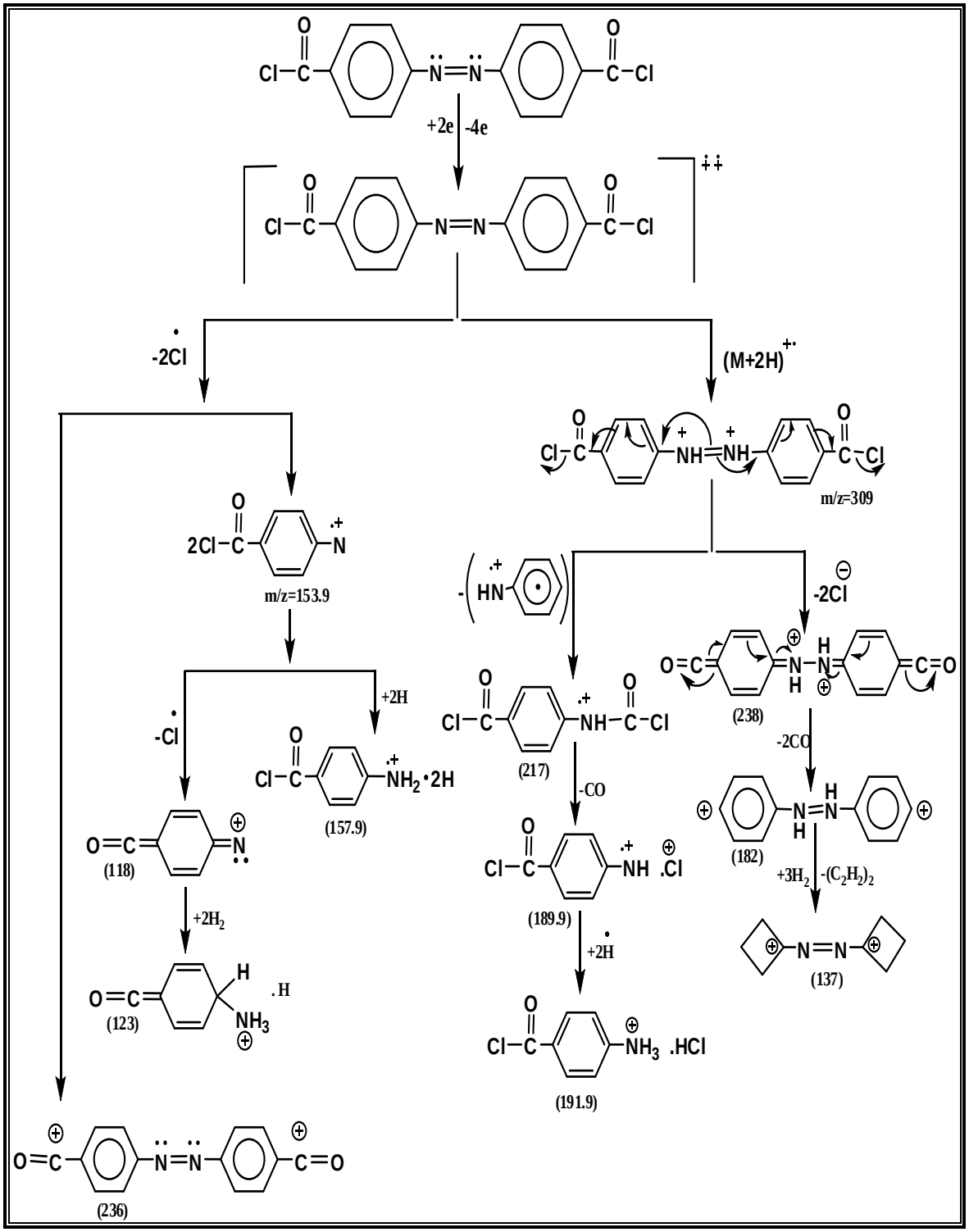
C.H.N- analysis of this compound [II], showed good agreement with the calculated / found result, Table (3-4).

FT-IR spectrum of compound [II] Fig (3-2), showed stretching bonds vibration of acid chloride carbonyl C=O (1774asy,1712sym) and azo-group N=N at 1597cm^{-1} respectively, all these data are given in Table (3-1).

While ^{1}H-NMR spectrum of this compound [II] Fig (3-3), showed aromatic (-CH) signals at (7.9 - 8.2) ppm Table (3-2).

^{13}C-NMR spectrum Fig (3-3), showed (C=O) carbon signal and aromatic carbon signals at δ(167 and 122 - 135) ppm respectively, as shown in Table (3-4).

Mass spectral analysis of compound [II] Fig (3-5), showed molecular ion [$M^{+.2}$] and [$M+2H^{.+2}$] ions at m/z (307 and 309) respectively, as well as to the following fragments m/z (238, 236, 182, and 137), these ions probably obtained by decomposition of [$M^{+.2}$] and [$M+2H^{.+2}$] with charge is considered to be localized on carbonyl-oxygen atoms of both ends of molecule compound [II] at m/z (238, 236), then ion m/z (238) may be decompose to hydrozo-benzene ions m/z (182), and the latter ion decompose to give m/z (137). Other fragmented ions m/z = (153.9, 217, 157.9, 189.9, 191.9, 123), probably obtained by decompose ion of [$M^{+.}$] and [$M+2H^{+.}$] ions, with charge is considered to be localized on azo-nitrogen atoms at the middle of symmetrical molecule of compound [II] at m/z = (217, 153.9), which probably decomposed to another fragmented ions would be identified by presence of chlorine atoms, according to the ion-isotopes peaks of chlorine (35/37) abundances. While fragmented ion (m/z 153.9) probably lose of chlorine-atom as a radical to give ions m/z (118, 123). All these fragmented and decomposed ions are summarized in Table (3-5) probably would be concluded as in following scheme (3-4) of suggested mechanism.



Scheme (3-4) : Suggested fragmentation mechanism of azobenzen-p,p'-diacid chloride [II]

3.3. Synthesis of azobenzen-p,p'-[(dibenzoic acid-2-yl) dicarboxamide] [III]:

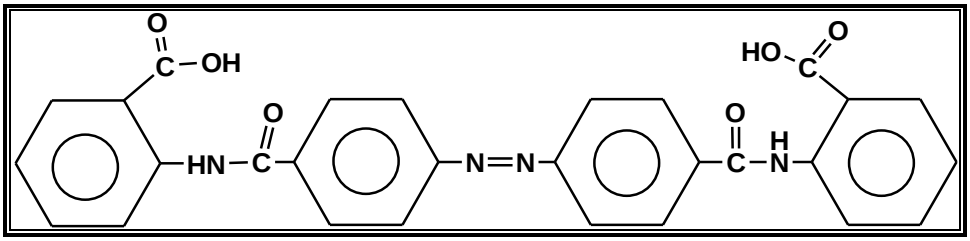
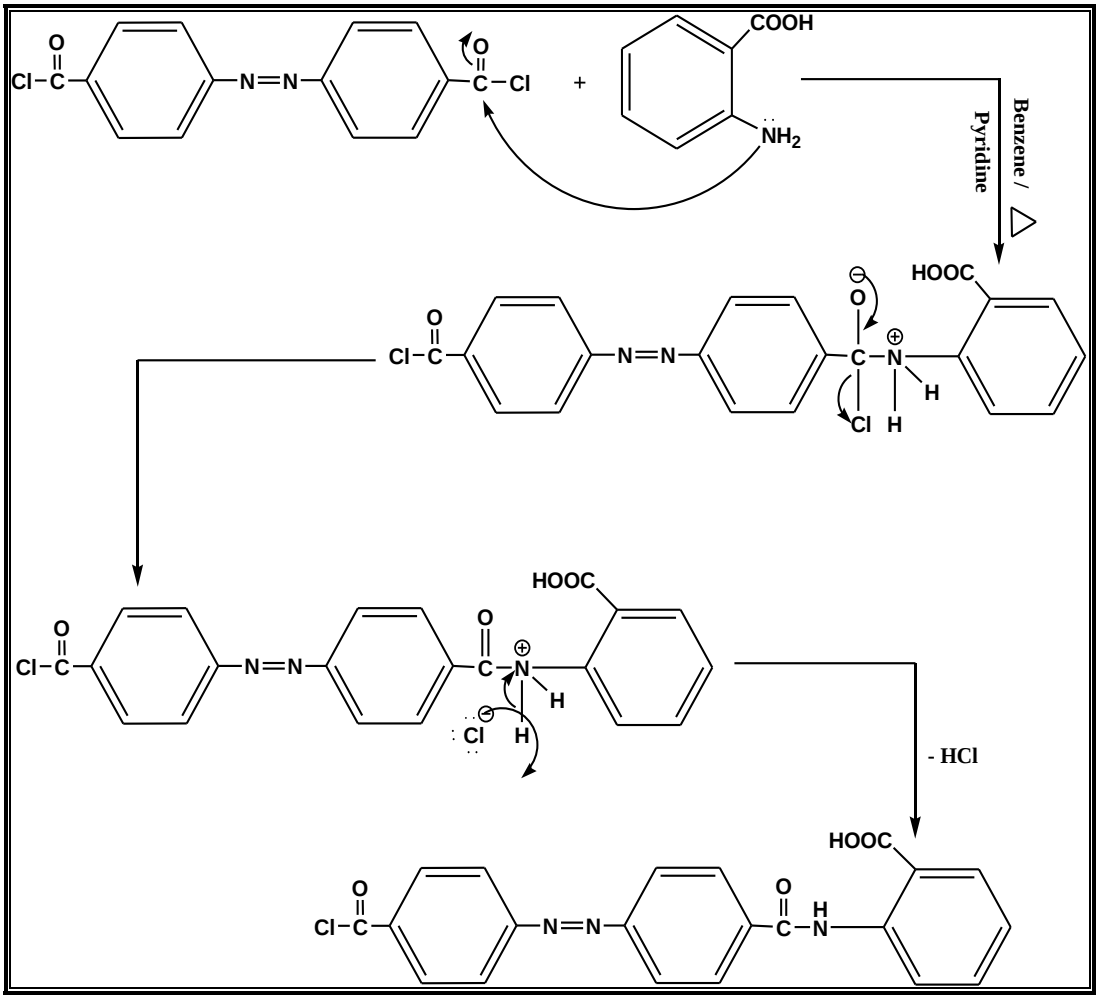


Figure (3-3): Structure of compound [III]

Condensation of azobenzen-p,p'-diacid chloride [II], with anthranilic acid in molar ratio (1:2) in the presence of pyridine, give azobenzen-p,p'-[(dibenzoic acid-2-yl)dicarboxamide] [III], according to the following mechanistic-steps [169].



Scheme (3-5) : Mechanism of formation azobenzen-p,p'-[(dibenzoic acid-2-yl)dicarboxamide] [III]

Compound [III], was characterized by C.H.N- analysis, FT-IR, ^{1}H-NMR, ^{13}C-NMR and Mass spectral analysis.

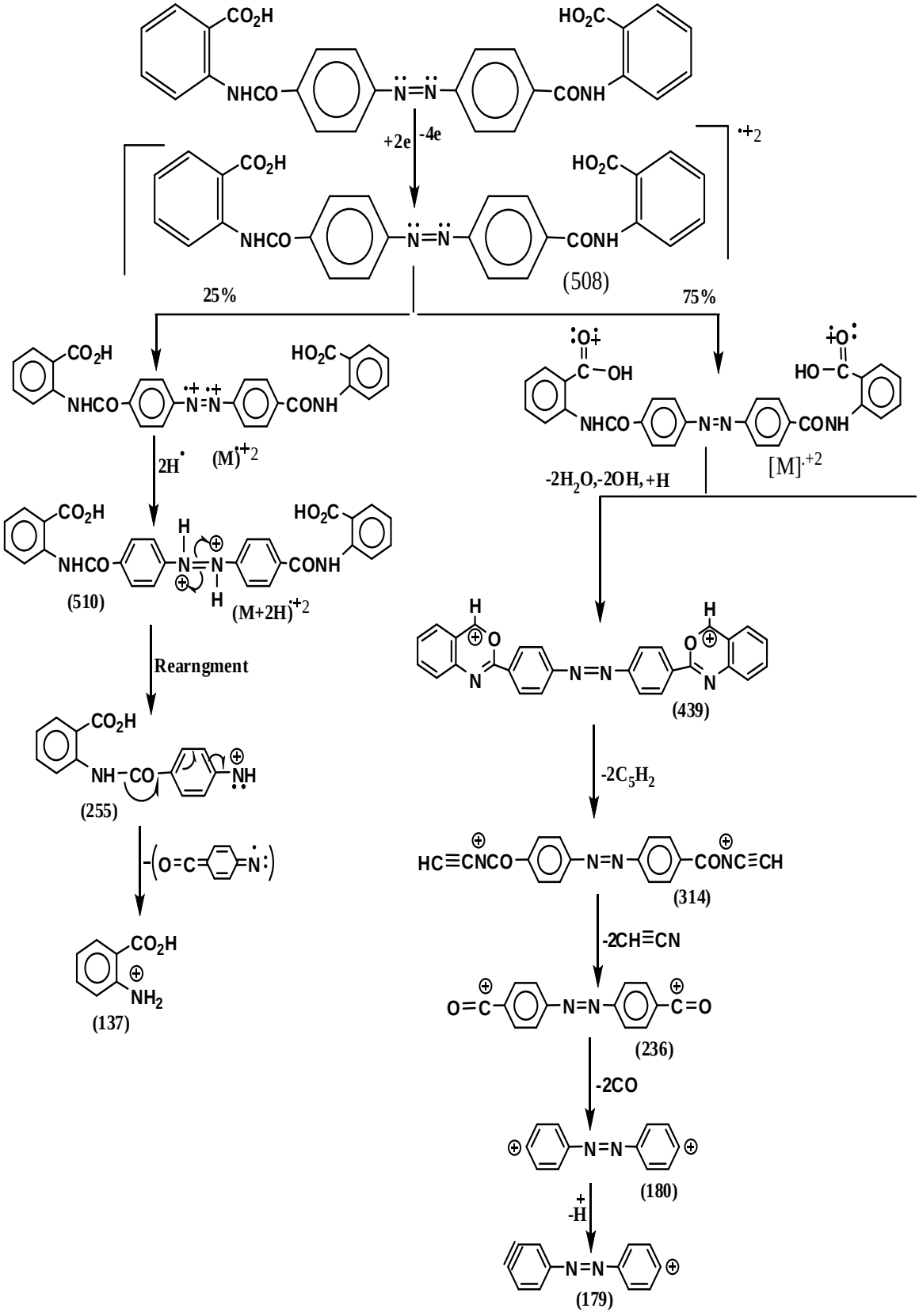
C.H.N- analysis was found to be agreed with calculated results Table (3-4).

FT-IR spectrum Fig (3-6), showed stretching bands of (OH, NH, C=O, and N=N) groups at 3430 (broad), 3232, 1675 and 1535 cm^{-1} respectively, beside (CO), amide II and I bands at (1608, 1589)cm^{-1} respectively Table (3-1).

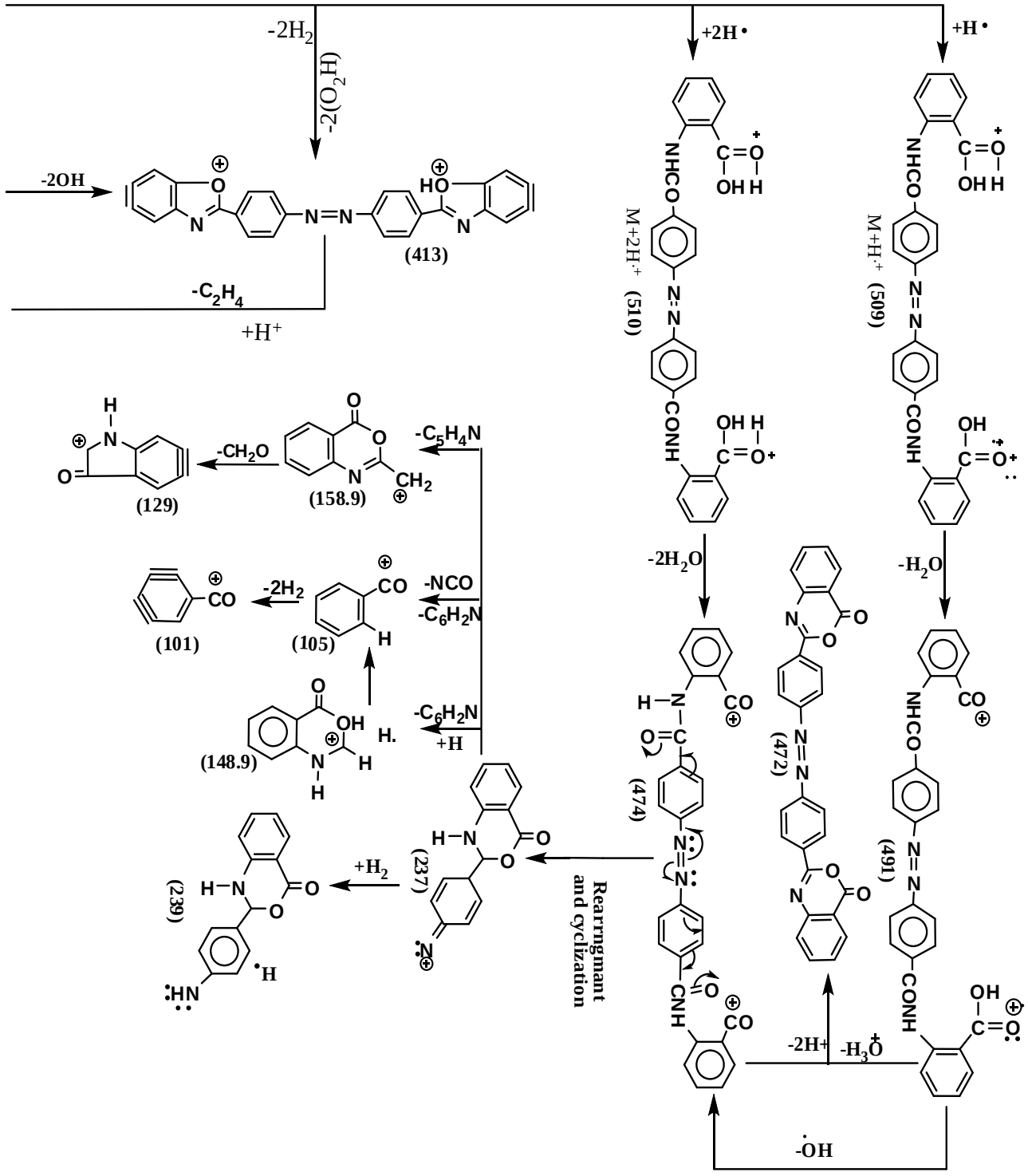
^{1}H-NMR spectral analysis of compounds [III] Fig (3-7), showed hydroxyl protons signal (OH) at δ (12.25) ppm, -NH and aromatic -CH as (16H) protons signals at δ (7.1 - 8.1) ppm Table (3-2).

But ^{13}C-NMR spectrum of this compound [III] Fig (3-8), showed carbonyl carbons of carboxyl and carboxamide as a singlet signals at δ (191, 164) ppm respectively, with aromatic carbons signals at δ (122 - 140) ppm, and (C=N) at 153. All these data are summarized in Table (3-3).

While Mass spectrum of compounds [III] Fig (3-9), showed, $(M+H)^{+.2}$ and $(M+2H)^{+.2}$ ions at m/z (509 and 510) respectively, with fragmented ions at m/z (491,474, 472, 439, 413, 236, 180, 179), probably obtained by decomposition of $(M)^{\cdot+2}$,$(M+H)^{\cdot+2}$ or $(M+2H)^{\cdot+2}$, with charge is considered to be localized on carbon-oxygen atoms for both ends of molecule. Rearrangement of fragmented ion m/z (474) probably gives ions m/z (148.9, 158.9, 129, 105 and 101). Also other fragmented ions m/z (510, 255, 137), probably obtained by decomposition of $[M^{\cdot+2}]$ ions, with charge is considered to be localized on azo-nitrogen atoms at the middle of symmetrical molecule of compound [III]. All these fragmented and decomposed ions would be concluded in the following suggested mechanism shown in the Scheme (3-6). All these fragments are summarized in Table (3-6).



Scheme (3-6) : Suggested fragmentation mechanism of azobenzen-p,p'-[(dibenzoic acid-2-yl)di carboxamide][III]


-2H2
-2(O2H)
-2OH
(413)
-C2H4
+H+
+2H•
+H•
M+2H+
(510)
M+H+
(509)
-2H2O
-H2O
-CH2O
-C5H4N
(129)
(158.9)
-2H2
-NCO
-C6H2N
(101)
(105)
-C6H2N
+H
(148.9)
H.
(474)
(472)
(491)
Rearrngmant
and cyclization
(237)
+H2
(239)
-2H+
-H3O+
-OH

3.4. Synthesis of azobenzen-p,p'-di[3,1-benzoxazin-4-one-2-yl] [IV]:

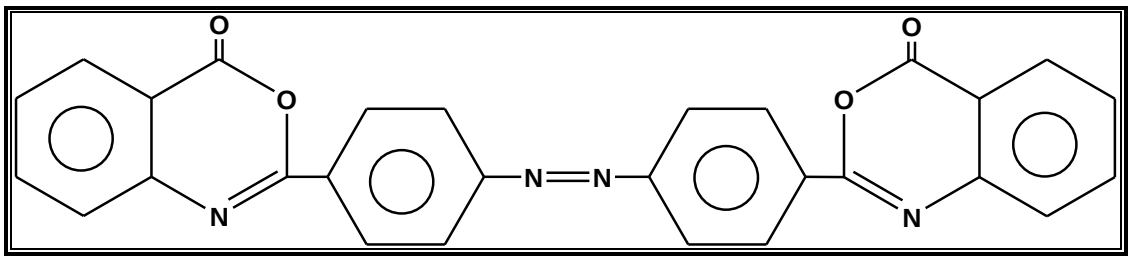


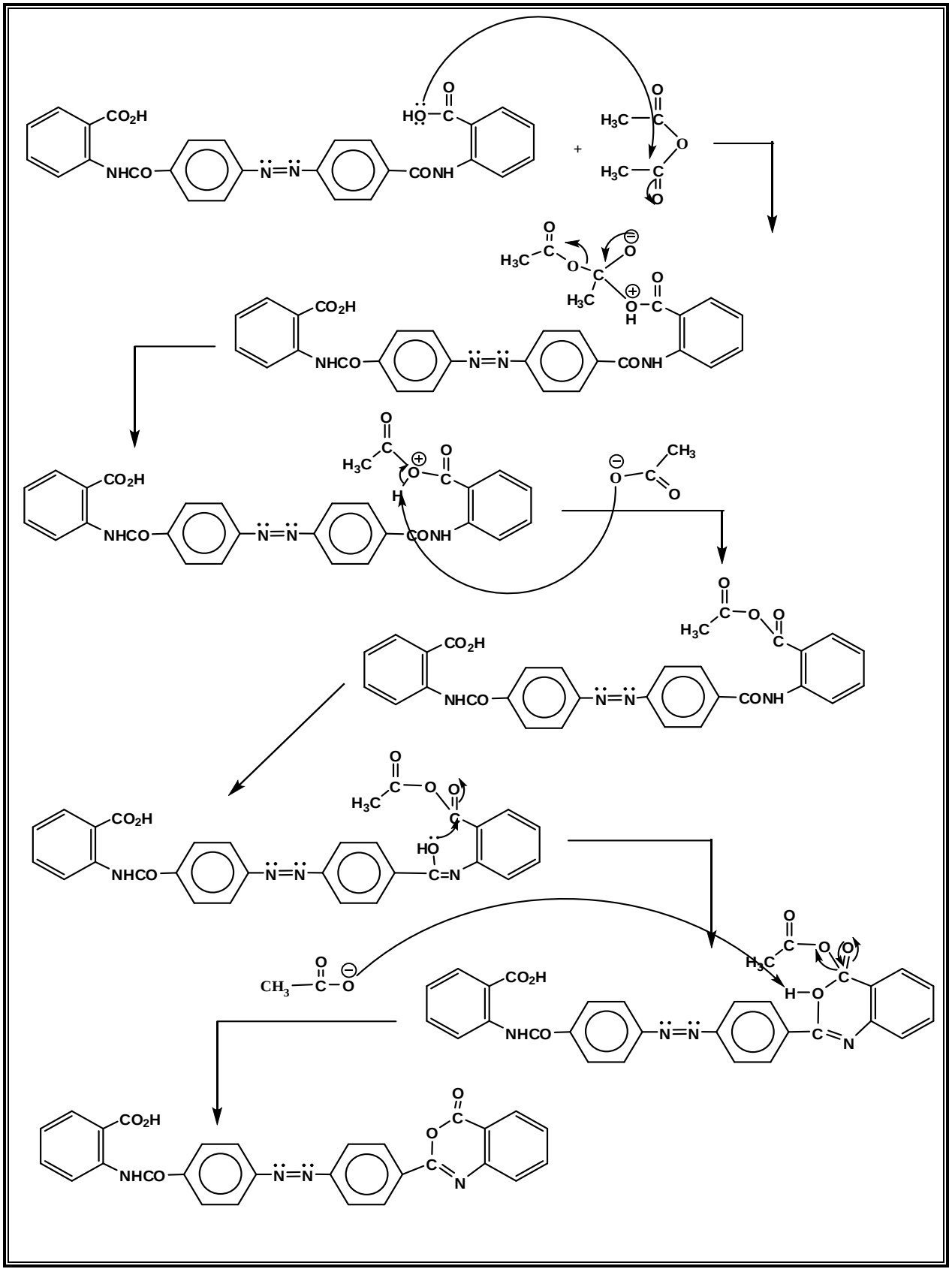
Figure (3-4): Structure of compound [IV]

Azobenzen-p,p'-di[3,1-benzoxazin-4-one-2-yl] [IV], was synthesized by two methods:-

First Methods, involved heating azobenzen-p,p'-[(dibenzoic acid-2yl)dicarboxamide] [III], with excess of thionyl chloride in presence of pyridine, to give compound [IV].

While the **Second Method or (Classical Method),** was involved heating compound [III] with acetic anhydride in N,N-dimethylformamide (DMF), also give compound [IV]. This compound [IV], was prepared by both methods identified by melting point and mixed melting point, (unchanged melting point of mixture of compound [IV] prepared by both methods), than melting points of same compound [IV] prepared by each method.

Formation of compound [IV], from reaction of compound [III], with acetic anhydride, would follow these mechanistic path-way [171].



Scheme (3-7) : Mechanism of formation azobenzen-p,p'-di[3,1-benzoxazin-4-one-2-yl][IV]

Compound [IV], was characterized by C.H.N- analysis, FT-IR, ^{1}H-NMR, ^{13}C-NMR and Mass spectral analysis.

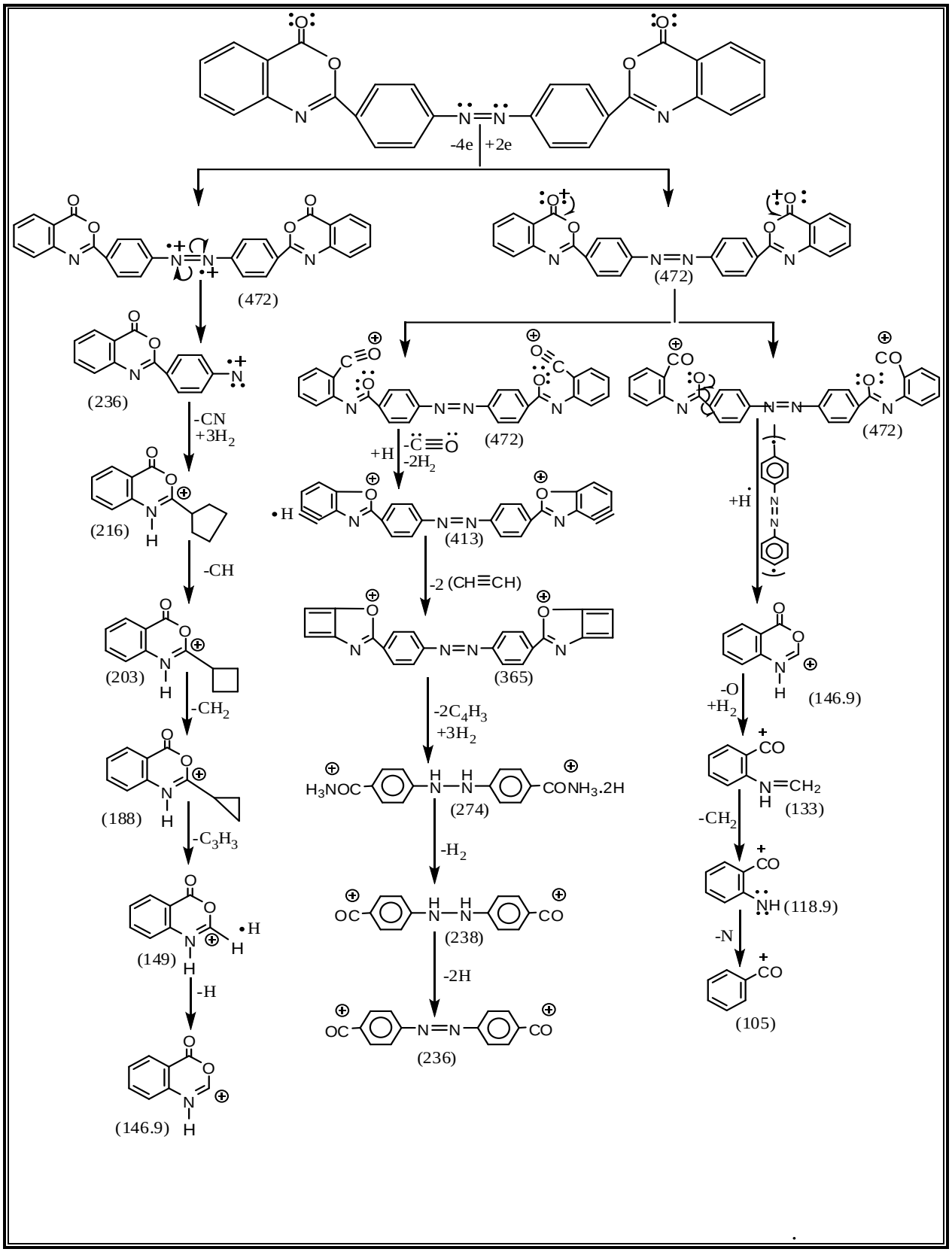
C.H.N- analysis was found to be identical to calculate result Table (3-4).

FT-IR spectral analysis of compounds [IV] Fig (3-10), showed stretching vibration bands ester (C=O), (C=N) and (N=N) bands at (1762, 1604) cm^{-1} and (1425) cm^{-1} respectively. All these bands were summarized in Table (3-1).

^{1}H-NMR spectral analysis of compound [IV] Fig (3-11), showed only aromatic (–CH) as (16H) proton at δ (7.5-8.4) ppm. All these signals are summarized in Table (3-2).

^{13}C-NMR spectral analysis for compound [IV] Fig (3-12), showed carbonyl carbons (C=O), azo-methane carbon (C=N) carbons, and aromatic carbons at δ (166, 153, and 119 - 140) ppm respectively. All these signals are summarized in Table (3-3).

While Mass spectrum of this compound [IV] Fig (3-13), does not show molecular ion [$M^{\cdot+2}$], but showed fragmented ions m/z = (413, 365, 274, 238, 236 and 146.9, 132.9, 118.9, 105) probably obtained from decomposition of molecular ion $M^{\cdot+2}$ with charge is considered to be localized on carbonyl-oxygen atoms for both ends of azobenzen-p,p'-di[3,1-benzoxazin-4-one-2yl] molecule. Also other fragments ions m/z (236, 216, 203, 188, 149, 146.9), probably obtained by decomposition of molecular ion $M^{\cdot+2}$, with charge is considered to be localized on azo-nitrogen atoms at the middle of symmetrical molecule of compound [IV]. All these decomposed ions would be attributed to the following fragments suggested mechanism in Scheme (3-8). All these fragments were summarized in Table (3-7).



Scheme (3-8) : Suggested fragmentation mechanism of azobenzen-p,p'-di[3,1-benzoxazin-4-one-2-yl][IV]

- **Series One:**

3.5. Synthesis of azobenzen-p,p'-di[3-substituted-4(3H)quinazolinone-2-yl] [Va-Vp]:

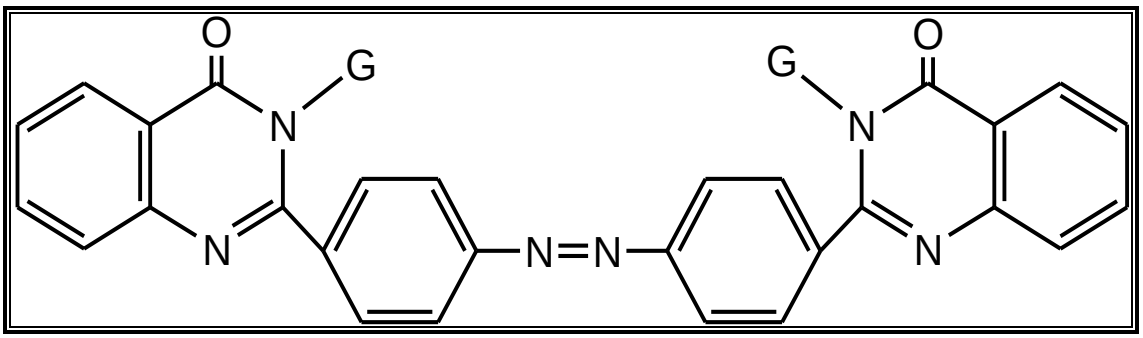
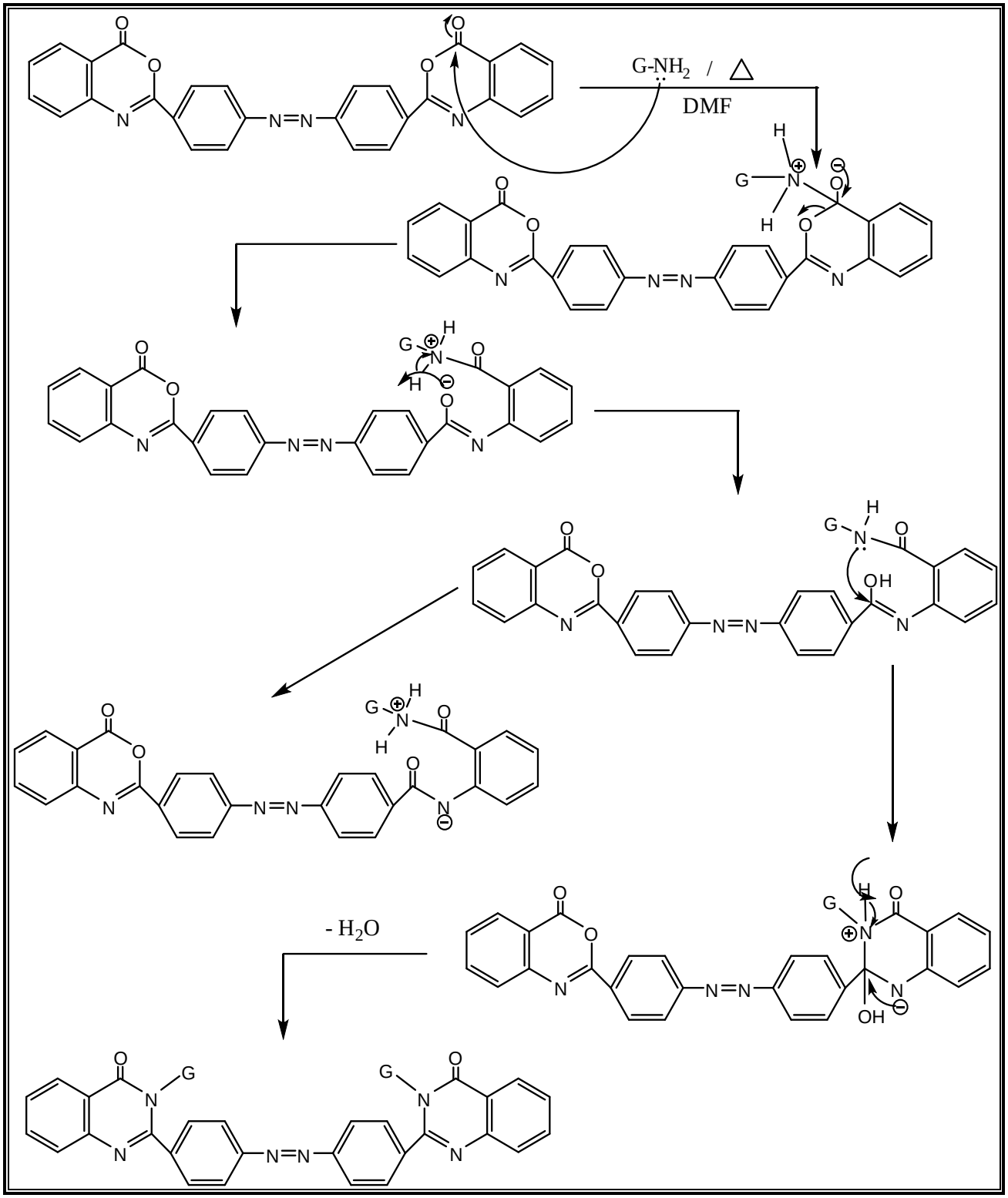


Figure (3-5): Structure of compound [V]

Heating (1:2) molar ratio of azobenzen-p,p'-di[3,1-benzoxazin-4-one-2-yl] [IV], and amino-moiety compounds like hydrazine hydrate, hydroxyl amine, quinidine, urea, thiourea, semicarbazide, thiosemicarbazied, aromatic amine, hetro amine and aliphatic amine, give azobenzen-p,p'-di[3-substituted-4(3H)quinazolinone-2-yl] [Va-Vp], these compounds are characterized by FTIR-spectral analysis, many of them are characterized by ^{1}H NMR, ^{13}C NMR, and some of these compounds by Mass spectral analysis.

Formation of compounds [Va-Vp], via reaction of compound [IV] with amino-moieties compounds, would follow this mechanistic path-way [169].



Scheme (3-9) : Mechanism of formation azobenzen-p,p'-di[3-substituted-4(3H)quinazolinone-2-yl][V]

FT-IR spectral analysis of compounds [Va-Vp] Figs [(3-14) - (3-55)], using KBr disk, showed many absorption bands of stretching and bending vibration of different groups, in general the FT-IR showed to have stretching characteristic quinazolin-4-one bands C=O, C=N, and NH_2 at (1680 - 1620), (1591 - 1635) and (3207 - 3277) cm^{-1} respectively, and showed stretching bands of azo-group (N=N) at (1489 - 1444) cm^{-1}, as well as to the other functional groups stretching bands of 3-substituted moiety, are shown in Table (3-8).

^{1}H-NMR spectrum of compounds [V(a, b, c, g, j, k, l, n, o, p)] Figs [(3-15) -(3-56)], were obtained in DMSO-d6 as solvents and with TMS as internal standard, showed beside quinazoline aromatic proton as a multiplet signals at δ (6.5 - 9.2) ppm, some proton signals of 3-substituted moiety like, NH_2, OH, CH_2, CH_3 protons signals which were shown in Table (3-9).

As well as ^{13}C-NMR obtained from a ^{13}C-NMR spectrometer operating in the normal mode consists of series moderate to sharp signals. Each signal represents a different ^{13}C-NMR. In addition, the calibration signals TMS as an internal standard. ^{13}C-NMR spectral analysis of compounds [V(a, b, c, g, j, k, l, n, o, p)] Fig [(3-16) - (3-57)], showed quinazolinone, (aromatic, C=O, C=N) carbon signals at δ (110 - 140), (163 -180), (152 - 164) ppm, respectively, beside to other carbon signals of 3-substituted moiety, CH_3, external C=O amide, C=S, C=NH, CH_2 carbons signal, All these signals are summarized in Table (3-10).

3.5.1. Synthesis of Azobenzen-p,p'-di[3-amino-4(3H)quinazolinone-2-yl] [Va]:

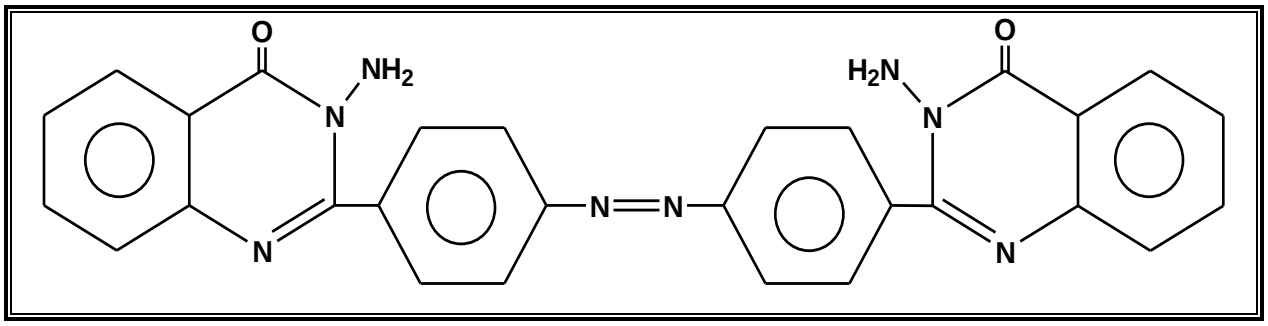


Figure (3-6): Structure of compound [Va]

Azobenzen-p,p´-di[3-amino-4(3H)quinazolinone-2-yl] [Va], was characterized by C.H.N- analysis data found agreement of practical with theoretical data Table (3-4).

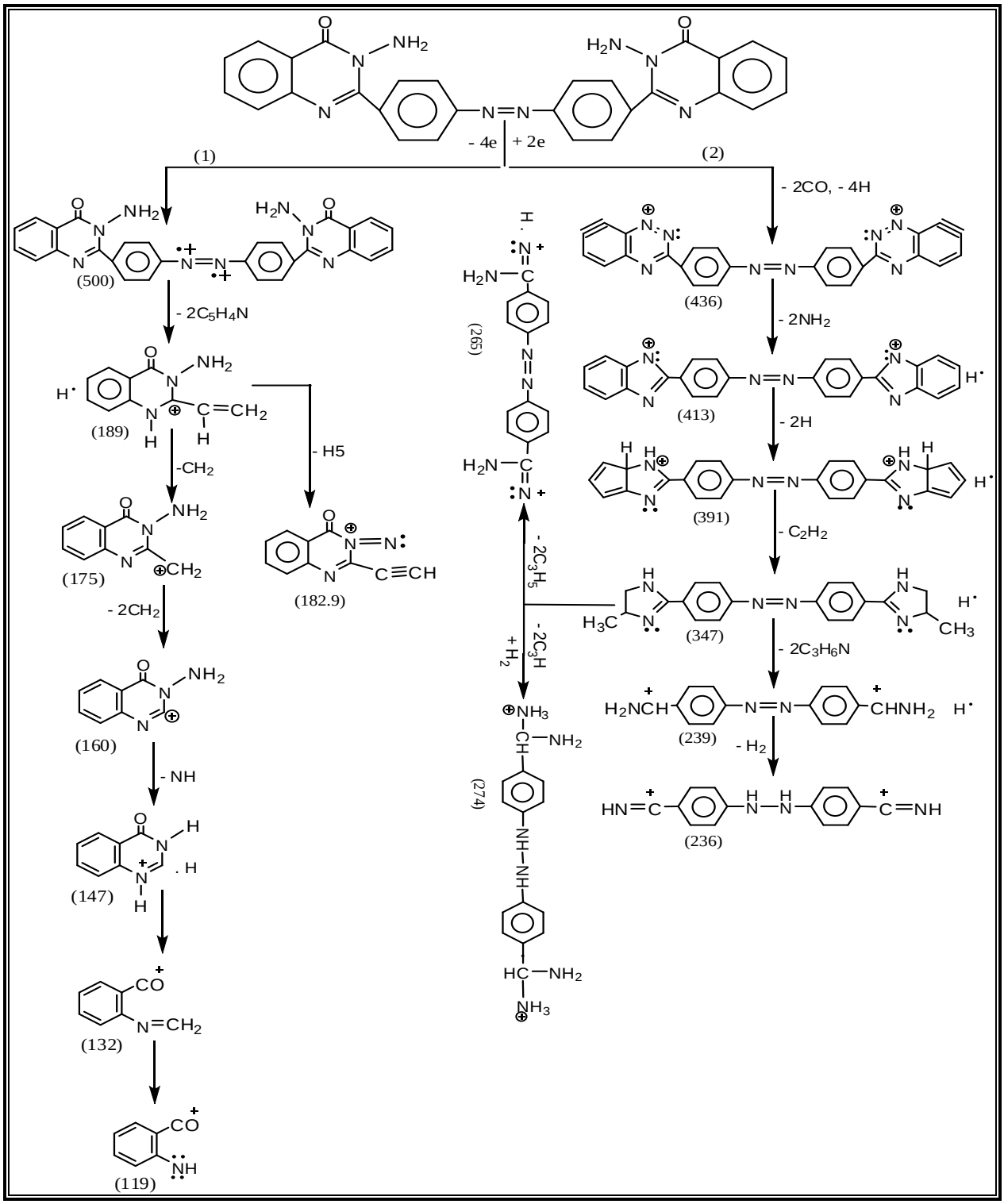
While FT-IR spectrum of compound [Va] Fig (3-14), showed quinazolin-4-one (C=O), (C=N) and (N=N) azo stretching bands at 1664, 1635 and 1467 cm^{-1} respectively, beside to ($–NH_2$) stretching vibration of aromatic rings at (3307asy – 3215sym) cm^{-1}, all these data are given in Table (3-8).

^{1}H-NMR spectrum of this compound [Va] Fig (3-15), showed quinazolin, aromatic as a multiple protons signals with combination NH_2 protons as (20H) protons of (7.2 - 8.1) ppm. As shown in Table (3-9).

But ^{13}C-NMR spectrum of compound [Va] Fig (3-16), showed quinazolinone (C=O), (C=N) and aromatic carbon, signals at δ (170, 151) and (121 - 145) ppm respectively. All these data are shown in Table (3-10).

While Mass spectrum of compound [Va] Fig (3-17), does not show molecular [$M^{\cdot+2}$], but showed fragmented ions at m/z (436, 413, 391, 347, 239, 236), probably obtained from decomposition of molecular ion [$M^{\cdot+2}$], with charge is considered to be localized on carbonyl-oxygen atoms for both ends of azobenzen-p,p'-[3-amino-4(3H)quinazolinone-2-yl] molecule. Also other fragments ions at m/z (189, 183, 175, 160, 147, 132, and 119), probably obtained by decomposition of molecular ion $M^{\cdot+2}$, with charge is considered to be localized on azo-nitrogen atoms at the middle of symmetrical molecule of

compound [Va].All these decomposed ions would be attributed to the following fragments of suggested mechanism in Scheme (3-10). All these fragments were summarized in Table (3-11).



Scheme (3-10) : Suggested fragmentation mechanism of azobenzen-p,p'-di[3-amino-4(3H)quinazolinone-2-yl] [Va]

3.5.2. Synthesis of azobenzen-p,p'-di[3-hydroxy-4(3H)quinazolinone-2-yl] [Vb]:

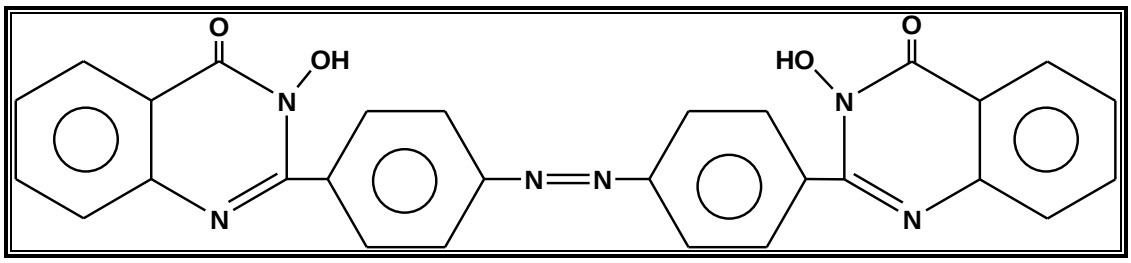


Figure (3-7): Structure of compound [Vb]

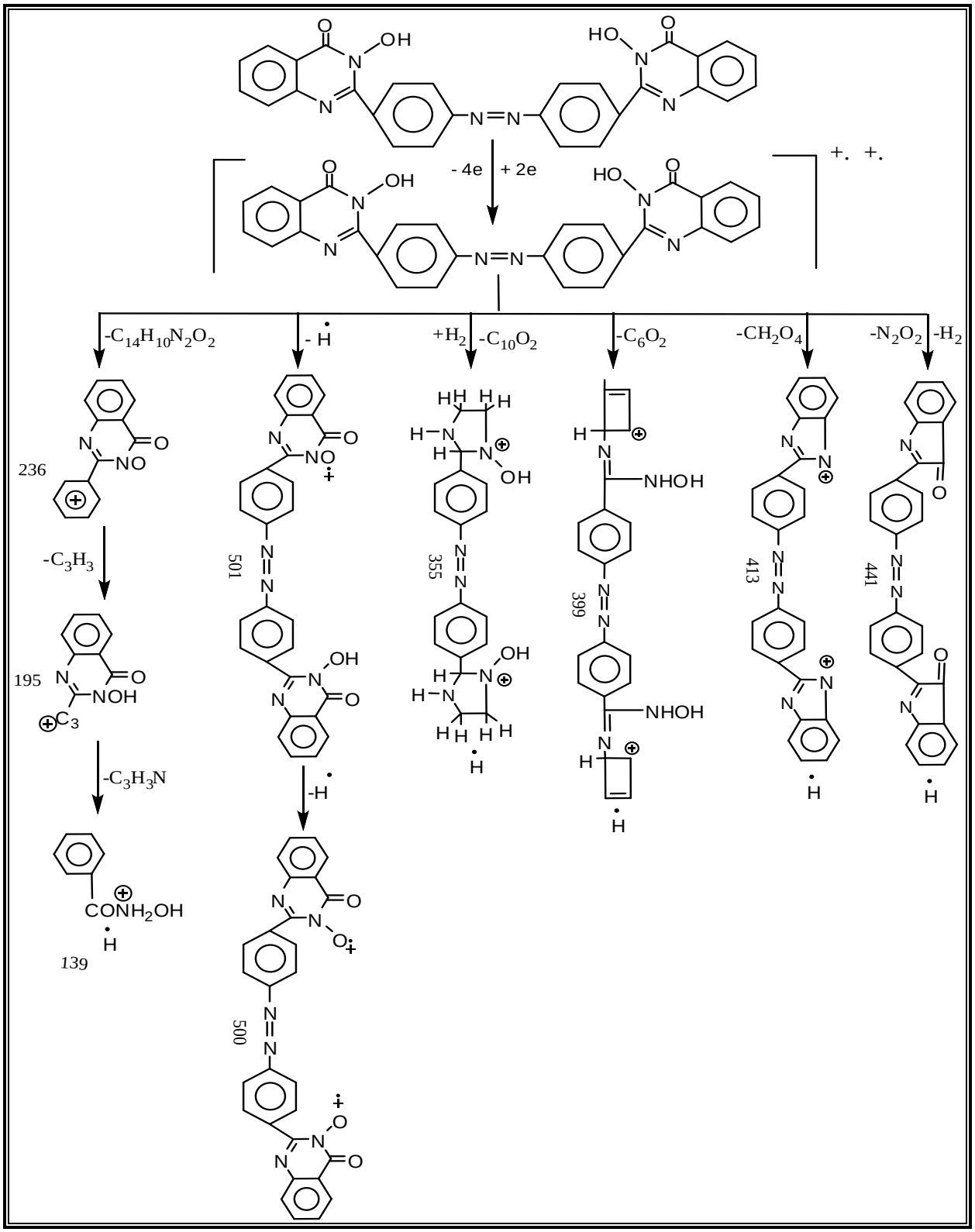
Azobenzen-p,p'-di[3-hydroxy-4(3H)quinazolinone-2-yl] [Vb], FT-IR spectrum Fig(3-18), showed beside stretching (C=O), and (C=N) of quinazolin-4-one ring at (1705 and 1606) cm^{-1}, stretching bands of (OH) and (N=N) azo group at (3365 and 1446) cm^{-1} respectively, all these data are given in Table (3-8).

^{1}H-NMR spectrum of this compound [Vb] Fig (3-19), showed aromatic (18H) protons as a multiple protons signals with hydroxyl group (2H) protons of (5.4 – 9.9) and (10.2) ppm respectively Table (3-9).

While ^{13}C-NMR spectrum of this compound [Vb] Fig (3-20), showed multiple signals of aromatic carbons, with carbonyl (C=O), and azo-methine (C=N) carbons signals of qunazolinone ring at (110 - 142) and (164 and 158) ppm respectively, which are shown in Table (3-10).

Mass spectrum of compound [Vb] Fig (3-21), showed molecular $(M+H)^{+.2}$ ion at m/z (501) with fragmented ions at m/z (441, 413, 399, 355), probably obtained from decomposition of molecular ion $M^{\cdot+2}$, with charge is considered to be localized on carbonyl-oxygen atoms for both ends of azobenzen-p,p'-[3-hydroxy-4(3H)quinazolinone-2-yl] molecule. Also other fragments ions at m/z = (236, 195 and 139), probably obtained by decomposition of molecular ion $M^{\cdot+2}$, with charge is considered to be localized on azo-nitrogen atoms at the middle of symmetrical molecule of compound [Vb]. All these decomposed ions would be

attributed to the following fragments suggested mechanism in Scheme (3-11). All these fragments were summarized in Table (3-12).



Scheme (3-10) : Suggested fragmentation mechanism of azobenzen-p,p'-di[3-hydroxy-4(3H)quinazolinone-2-yl] [Vb]

3.5.3. Synthesis of Azobenzen-p,p'-di[3,p-touldino-4(3H)qunazolinone-2-yl] [Vc]:

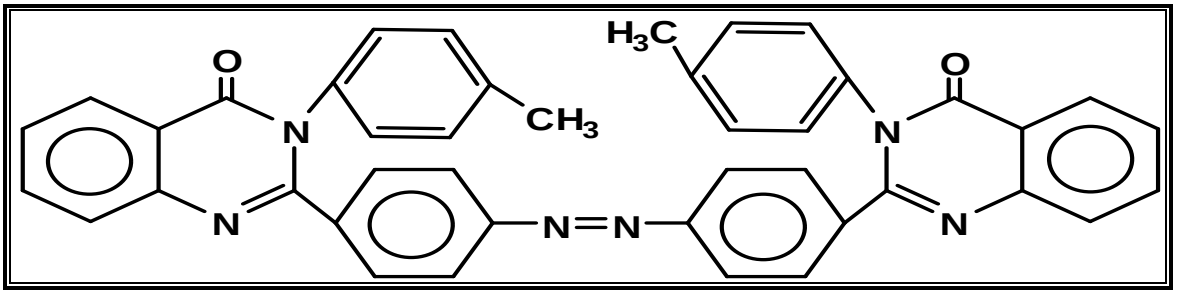


Figure (3-8): Structure of compound [Vc]

Azobenzen-p,p'-di[3,p-touldino-4(3H)qunazolinone-2-yl] [Vc], FT-IR spectrum Fig (3-22), showed beside stretching (C=O), and (C=N) of quinazolin-4-one ring at (1680 and 1620) cm^{-1}, stretching bands of (CH_3) and (N=N) azo group at (2920 and 1453) cm^{-1} respectively, all these data are given in Table (3-8).

^{1}H-NMR spectrum of this compound [Vc] Fig (3-23), showed aromatic protons as a multiple protons signals with methyl group, (3H) protons of δ (6.8 – 8.7) and δ(3.8) ppm respectively Table (3-9).

While ^{13}C-NMR spectrum of this compound [Vc] Fig (3-24), showed multiple signals of aromatic carbons, with carbonyl (C=O), and azo-methine (C=N) carbons signals of qunazolinone ring at (110 - 148), (164 and 152) ppm respectively, and methyl group at (71)ppm, which are shown in Table (3-10).

3.5.4. Synthesis of Azobenzen-p,p'-di[3,p-(benzenesulphonamido)-4(3H)quinazolinone-2-yl] [Vd]:

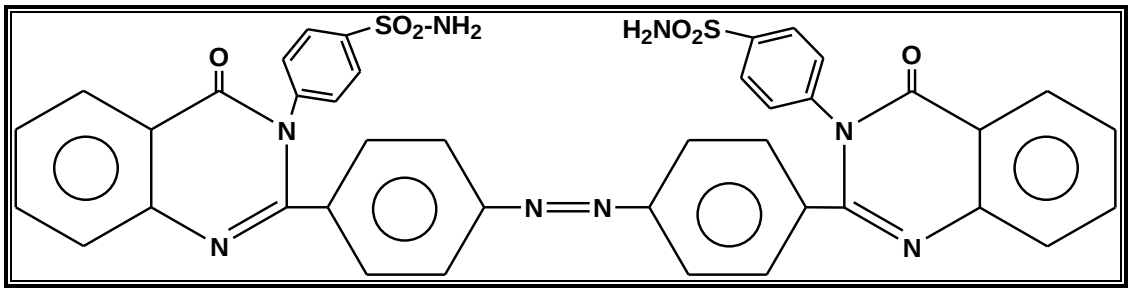


Figure (3-9): Structure of compound [Vd]

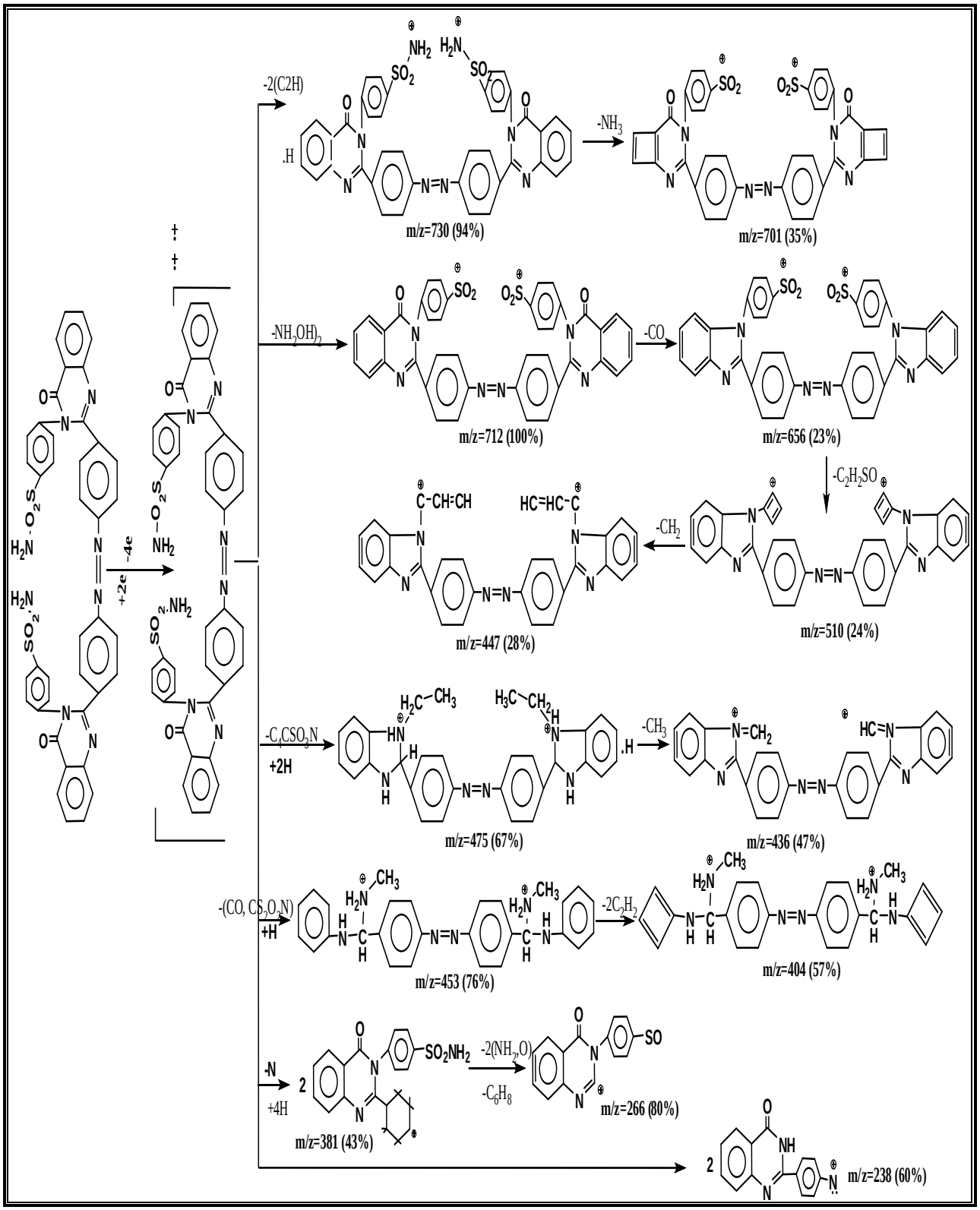
Azobenzen-p,p'-di[3,p-(benzenesulphonamido)-4(3H)quinazolinone-2-yl] [Vd], FT-IR spectrum Fig (3-25), shows stretching frequencies bonds of quinazolin-one ring (C=O), and (C=N) at 1670 and 1610 cm^{-1}, benzene sulphoneamido (NH_2) stretching and azo group bands at (3464, 3236) and 1450 cm^{-1} respectively, all these data are given in Table (3-8).

^{1}H-NMR spectrum of this compound [Vd] Fig (3-26), showed aromatic protons as a multiple protons signals with NH_2 group, (2H) protons of δ (5.9 – 9.9) and δ (10.3) ppm respectively Table (3-9).

While ^{13}C-NMR spectrum of this compound [Vd] Fig (3-27), showed multiple signals of aromatic carbons, with carbonyl (C=O), and azo-methine (C=N) carbons signals of qunazolinone ring at (119 - 149), (169 and 153) ppm respectively, which are shown in Table (3-10).

Mass spectrum of this compound [Vd] Fig (3-28), showed molecular [$M^{\cdot+2}$] at m/z (780), as well as to fragmented ions at m/z (730, 712, 701, 656, 510, 487, 475, 453, 436, 401), probably obtained from decomposition of molecular ion $M^{\cdot+2}$, with charge is considered to be localized on carbonyl-oxygen atoms for both ends of compound [Vd] molecule. Also other fragments ions at m/z (381, 266 and 236), probably obtained by decomposition of molecular ion M^{+}, with charge is considered to be localized on azo-nitrogen atoms at the middle of symmetrical molecule of azobenzen-p,p'-di[3-(benzenesulphonamido)-4(3H)quinazolinone-2-yl] [Vd]. All these decomposed ions would be concluded

in the following fragments suggested mechanism in Scheme (3-12). All these fragments were summarized in Table (3-13).



Scheme (3-11) : Suggested fragmentation mechanism of azobenzen-p,p'-di[3-(benzenesulphonamido)-4(3H)quinazolinone-2-yl] [Vd]

3.5.5. Synthesis of Azobenzen-p,p'-di[3,2'-(pyrimidin-2-yl)-4(3H)-quinazolinone-2-yl] [Ve]:

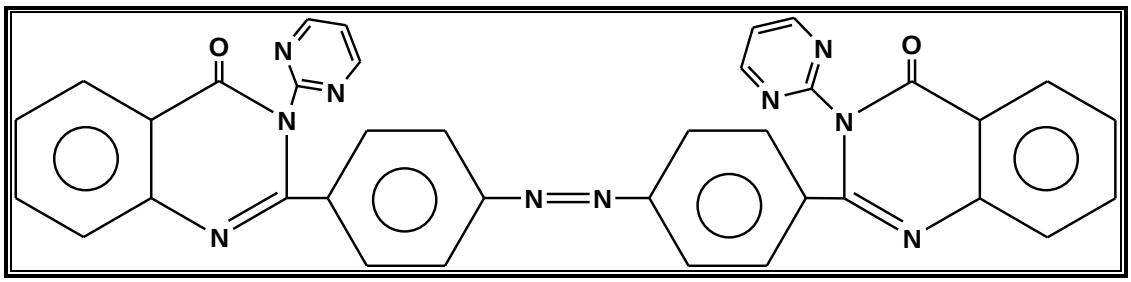


Figure (3-10): Structure of compound [Ve]

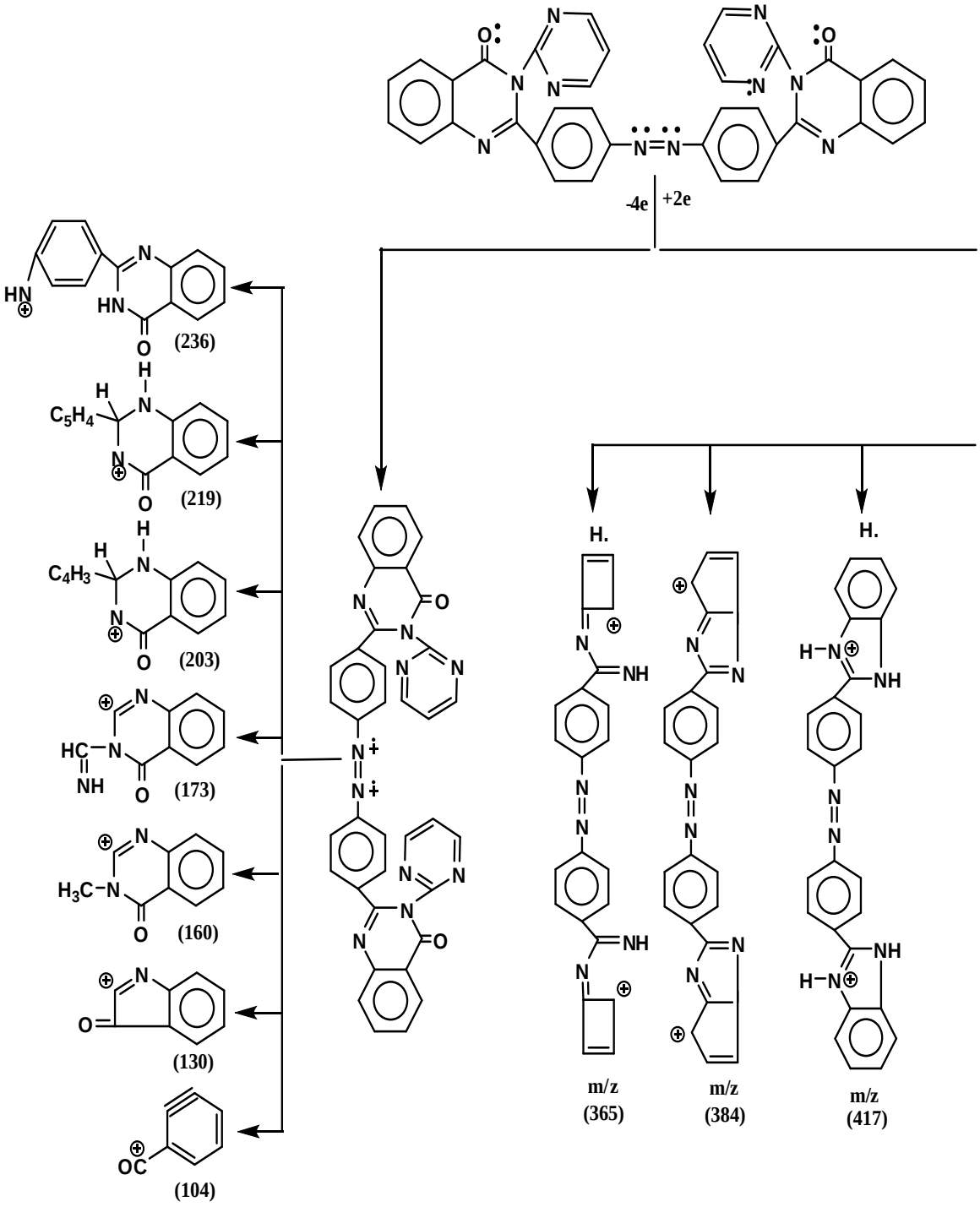
Azobenzen-p,p'-di[3,2'-(pyrimidin-2-yl)-4(3H)quinazolinone-2-yl] [Ve], FT-IR spectrum Fig (3-29), shows beside quinazolinone carbonyl ring (C=O), and azo-methane (C=N) stretching vibration bands at 1676, 1625 cm^{-1}, and azo group (N=N) and pyrimidine (C=N) stretching bands at (1455, 1600 cm^{-1} respectively, all these data are given in Table (3-8).

^{1}H-NMR spectrum of this compound [Ve] Fig (3-30), showed aromatic protons as a multiple protons signals group, of δ (7.18 – 8.6) ppm respectively Table (3-9).

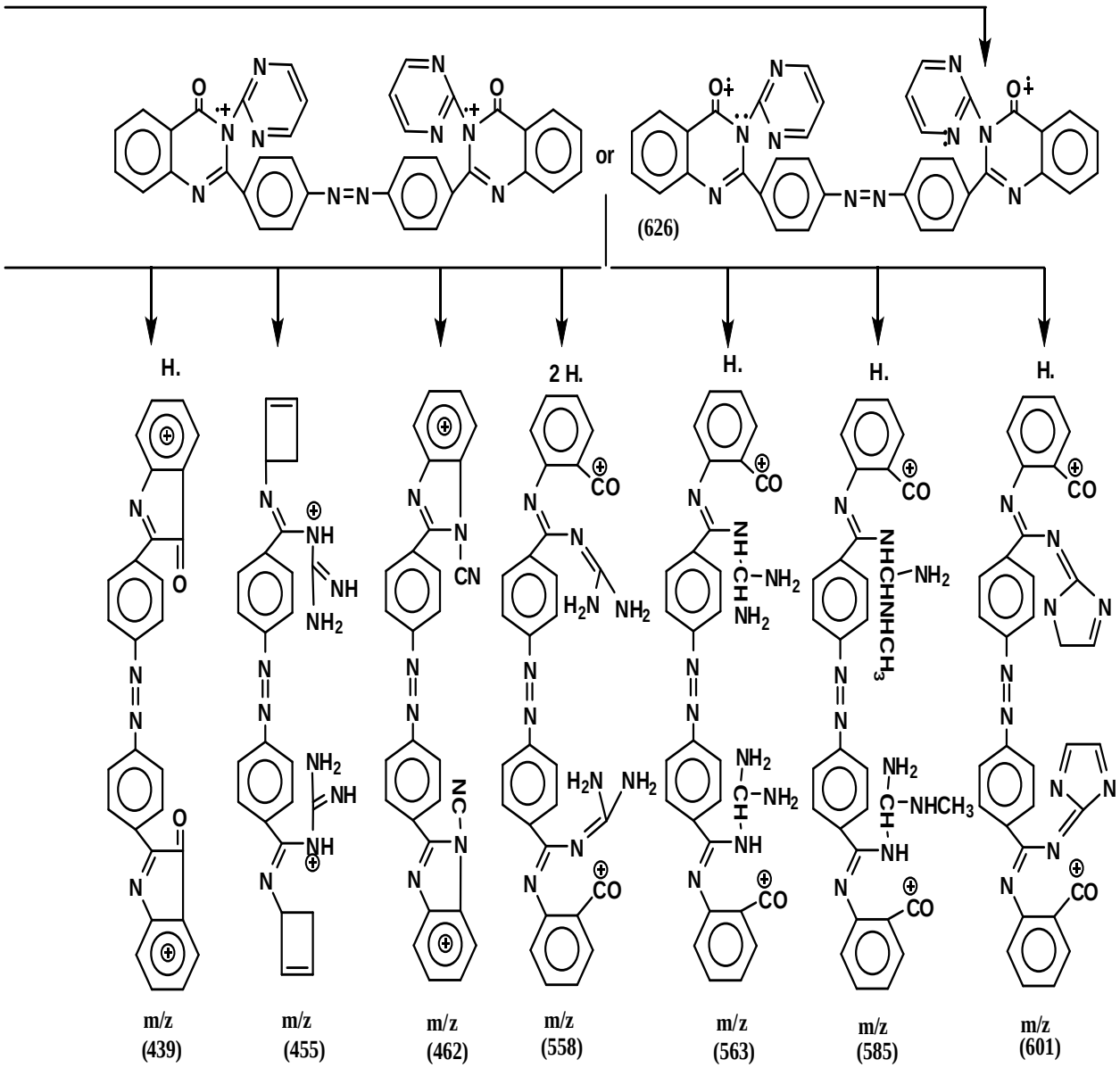
While ^{13}C-NMR spectrum of this compound [Ve] Fig (3-31), showed multiple signals of aromatic carbons, with carbonyl (C=O), and azo-methine (C=N) carbons signals of qunazolinone ring at δ (117 - 147) and δ (168 and 156) ppm respectively, which are shown in Table (3-10).

Mass spectrum of this compound [Ve] Fig (3-31), does not show molecular ion [$M^{\cdot+2}$] at m/z (626), but shows fragmented ions at m/z (601, 585, 563, 558, 462, 455, 439, 417, 384, 365), probably obtained from decomposition of molecular ion $M^{\cdot+2}$, with charge is considered to be localized on carbonyl-oxygen atoms for both ends of azobenzen-p,p'-di[3,2'-(pyrimidin-2-yl)-4(3H)quinazolinone-2-yl] molecule. Also another fragments ions at m/z (236, 219, 203, 173, 160, 130, 104), probably obtained by decomposition of molecular ion $M^{\cdot+2}$, with charge is considered to be localized on azo-nitrogen atoms at the middle of symmetrical molecule of this compound [Ve]. All these decomposed

ions would be concluded in the following fragments suggested mechanism in Scheme (3-13). All these fragments were summarized in Table (3-14).



Scheme (3-13) : Suggested fragmentation mechanism of azobenzen-p,p'-di[3,2'-(pyrimidin-2-yl)-4(3H)quinazolinone-2-yl][Ve]


or
(626)
H.
2 H.
H.
H.
H.
m/z (439)
m/z (455)
m/z (462)
m/z (558)
m/z (563)
m/z (585)
m/z (601)

- **Series Two:**

3.6. Synthesis of Azobenzen-p,p'-di[3,N-substituted-4(3H)-quinazolinone-2-yl] [Vo, Vp, VIA, VIB]

Condensation (1:2) malar ratio of azobenzen-p,p'-di[3-amino-4(3H)-quinazolinone-2-yl] [Va], with potassium cyanate or thiocyante, 5-nitrofurfural or benzenesulphonyl chloride, give compound [Vo, Vp, VIA, VIB] respectively.

3.6.1. Synthesis of Azobenzen-p,p'-di[3,N-urido-4(3H)quinazolinone-2-yl] [Vo]

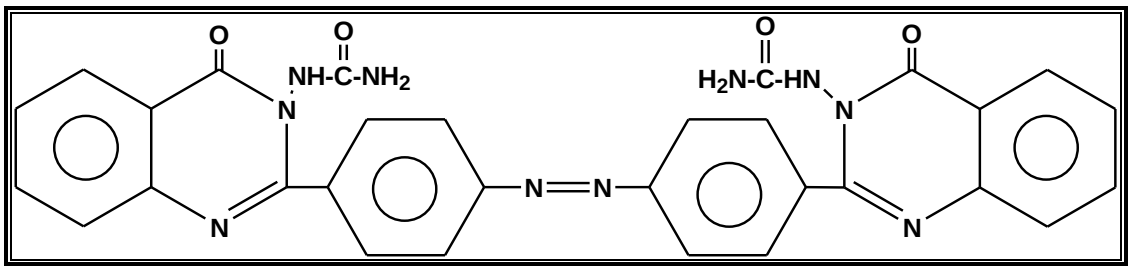


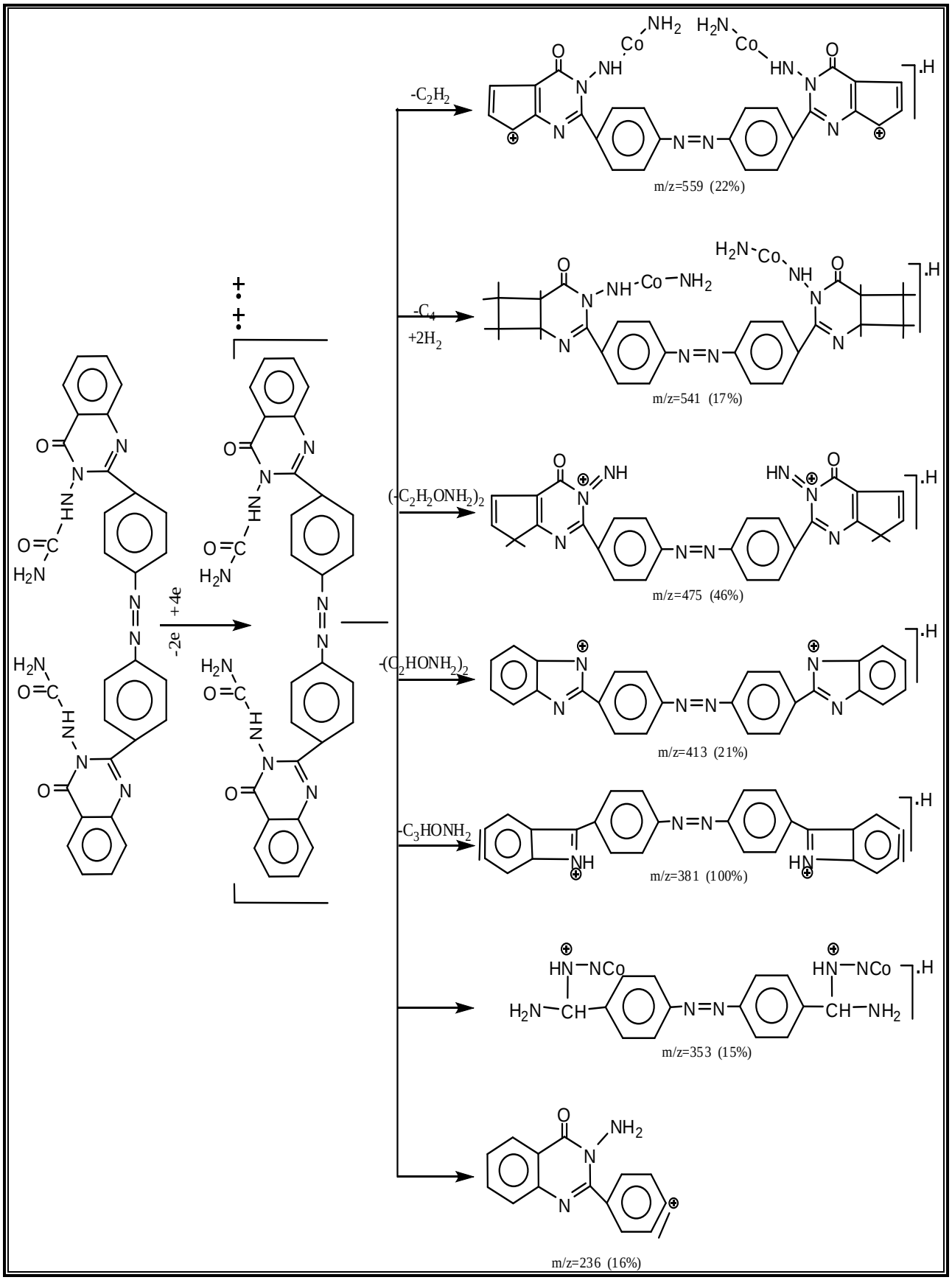
Figure (3- 12): Structure of compound [Vo]

Azobenzen-p,p'-di[3,N-urido-4(3H)quinazolinone-2-yl] [Vo], was characterized by melting and mixed melting point (unchanged melting point of mixture of this compound) [Vo], with that compound prepared by condensation of azobenzen-p,p'-di[1,3-benzoaxzine-4-one-2-yl] [IV], with semicarbazide in a malar ratio (1:2) respectively, and identify of both FT-IR spectrums Fig (3-50).

^{1}H-NMR spectrum of this compound [Vo] Fig (3-51), showed aromatic protons as a multiple protons signals with (NH) and (NH_2) group, of δ (7.08 – 8.24), (9.5 and 10.47) ppm respectively Table (3-9).

While ^{13}C-NMR spectrum of this compound [Vo] Fig (3-52), showed multiple signals of aromatic carbons, with carbonyl exo and endo rings (C=O) , and carbons signals of qunazolinone ring at δ (119 - 140) and (160 and 177) ppm respectively, which are shown in Table (3-10).

Mass spectrum of this compound [Vo] Fig(3-53), does not show molecular ion [$M^{\cdot+2}$] (586), but showed fragmented ions m/z (559, 541,475, 413, 381, 353) probably obtained from decomposition of molecular ion, with charge is considered to be localized on carbonyl – oxygen atoms for both ends of azobenzen-p,p'-di[3-N-urido-4(3H)quinazolinone-2-yl] molecule [Vo]. Also another fragmented ions at m/z (236), probably obtained by decomposition of molecular ion $M^{\cdot+2}$ at m/z (586), with charge is considered to be localized on azo-nitrogen atoms at the middle of symmetrical molecule of compound [Vo]. All these decomposition ions probably are summarized in Table (3-15), would be concluded in the following scheme (3-14) of suggested mechanism.



Scheme (3-14) : Suggested fragmentation mechanism of azobenzen-p,p'-di[3,N-urido-4(3H)quinazolinone-2-yl][Vo]

3.6.2. Synthesis of Azobenzen-p,p'-di[3,N-thiourido-4(3H)-quinazolinone-2-yl] [Vp]:

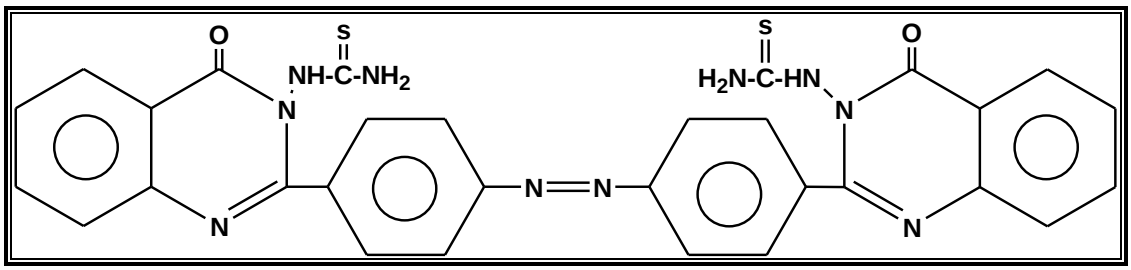


Figure (3- 13): Structure of compound [Vp]

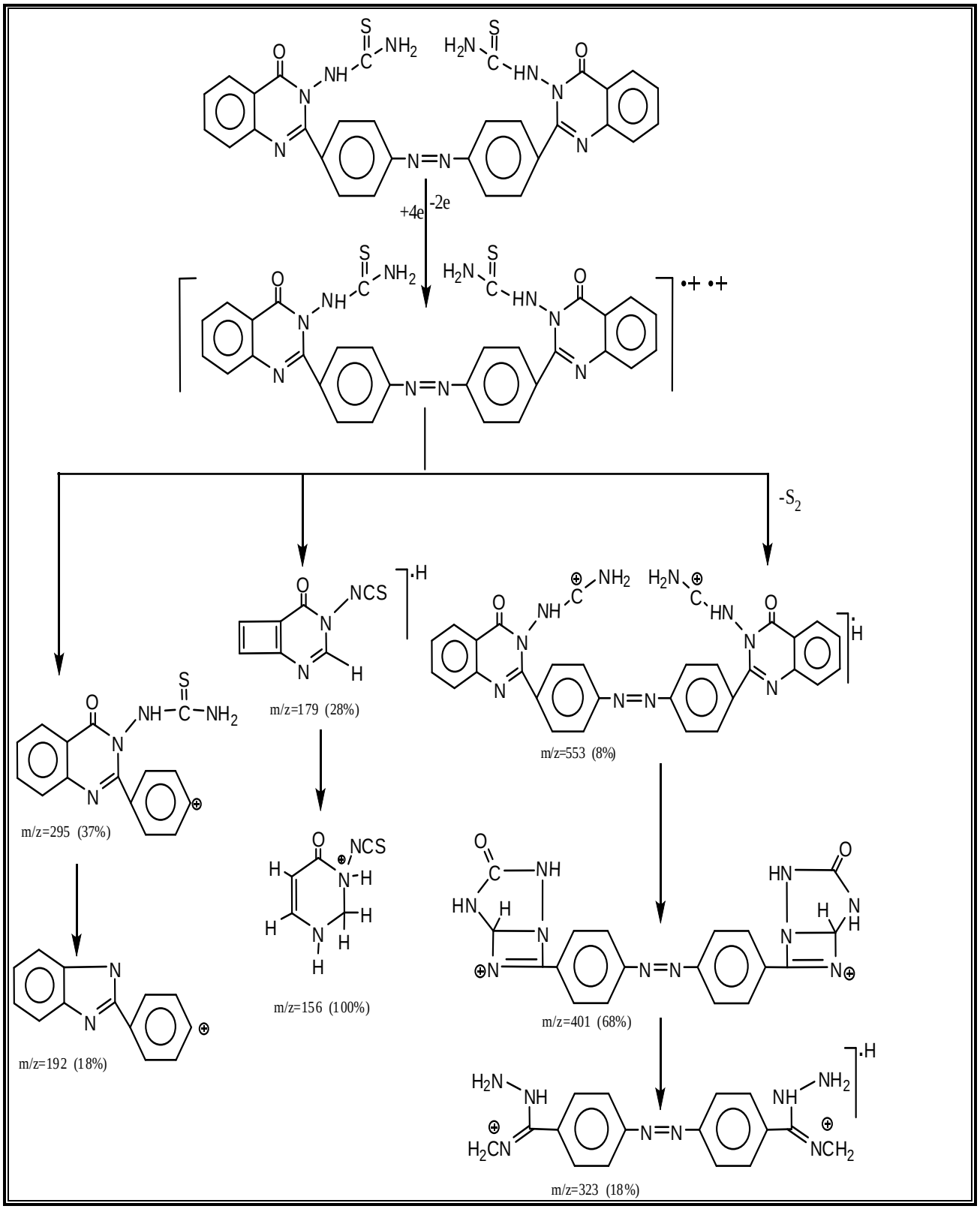
Azobenzen-p,p'-di[3,N-thiourido-4(3H)quinazolinone-2-yl] [Vp], was characterized by melting and mixed melting point (unchanged melting point of mixture of this compound [Vp]), with that compound prepared by condensation of azobenzen-p,p'-di[3,1-benzoaxzine-4-one-2-yl] [IV], with thiosemicarbazide in a malar ratio (1:2) respectively, and identify of both FT-IR spectrums Fig (3-54).

^{1}H-NMR spectrum of this compound [Vp] Fig (3-55), showed aromatic protons as a multiple protons signals with (NH) and (NH_2) group, of δ (7.15 – 8.24), (10.3 and 10.7) ppm respectively Table (3-9).

While ^{13}C-NMR spectrum of this compound [Vp] Fig (3-56), showed multiple signals of aromatic carbons, with endo carbonyl and exo thiocarbonyl, and carbons signals of qunazolinone ring at δ (110 - 133) and (180 and 194) ppm respectively, which are shown in Table (3-10).

Mass spectrum of this compound [Vp] Fig (3-57), showed $[M+H]^{\cdot+2}$ ion at m/z (619) in the extensional part of this spectrum (using NL: 5.57 4), as well as the fragmented ions m/z (553, 401, 323), probably obtained from decomposition of molecular ion $M^{\cdot+2}$ (618) or $(M+H)^{\cdot+2}$ (619) ion, with charge considered to be localized on carbonyl-oxygen atoms for both ends of azobenzen-p,p'-di[3-N-thiourido-4(3H)quinazolinone-2-yl] molecule [Vp]. Also another fragmented ions at m/z (295, 192, 179, 156), probably obtained from decomposition of molecular ion $M^{\cdot+2}$ or $(M+H)^{\cdot+2}$ ions of this compound [Vp],

with charge is considered to be localized on azo-nitrogen atoms at the middle of symmetrical molecule of compound [Vp]. All these decomposition ions probably are summarized in Table (3-16), would be concluded in the following scheme (3-15) of suggested mechanism.



Scheme (3-15) : Suggested fragmentation mechanism of azobenzen-p,p'-di[3,N-thiourido-4(3H)quinazolinone-2-yl][Vp]

3.6.3. Synthesis of azobenzen-p,p'-di[3,N-benzenesulphonamido-4(3H)-quinazolinone-2-yl] [VIA]:

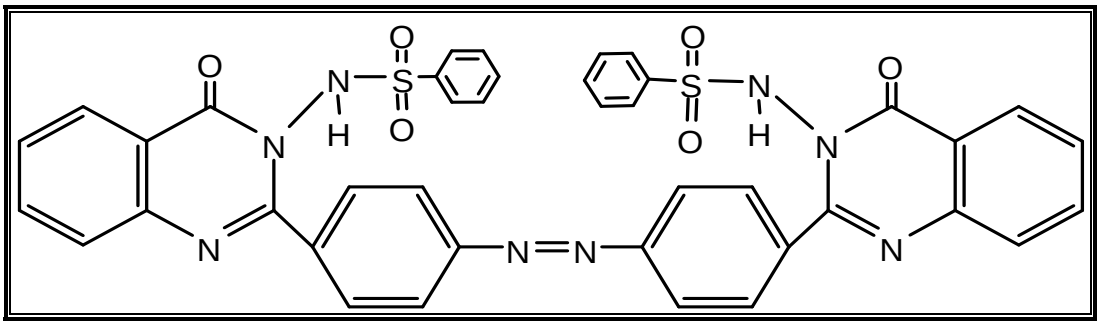


Figure (3-14): Structure of compound [VIA]

Azobenzen-p,p'-di[3,N-benzenesulphonamido-4(3H)quinazolinone-2-yl] [VIA], was synthesized by condensation of azobenzen-p,p'-di[3-amino-4(3H)quinazolinone-2-yl] [Va], with benzenesulphonylchloride in a malar ratio (1:2), characterized by FTIR, ^{1}H NMR, and ^{13}C NMR spectral analysis.

FT-IR spectral analysis of this compound [VIA] Fig (3-58), showed stretching frequency of quinazolin ring C=O and C=N bands at 1678 and 1620 cm^{-1} respectively, beside sulphonamido (NH) and azo (N=N) stretching bands at 3271 and 1446 cm^{-1} respectively. All these bands are summarized in Table (3-17).

^{1}H-NMR spectrum of this compound [VIA] Fig (3-59), showed all aromatic (-CH) and (-NH) sulphonamido proton as a cluster of multiple (28 H) signals at a range δ (6.8 – 8.8) and (4.04) ppm. All these signals are summarized in Table (3-19).

While ^{13}C-NMR spectrum of compound [VIA] Fig (3-60), showed aromatic (-CH), carbonyl carbon (C=O), and azomethin (–C=N) carbon signals of quinazolin ring as multiple at δ (107 - 143), (167) and (152) ppm respectively. All these signals are summarized in Table (3-20).

3.6.4. Synthesis of Azobenzen-p,p'-di[3,N(5'-nitrofurfuryidin-2'-ylimino)-4(3H)-quinazolinone-2-yl] [VIB]:

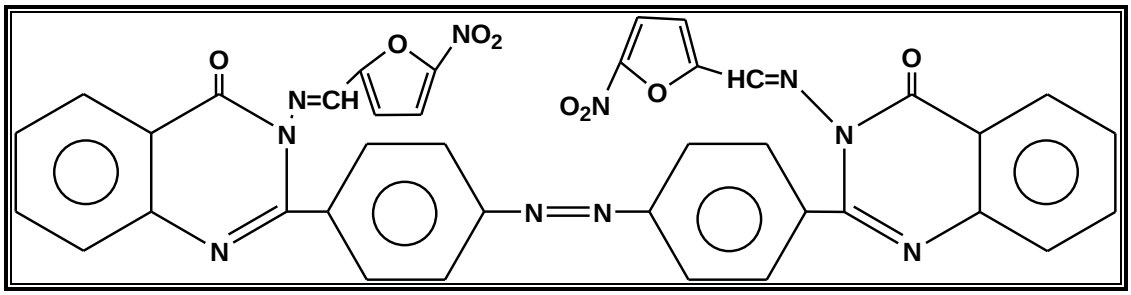


Figure (3- 15): Structure of compound [VIB]

Azobenzen-p,p'-di[3,N(5'-nitrofurfuryidin-2'-ylimino)-4(3H)quinazolinone-2-yl] [VIB], FT-IR spectrum Fig (3-61), showed stretching frequency of quinazolin ring C=O and C=N bands at 1689 and 1643 cm^{-1} respectively, as well as starching bands of azo N=N group at 1450 cm^{-1}, and asymmetric and symmetrical starching bands of NO_2 at 1535, 1302 cm^{-1} respectively. All these bands are summarized in Table (3-17).

- **Series Three:**

3.7. Synthesis of azobenzen-p,p'-di[3,O-substituted-4(3H)-quinazolinone-2-yl] [VIIA, VIIB]:

Condensation of azobenzen-p,p'-di[3-hydroxy-4(3H)quinazolinone-2-yl] [Vb], with benzyl chloride or acetyl chloride in a molar ratio (1:2), give azobenzen-p,p'-di[3,O-benzyl-4(3H)quinazolinone-2-yl] [VIIA], and azobenzen-p,p'-di[3,O-acetyl-4(3H)quinazolinone-2yl] [VIIB] respectively. These compounds are characterized by FT-IR, ^{1}H-NMR, and ^{13}C-NMR spectral analysis.

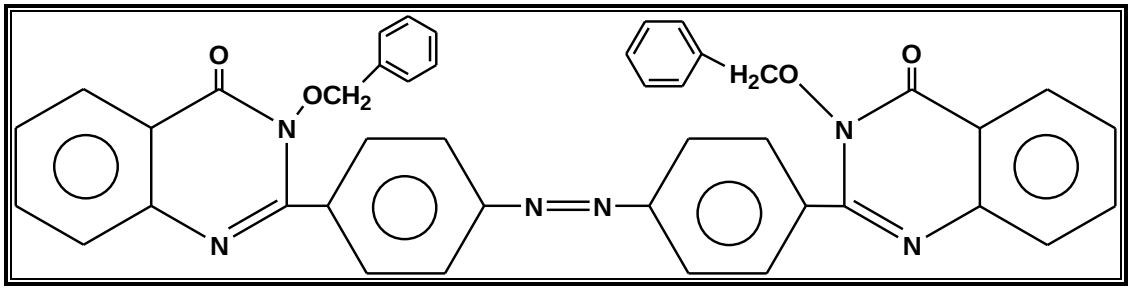


Figure (3-16): Structure of compound [VIIA]

FT-IR spectral analysis of compounds [VIIA] Fig (3-62), showed stretching band of azo (–N=N) at 1450 cm^{-1}, beside quinazolinone ring stretching C=O and C=N bands at 1666, 1604 cm^{-1} respectively. All these bands are summarized in Table (3-18).

But ^{1}H-NMR spectrum of compounds [VIIA] Fig (3-63), showed quinazolinone ring and phenyl ring protons as multiple (26H) protons, at δ (6.6 – 9.3) ppm, beside two methylene protons as (4H) protons at (4.7) ppm. All these signals are summarized in Table (3-19).

While ^{13}C-NMR spectrum of compound [VIIA] Fig (3-64), showed quinazolinone carbon as aromatic, (C=O), (C=N) carbons signal at δ (109 - 145), (168), (152) ppm respectively, beside methylene (-CH_2) carbon at δ (75.2) ppm. All these signals are summarized in Table (3-20).

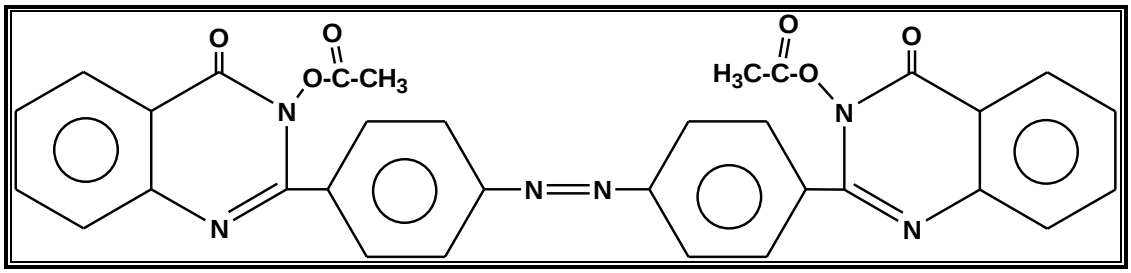


Figure (3-17): Structure of compound [VIIB]

FT-IR spectral analysis of compound [VIIB] Fig (3-65), showed (C=O) of (CH_3-CO) bands and azo (N=N) stretching bands at (1770, 1460) cm^{-1}, as well as to quinazolinone (C=O), (C=N) stretching bands of uredo group at (1625 and 1595) cm^{-1} respectively, which are given in Table (3-18).

^{1}H-NMR spectrum of compound [VIIB] Fig (3-66), showed quinazolinone ring protons as a multiple (16H) at δ (6.7 – 8.07) ppm, and methyl protons of acetyl groups as a singlet signal at δ (5.3) ppm, All these signals are summarized in Table (3-19).

^{13}C-NMR spectrum of compound [VIIB] Fig (3-67), showed quinazolinone ring as aromatic carbonyl carbon of (C=O), and (C=N) carbons as a multiple signals at δ (110 - 148) ppm, and singlet signals at δ (169 and 153) ppm respectively, beside carbon signal of methyl group at δ (71.9) ppm. All these signals are summarized in Table (3-20).

- **Series Four:**

3.8. Synthesis of Azobenzen-p,p'-di[3-hyrdo-4-quinazolinone-2-yl] [VIII]:

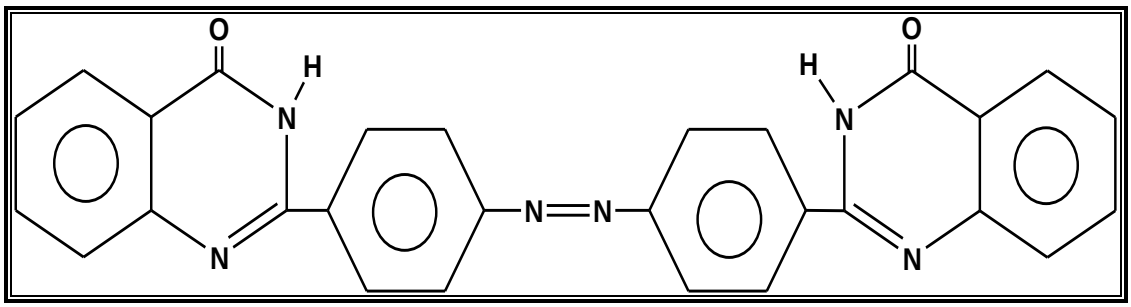


Figure (3-18): Structure of compound [VIII]

Heating (1:2) molar ratio of azobenzen-p,p'-di[3,1-benzoxazin-4-one-2-yl] [IV], with ammonium hydroxide and ammonium acetate, give azobenzen-p,p'-di[3-hydro-4-quinazolinone-2-yl] [VIII], which was characterized by FT-IR spectral analysis, ^{1}H-NMR, ^{13}C-NMR, and Mass spectral analysis.

FT-IR spectral analysis of compound [VIII] Fig (3-68), showed stretching bands of azo-group (N=N) at (1446) cm^{-1}, beside 3-hydro-4-quinazolinone ring starching bands (NH), (C=O), and (C=N), at (3271, 1674, 1596 cm^{-1}) respectively, which were given in Table (3-21).

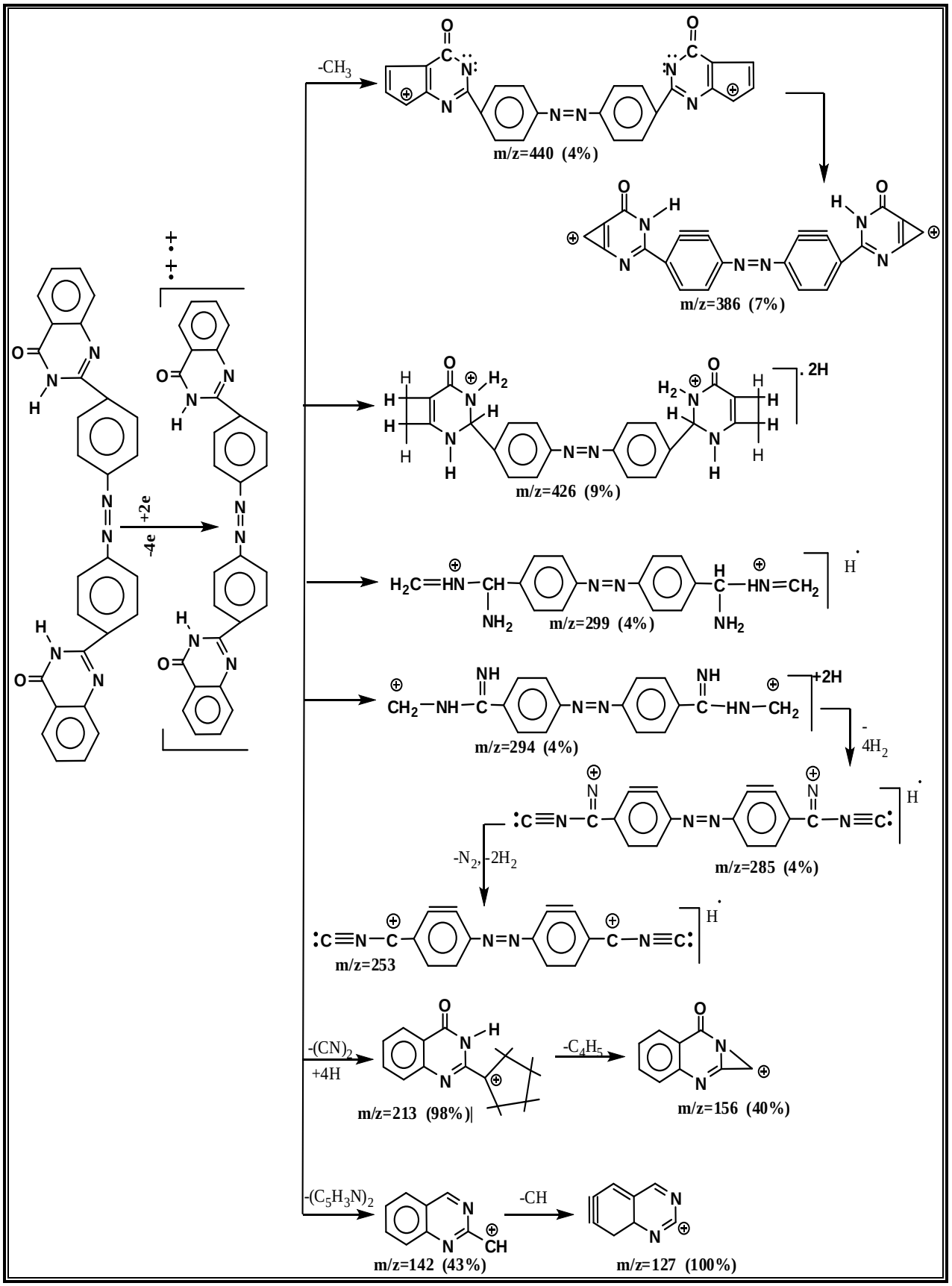
^{1}H-NMR spectrum of compound [VIII] Fig (3-69), showed aromatic (CH), and (NH) quinazolinone protons as a multiplet signals of (18H) at δ(7.1 - 8.7) ppm, which were shown in Table (3-22).

While ^{13}C-NMR spectrum of this compound [VIII] Fig (3-70), showed aromatic carbon of quinazolinone (C=O), and azomethine (C=N) carbons as a multiplet signals at (119 - 140), (160 and 150) ppm, respectively, All these signals are summarized in Table (3-23).

Mass spectral analysis of this compound [VIII] fig (3-71), showed [$M^{\cdot+2}$] ion at m/z (470) in the extensional part of this spectrum (using NL:8.01E6), as well as the fragmented ions m/z (440, 426, 386, 299, 294, 285, 253), probably obtained from decomposition of molecular ion, with charge considered to be

localized on carbonyl-oxygen atoms for both ends of azobenzene-p,p´-di[3-hydro-4-quinazolinone-2-yl] molecule [VIII].

Also other fragmented ions at m/z (213, 156, 141, 127), probably obtained from decomposition of molecular ion $M^{\cdot+2}$, with charge is considered to be localized on azo-nitrogen atoms at the middle of symmetrical molecule of compound [VIII]. All these decomposed ions are summarized in Table (3-24), probably would be concluded in the following scheme (3-16) of suggested mechanism.



Scheme (3-16) : Suggested fragmentation mechanism of azobenzen-p,p'-di[3-hydro-4-quinazolinone-2-yl] [VIII]

3.9. Synthesis of azobenzen-p,p'-di[4-chloro-quinazoline-2-yl] [IX]:

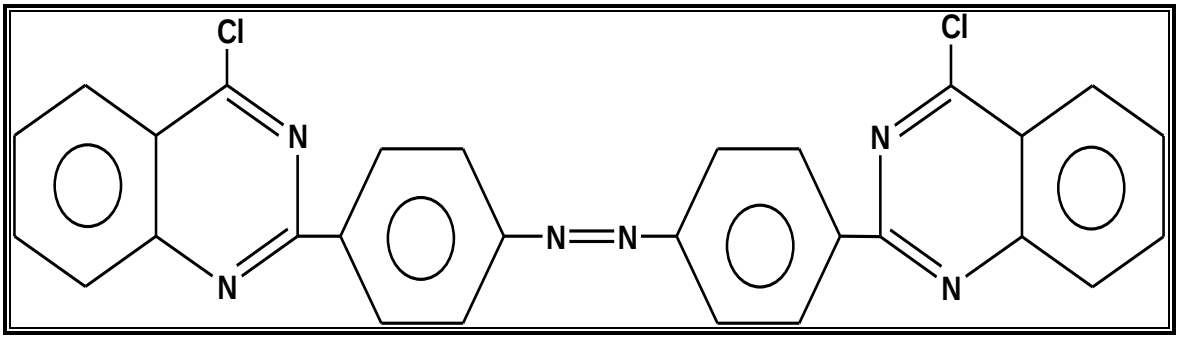


Figure (3-19): Structure of compound [IX]

Treatment of azobenzen-p,p'-di[3-hydro-4-quinazolinone-2-yl] [VIII], with phosphorus pantachloride / phosphorus oxychloride, give azobenzen-p,p'-di[4-chloro-quinzoline-2yl] [IX], which characterized by FT-IR, ^{1}H-NMR, ^{13}C-NMR and mass spectral analysis.

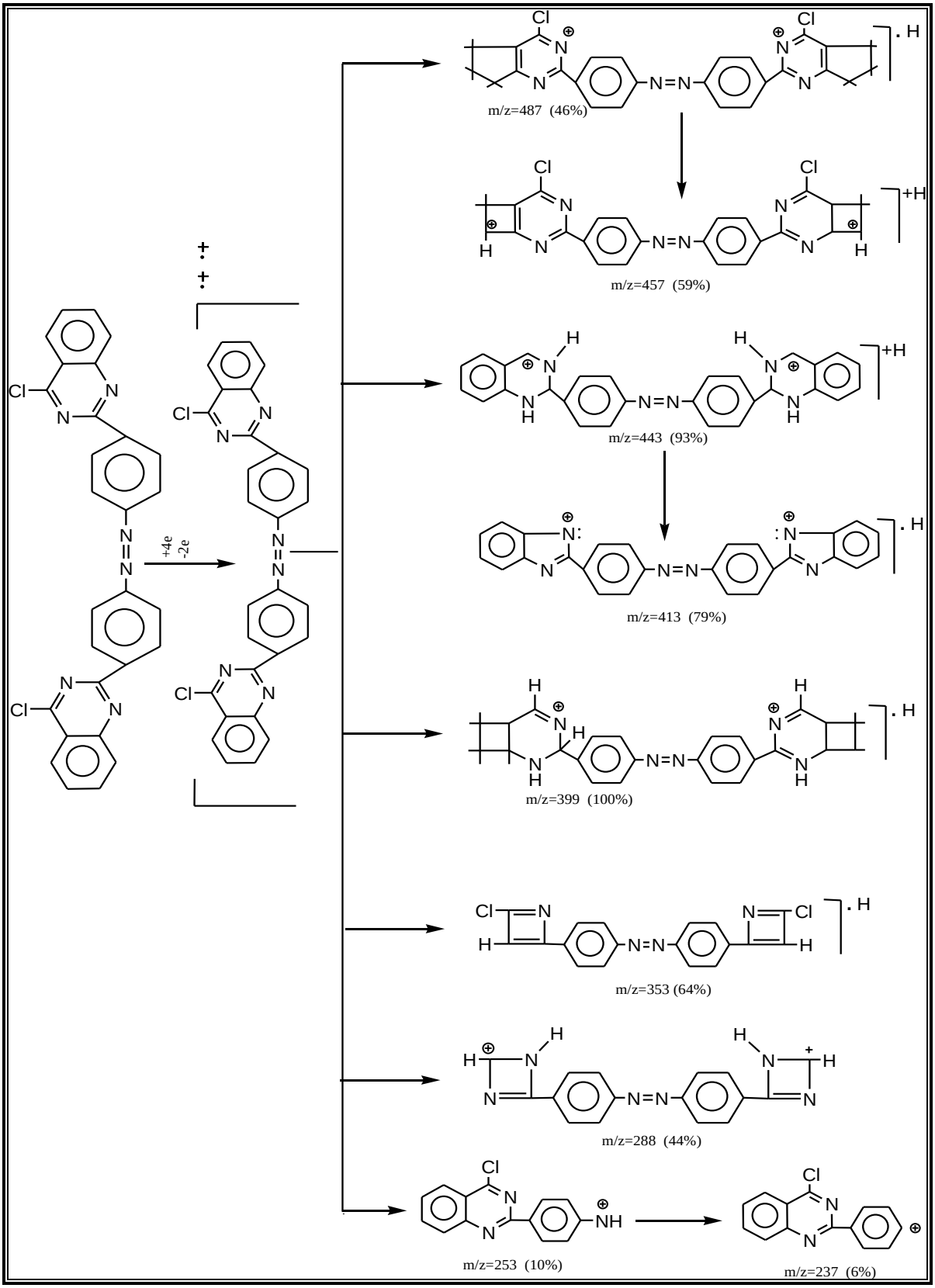
FT-IR spectrum of this compound [IX] Fig (3-72), showed azo starching band (N=N) at 1435 cm^{-1}, beside quinazoline (C=N) starching bands at 1605 cm^{-1} respectively, which are given in Table (3-21).

^{1}H-NMR spectrum of compound [VIII] Fig (3-73), showed aromatic (-CH) protons as a multiplet signals of (16H) at (6.3 - 8.8) ppm, which were shown in Table (3-22).

While ^{13}C-NMR spectrum of this compound [VIII] Fig (3-70), showed aromatic carbon, and azomethine (C=N) carbons as a multiplet signals at (120 - 144), (152) ppm respectively, All these signals are summarized in Table (3-74).

Mass spectrum of compound [IX] Fig (3-75), showed molecular ion $M^{\cdot+2}$ at m/z (507), in the extensional part of this spectrum using (NL:1.6E5), as well as fragmented ions m/z (487, 457, 413, 399, 353, 288), probably obtained from decomposition of molecular ion with charge is considered to be localized on quinazolin rings for both ends of azobenzen-p,p'-di[4-chloro-quinazolinone-2-yl] molecule [IX].

Also other fragmented ions at m/z (253, 237), probably obtained from decomposition of molecular ion $M^{\cdot+2}$ at m/z (507), with charge is considered to be localized on azo-nitrogen atoms at the middle of symmetrical molecule of compound [IX]. All these decomposed ions are summarized in Table (3-25), probably would be concluded in the following scheme (3-17) of suggested mechanism.



Scheme (3- 17) : Suggested fragmentation mechanism azobenzen-p,p'-di[4-chloro-quinzoline-2-yl] [IX]

3.9.1. Synthesis of azobenzen-p,p'-di[4-subsitituted-quinazolin-2-yl] [IXA, IXB]:

Substitution reaction of chlorine in azobenzen-p,p'-di[4-chloro-quinazolin-2-yl] [VIII], with p-tolidin or ethylenediamine, give azobenzen-p,p'-di[4,N-toluidino-quinazolin-2-yl] [IXA], and azobenzen-p,p'-di[4,N-aminoethylamine-quinazolin-2-yl] [IXB] respectively.

-Azobenzen-p,p'-di[4,N-toluidino-quinazolin-2-yl] [IXA], was characterized by FT-IR, ^{1}H-NMR and ^{13}C-NMR spectral analysis.

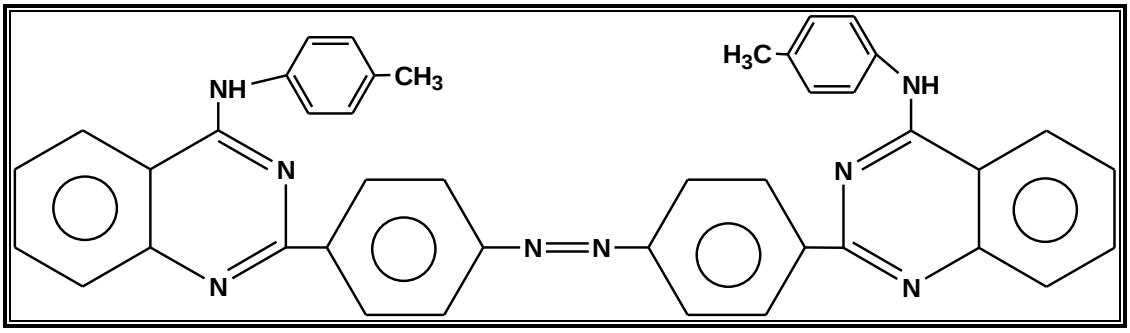


Figure (3-20): structure of compound [IXA]

FT-IR spectral analysis of compound [IXA] Fig (3-76), showed (NH) stretching bands of amino group (NH) and azo (N=N) at (3421, 1436) cm^{-1} respectively. All these bands are summarized in Table (3-21).

While ^{1}H-NMR spectrum of this compound [IXA] Fig (3-77), showed singlet signal of methyl protons as (6H) at δ (3.5) ppm and (NH) at δ(7.5)ppm, as well as aromatic ring (CH) proton and amino proton as a multiplet signal of (26H) proton at δ (7.2 - 8.7) ppm. All these signals are summarized in Table (3-22).

But ^{13}C-NMR spectrum of compound [IXA] Fig (3-78), showed methyl carbon (CH_3) as a singlet signal at δ (93) ppm, beside quinazolin ring (aromatic carbon and azomethine carbon (C=N) carbon) as a multiplet signals at δ (117 - 146 and 153) ppm respectively. All these signals are summarized in Table (3-23).

-Azobenzen-p,p'-di[4,N-aminoethylamine-quinazolin-2-yl] [IXB], was characterized by FT-IR, ^{1}H-NMR and ^{13}C-NMR spectral analysis.

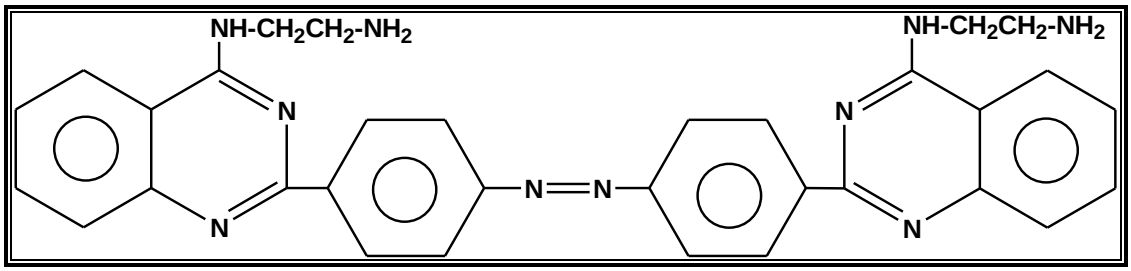


Figure (3-21): Structure of compound [IXB]

FT-IR spectrum Fig (3-79), showed both (NH) and (NH_2) starching bands at 3421, 3305, 3282 cm^{-1} and azo starching bands (N=N) at 1436 cm^{-1}, beside quinazolin ring azomethine (C=N) at 1641, 1598 cm^{-1} respectively, which are given in Table (3-21).

While ^{1}H-NMR spectrum of this compound [IXB] Fig (3-80), showed singlet signal of methyl protons at δ (2.1) ppm, and as well as aromatic ring (CH) proton and amino proton as a multiplet signal of (24H) proton at δ (7.5 – 7.8) ppm. All these signals are summarized in Table (3-22).

But ^{13}C-NMR spectrum of compound [IXB] Fig (3-81), showed methyl carbon (CH_3) as a singlet signal at δ (83.3) ppm, beside quinazolin ring (aromatic carbon and azomethine carbon (C=N) carbon) as a multiplet signals at δ (120 - 135 and 153) ppm respectively. All these signals are summarized in Table (3-23).

- **Series Five:**

3.10. Synthesis of azobenzen-p,p'-di[3-substituted-4(3H)-quinazolin-thion-2-yl] [X(A, B, C, D, E, F, G, I, J, K, L, P), XI']:

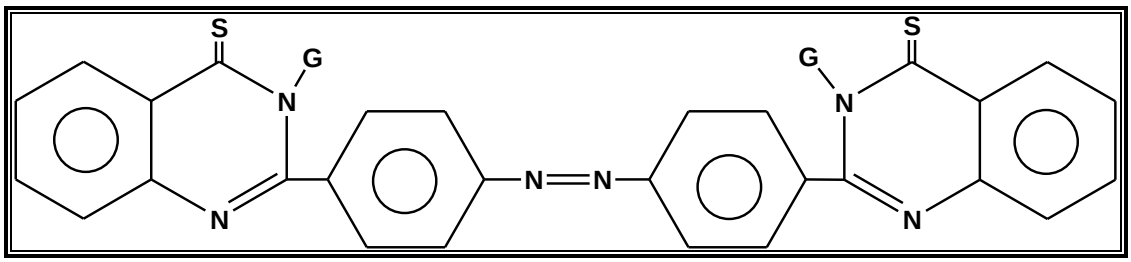
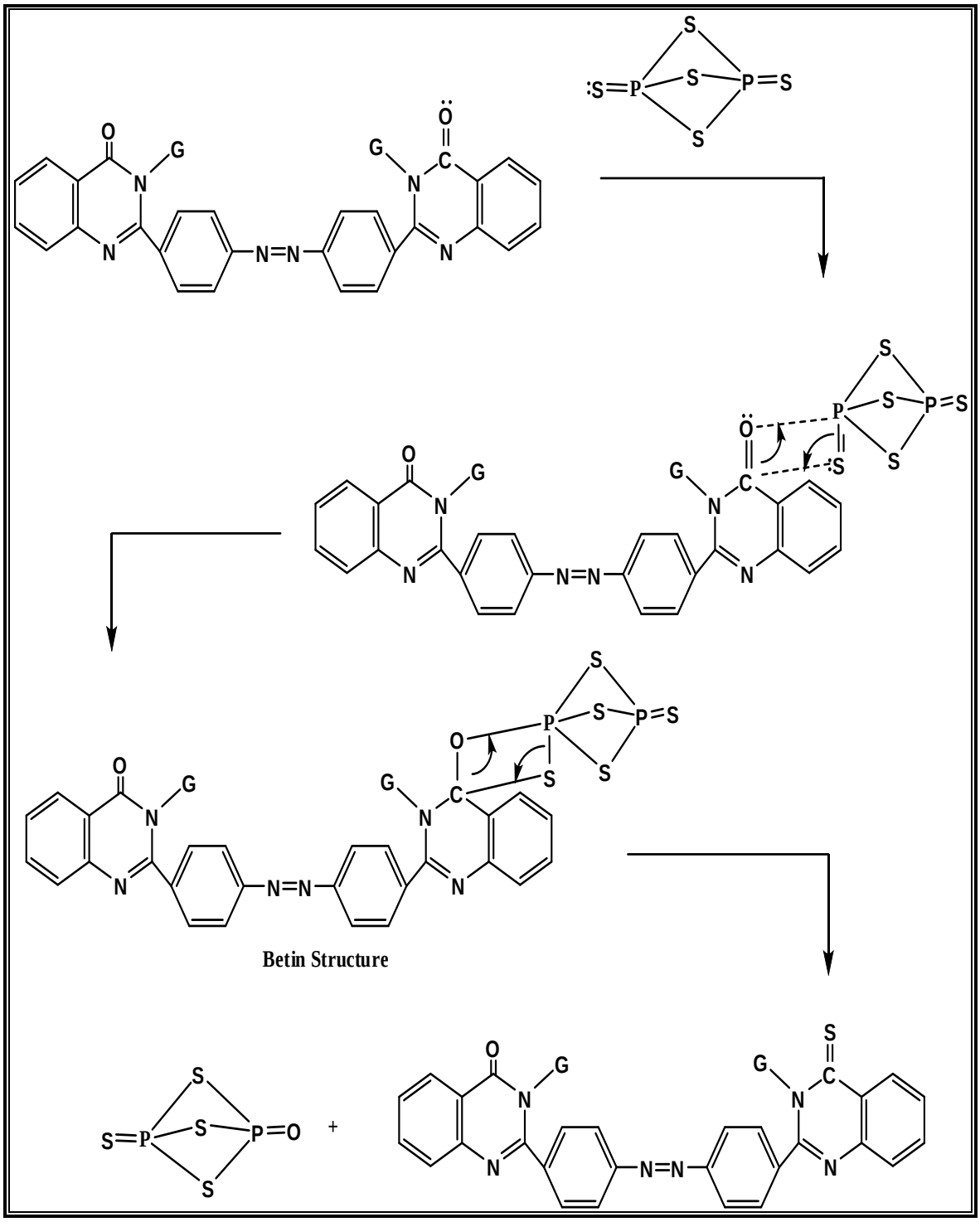


Figure (3-22): Structure synthetic of compound [X]

Whenever heating some of azobenzen-p,p'-di[3-substituted-4(3H)quinazolinone-2-yl], [V(a, b, c, d, e, f, g, i, j, k, l, k, p), VIII], with excess of phosphorouspenta sulphide in pyridine, give azobenzen-p,p'-di[3-substituted-4(3H)quinazolinthion-2-yl] [X(A, B, C, D, E, F, G, I, J, K, L, P), IX'], these compounds were characterized by FT-IR, some of them characterized by ^{1}H-NMR, ^{13}C-NMR [X(A, B, F, G, P), IX'], and mass spectral analysis for compounds [X(A, B, D, E)] .

Formation of compounds [X derivatives and XI'], from reaction of [V derivatives and VIII], with phosphorus penta sulphide (P_2S_5), would follow this reaction path-way [171] scheme (3-18).



Scheme (3-18) : Mechanism of formation azobenzen-p,p'-di[3-substituted-4(3H)-quinazolin-thion-2-yl] [X(A, B, C, D, E, F, G, I, J, K, L, P), XI']

FT-IR spectrum analysis of compounds [X(A, B, C, D, E, F, G, I, J, K, L, P), IX'], Figs [(3-82), (3-107)], were found to have stretching quinazolin-4-thion bands of (C=S, C=N) at (1394 - 1327, 1625 - 1558) cm^{-1} respectively, and stretching bands of (N=N) azo groups at (1450 - 1440) cm^{-1}, as well as to the other functional group starching bands of 3-substituted moiety, are shown in Table (3-26).

^{1}H-NMR spectrum of compound [X(A, B, F, G, P), IX'] Figs. [3(83, 87, 95, 106)], showed beside quinazolin aromatic protons as a multiplet signals at δ (6.6 - 9.6) ppm, some proton signals of 3-substituted moiety like, NH_2, OH, $NHCSNH_2$, NH, protons signals, which were shown in Table (3-27).

As well as ^{13}C-NMR spectral analysis of compounds [X(A, B, F, G, P), IX'] Figs [3(84, 88, 96, 100, 107)] respectively, showed quinazolin-4-thion aromatic, (C=S), (C=N) carbon signals at δ (110 - 148), (185 - 190), (151 - 153) ppm respectively, beside to the other carbon signals of 3-substituted moiety, are shown in Table (3-28).

3.10.1. Synthesis of azobenzen-p,p'-di[3-amino-4(3H)quinazolin-thion-2-yl] [XA]

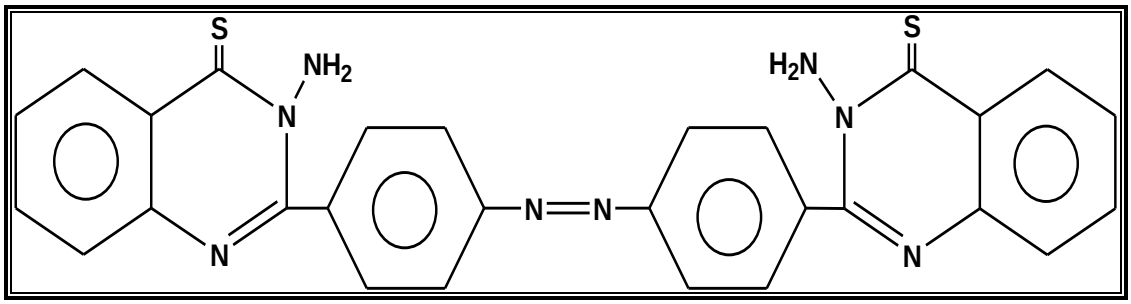


Figure (3-23): structure of compound [XA]

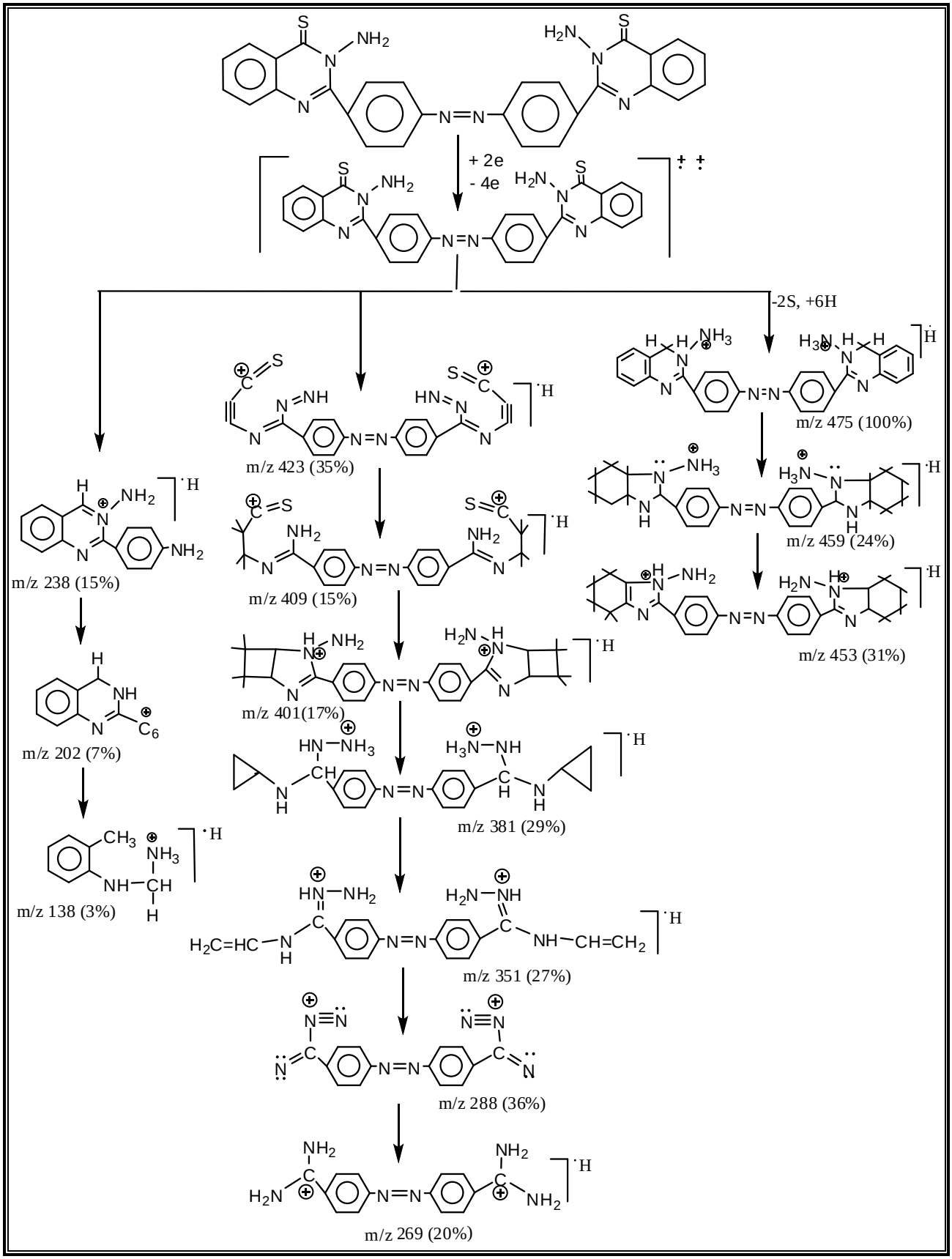
Azobenzen-p,p'-di[3-amino-4(3H)quinazolin-thion-2-yl] [XA], FT-IR spectrum Fig (3-82), showed C=S, C=N stretching bands of quinazolin-4-thion, and N=N stretching bands at (1392, 1608 and 1450) cm^{-1} respectively, beside to NH_2- stretching bands at (3460 – 3394) cm^{-1}. All these bands are given in Table (3-26).

^{1}H-NMR spectral analysis of compound [XA] Fig (3-83), showed quinazoin-4-thion aromatic protons as multiplet signals at δ (6.6 - 7.9) ppm in combination with NH_2- protons at (4.2 - 5.4) ppm as (20 H) protons. All these signals are summarized in Table (3-27).

But ^{13}C-NMR spectral analysis for compound [XA] Fig (3-84), showed quinazolin-4-thion ring (C=S, C=N, and aromatic carbon signals) at δ (180, 153, and 110 - 145) ppm respectively. All these signals are given in Table (3-28).

Mass spectrum of compound [XA] Fig (3-85), showed molecular ion [$M^{\cdot+2}$] at m/z (532), in the extensional part of this spectrum using (NL:1.75E5), as well as fragmented ions m/z (475, 459, 453, 423, 409, 401, 381, 351, 288, 269), probably obtained from decomposition of molecular ion with charge is considered to be localized on thion-sulpher atoms for both ends of azobenzen-p,p'-di[3-amino-4(3H)quinazolinthion-2yl] [XA] molecule. Also other fragmented ions at m/z (238, 202, 138), probably obtained from decomposition of molecular ion $M^{\cdot+2}$ of this compound, with charge is considered to be localized on azo-nitrogen atoms at the middle of symmetrical molecule of

compound [XA]. All these decomposed ions probably are summarized in Table (3-29), would be concluded in the following scheme (3-19) of suggested mechanism.



Scheme (3-19) : Suggested fragmentation mechanism of azobenzen-p,p´-di[3-amino-4(3H)quinazolin-thion-2-yl] [XA]

3.10.2. Synthesis of azobenzen-p,p'-di[3-hydroxy-4(3H)quinazolin-thion-2-yl] [XB]:

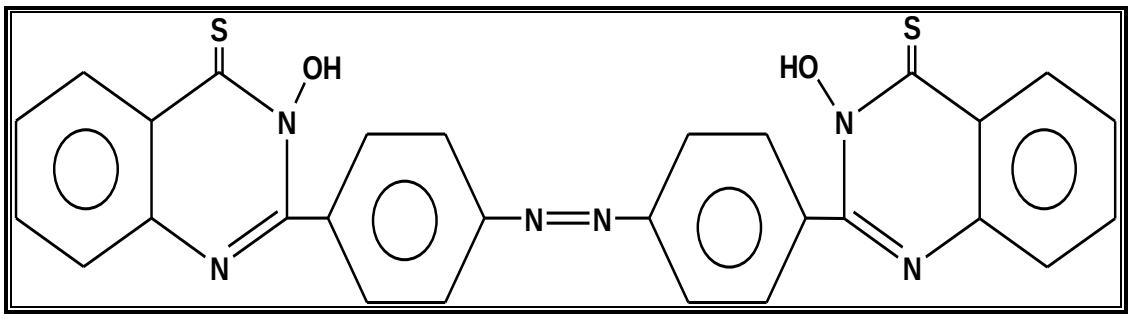


Figure (3-24): structure of compound [XB]

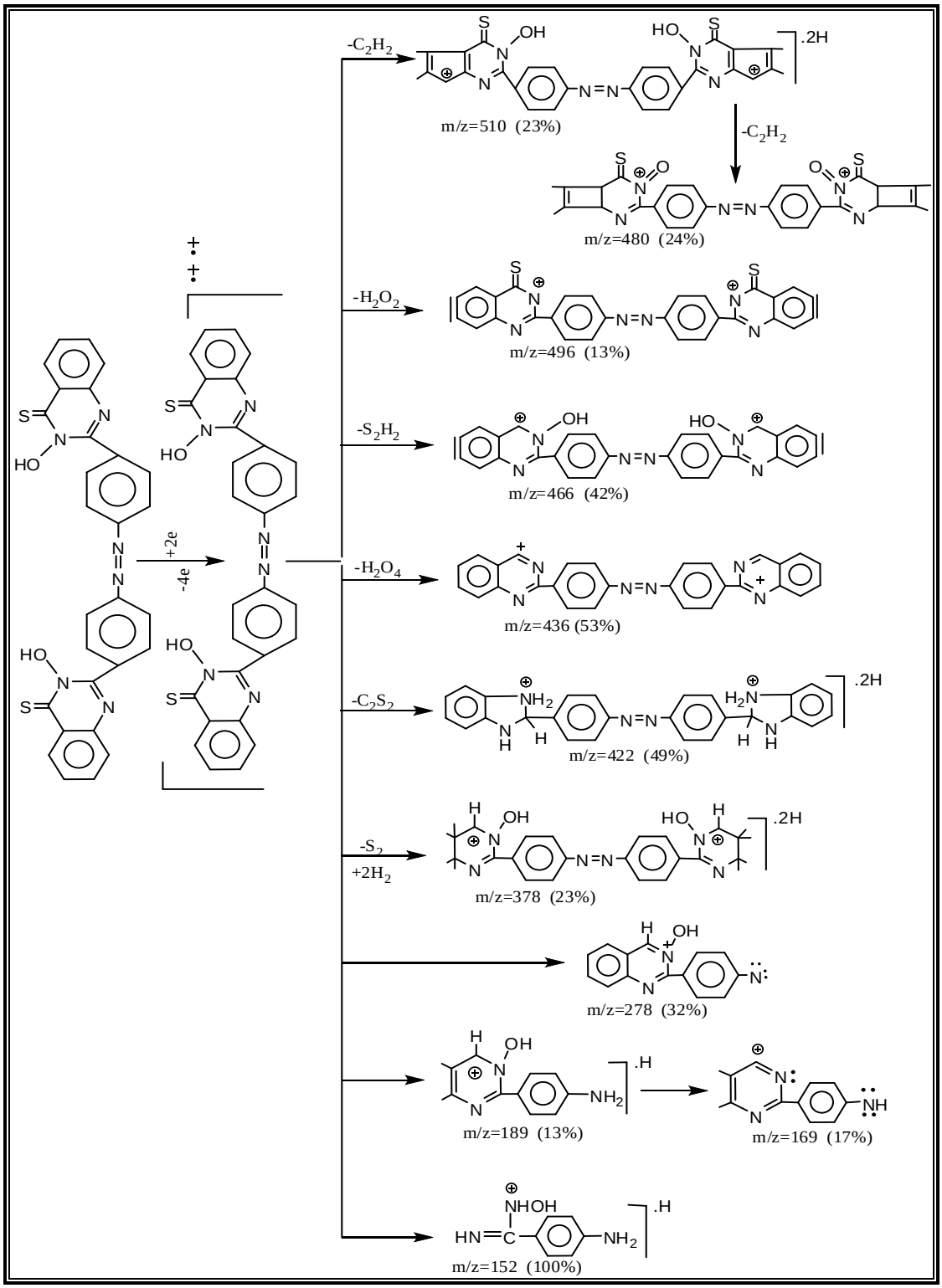
Azobenzen-p,p'-di[3-hydroxy-4(3H)-quinazolinthion-2-yl] [XB], FT-IR spectrum Fig (3-86), showed C=S, C=N stretching bands of quinazolin-4-thion ring, and N=N stretching bands at (1375, 1604 and 1446) cm^{-1} respectively, beside to -OH stretching bands at (3174 – 2806) cm^{-1}. All these bands are summarized in Table (3-26).

^{1}H-NMR spectral analysis of compound [XB] Fig (3-87), showed quinazoin-4-thion aromatic protons as a multiplet signals of (18H) protons at (7.2 - 7.85) ppm, and a single signal of (OH) protons as (2H) protons at 10.7 ppm. All these signals are summarized in Table (3-27).

^{13}C-NMR spectral analysis for compound [XB] Fig (3-88), showed quinazolin-4-thion ring (C=S, C=N, and aromatic carbon signals) at (184, 158, and 120 - 140) ppm respectively. All these signals are summarized in Table (3-28).

Mass spectrum of compound [XB] fig (3-89), showed molecular ion $M^{\cdot+2}$ at m/z (534), in the extensional part of this spectrum using (NL:3.95E6), as well as fragmented ions at m/z (510, 496, 466, 436, 422, 378), probably obtained from decomposition of molecular ion with charge is considered to be localized on thion-sulpher atoms for both ends of azobenzen-p,p'-di[3-hydroxy-4(3H)quinazolinthion-2-yl] molecule [XB]. Also other fragmented ions at m/z (189, 169, 152), probably obtained from decomposition of molecular ion $M^{\cdot+2}$ of this compound, with charge is considered to be localized on azo-nitrogen atoms

at the middle of symmetrical molecule of compound [XB]. All these decomposed ions are summarized in Table (3-30), probably would be concluded in the following scheme (3-20) of suggested mechanism.



Scheme (3-20) : Suggested fragmentation mechanism of azobenzen-p,p'-di[3-hydroxy-4(3H)quinazolin-thion-2-yl] [XB]

3.10.3. Synthesis of azobenzen-p,p'-di[3(p-benzensulphonamido)-4(3H)quinazolinthion-2-yl] [XD]:

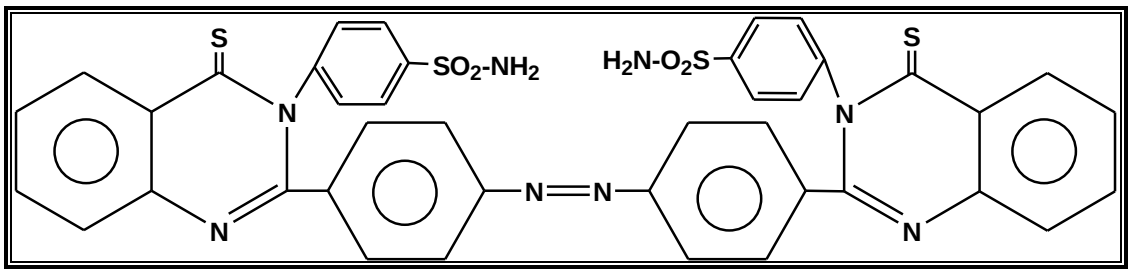
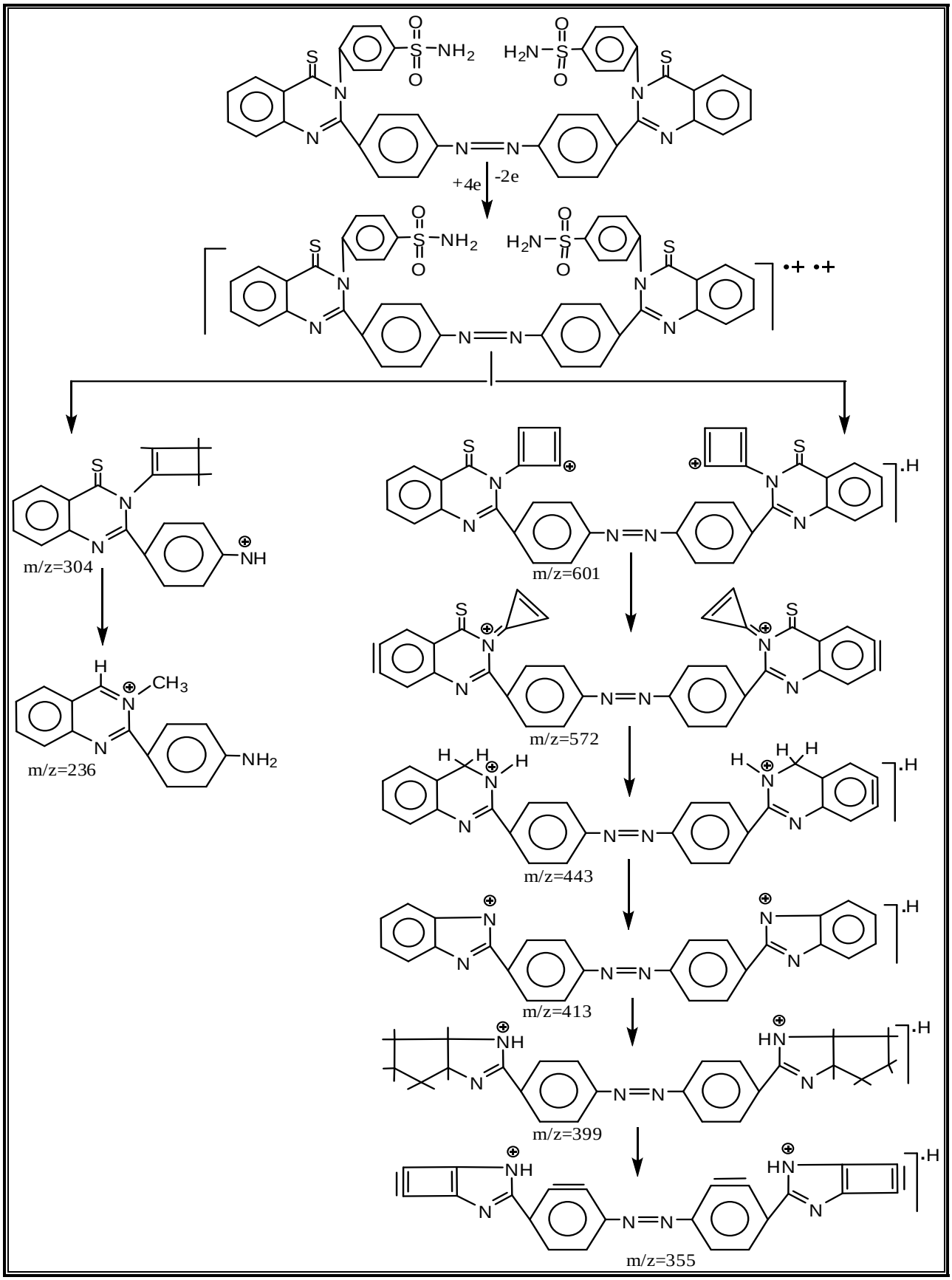


Figure (3-25): structure of compound [XD]

Azobenzen-p,p'-di[3(p-benzensulphonamido)-4(3H)quinazolin-thion-2-yl] [XD], FT-IR spectrum Fig (3-91), showed C=S, C=N stretching bands of quinazolin-4-thion ring, and N=N stretching bands at (1296, 1664 and 1450) cm^{-1} respectively, beside to stretching band (NH_2) at (3471 - 3367) cm^{-1}. All these bands are summarized in Table (3-26).

Mass spectrum of compound [XD] Fig (3-92), does not show molecular ion $M^{\cdot+2}$ at m/z (812), but showed fragmented ions m/z (601, 572, 443, 413, 399, 355), probably obtained from decomposition of molecular ion with charge is considered to be localized on thion-sulpher atoms for both ends of azobenzen-p,p'-di[3(p-benzensulphonamido)-4(3H)quinazolinthion-2-yl] molecule [XD]. Also other fragmented ions at m/z = (304, 236), probably obtained from decomposition of molecular ion $M^{\cdot+2}$ of this compound, with charge is considered to be localized on azo-nitrogen atoms at the middle of symmetrical molecule of compound [XD]. All these decomposition ions are summarized in Table (3-31), probably would be concluded in the following scheme (3-21) of suggested mechanism.



Scheme (3-21) : Suggested fragmentation mechanism of azobenzen-p,p'-di[3(p-benzensulphonamido)-4(3H)quinazolin-thion-2-yl] [XD]

3.10.4. Synthesis of azobenzen-p,p'-di[3(2'-pyrimidino)-4(3H)-quinazolin-thion-2-yl] [XE]:

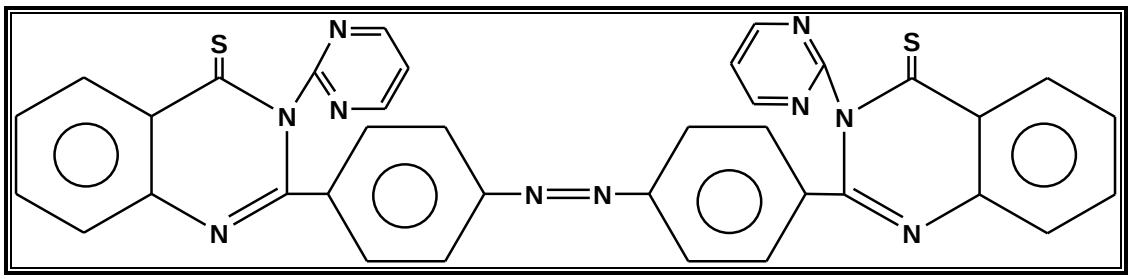
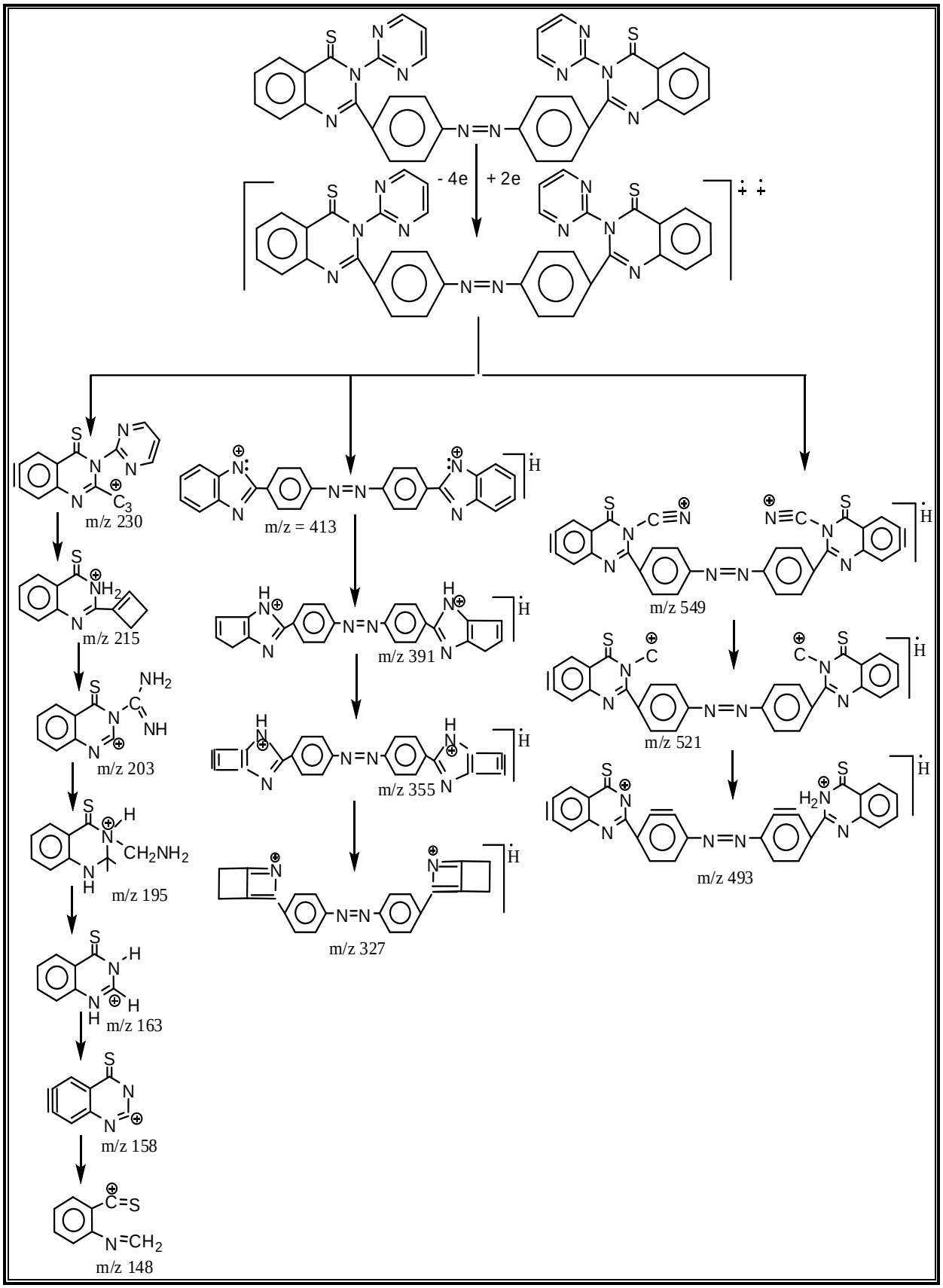


Figure (3-26): structure compound of [XE]

Azobenzen-p,p'-di[3(2'-pyrimidino)-4(3H)-quinazolin-thion-2-yl] [XE], FT-IR spectrum Fig (3-93), showed C=S, C=N stretching bands of quinazolin-4-thion ring, and N=N stretching bands, at (1354, 1616 and 1450) cm^{-1} respectively. All these bands are summarized in Table(3-26).

As well as ^{13}C-NMR spectrum for compound [XE] Fig (3-94), showed quinazolin-4-thion ring [C=S, (C=N), and aromatic carbons as a singlet signals and multiplet signals) at δ [179, (150, 152) and 112 – 149] ppm respectively. All these signals are summarized in Table (3-28).

Mass spectrum of compound [XE] Fig (3-95), showed molecular ion [$M^{\cdot+2}$] at m/z (658), in the extensional part of this spectrum using (NL:1.55E5), as well as fragmented ions at m/z (549, 521, 493, 413, 391, 355, 327), probably obtained from decomposition of molecular ion with charge is considered to be localized on thion-sulpher atoms for both ends of azobenzen-p,p'-di[3(2'-pyrimidino)-4(3H)quinazolin-thion-2-yl] molecule [XE]. Also other fragmented ions at m/z (230, 215, 203, 195, 163, 158, 148), probably obtained from decomposition of molecular ion $M^{\cdot+2}$ of this compound, with charge is considered to be localized on azo-nitrogen atoms at the middle of symmetrical molecule of compound [XF]. All these decomposition ions are summarized in Table (3-32), probably would be concluded in the following scheme (3-22) of suggested mechanism.



Scheme (3-22) : Suggest mechanism of azobenzen-p,p'-di[3(2'-pyrimidino)-4(3H)quinazolinthion-2-yl] [XE]

Table (3-1): FT-IR spectral data (Wave number υ⁻) of the compounds main scheme

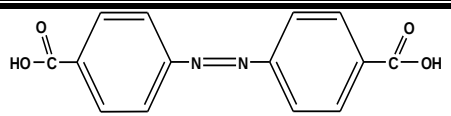
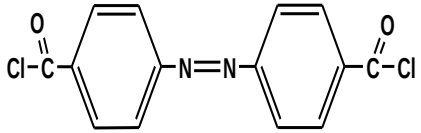
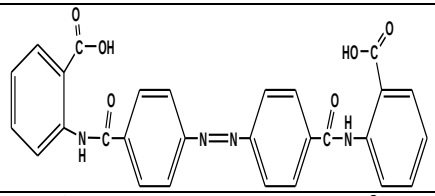
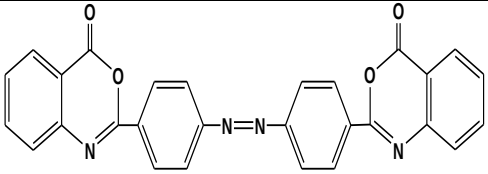
Comp. No.	Structure	υ (-OH)	υ (–NH)	υ (C=O)	υ (–N=N-)	υ (-C=N-) ring quinazolinion	υ(-NH) Amide II & I	others
[I]		3437-2544	-	1693 s,br	1575	–	-	υCH Ar. 3088
[II]		-	-	1774 1712	1597	–	-	υCH Ar. 3097
[III]		3232-2924	3435	1751 1676	1535	–	1589 1185	υCH Ar. 3012
[IV]		-	-	1762	1570	1604	-	υCH Ar. 3078

Table (3-2): ^{1}H-NMR spectral data (δ ppm) of the compounds main scheme

Comp. No.	-OH	Aromatic–H	–NH ring	Other
I	-	-	-	-
II	-	7.9-8.1	-	-
III	12	7.1-8.6	8.5	-
IV	-	7.5-8.4	-	-

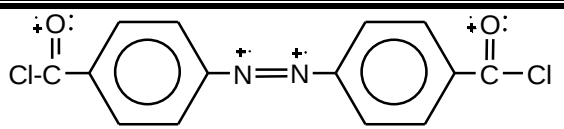
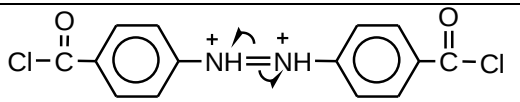
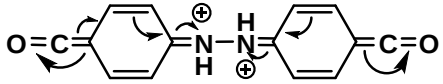
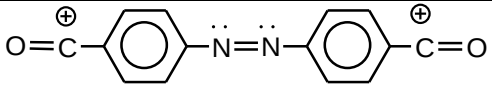
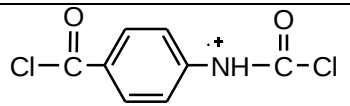
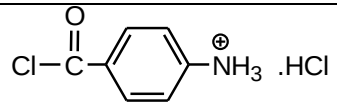
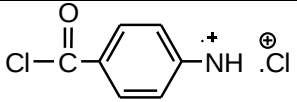
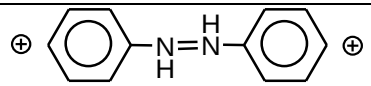
Table (3-3): ^{13}C-NMR spectral data (δ ppm) of the compounds main scheme

Comp. No.	Aromatic–C	-C=O	C=O amide	C=N ring	other
I	-	-	-	-	-
II	122-135	167	-	154	-
III	122-140	191	164	153	-
IV	119-140	166	-	153	-

Table (3-4): C.H.N- analysis data of the compounds main scheme

Comp. No.	Analysis found / calculate		
	C	H	N
[I]	62.24 / 62.4	3.70 / 3.8	10.36 / 10.0
[II]	71.48 / 71.45	3.82 / 3.81	17.8 / 18.23
[III]	54.7 / 54.00	2.60 / 2.52	9.12 / 8.95
[IV]	71.18 / 70.92	3.38 / 3.58	13.55 / 13.79
[Va]	67.2 / 67.48	4.0 / 4.11	22.4 / 22.13
[Ve]	69.0 / 69.09	3.51 / 3.43	22.36 / 22.58

Table (3-5): Fragmentation of azobenzene-p,p'-diacidchloride [II]

% Abundance	Fragments	Possible positive ion
3% (307)	$(M)^{+\cdot}$	
4% (309)	$(M–2H)^{+2}$	
7% (238)	M-Cl+2H	
10% (236)	M-2Cl	
38% (217)	M-C_6H_5	
20% (191.9)	M-C_7O	
11% (189.9)	M-C_7H_3NO	
18% (182)	M-$COCl_2$+2H	

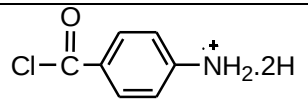
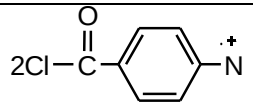
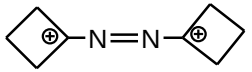
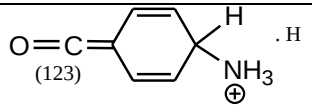
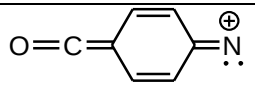
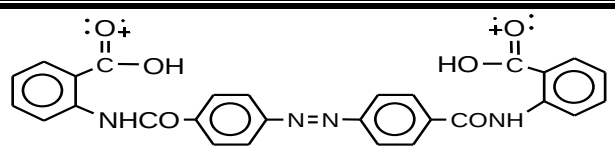
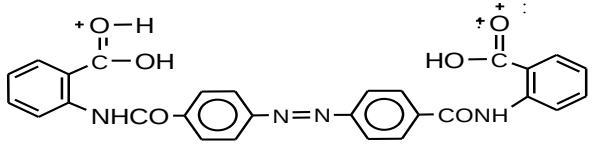
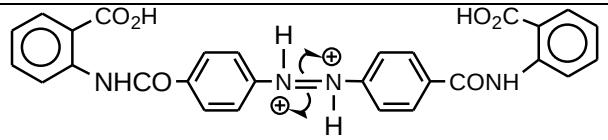
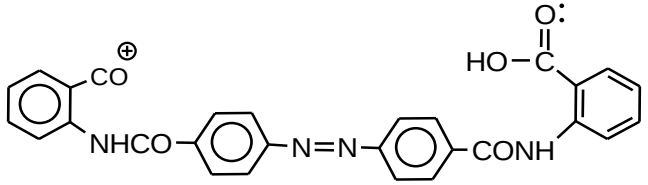
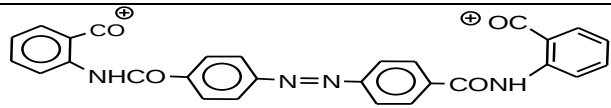
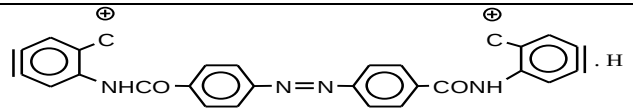
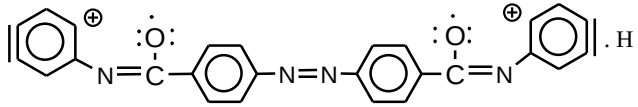
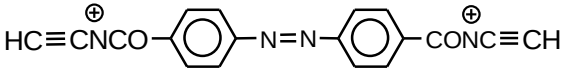
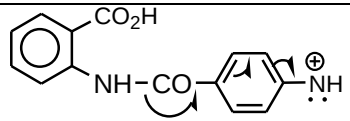
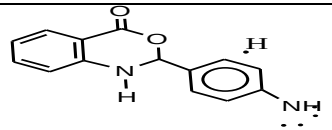
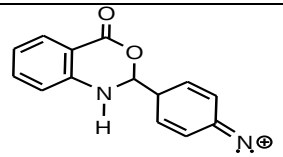
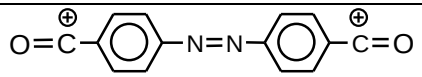
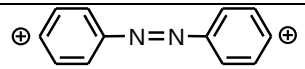
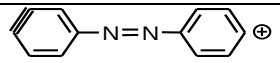
40% (157.9)	M-C_7H_3NOCl	
33% (153.9)	M-C_7H_3NOCl	
12% (137)	M-$C_6HO_2Cl_2$+4H	
50% (123)	M-C_7NOCl_2+H	
17% (118)	M-$C_7H_4NOCl_2$	

Table (3.6): Fragmentation of azobenzene-p,p'-[(dibenzoic acid-2yl)dicarboxamido] [III]

% Abundance	Fragments	Possible positive ion
4% (508)	$(M+H)^+$	
12% (509)	M+H	
5% (510)	M+2H	
23% (491)	M-OH	
5% (474)	$M-H_2O_2$	

% (439)	M-H_6O_4	
% (413)	M-$C_2H_8O_4$	
% (314)	M-$C_{10}H_{10}O_4$	
% (255)	M-$C_4H_9N_2O_3$	
% (239)	M-$C_{14}H_{10}N_2O_4$	
% (237)	M-$C_{14}H_{11}N_2O_4$	
% (236)	M-$C_4H_{12}N_2O_4$	
% (180)	M-$C_{16}H_{12}N_2O_6$	
% (179)	M-$C_{16}H_{13}N_2O_6$	

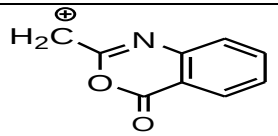
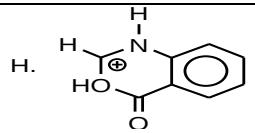
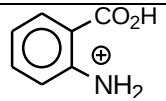
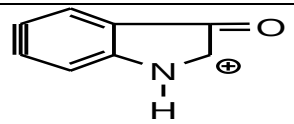
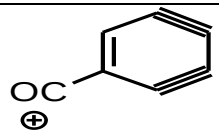
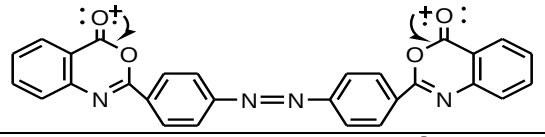
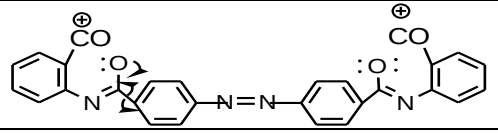
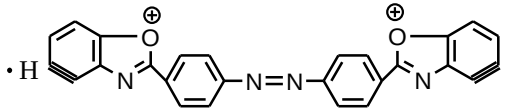
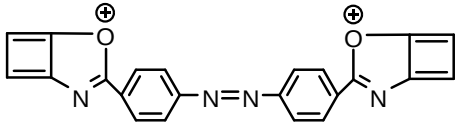
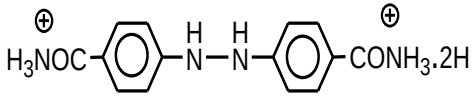
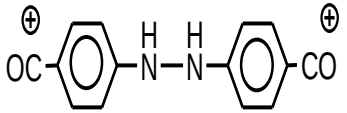
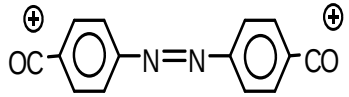
%(158.9)	M-$C_{20}H_{15}N_3O_4$	
% (148.9)	M-$C_{20}H_{15}N_3O_4$	
% (137)	M-$C_{21}H_{13}N_3O_4$	
% (129)	M-$C_{20}H_{17}N_3O_3$	
% (101)	M-$C_{21}H_{19}N_4O_5$	

Table (3-7): Fragmentation of azobenzene-p,p'-di[1,3-benzoxazine-4-one-2-yl] [IV]

% Abandance	Fragments	Possible positive ion
% (472)	$(M)^{+.2}$	
% (472)	$M^{.+2}$	
100% (413)	$M-2H_2O$	
10% (365)	$M-C_4H_2O_2$	
14% (274)	$M-C_{14}O_4$	
38% (238)	$M-C_{14}H_{10}N_2O_2$	
20% (236)	$M-C_{14}H_8N_2O_2$	

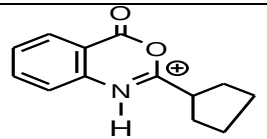
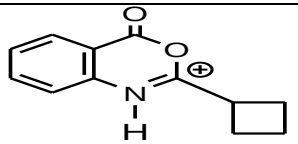
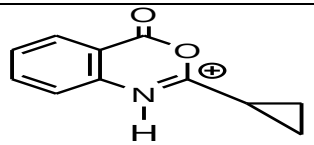
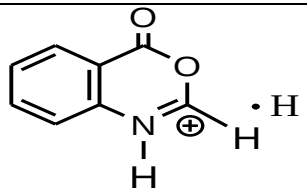
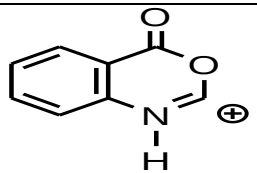
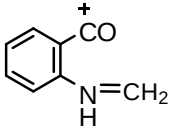
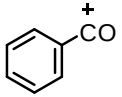
8% (216)	M-$C_{15}H_3N_3O_2$	
33% (203)	M-$C_{16}H_4N_3O_2$	
4% (188)	M-$C_{17}H_6N_3O_3$	
3% (149)	M-$C_{20}H_{10}N_3O_2$	
10% (146.9)	M-$C_2H_{11}N_3O_2$	
13% (132)	M-$C_{13}H_6O_2$	
20% (105)	M-$C_{14}H_8NO$	

Table (3-8): FT-IR spectral data (Wave number □–) of the compounds series one

COMP. NO.	ῡ(-NH_2) & ῡ(-NH)	ῡ(C=O)	ῡ(-OH)	ῡ(-N=N-)	ῡ (-C=N-)	ῡ(–NO_2)	ῡ(-C=S)	ῡ(-CH)
Va	3307 3217	1664	-	1583	1606	-	-	Ar. 3051
Vb	-	1705	3365-2571	1446	1606	-	-	Ar.3032
Vc	-	1680	-	1453	1664	-	-	Al. 2862 Ar. 3008
Vd	3464 3236	1670	-	1450	1596	-	-	Ar. 3050
Ve	-	1676	-	1455	1625 1600	-	-	Ar. 3068
Vf	-	1666	-	1450	1606	1525 1390	-	Ar. 3118

Comp. No	ῡ(NH_2) & ῡ(NH)	ῡ(C=O)	ῡ(OH)	ῡ(-N=N-)	ῡ(-C=N)	ῡ($-NO_2$)	ῡ(-C=S)	ῡ(-CH)
Vg	3433 3213	1661	-	1450	1610	-	-	3050
Vh	-	1629	-	1454	1571	-	-	3078 3043
Vi	3275 3210	1666	-	1446	1624	-	-	3116
Vj	3414 3332 3221	1620	-	1448	1510	-	-	3095
Vk	3367 3217	1654	-	1446	1600	-	-	3036
Vl	3367 3174	1697	-	1450	1624	-	-	3082
Vm	-	1658	-	1451	1637	-	1292	Al 2877 Ar 3078

Comp. No.	ῡ(-NH_2) & (-NH)	ῡC=O)	ῡ(-OH)	ῡ(-N=N-)	ῡ(-C=N)	ῡ(-NO_2)	ῡ(-C=S)	(-CH)
Vn	3226	1654	-	1454	1604	-	-	Ar.3078
Vo	3444 3398 3186	1670	-	1450	1600	-	-	3012
Vp	3429 3309 3212	1670	-	1469	1604	-	1246	3117

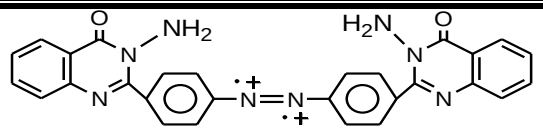
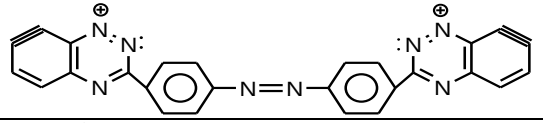
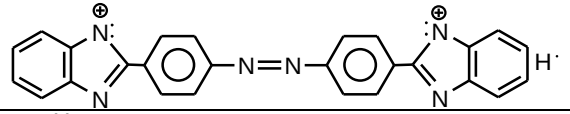
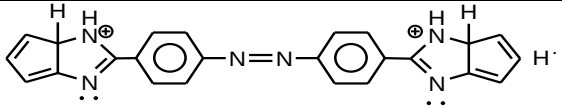
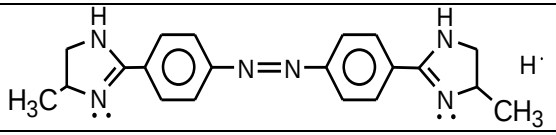
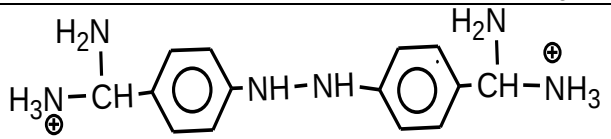
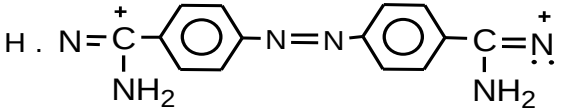
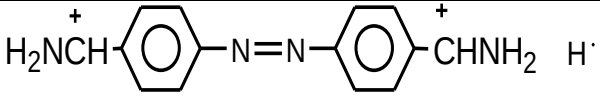
Table (3-9): ^{1}H-NMR spectral data (δ ppm) of the compounds series one

Comp. No.	–OH	Aromatic–H	–NH_2	–NH ring	Others
Va	-	7.2-8.1	7.2	-	-
Vb	10.21	6.8-9	-	-	-
Vc	-	6.6-8.7	-	-	3.8
Vd	-	6.5-8.8	10.5	-	-
Ve	-	7.18-8.6	-	-	-
Vg	-	6.3-8.4	-		CH2
Vj	-	6.3-8.8	8.3	8.5	-
Vk	-	6.2-8.4	-	-	-
Vl	-	6.2-9.9	-	-	-
Vo	-	7.08-8.24	9.5	10.47	-
Vp	-	7.15-8.24	10.3	10.7	-

Table (3-10): ^{13}C-NMR spectral data (δ ppm) of the compounds series one

Comp. No.	Aromatic -C	-C=O	C=N	Other
Va	121-145	170	151	-
Vb	110-142	168	158	-
Vc	110-148	164	152	71 CH_3
Vd	119-149	169	153	-
Ve	117-147	168	156	-
Vg	111-143	164	153	71 & 66
Vj	119-140	162	153	-
Vk	120-145	161	158	183 C=O Exo
Vl	110-145	162	158	192 C=S Exo
Vo	119-140	160	153	177 C=O Exo
Vp	110-133	180	153	194 C=S Exo

Table (3- 11): Fragmentation of azobenzene p,p'-di[3-amino-4(3H)quinazolinone-2yl] [Va].

% Abandance	Fragments	Possible positive ion
% (500)	$(M)^{+.2}$	
15% (436)	$M-C_2H_6O_2$	
57% (413)	$M-C_2H_4N_2O_2$	
15% (391)	$M-C_4H_6N_2O_2$	
5% (347)	$M-C_8N_2O_2$	
5% (274)	$M-C_{14}N_2O_2+2H$	
6% (265)	$M-C_{14}H_8N_2O_2$	
5% (239)	$M-C_{14}H_6N_4O_2$	

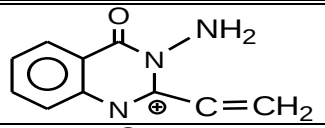
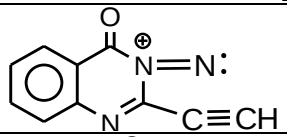
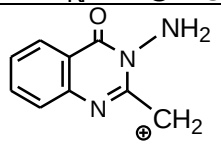
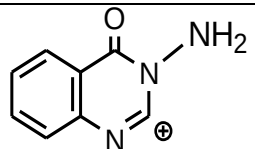
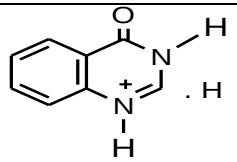
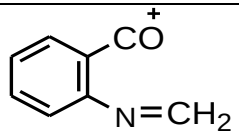
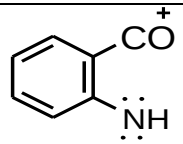
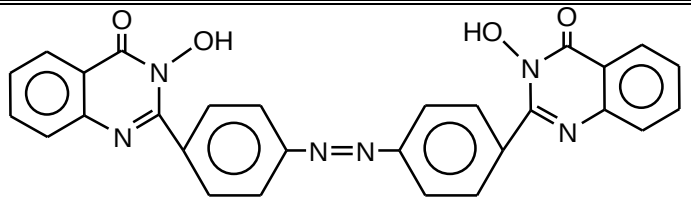
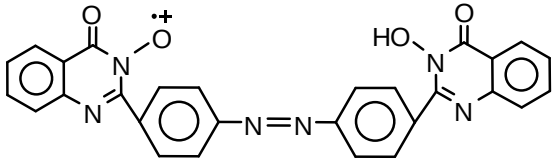
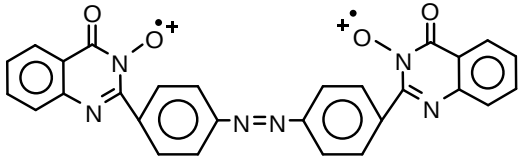
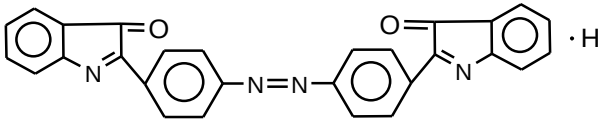
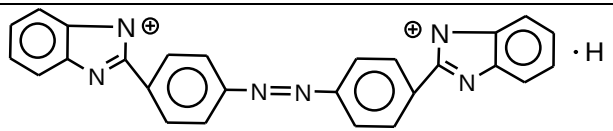
9% (189)	M-$C_{16}H_6N_6O_2$	
12% (182.9)	M-$C_{16}H_{10}N_6O_2$	
37% (175)	M-$C_{11}H_{12}N_5O$	
20% (160)	M-$C_{20}H_{12}N_5O$	
60% (147)	M-$C_{20}H_{14}N_6O$	
15% (132)	M-$C_{20}H_{14}N_7O$	
10% (119)	M-$C_{21}H_{15}N_7O$	

Table (3-12): Fragmentation of azobenzene p,p'-di[3-hydroxy-4(3H)quinazolinone-2yl] [Vb]

Abandance %	fragments	Possible positive ion
2% (502)	$M^{\cdot+2}$	
12% (501)	M-H	
13% (500)	M-2H	
15% (441)	$M-H_2N_2O_2$	
10% (413)	$M-C_2H_2O_4$	

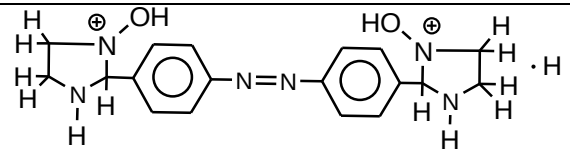
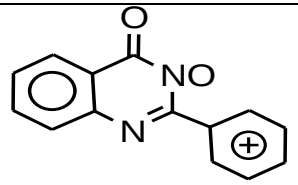
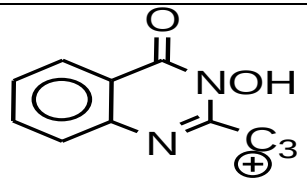
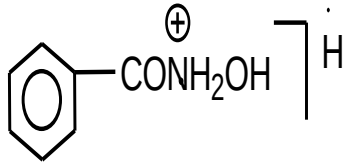
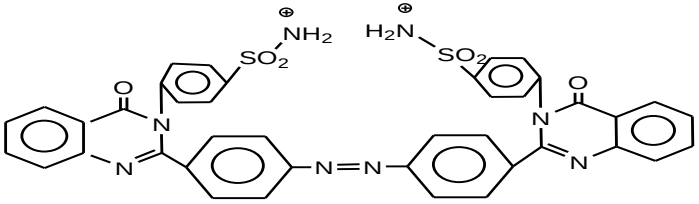
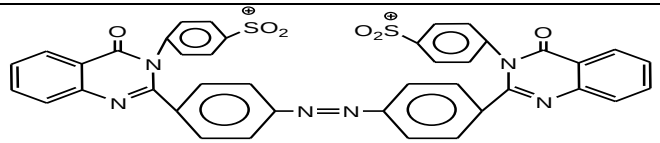
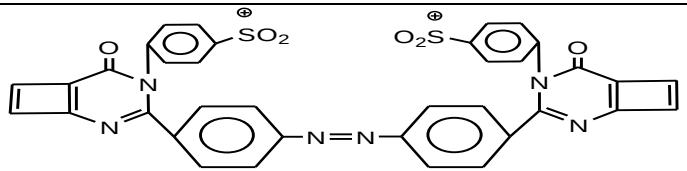
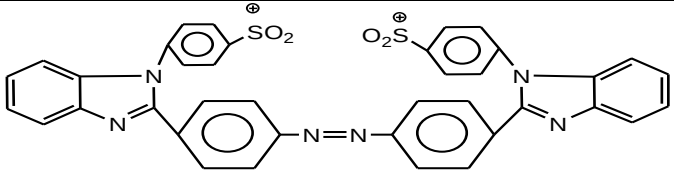
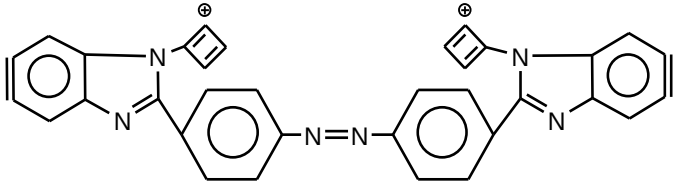
56% 355	M-$C_{10}O_2$+H_2	
22% 236	M-$C_{14}H_{10}N_2O_2$	
100% 195	M-$C_{17}H_{13}N_4O_2$	
11% 139	M-$C_{21}H_{10}N_3O_2$	

Table (3- 13): Fragmentation of azobenzene p,p'-di[3-banzensulphonamido-4(3H)quinazolinone-2yl] [Vd]

% Abandance	fragments	Possible positive ion
30% (730)	M-C_4H_2	
100% (712)	M-$N_2H_6O_2$	
35% (701)	M-$C_4H_7N_2$	
23% (656)	M-$C_2H_6O_4$	
24% (510)	M-$C_6H_8N_2O_7S$	

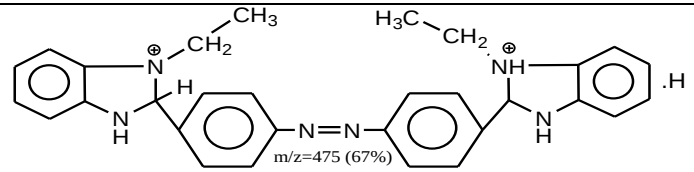
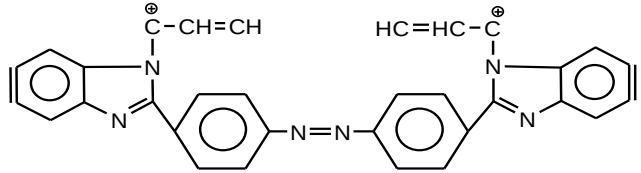
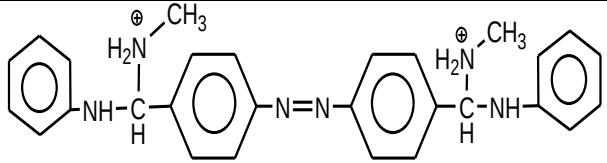
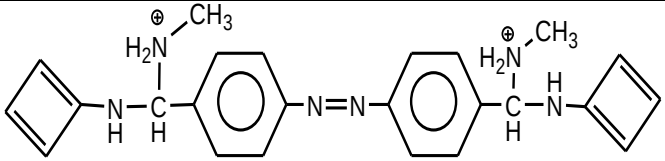
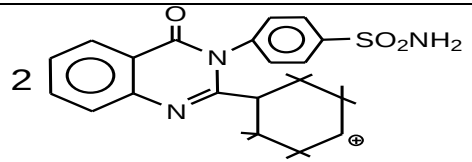
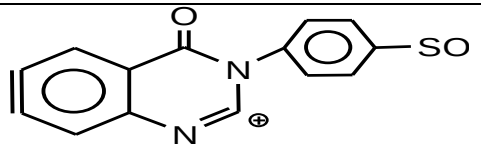
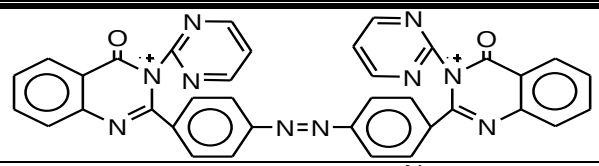
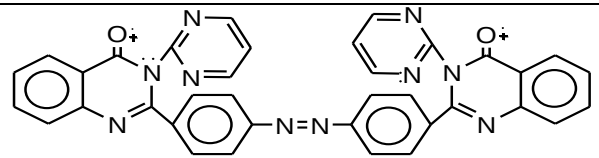
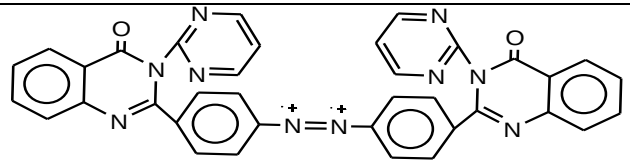
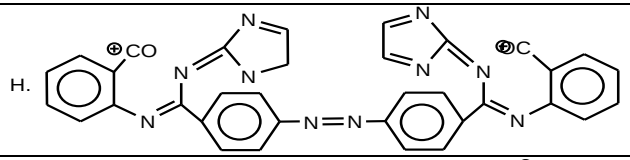
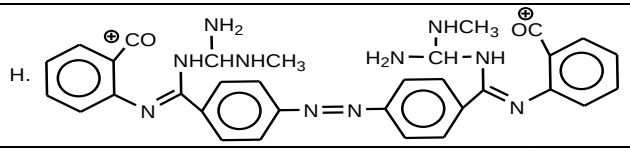
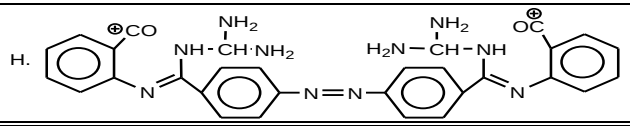
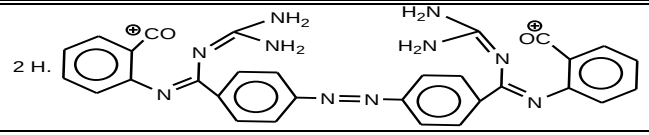
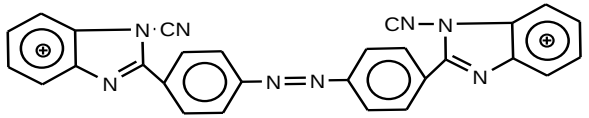
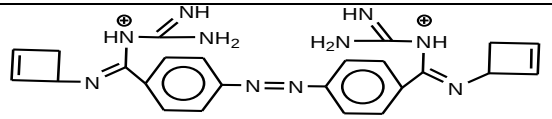
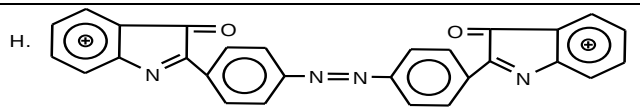
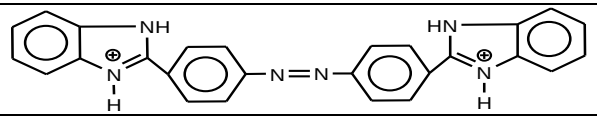
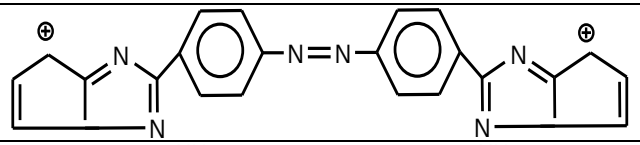
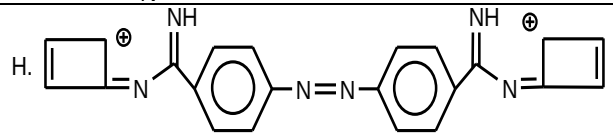
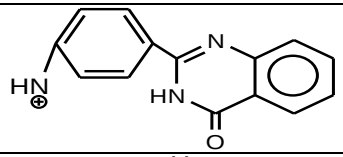
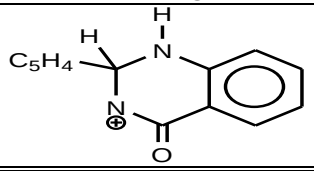
67% (475)	M-$C_{14}N_2O_6S_2$ +2H	
28% (447)	M-$C_8H_{12}N_2O_6S_2$	
76% (453)	M-$C_{12}H_{13}N_2O_6S_2$	
57% (404)	M-$C_{16}N_2O_2S_2$	
43% (381)	M-$C_{20}H_{11}N_2O_3S$	
80% (266)	M-$C_{26}H_{22}N_8O_4S$	

Table (3- 14): Fragmentation of azobenzene p,p'-di[3,P-pyrimidino-4(3H)quinazolinone-2yl] [Ve]

% Abundance	fragments	Possible positive ion
3% (626)	$M^{\cdot+2}$	
3% (626)	$M^{\cdot+2}$	
3% (626)	$M^{\cdot+2}$	
55% (601)	$M-C_2H_2$	
60% (585)	$M-C_2H_2N+H$	
43% (563)	$M-C_6+2H_3$	

12% (558)	M-C_6 +2H	
11% (462)	M-$(C_4H_2N_2)_2$ +2H	
90% (455)	M-$C_{12}O_2$ +2H	
31% (439)	M-$C_8H_6N_6$	
8% (417)	M-$C_{10}H_2O_2N_4$	
17% (384)	M-$C_{12}H_4N_4O_2$	
9% (365)	M-$C_{18}H_4N_4O_2$	
77% (236)	M-$C_{22}H_2N_7O$	
25% (219)	M-$C_{23}H_{12}N_8O$	

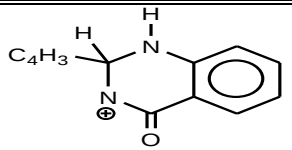
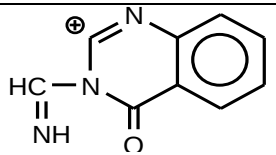
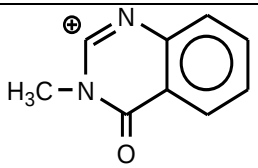
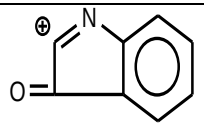
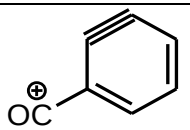
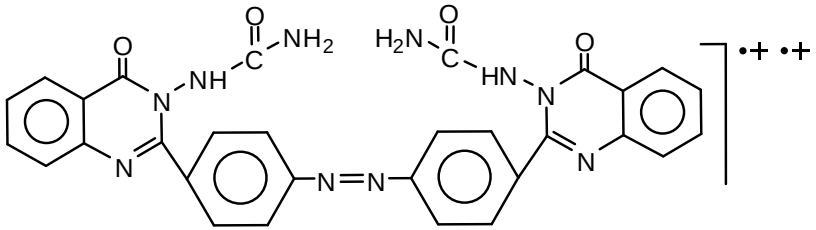
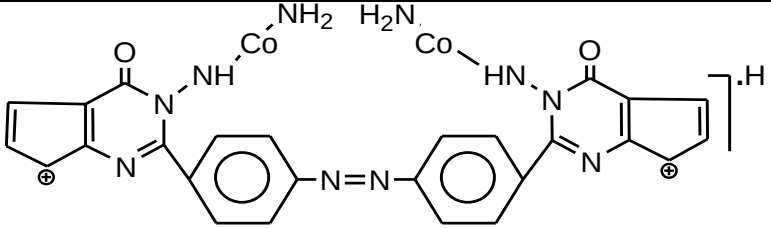
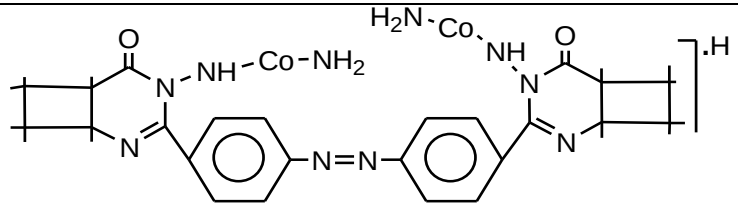
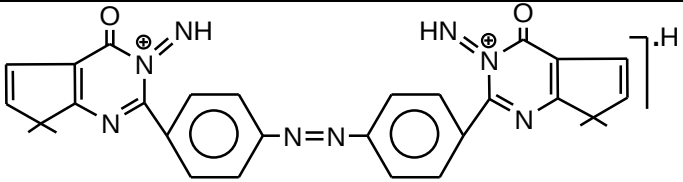
22% (203)	M-$C_{24}H_{13}N_8O$	
23% (173)	M-$C_{27}H_{16}N_7O$	
55% (160)	M-$C_{27}H_{15}N_4O$	
13% (130)	M-$C_{28}H_{17}N_9O$	
21% (104)	M-$C_{29}H_{19}N_{10}O$	

Table (3-15): Fragmentation of azobenzene p,p'-di[3,N-urido-4(3H)quinazolinone-2yl] [Vo]

% Abandance	Fragments	Possible positive ion
(586)	$M^{\cdot+2}$	
22% (559)	$M\text{-}C_2H_2$	
17% (541)	$M\text{-}C_2\text{+}H_2$	
46% (475)	$M\text{-}C_2H_6N_2O_2$	

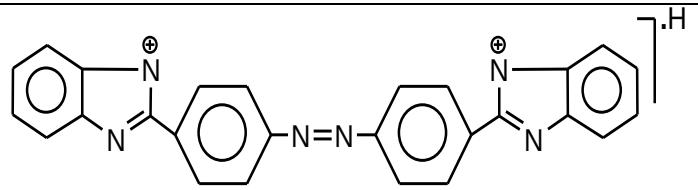
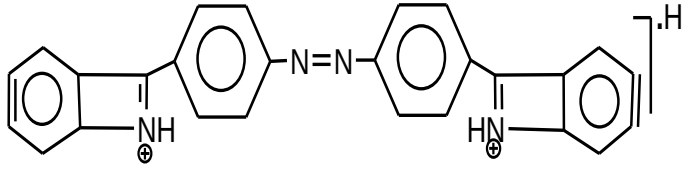
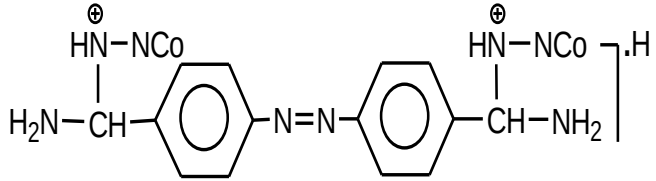
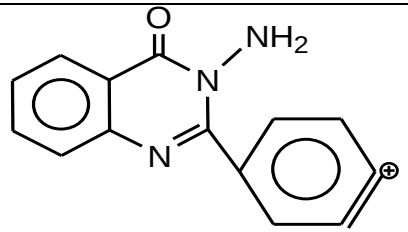
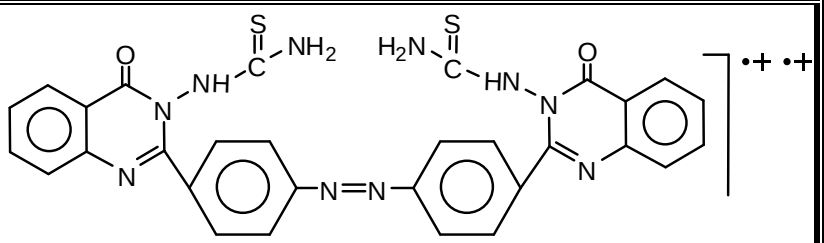
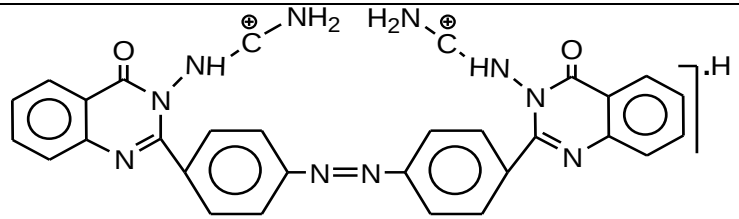
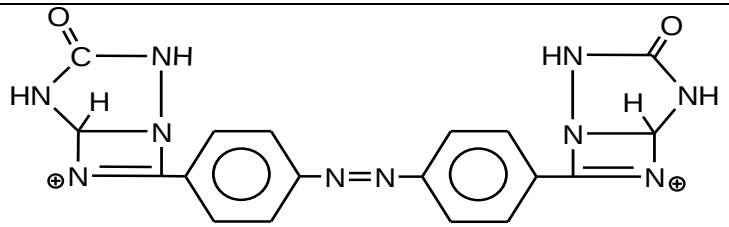
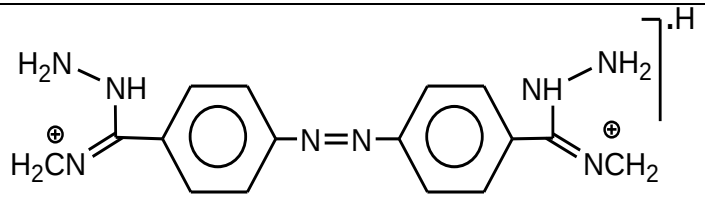
21% (413)	M-$C_4H_6N_4O_2$	
40% (381)	M-$C_4H_8N_8O_2$	
15% (353)	M-$C_{14}H_6N_2O_2$	
16% (236)	M-$C_{16}H_{13}N_7O$	

Table (3-16): Fragmentation of azobenzene p,p'-di[3,N-thioureido-4(3H)quinazolinone-2yl] [Vp]

% Abandance	Fragment	Possible positive ion
11% (619)	$[M+H]^{\cdot+2}$	
8% (553)	$M\text{-}S_2$	
68% (401)	$M\text{-}C_{12}H_8S_2$	
18% (323)	$M\text{-}C_{14}H_6N_2O_2S_2$	

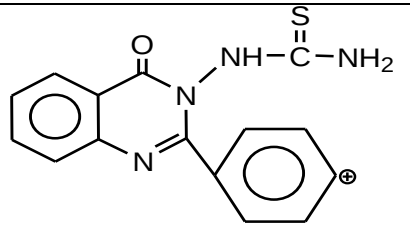
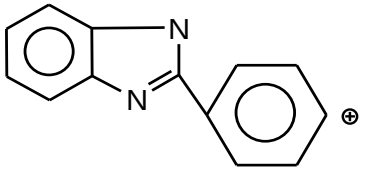
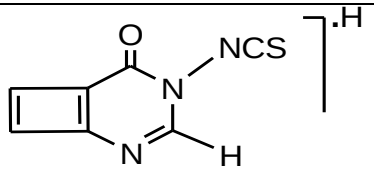
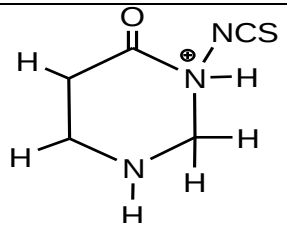
37% (295)	M-$C_{13}H_{10}N_6SO$	
18% (192)	M-$C_{17}H_{13}N_8O_2S_2$	
28% (179)	M-$C_{23}H_{19}N_7SO$	
100% (156)	M-$C_{25}H_{16}N_7SO$	

Table (3-17): FTIR- spectral data (Wave number υ–) of the compounds series two.

Comp. No.	υ(-NH_2) & (-NH)	υ (C=O)	υ (-N=N-)	υ (-C=N-)	υ (-CH)	others
VIA	3174	1678	1450	1604	3059	-
VIB	-	1689	1450	1643	3039	NO_2 1508 Asy. 1338 sym.

Table (3-18): FTIR- spectral data (Wave number υ–) of the compounds series three.

Comp. No.	υ(-NH_2) & (-NH)	υ(C=O)	υ (-N=N-)	υ(-C=N-)	υ(-CH)	Others
VIIA	-	1666	1450	1604	2924 3009	-
VIIB	-	1770 1625	1460	1595	2954 2842 3095	-

Table (3-19): ^{1}H-NMR spectral data (δ ppm) of the compounds Series two &three

Comp. No.	Aromatic -H	NH2 & NH	Others
VIA	6.8-8.8	4.03	-
VIIA	6.6-9.3	-	4.7 CH2
VIIB	6.7-8.07	-	5.3 CH3

Table (3-20): ^{13}C-NMR spectral data (δ ppm) of the compounds Series two &three

Comp. No.	Aromatic -H	-C=O	C=N	Others
VIA	107-143	167	152	-
VIIA	109-143	168	153	75 CH2
VIIB	110-148	169	153	71 CH3

Table (3-21): FT-IR spectral data (Wave number ῡ) of the compounds series four

Comp. No.	υ(-NH_2) & (-NH)	υ(C=O)	υ(-N=N-)	υ(-C=N)	υ(-CH)
VIII	3271	1674	1446	1596	3074 3002
IX	-	-	1450	1608	3064
IXA	3421	-	1436	1573	3070
IXB	3421 3305 3251	-	1431	1647	3164

Table (3-22): ^{1}H-NMR spectral data (δ ppm) of the compounds series four

Comp. No.	Aromatic -H	NH	Others
VIII	7.1-8.7	7.5	-
IX	6.38-8.8	-	-
IXA	7.2-8.7	7.5	3.5 CH3
IXB	7.5-7.8	6.5	3.34 CH2

Table (3-23): ^{13}C-NMR spectral data (δ ppm) of the compounds series four

Comp. No	Aromatic -C	C=O	C=N	Others
VIII	119-140	160	150	-
IX	120-144	-	152	-
IXA	117-146	-	153	93 CH3
IXB	120-135	-	151	83 CH2

Table (3-24): Fragmentation of azobenzene p,p´-di[3-hydro-quinazolinone-2yl] [VIII]

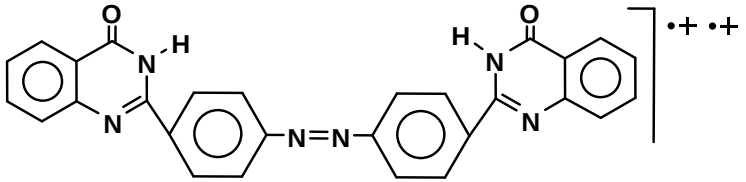
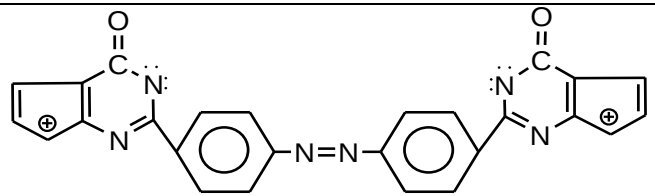
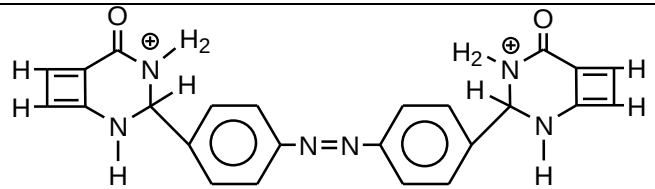
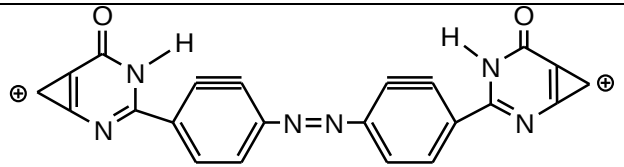
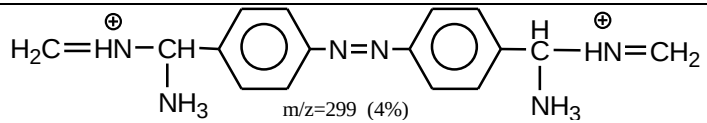
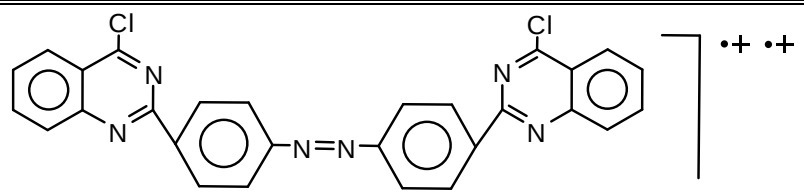
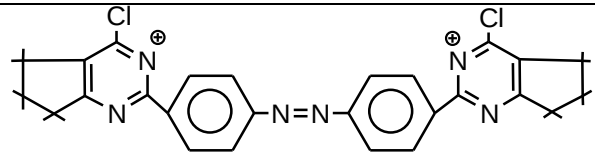
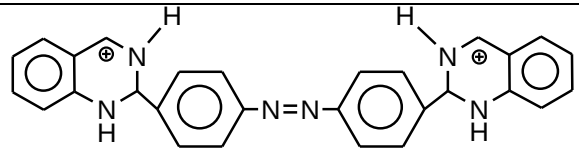
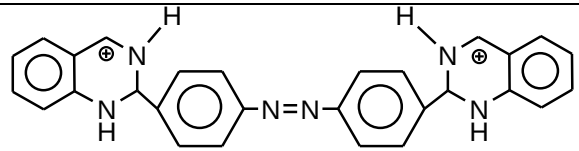
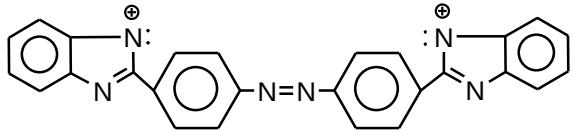
% Abandance	Fragments	Possible positive ion
22% (470)	$M^{\cdot+2}$	
4% (440)	$M\text{-}C_2H_4$	
9% (426)	$(M\text{-}C_4 +2H_2)$	
9% (386)	$(M–C_6H_{12})$	
4% (299)	$(M–C_{12}H_7O_2 +H)$	 m/z=299 (4%)

Table (3-25): Fragmentation of azobenzene p,p'-di[4-chloro-quinazolinone-2yl] [IX]

%Abundance	Fragments	Possible positive ion
7% (507)	$M^{\cdot+2}$	
46% (487)	$M\text{-}C_2H_2$	
59% (457)	$M\text{-}C_4H_2$	
93% (443)	$M\text{-}Cl_2 + 3H_2$	
79% (413)	$M\text{-}C_2Cl_2 + H$	

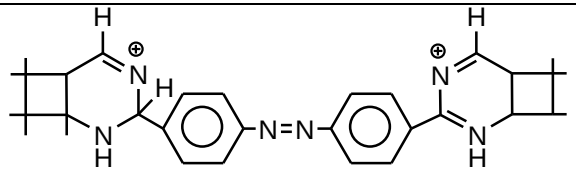
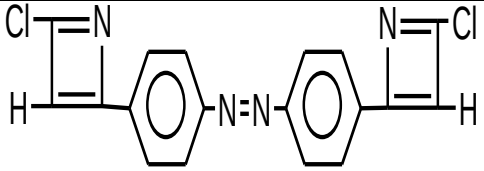
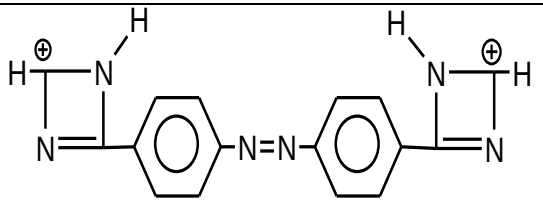
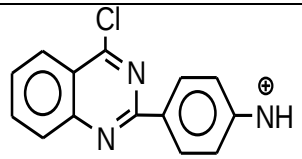
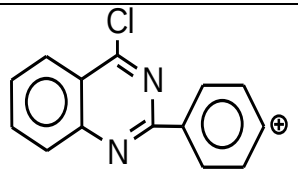
100% (399)	M-C_4H_2 +5H_2	
64% (353)	M-$C_{10}H_6N_2$	
44% (288)	M-$C_{12}H_4Cl_2$	
10% (253)	M-$C_{10}H_8Cl_2N_4$ +H	
6% (237)	M-$C_{14}H_4Cl_2N_2$ +H	

Table (3-26): FT-IR spectral data of the compounds series five

Comp. No.	υ(-NH_2) & (-NH)	υ(-OH)	υ(-N=N-)	υ(-C=N)	υ(-NO_2)	υ(-C=S)	υ(-CH)
XA	3410 3116	-	1450	1604	-	1300	3043
XB	-	3331- 2806	1446	1604	-	1375	3030
XC	-	-	1440	1649	-	1371	2931
XD	3471 3357	-	1450	1664 1556	-	1298	3068
XE	-	-	1450	1616		1354	3078
XF	-	-	1446	1637 1606	1242	1377	3045
XG	3431 3254	-	1473	1635	-	1396	2970 2822

XI	3410 3174	-	1450	1616	-	1384	-
XJ	3448 3379 3217	-	1446	1589	-	1346	3062
XK	3458 3358	-	1444	1593	-	1394	3057
XL	3433 3213	-	1450	1593	-	1327	3059
XP	3429 3213 3120	-	1450	1604	-	1392	3062
XI'	3251	-	1442	1558	-	1346	3062

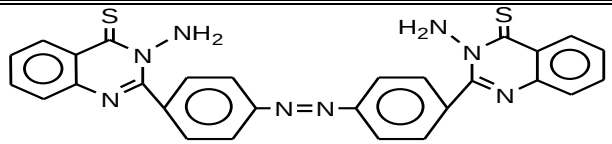
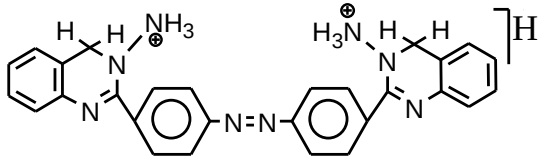
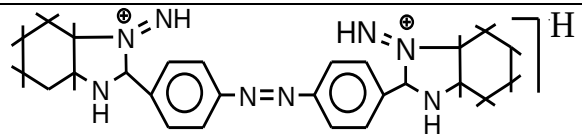
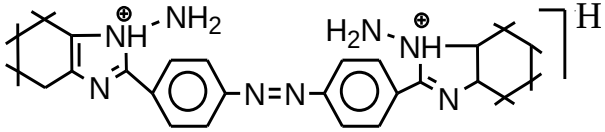
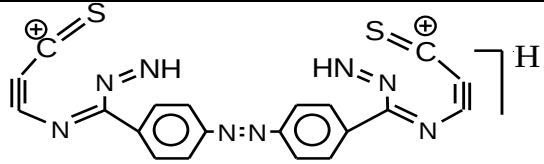
Table (3-27): ^{1}H-NMR spectral data (δ ppm) of the compounds series five

Comp. NO.	NH2 &NH	OH	Aromatic-H	Others
XA	5-5.4	-	6.6-7.9	-
XB	-	10.7	7.2-7.85	-
XG	9.2 & 4.5	-	7.1-9.2	CH2
XP	9 & 4.4	-	6.8-9.6	-
XI'	8.5	-	6.6-8.08	-

Table (3-28): ^{13}C-NMR spectral data (δ ppm)of the compounds series five

Comp. No.	Aromatic -C	C=S	C=N	Others
XA	110-145	180	153	-
XB	120-140	184	158	-
XE	112-149	179	153	-
XG	105-147	189	152	CH_2
XP	110-145	179 Endo	158	Exo C=S 192
XI'	107-149	172	153	-

Table (3-29): Fragmentation of azobenzene p,p'-di[3-amino-4(3H)quinazolinthion-2yl] [XA]

%Abundance	Fragments	Possible positive ion
3% (532)	$M^{\cdot+2}$	
100% (475)	$M\text{-}S_2 + 3H_2$	
24% (459)	$M\text{-}C_2S_2 + 7H$	
31% (453)	$M\text{-}C_2S_2 + 4H_2$	
35% (423)	$M\text{-}C_{10}H_{10}$	

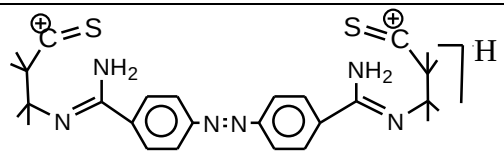
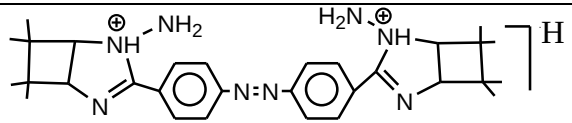
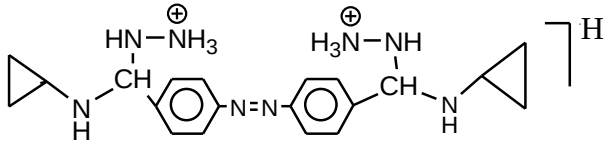
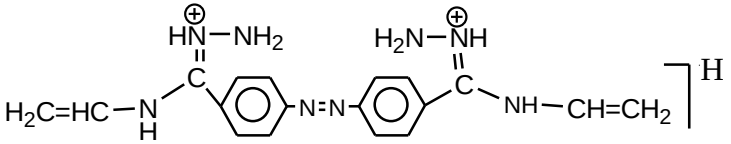
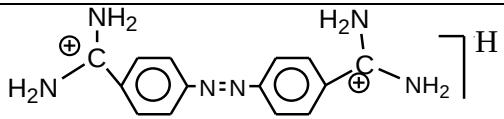
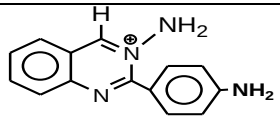
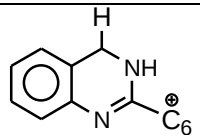
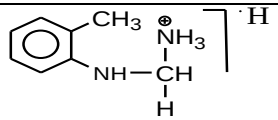
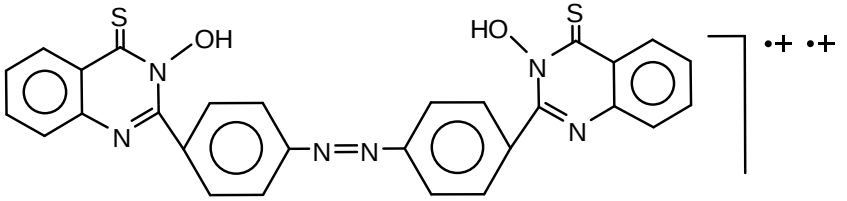
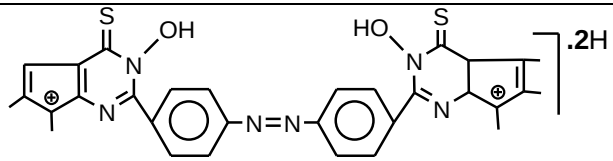
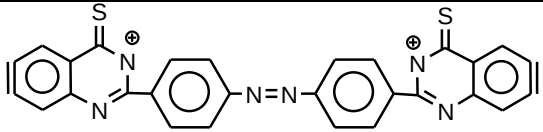
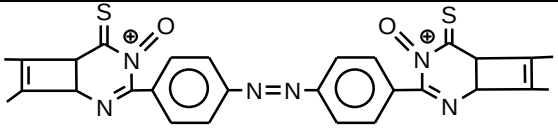
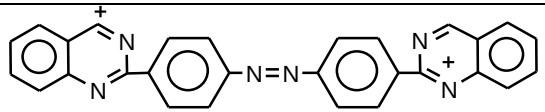
15% (409)	M-$C_{10}H_{10}N_2$	
17% (401)	M-$C_{10}S_2$ +2H	
29% (381)	M-$C_{16}S_2$	
27% (351)	M-$C_{16}S_2$ +2H	
20% (269)	M-$C_{14}H_6N_2S_2$	
15% (238)	M-$C_{14}H_7N_4S_2$	
7% (202)	M-$C_{14}H_{14}N_4S_2$	
3% (138)	M-$C_{20}H_9N_4S_2$	

Table (3-30): Fragmentation of azobenzene p,p'-di[3-hydroxy-4(3H)quinazolinthion-2yl] [XB]

% Abandance	Fragments	Possible positive ion
25 % (534)	$M^{\cdot+2}$	
23% (510)	$M-C_2H_2$	
13% (496)	$M-H_6O_2$	
24% (480)	$M-C_4H_6$	
53% (436)	$M-H_4S_2$	

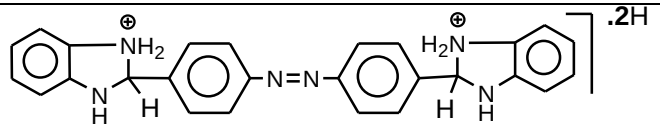
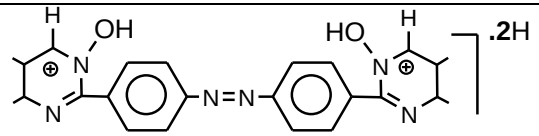
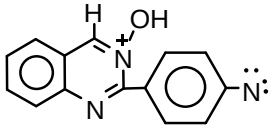
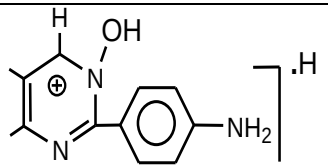
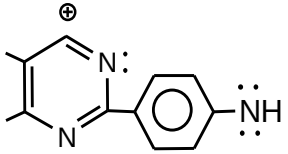
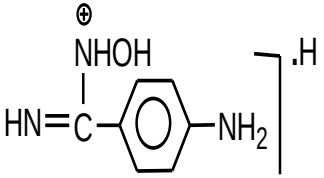
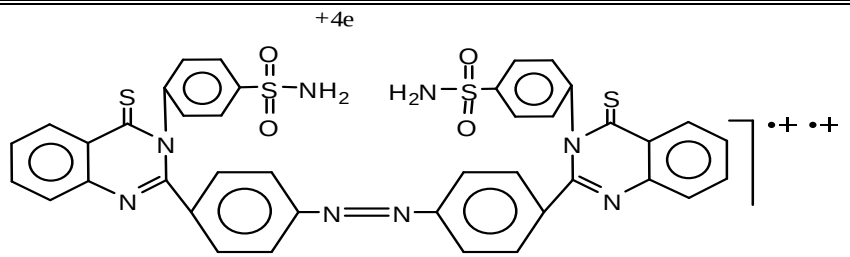
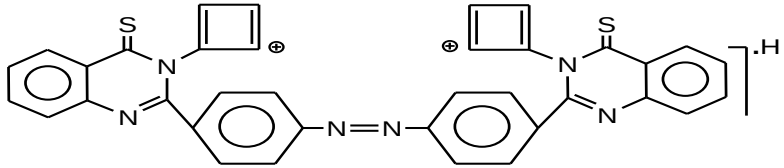
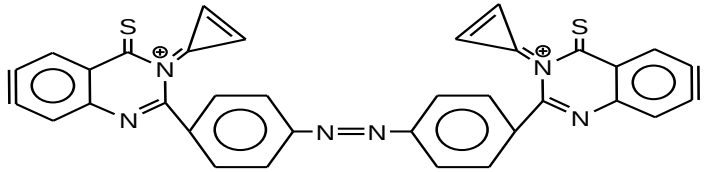
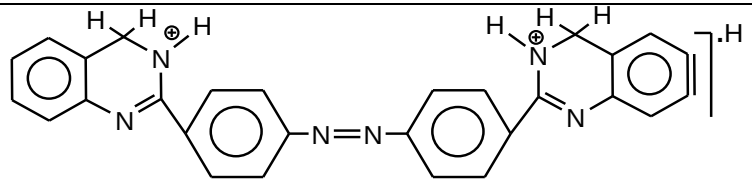
49% (422)	M-$C_2O_2S_2$ +3H_2	
23% (378)	M-C_6S_2 +H_2	
32% (278)	M-$C_{14}H_8N_3OS_2$	
13% (189)	M-$C_{18}H_8N_3OS_2$	
17% (169)	M-$C_{18}H_{11}N_3O_2S_2$	
100% (152)	M-$C_{21}H_9N_3OS_2$	

Table (3-31): Fragmentation of azobenzene p,p'-di[3-benzensulphonamido-4(3H)quinazolinthione-2yl] [XD]

%Abandance	Fragments	Possible positive ion
% (812)	$M^{\cdot+2}$	
17% (601)	$M\text{-}C_6H_6O_4S_2$	
35% (572)	$M\text{-}C_8H_{22}O_4S_2$	
15% (443)	$M\text{-}C_{12}H_6N_2O_4S4$	

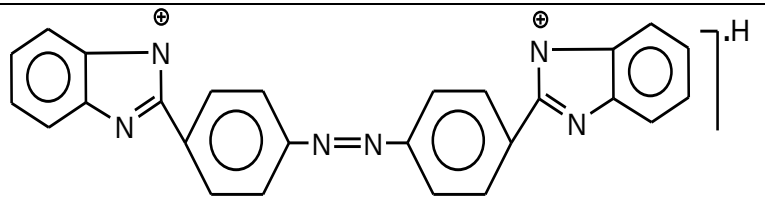
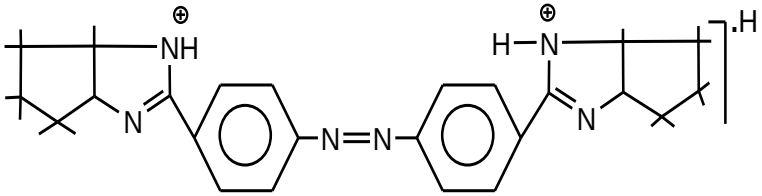
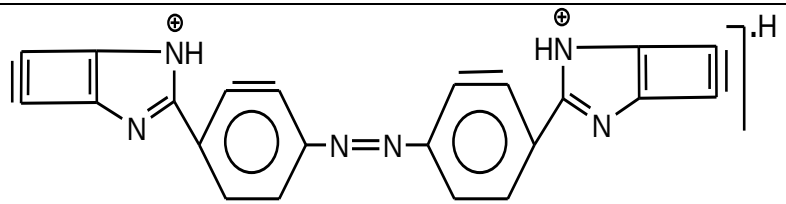
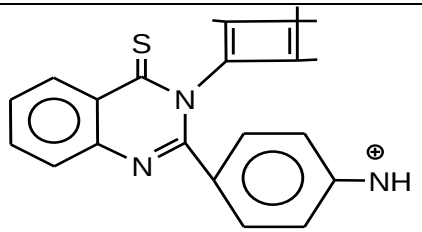
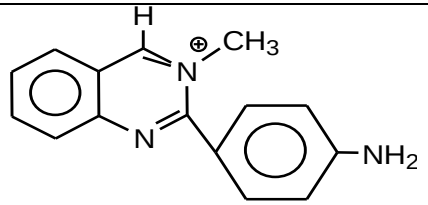
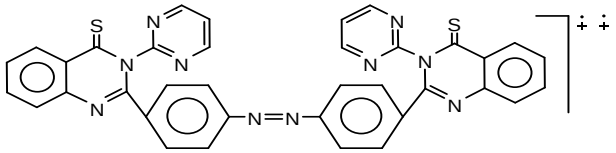
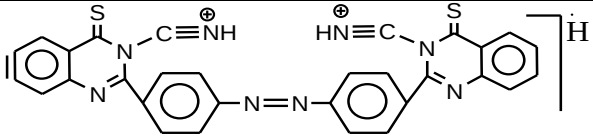
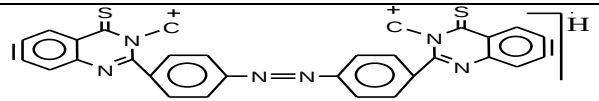
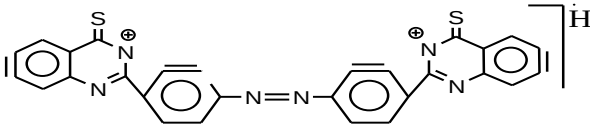
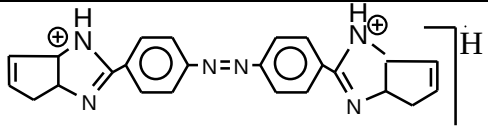
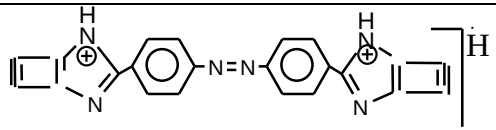
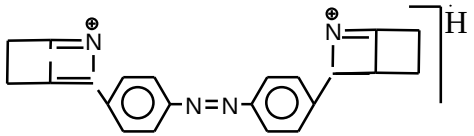
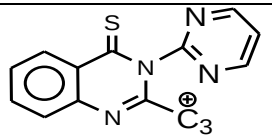
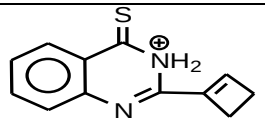
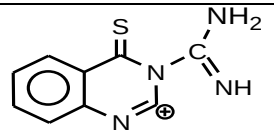
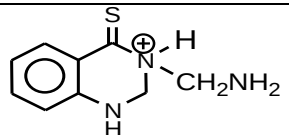
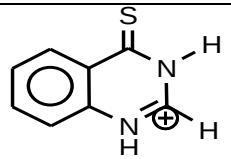
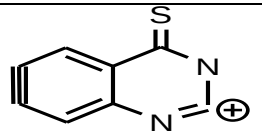
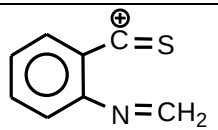
100% (413)	M-$C_{14}H_{12}N_2O_4S_4$	
90% (399)	M-$C_{16}N_2O_4S_4$ +2H	
80% (355)	M-$C_{18}H_{22}N_2O_4S_4$	
15% (304)	M-$C_{24}H_{14}N_5O_4S_3$	
40% (236)	M-$C_{25}H_{14}N_6O_4S_4$	

Table (3-32): Fragmentation of azobenzene p,p'-di[3(2'-pyrimidno-4(3H)quinazolinthion-2yl] [XE]

%Abandance	Fragment	Possible positive ion
33% (658)	$M^{\cdot+2}$	
23% (549)	$M\text{-}C_6H_8N_2$	
60% (521)	$M\text{-}C_6H_{10}N_4$	
53% (493)	$M\text{-}C_8H_{14}N_2$	
45% (391)	$M\text{-}C_{12}H_4N_2S_2$	
35% (355)	$M\text{-}C_{14}H_{12}N_4S_2$	

37% (327)	M-$C_{12}H_{12}N_6S_2$	
42% (230)	M-$C_{21}H_{15}N_6S$	
37% (215)	M-$C_{22}H_{11}N_8S$	
32% (203)	M-$C_{27}H_{15}N_8S$	
27% (195)	M-$C_{27}H_{12}N_7S$	
100% (163)	M-$C_{24}H_{14}N_5O_4S_3$	
100% (158)	M-$C_{28}H_{19}N_8S$	
65% (148)	M-$C_{28}H_{16}N_9S$	

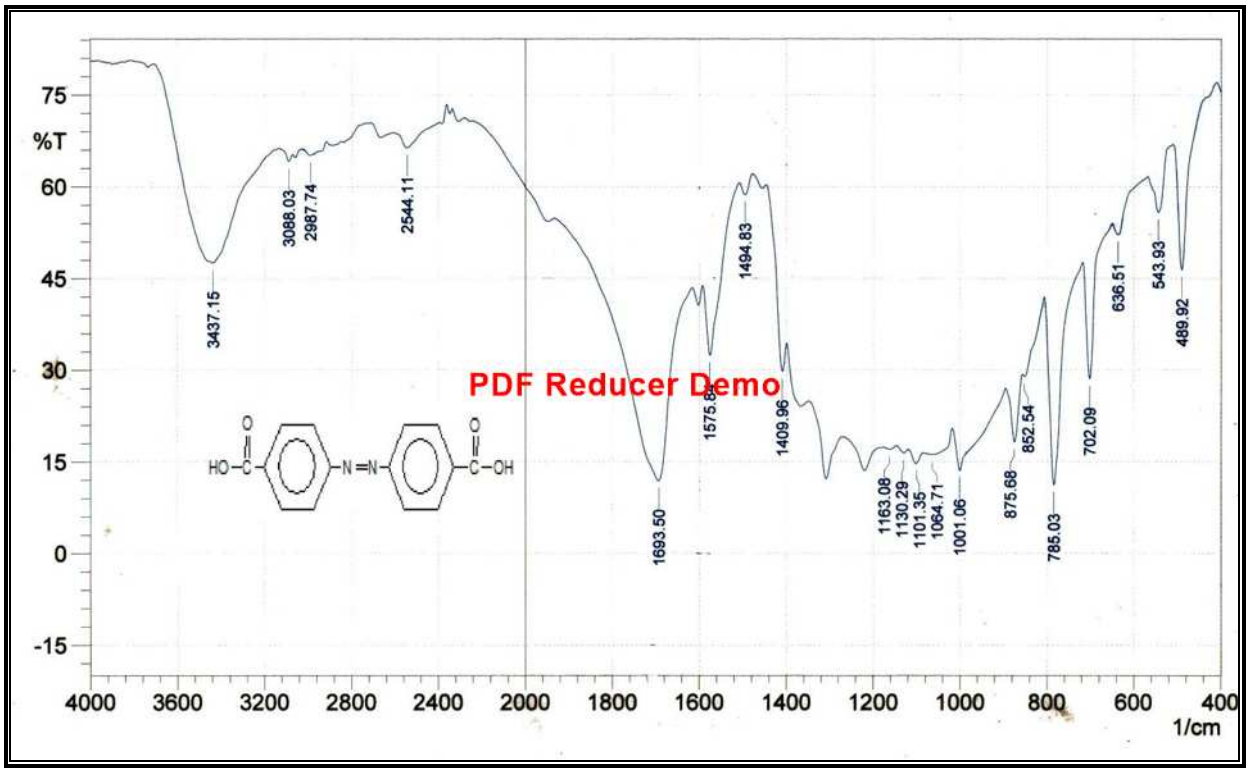


Fig (3-1). FT-IR spectrum of compound [I]

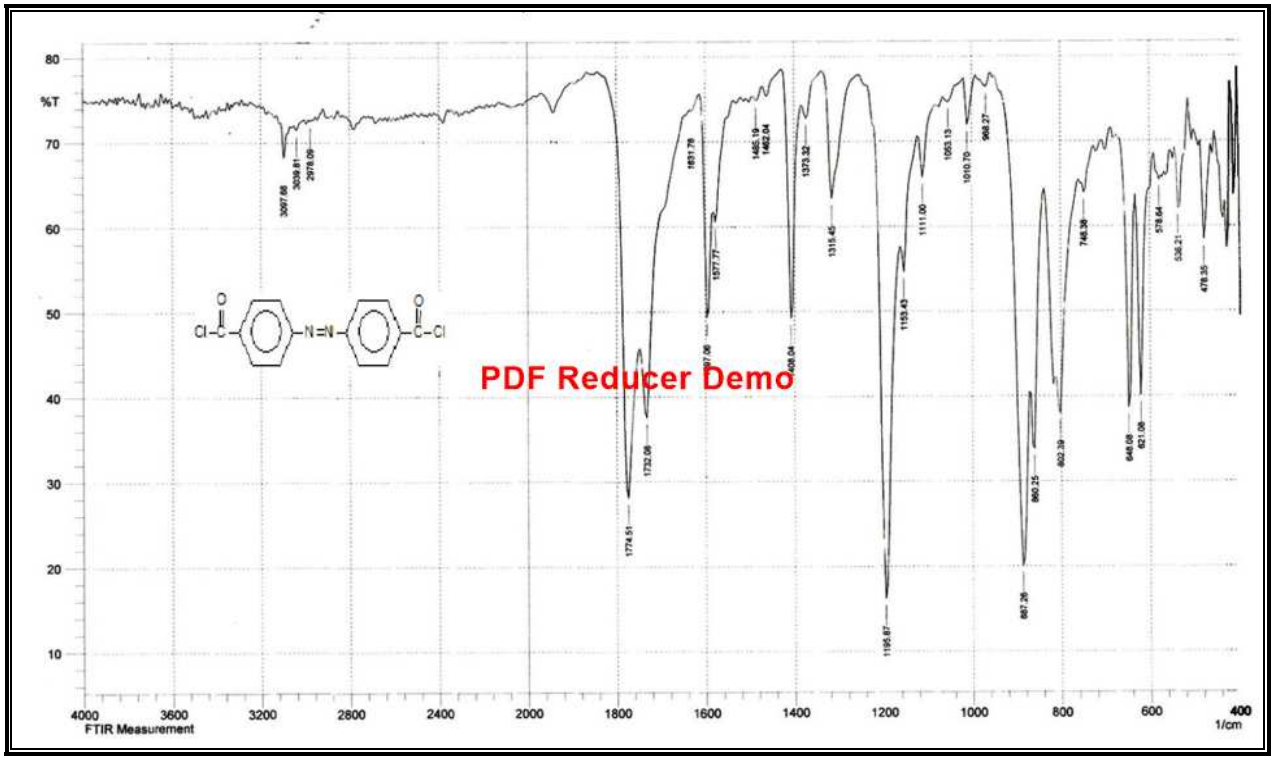


Fig (3-2). FT-IR spectrum of compound [II]

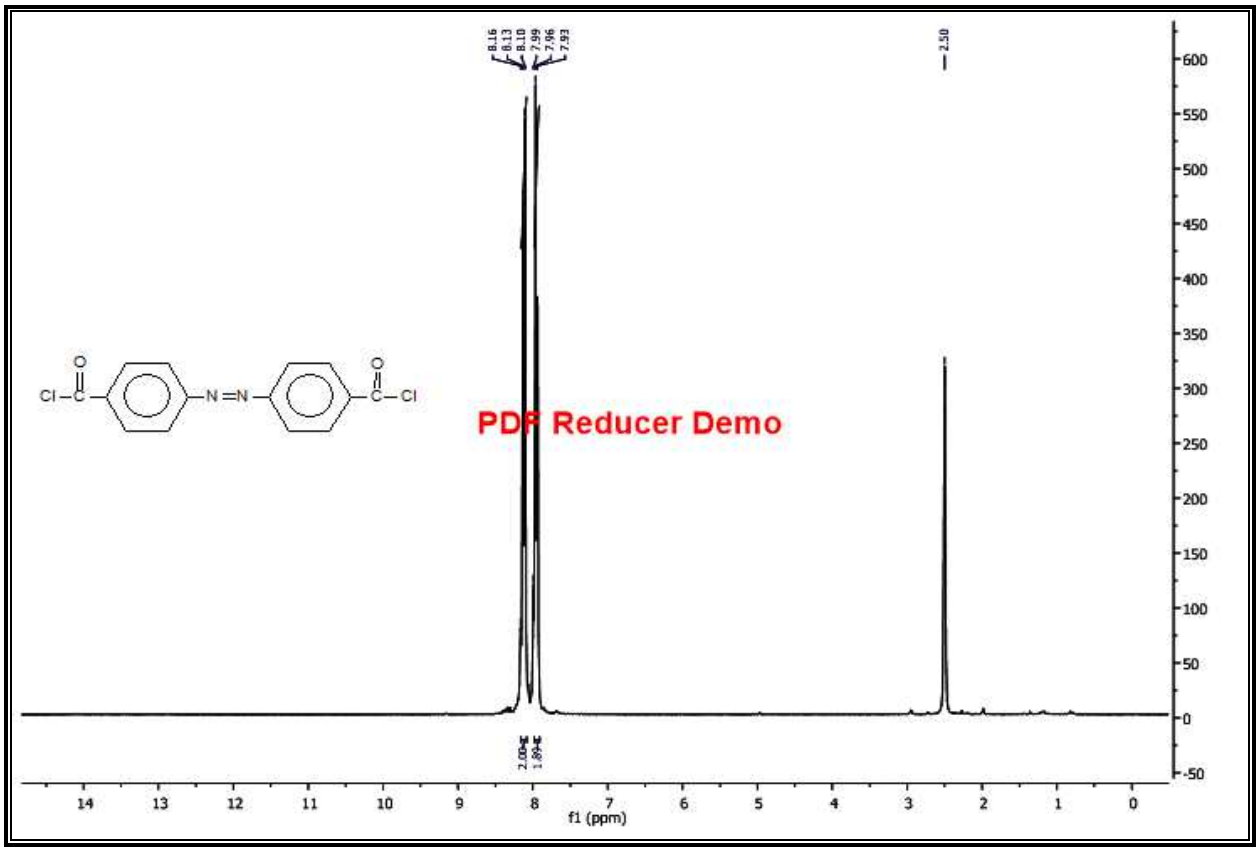


Fig (3-3). ^{1}H-NMR spectrum of compound [II]

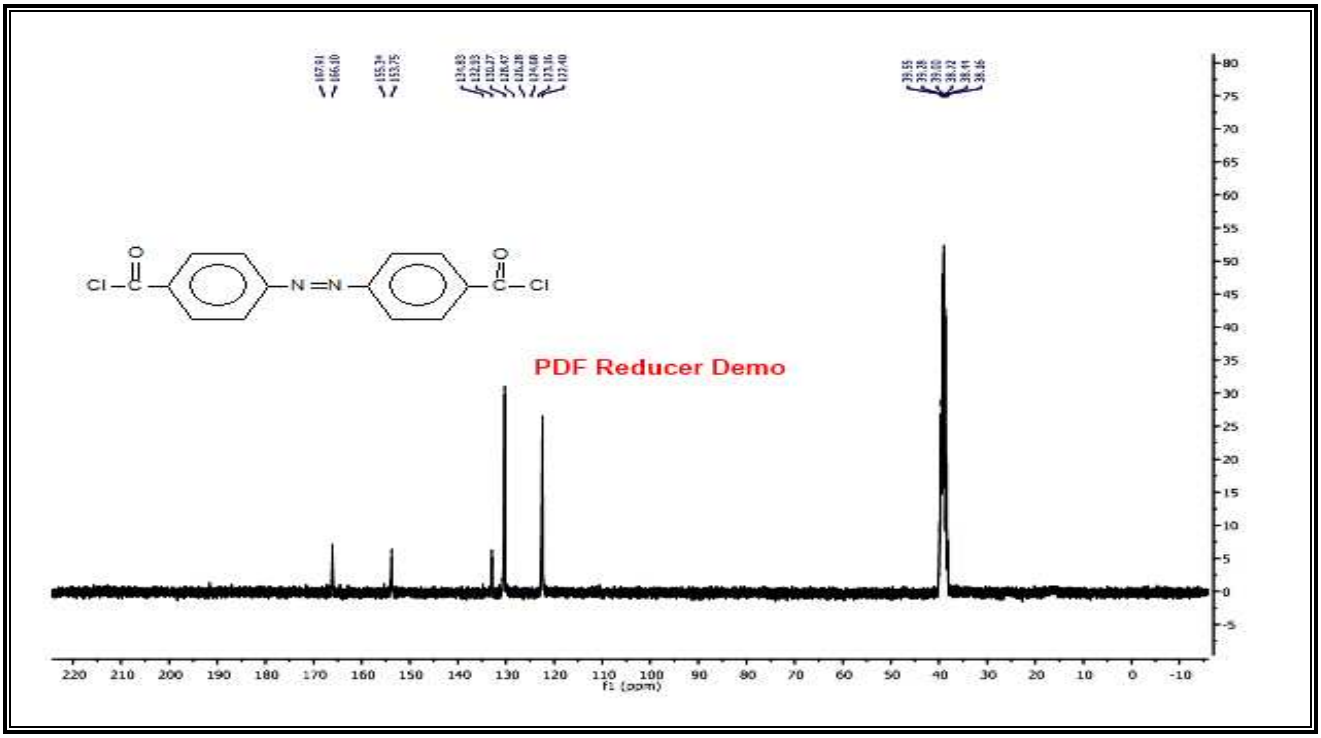


Fig (3-4). ^{13}C-NMR spectrum of compound [II]

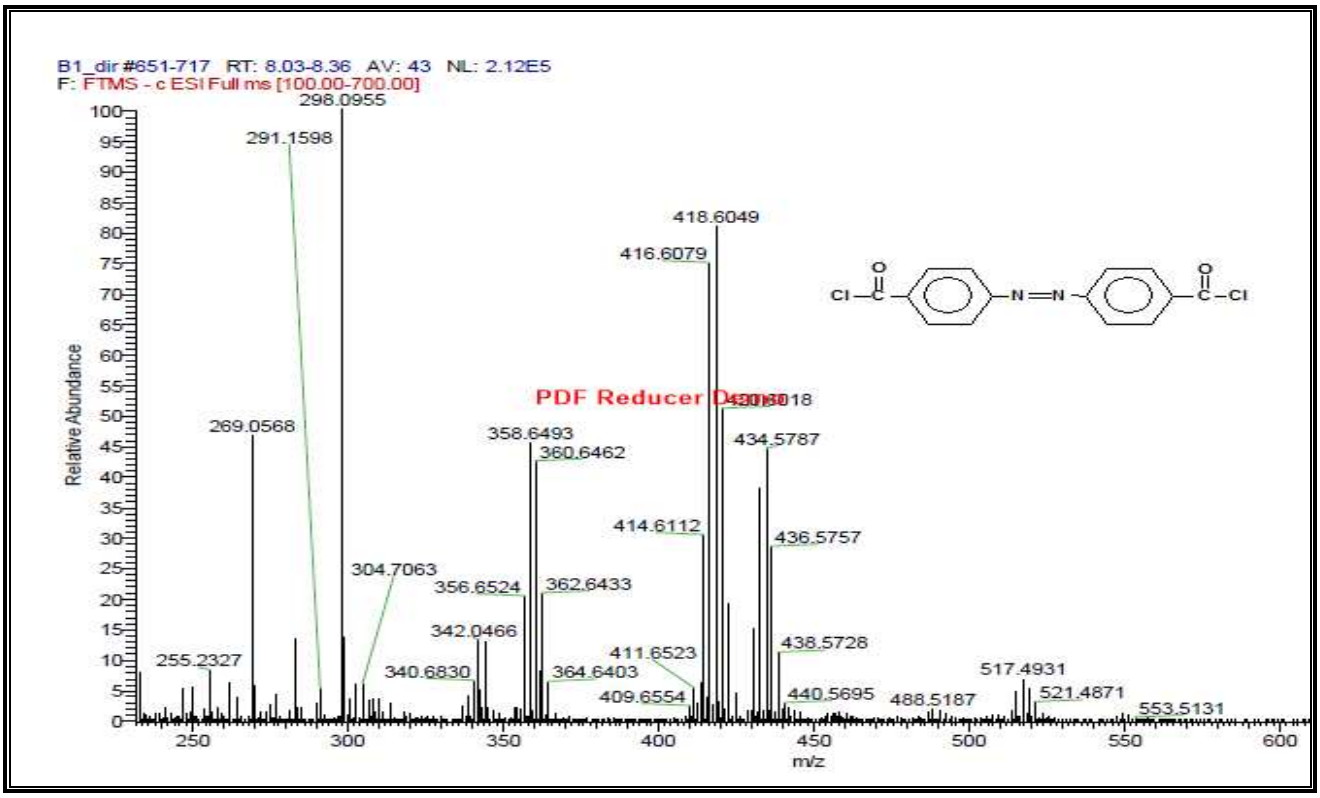


Fig (3-5). Mass spectrum analysis of compound [II]

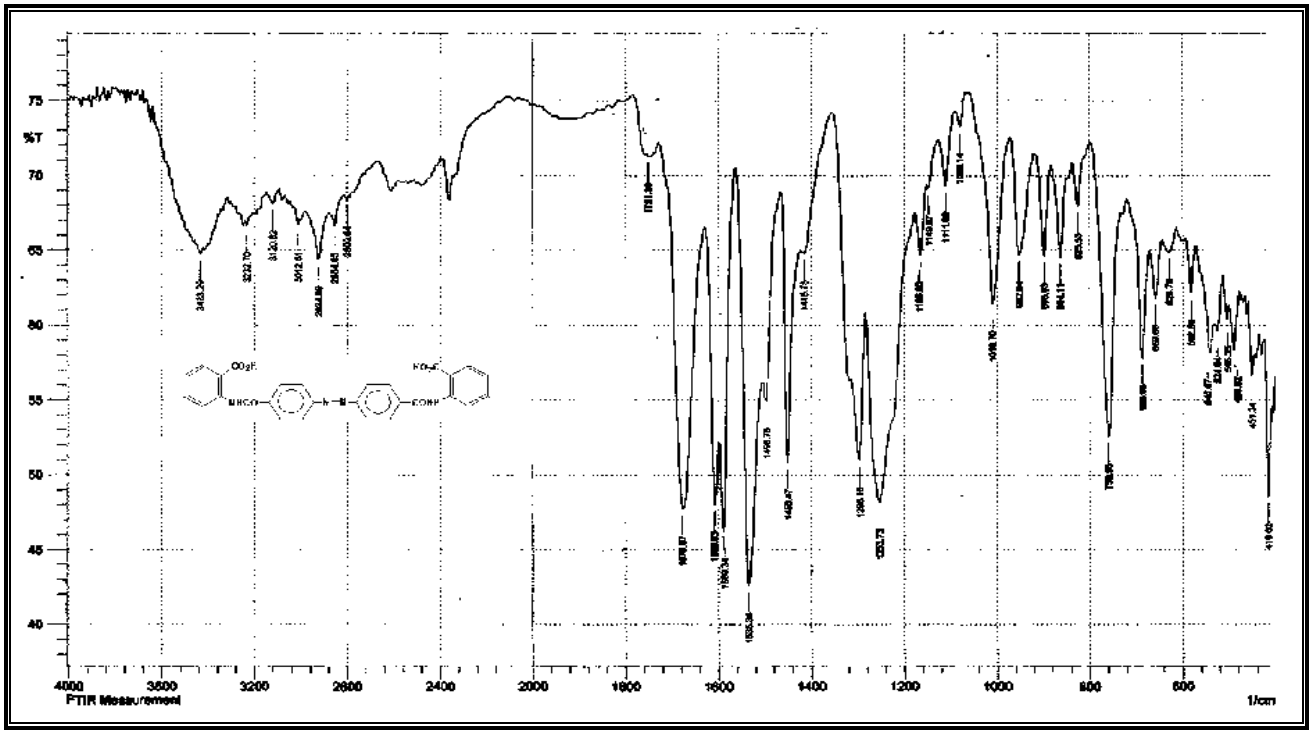


Fig (3-6). FT-IR spectrum of compound [III]

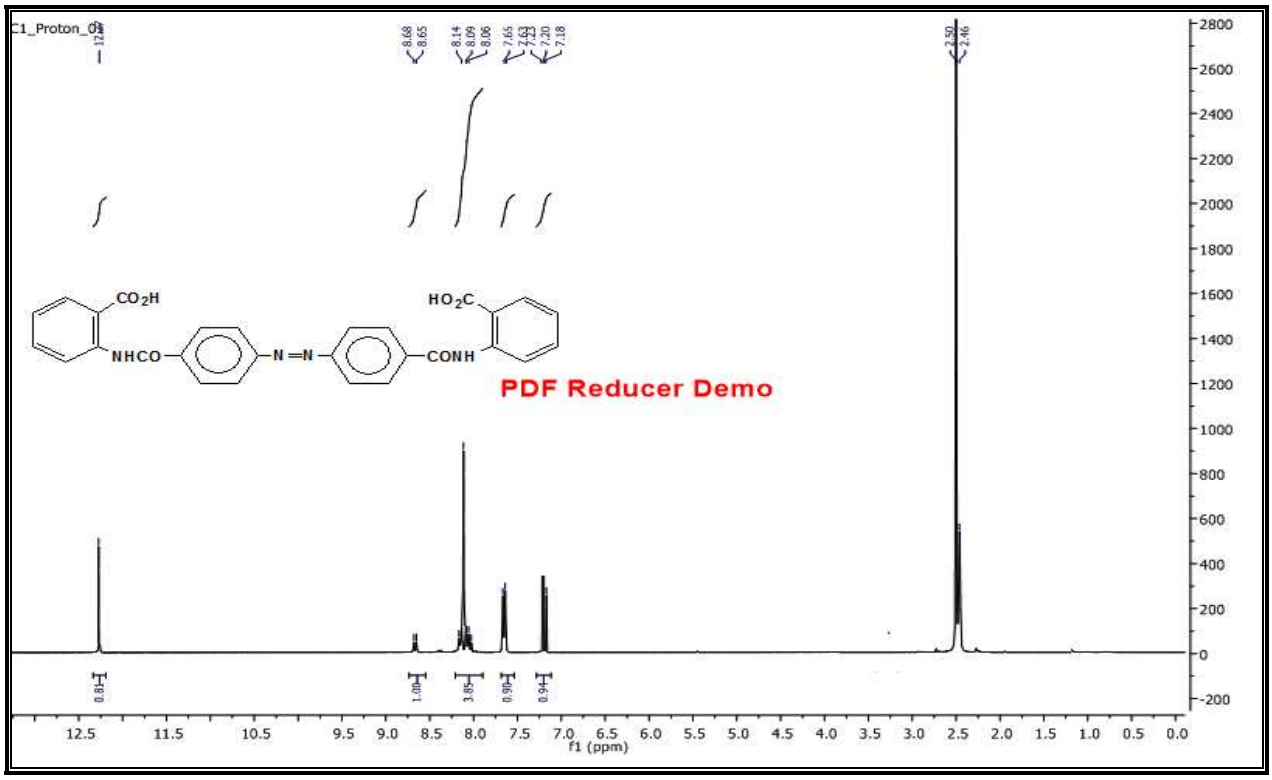


Fig (3-7). ^{1}H-NMR spectrum compound [III]

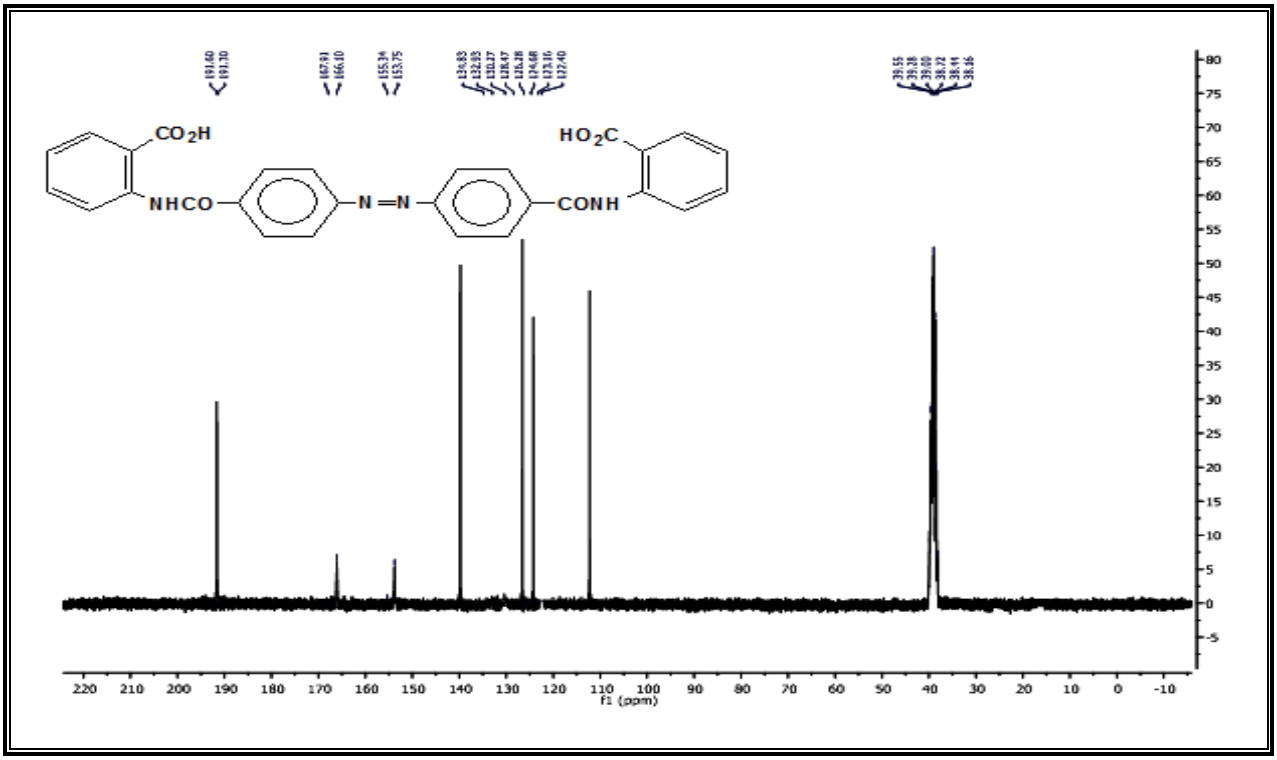


Fig (3-8). ^{13}C-NMR spectrum of compound [III]

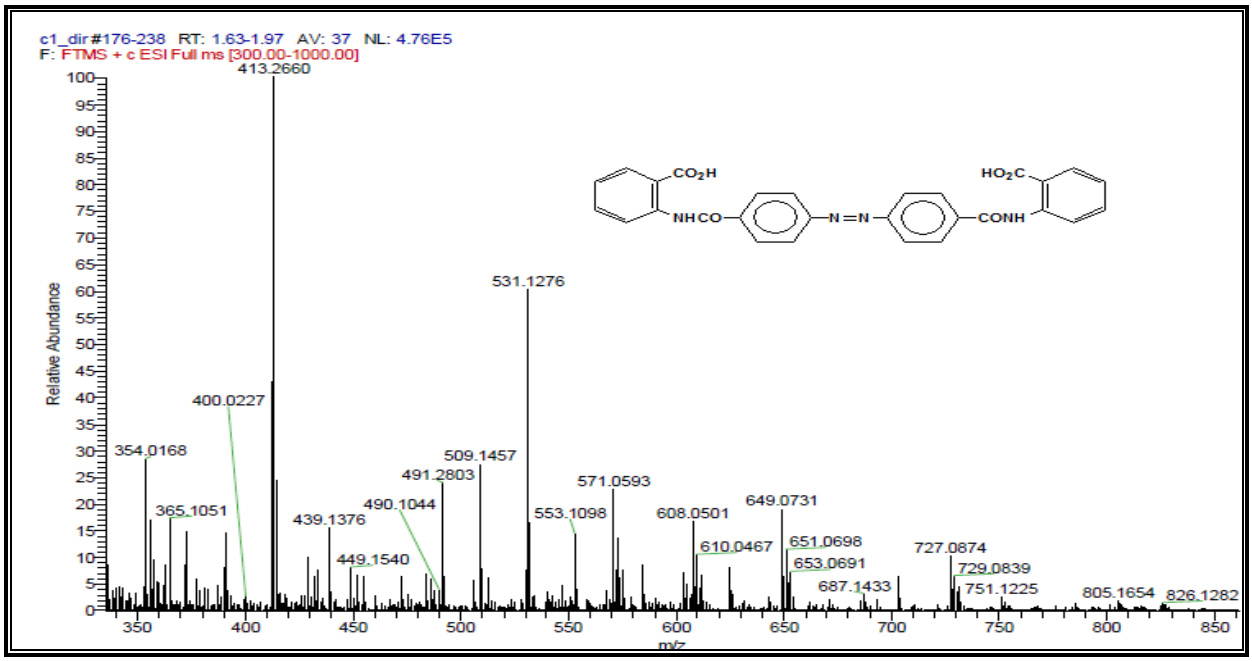


Fig (3-9). Mass spectrum analysis of compound [III]

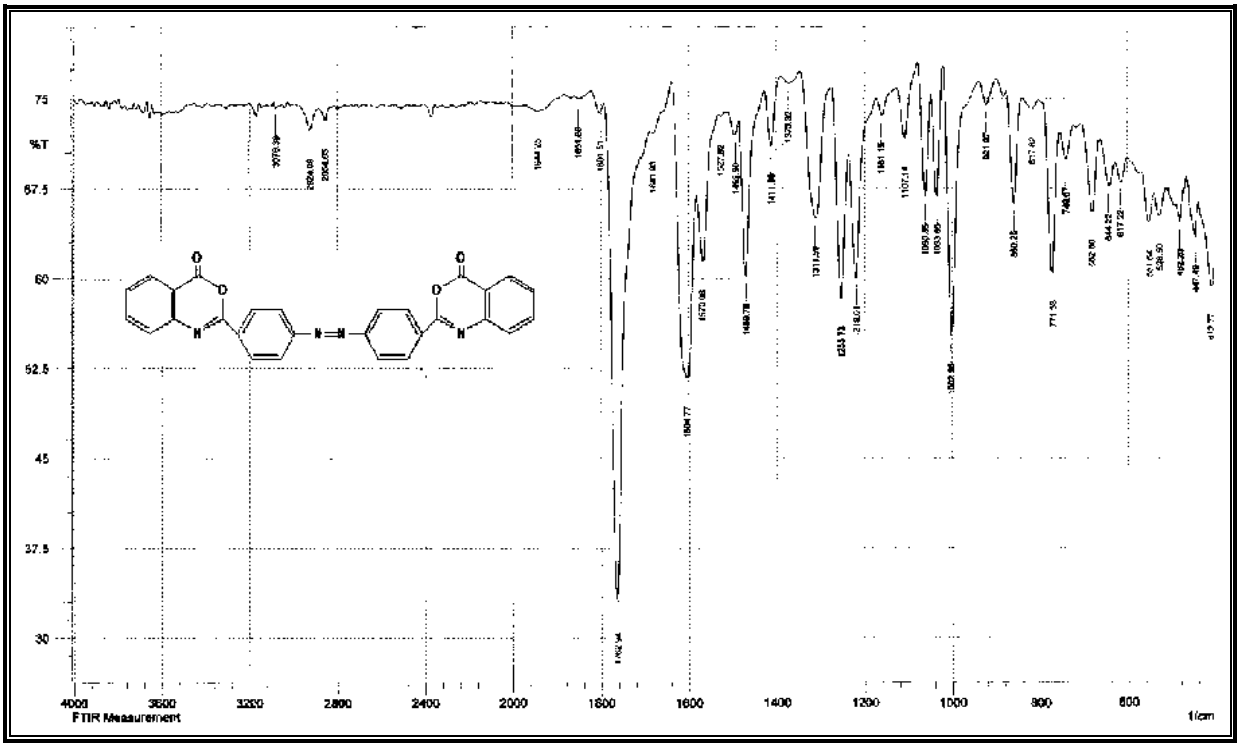


Fig (3-10). FT-IR spectrum of compound [IV]

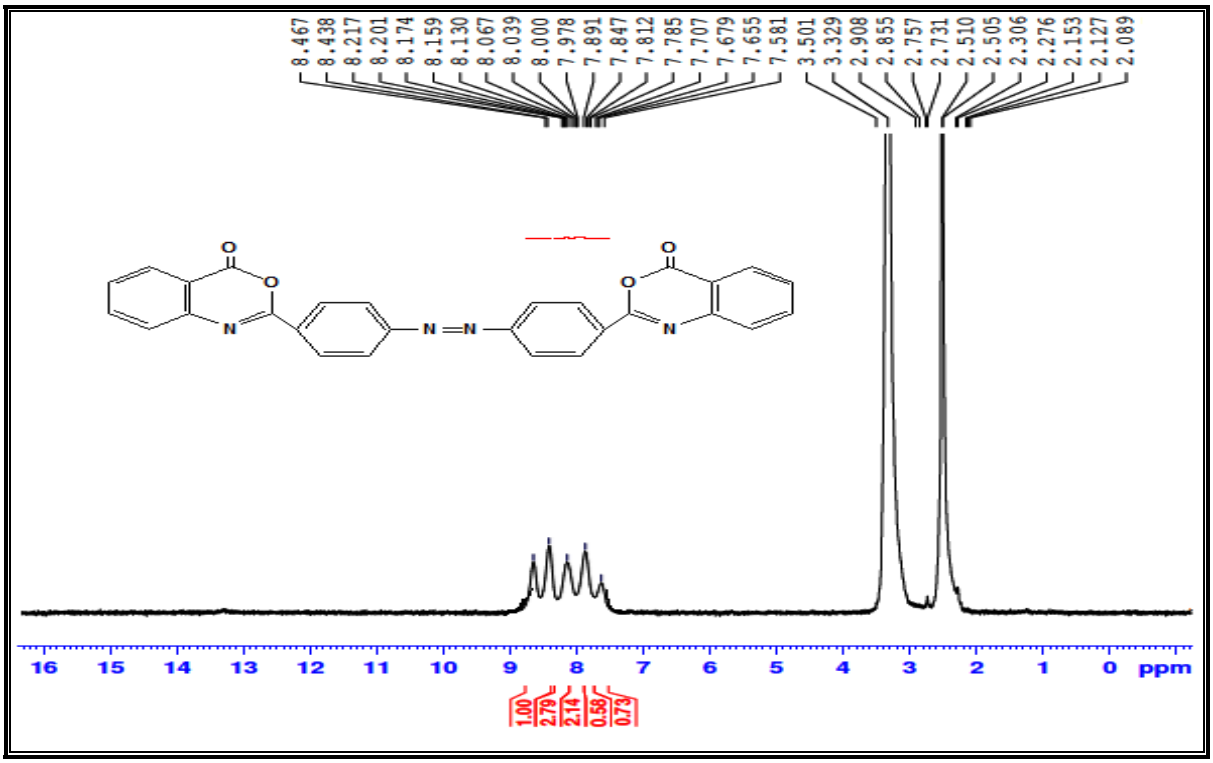


Fig (3-11). ^{1}H-NMR spectrum analysis of compound [IV]

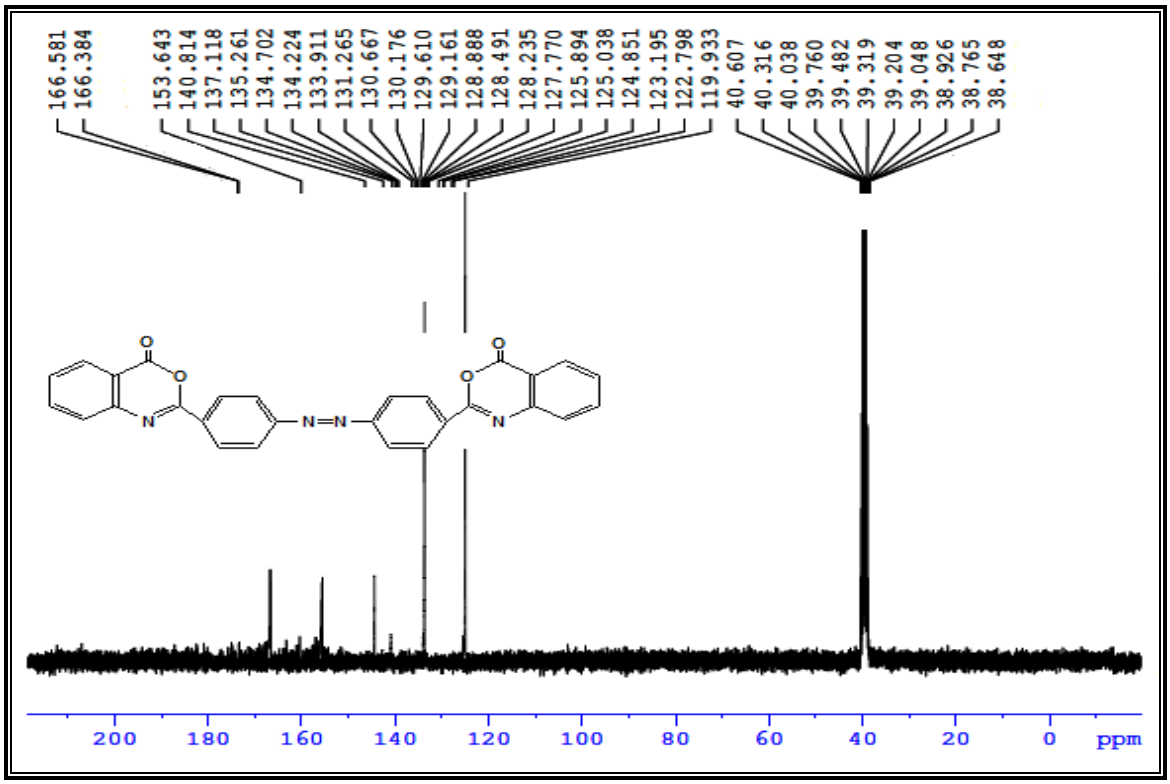


Fig (3-12). ^{13}C-NMR spectrum analysis of compound [IV]

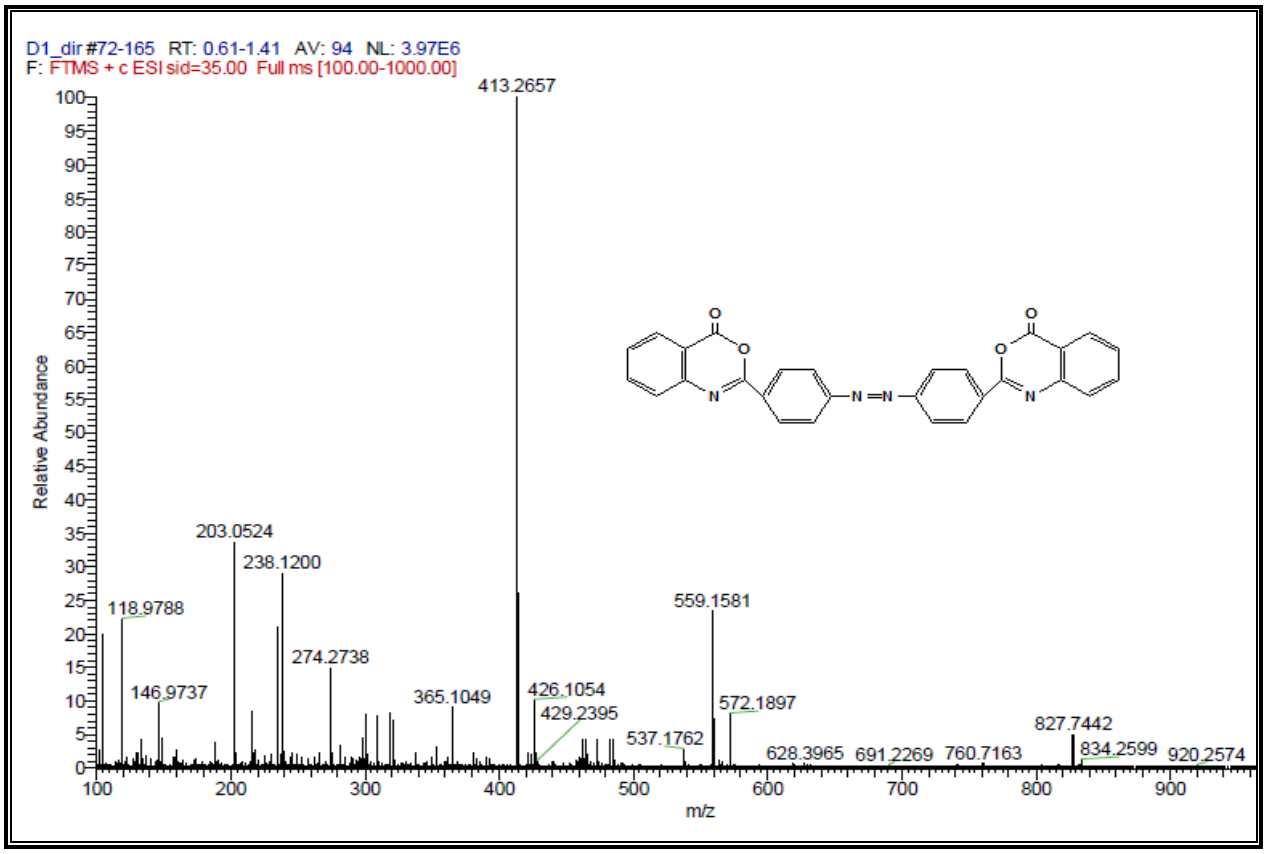


Fig (3-13). Mass spectrum analysis of compound [IV]

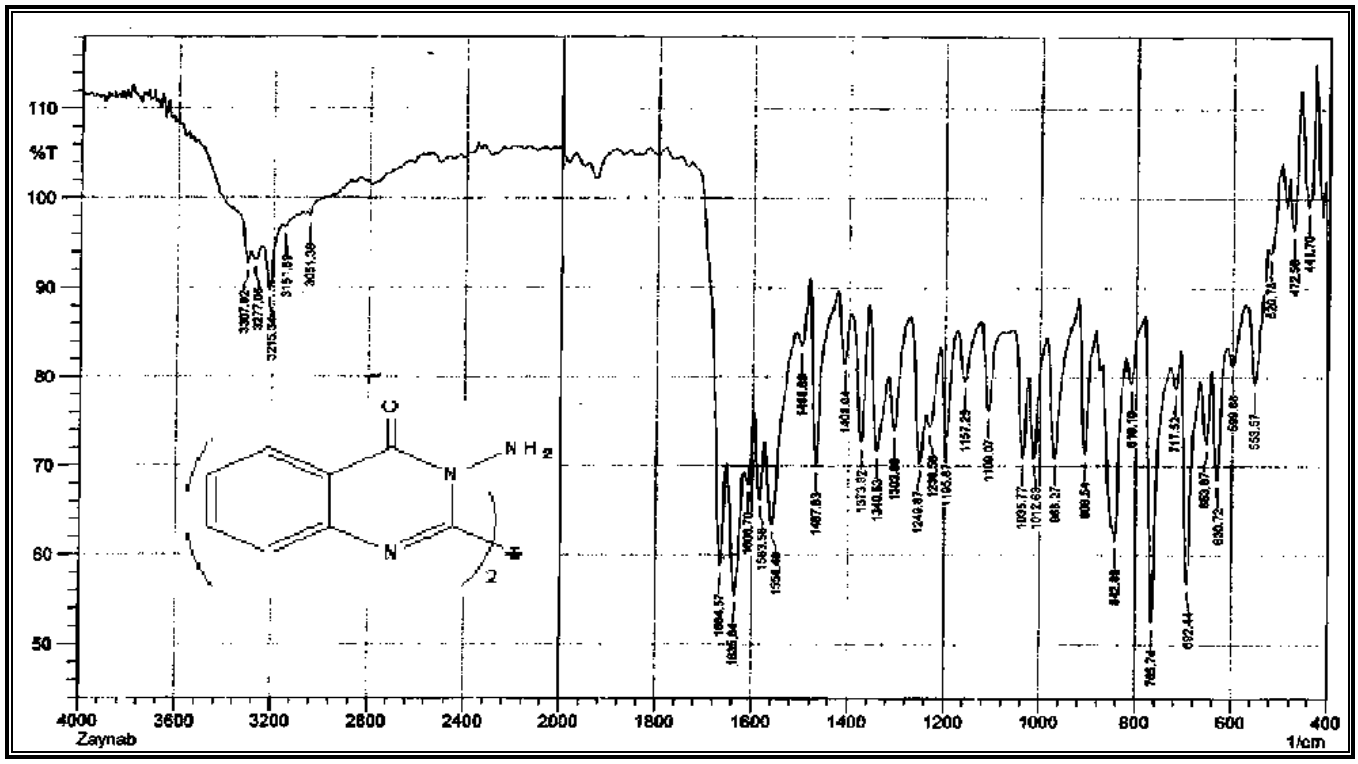


Fig (3-14). FT-IR spectrum analysis of compound [Va]

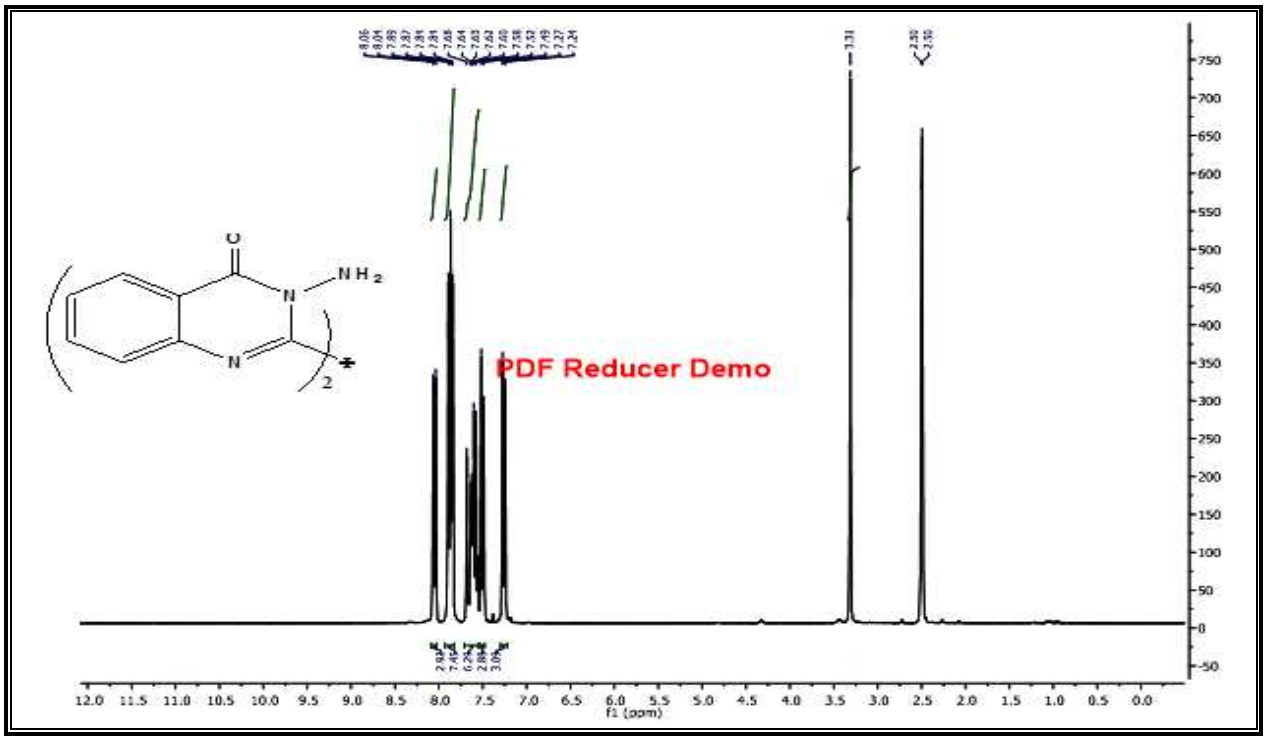


Fig (3-15). ^{1}H-NMR spectrum analysis of compound [Va]

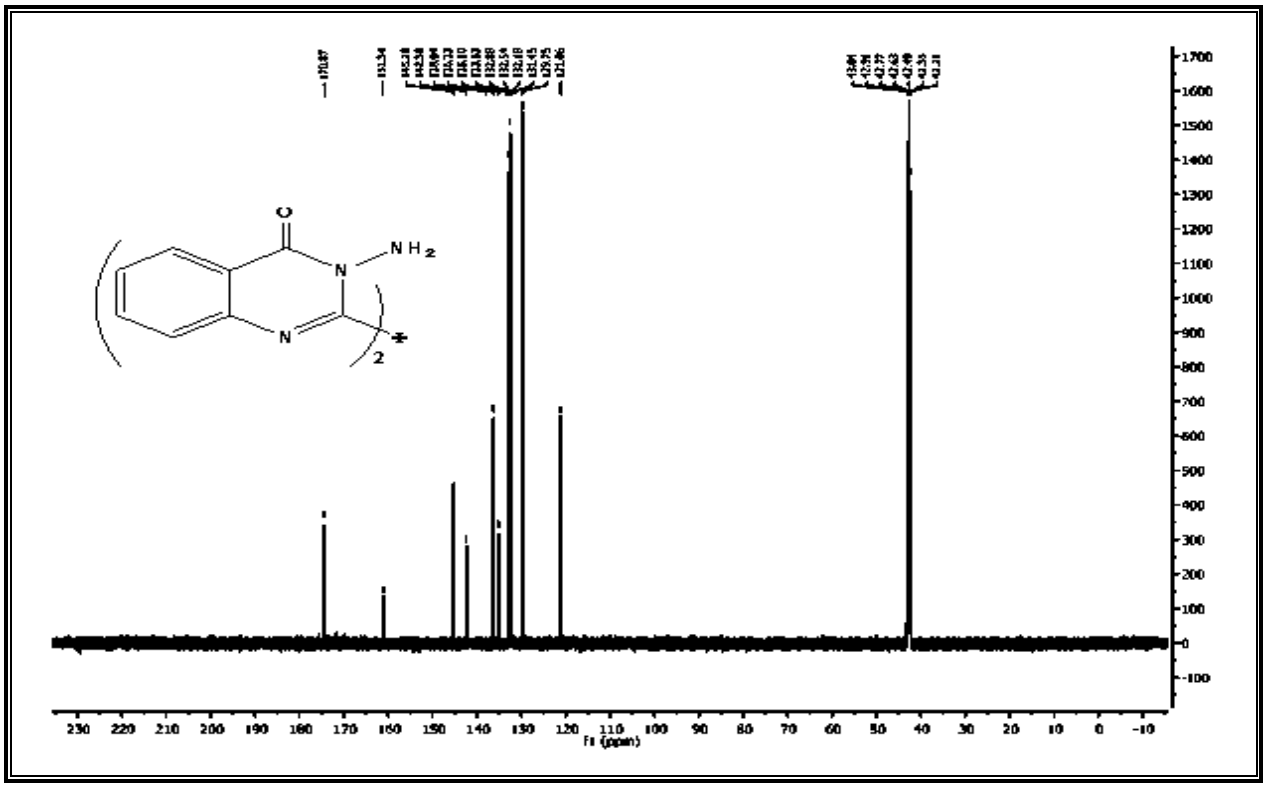


Fig (3-16). ^{13}C-NMR spectrum analysis of compound [Va]

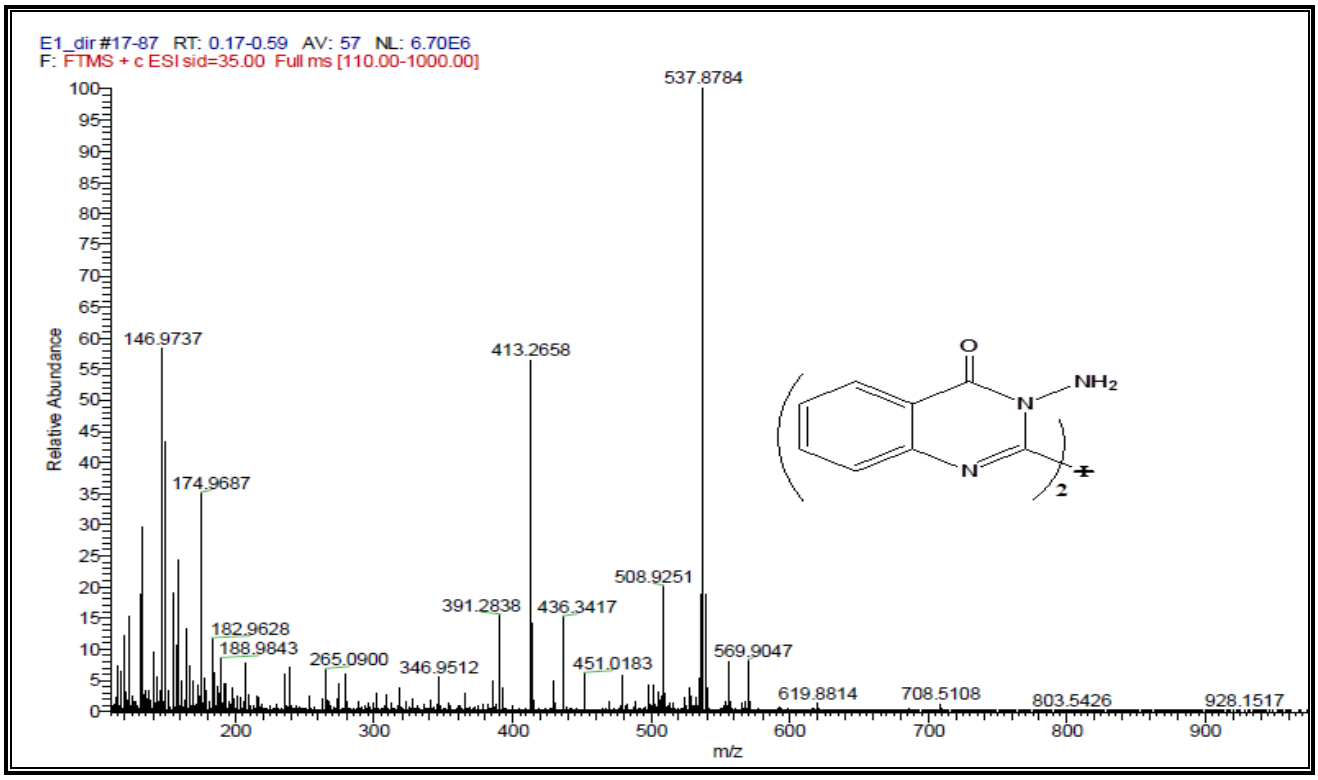


Fig (3-17). Mass spectrum analysis of compound [Va]

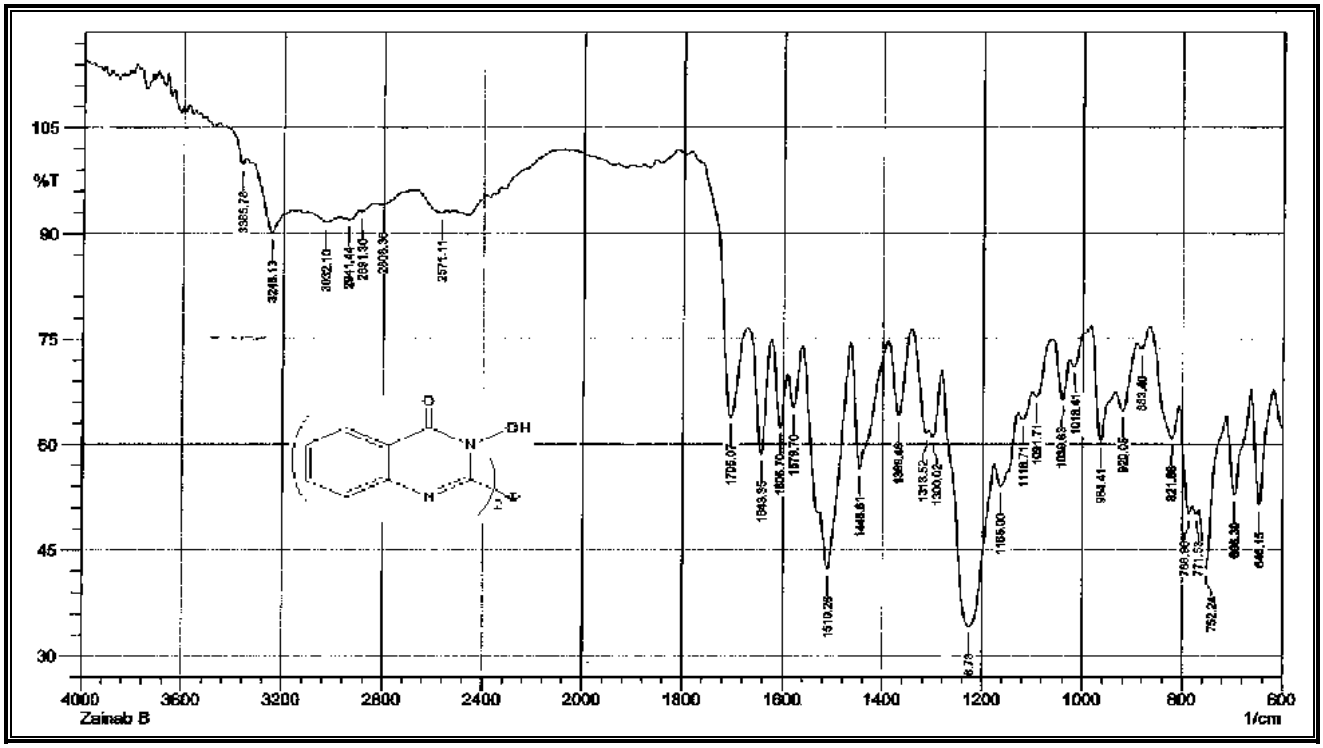


Fig (3-18). FT-IR spectrum analysis of compound [Vb]

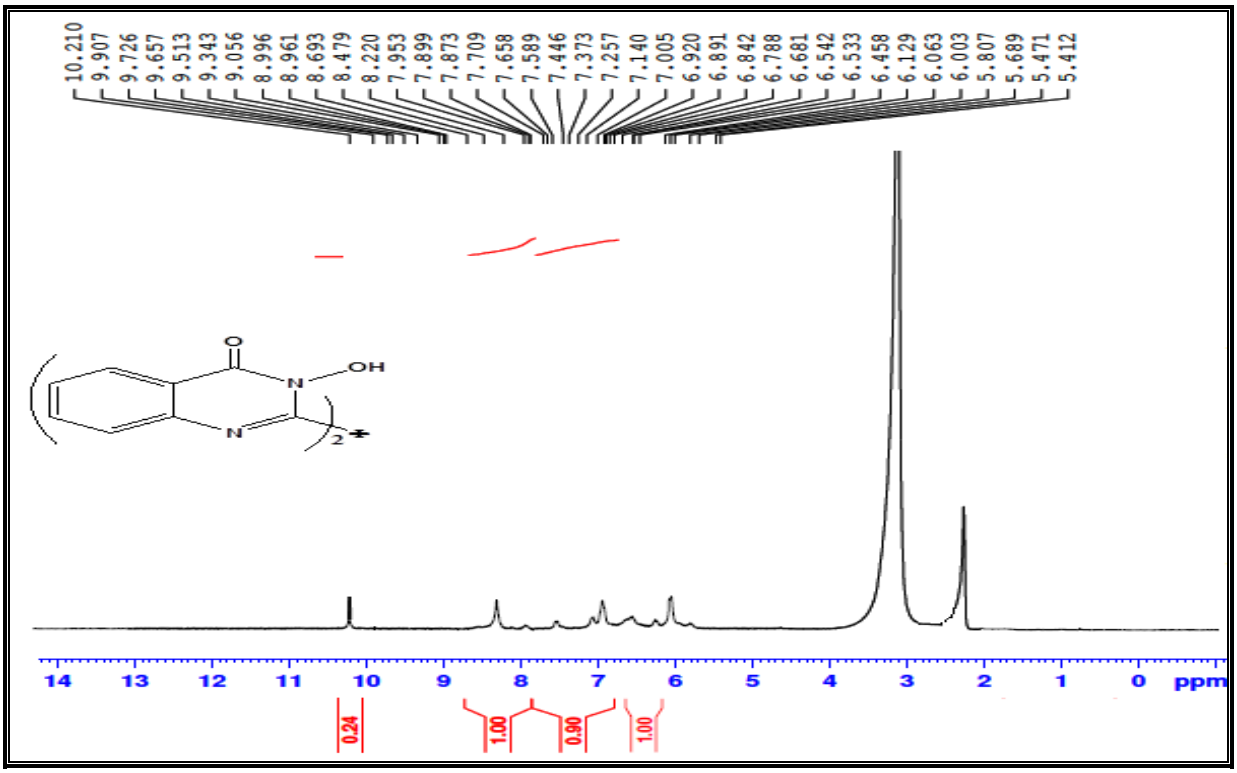


Fig (3-19). ^{1}H-NMR spectrum analysis of compound [Vb]

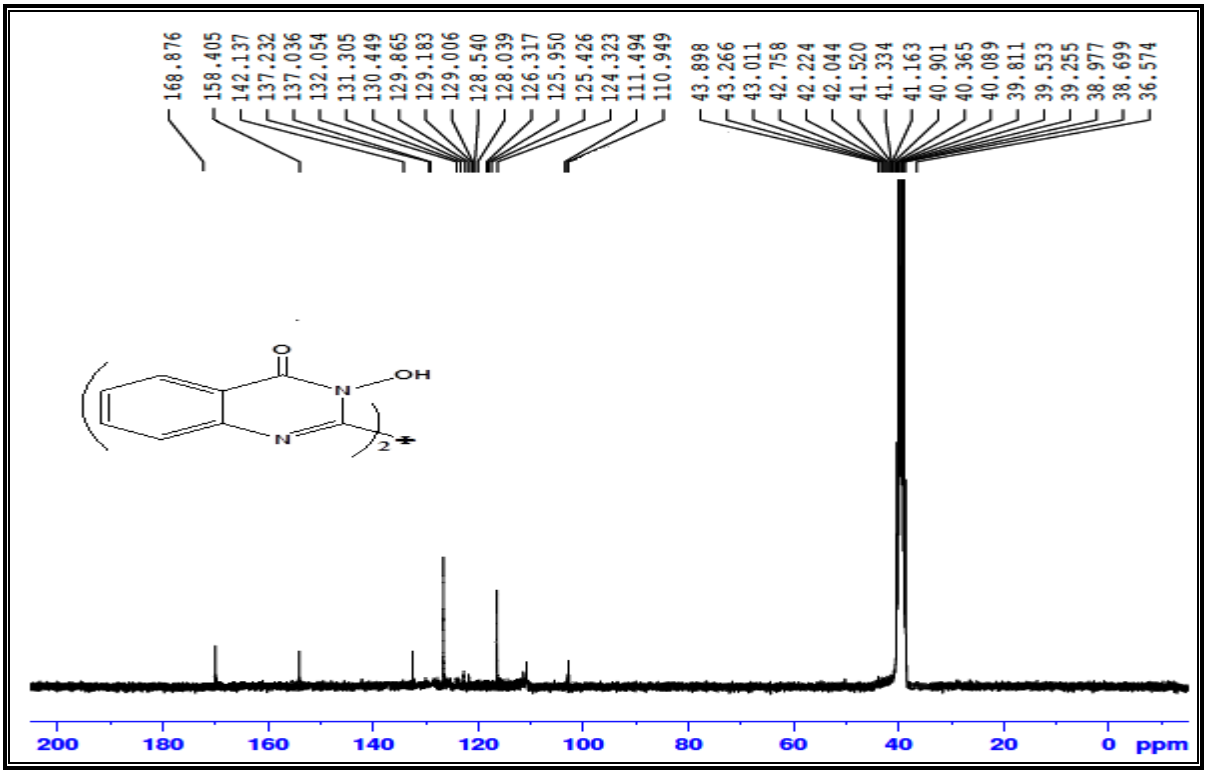


Fig (3-20). ^{13}C-NMR spectrum analysis of compound [Vb]

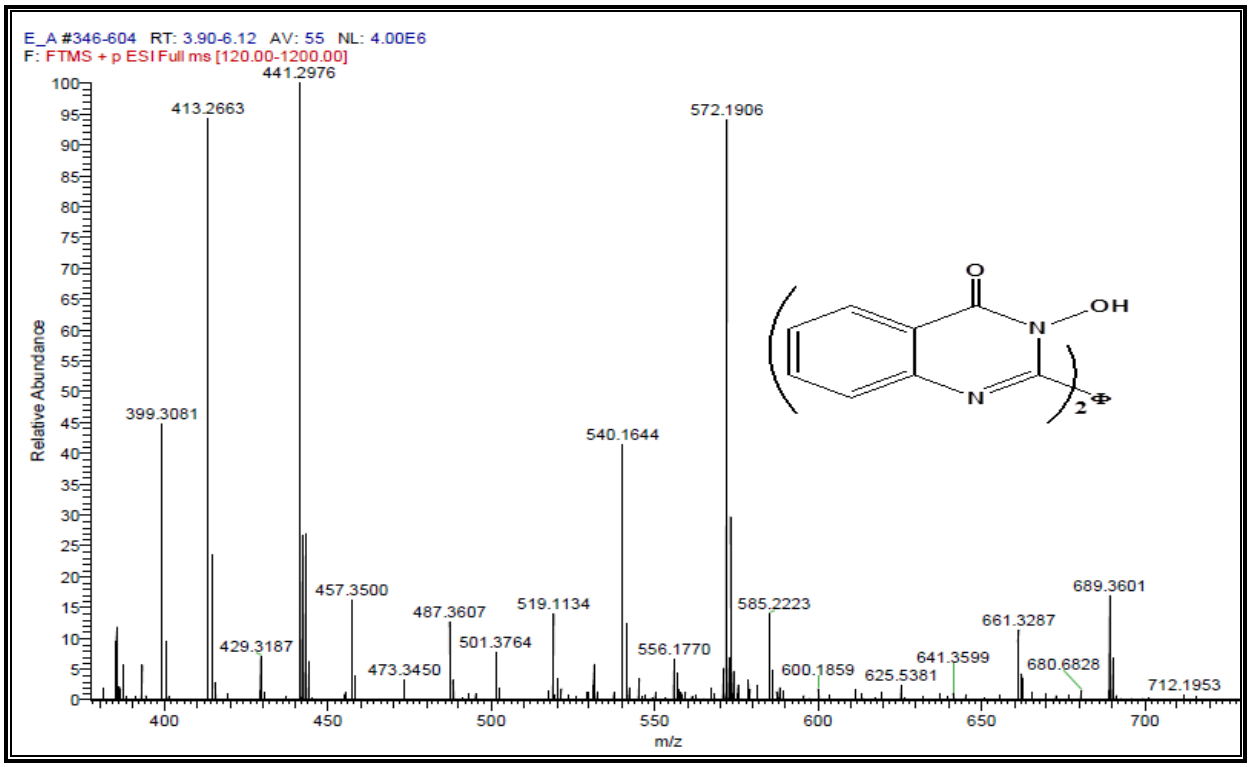


Fig (3-21). Mass spectrum analysis of compound [Vb]

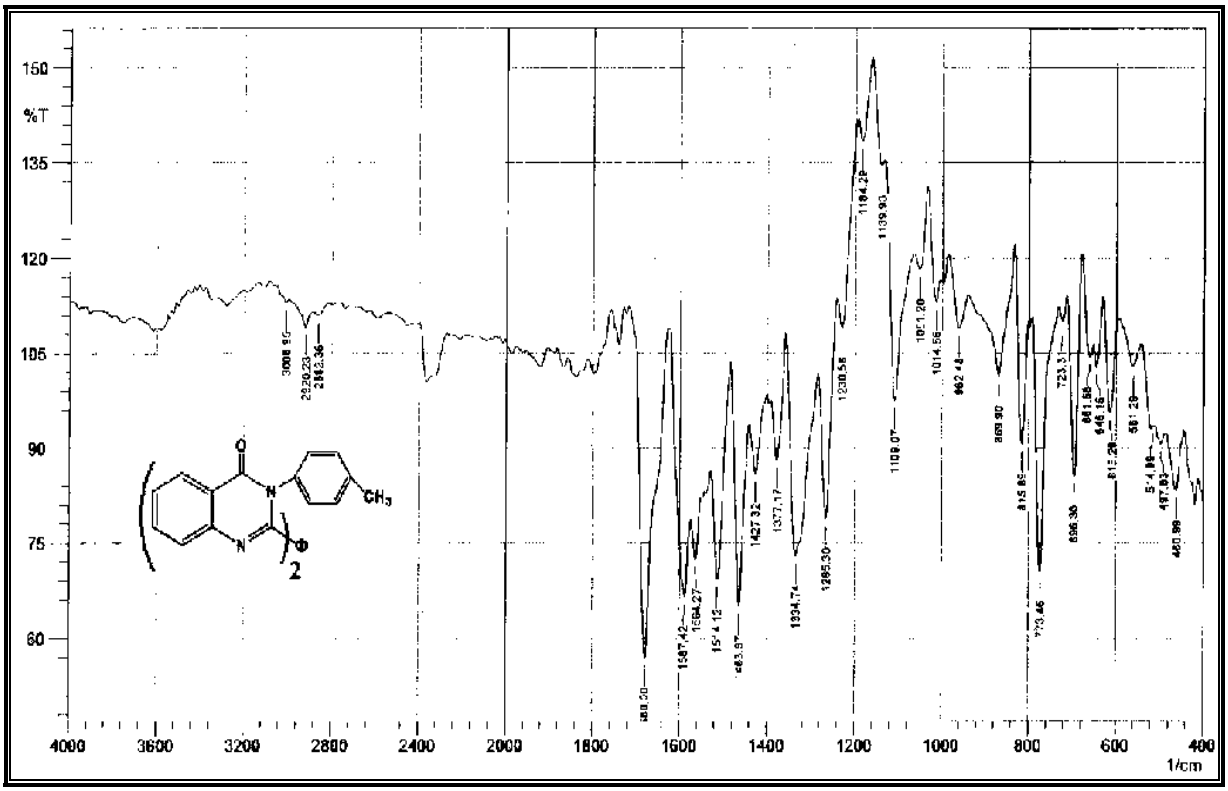


Fig (3-22). FT-IR spectrum analysis of compound [Vc]

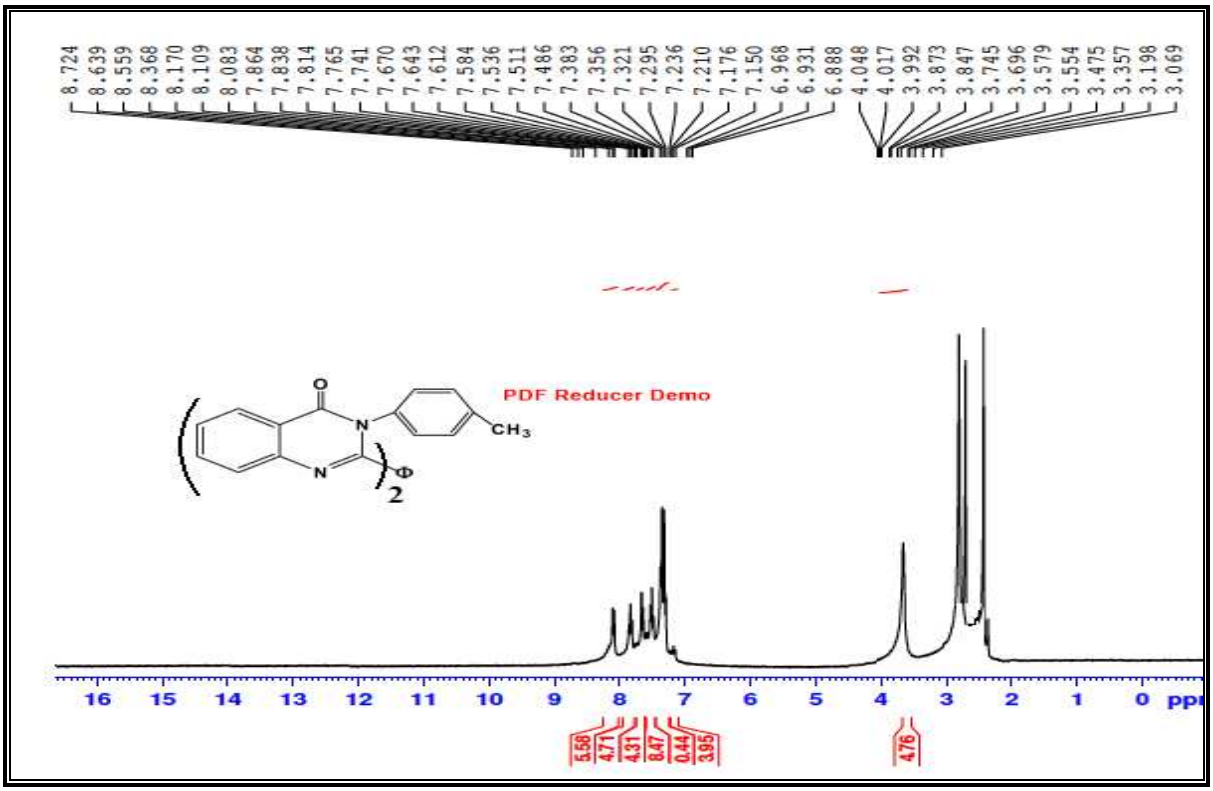


Fig (3-23). ^{1}H-NMR spectrum analysis of compound [Vc]

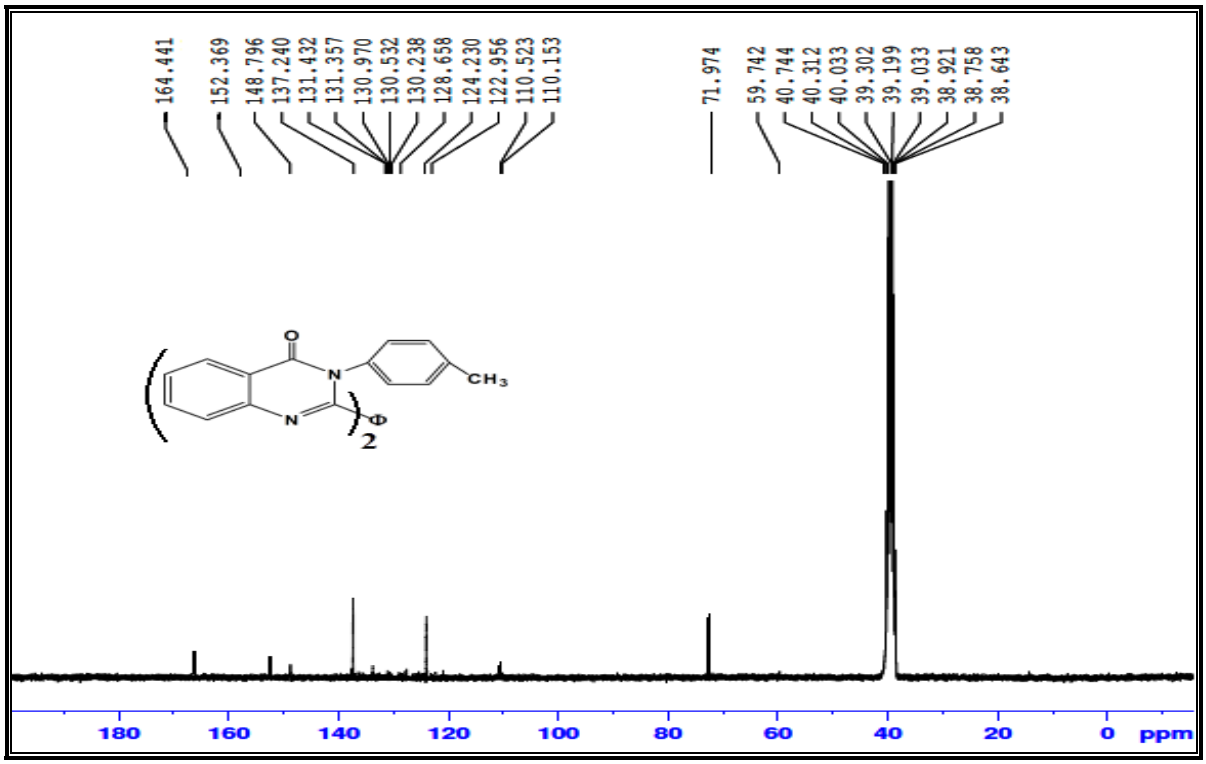


Fig (3-24). ^{13}C-NMR spectrum analysis of compound [Vc]

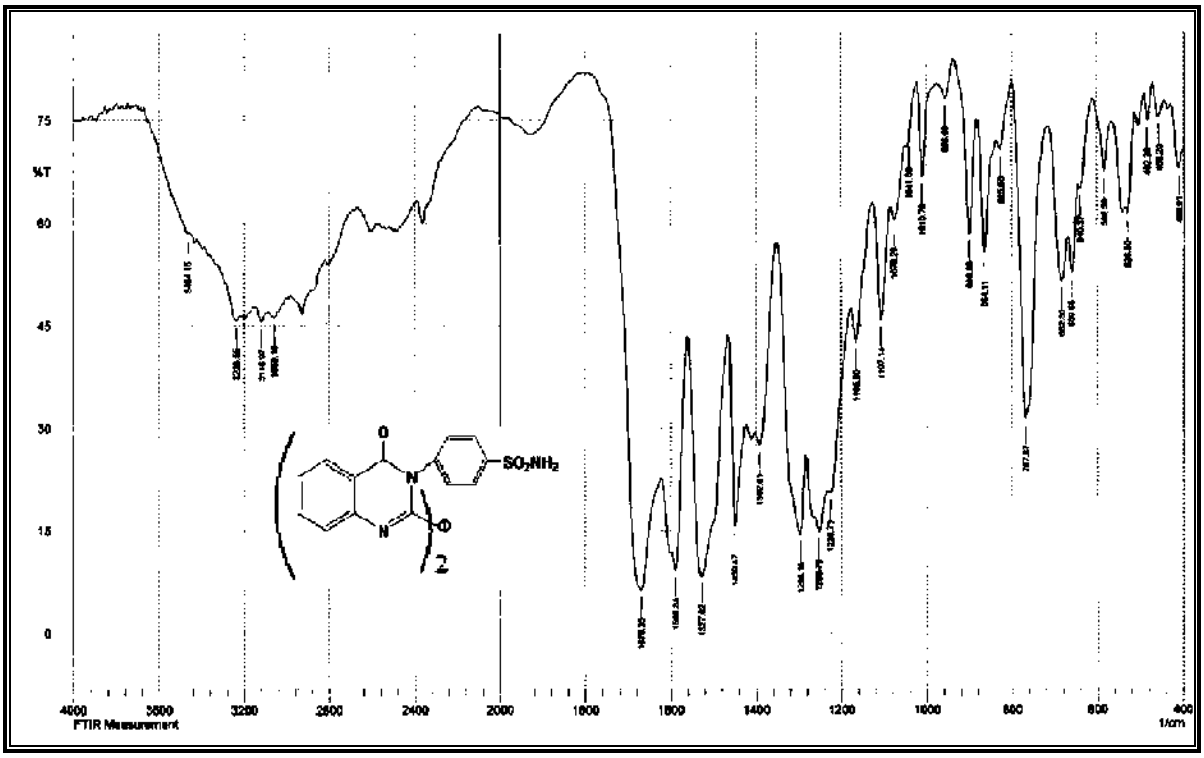


Fig (3-25). FT-IR spectrum analysis of compound [Vd]

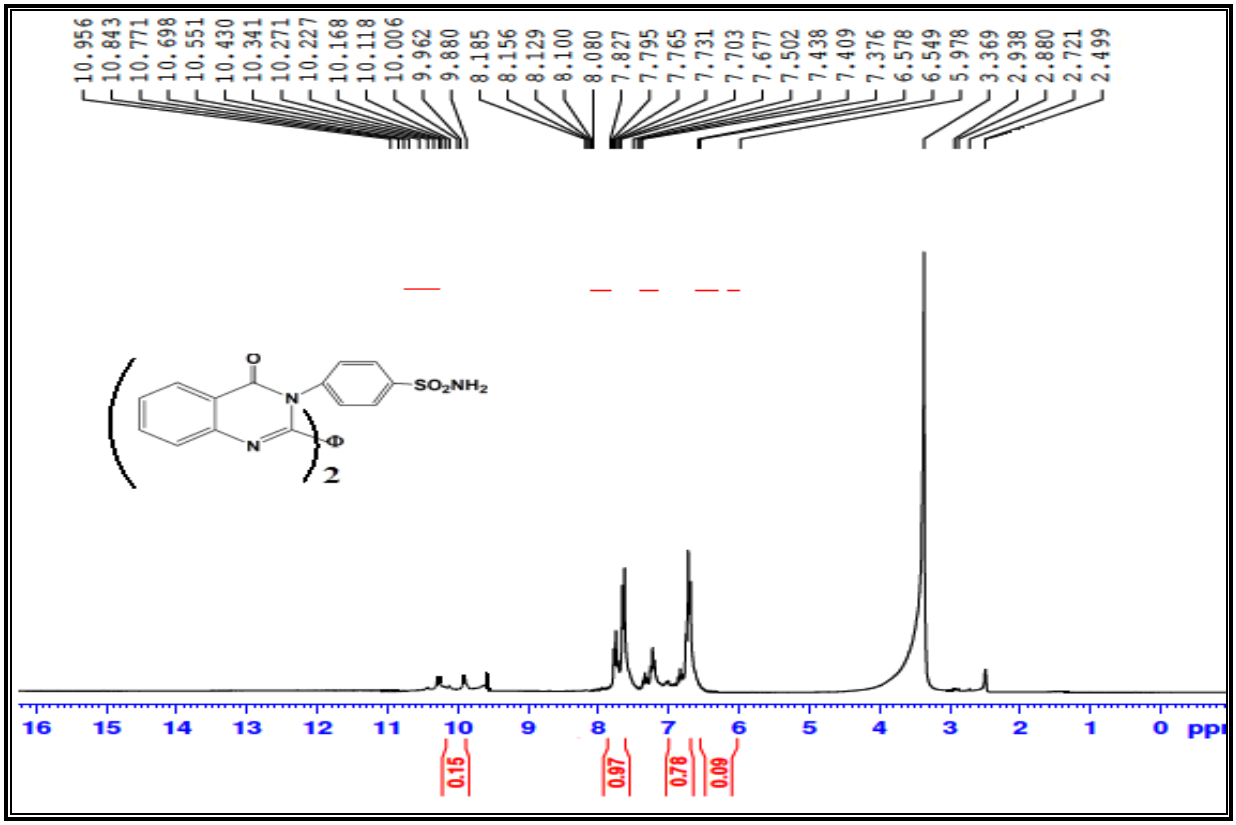


Fig (3-26). ^{1}H-NMR spectrum analysis of compound [Vd]

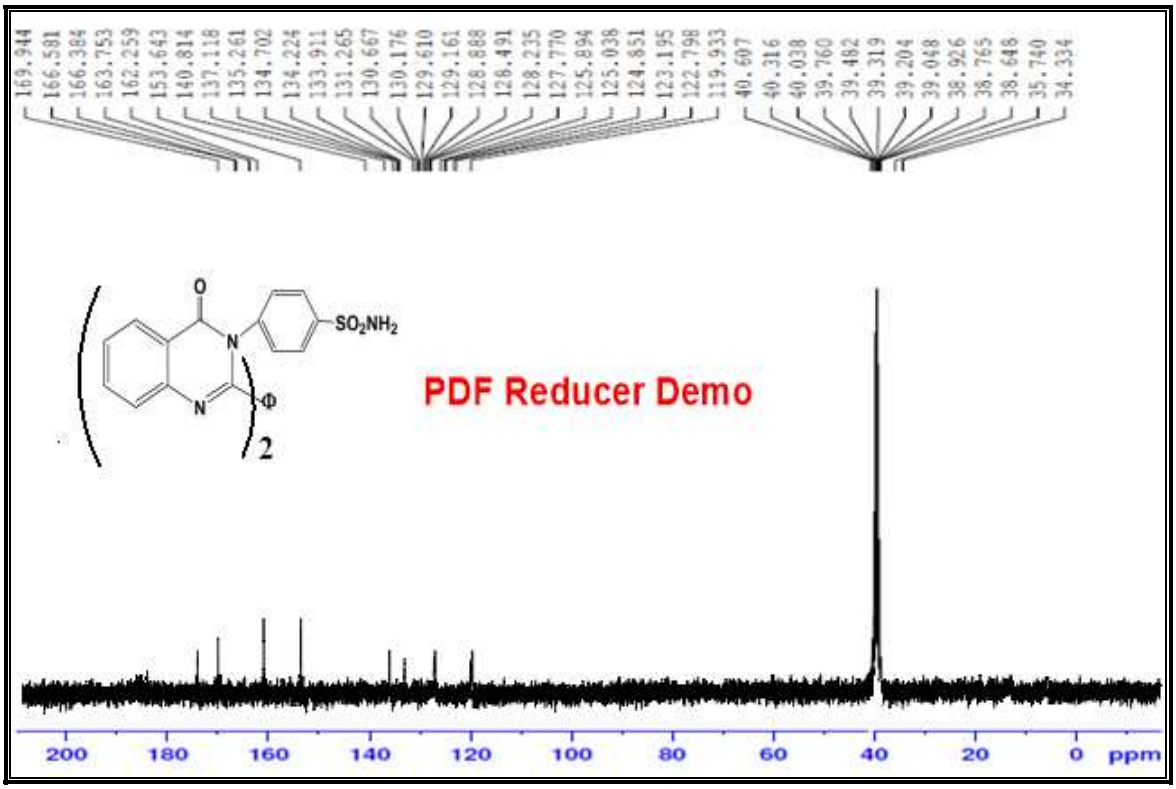


Fig (3-27). ^{13}C-NMR spectrum analysis of compound [Vd]

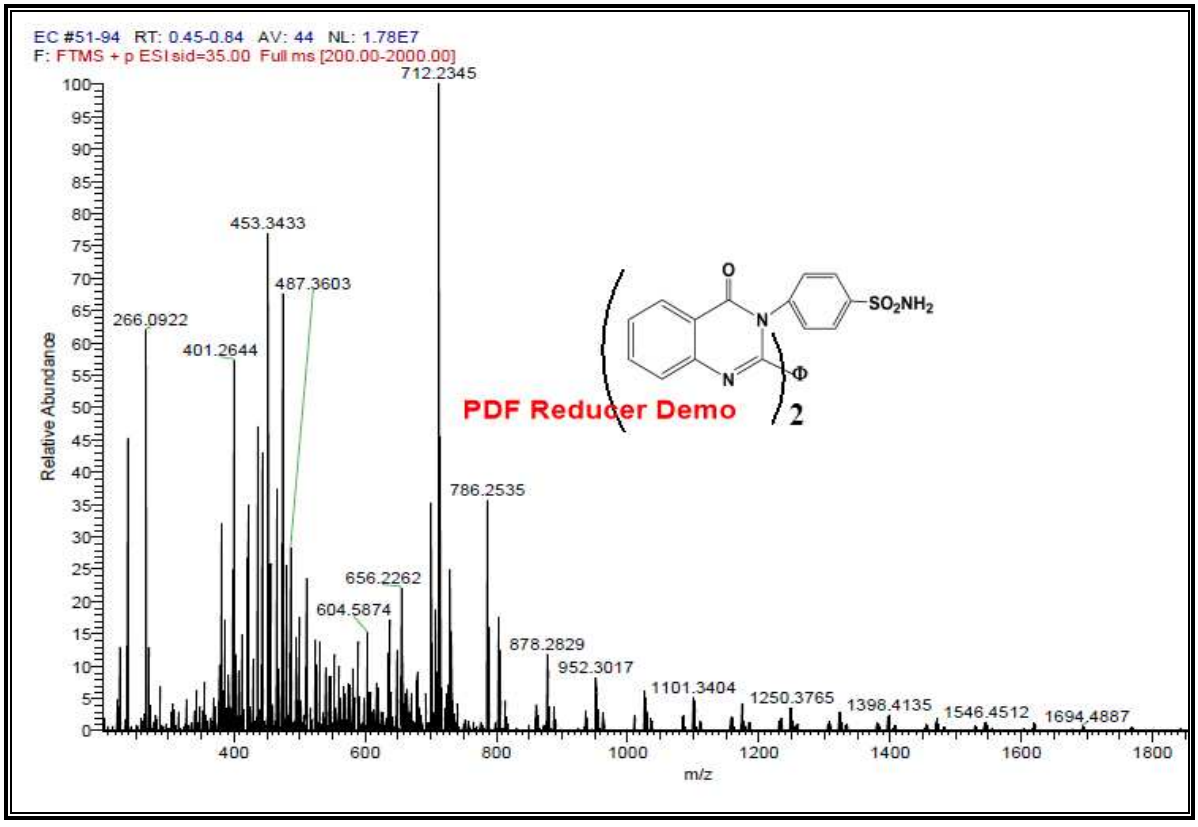


Fig (3-28). Mass spectrum analysis of compound [Vd]

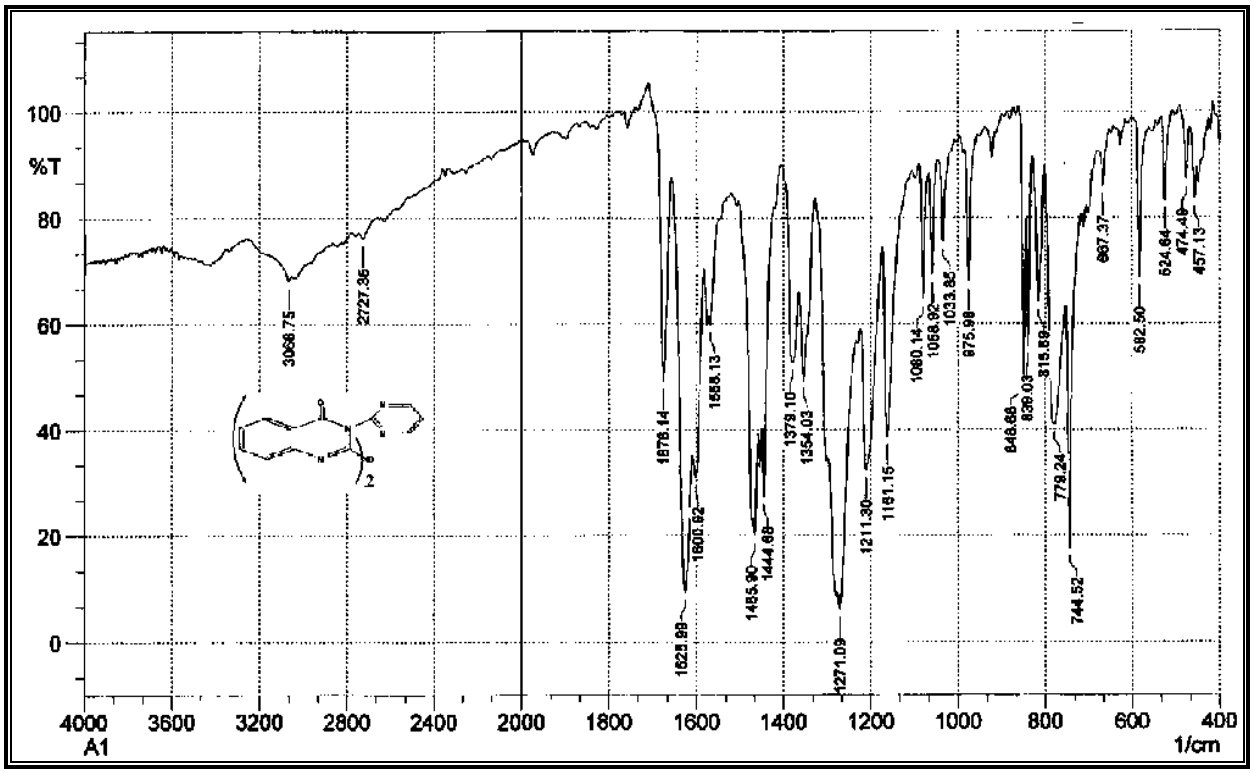


Fig (3-29). FT-IR spectrum analysis of compound [Ve]

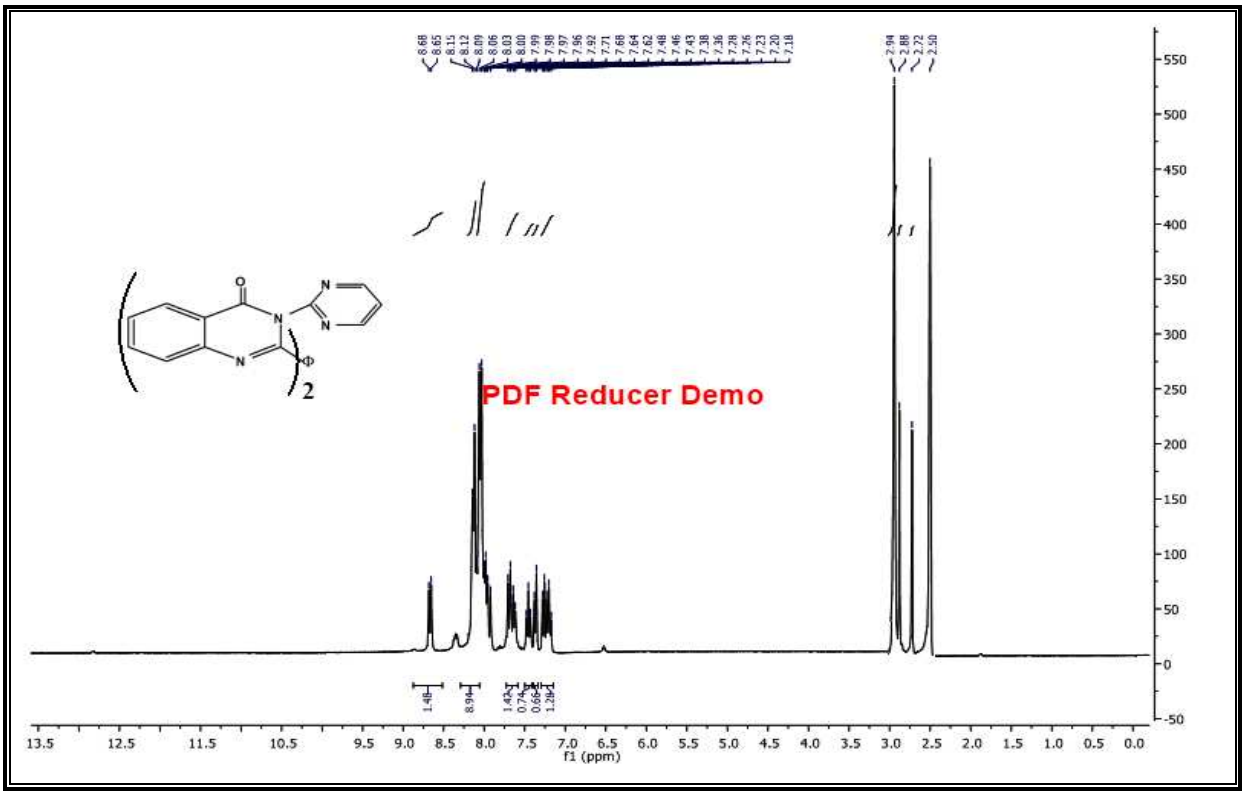


Fig (3-30). ^{1}H-NMR spectrum analysis of compound [Ve]

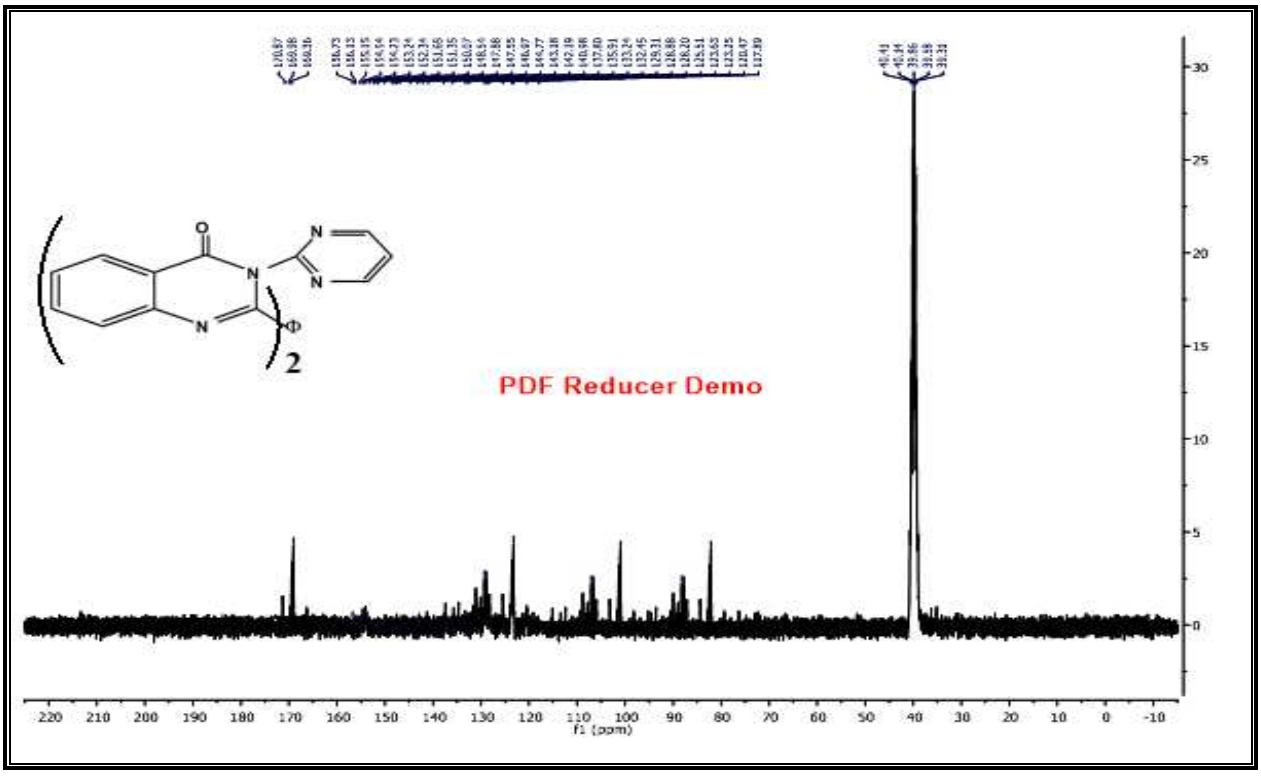


Fig (3-31). ^{13}C-NMR spectrum analysis of compound [Ve]

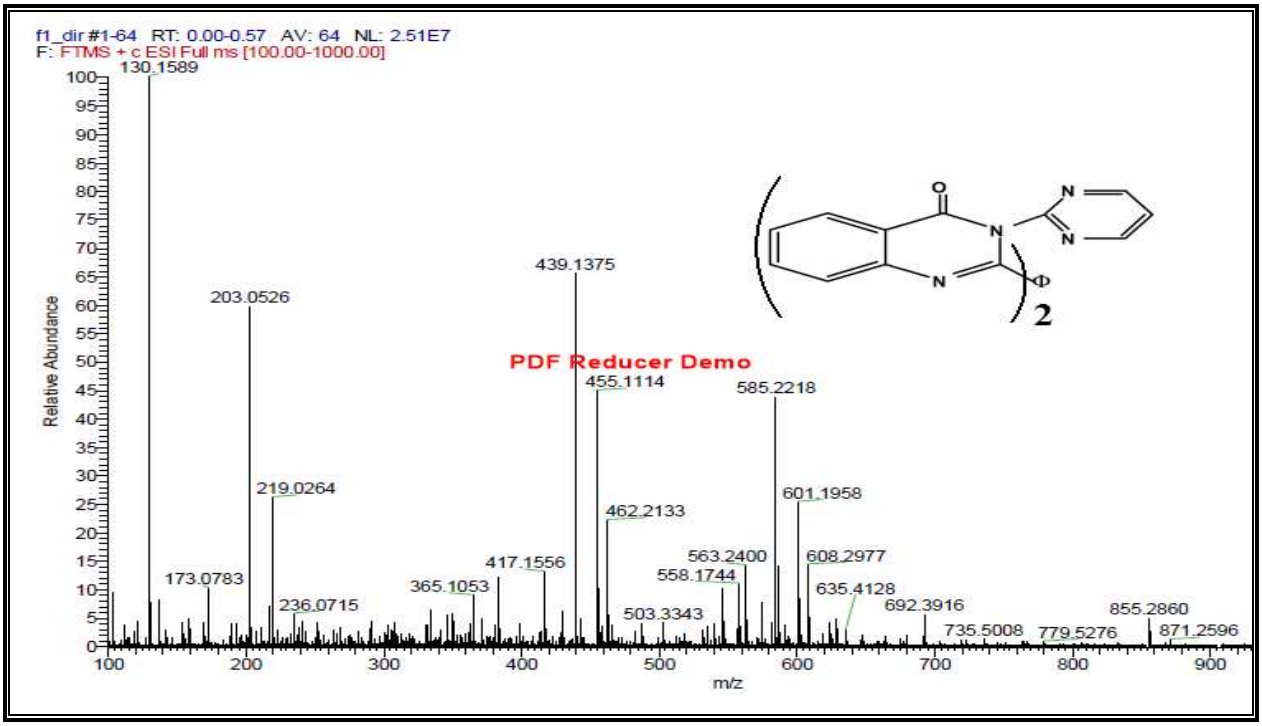


Fig (3-32). Mass spectrum analysis of compound [Ve]

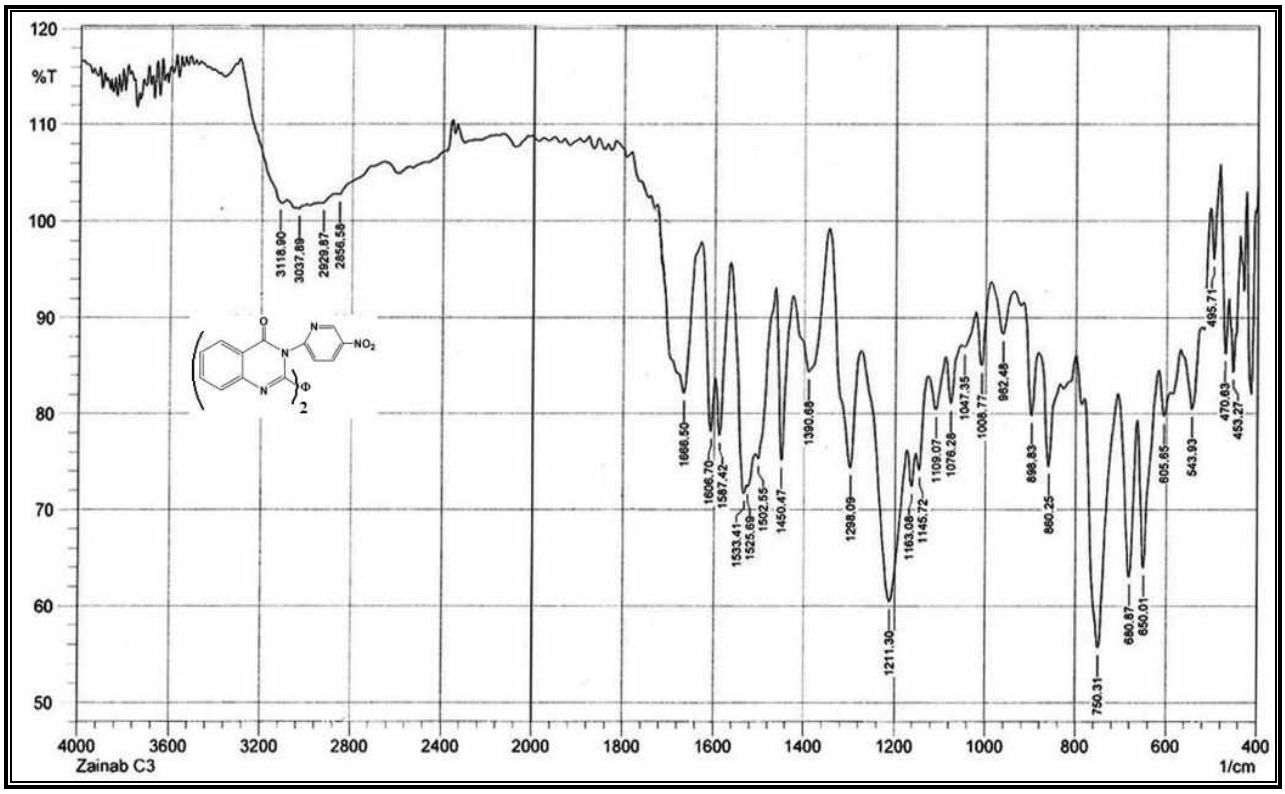


Fig (3-33). FT-IR spectrum analysis of compound [Vf]

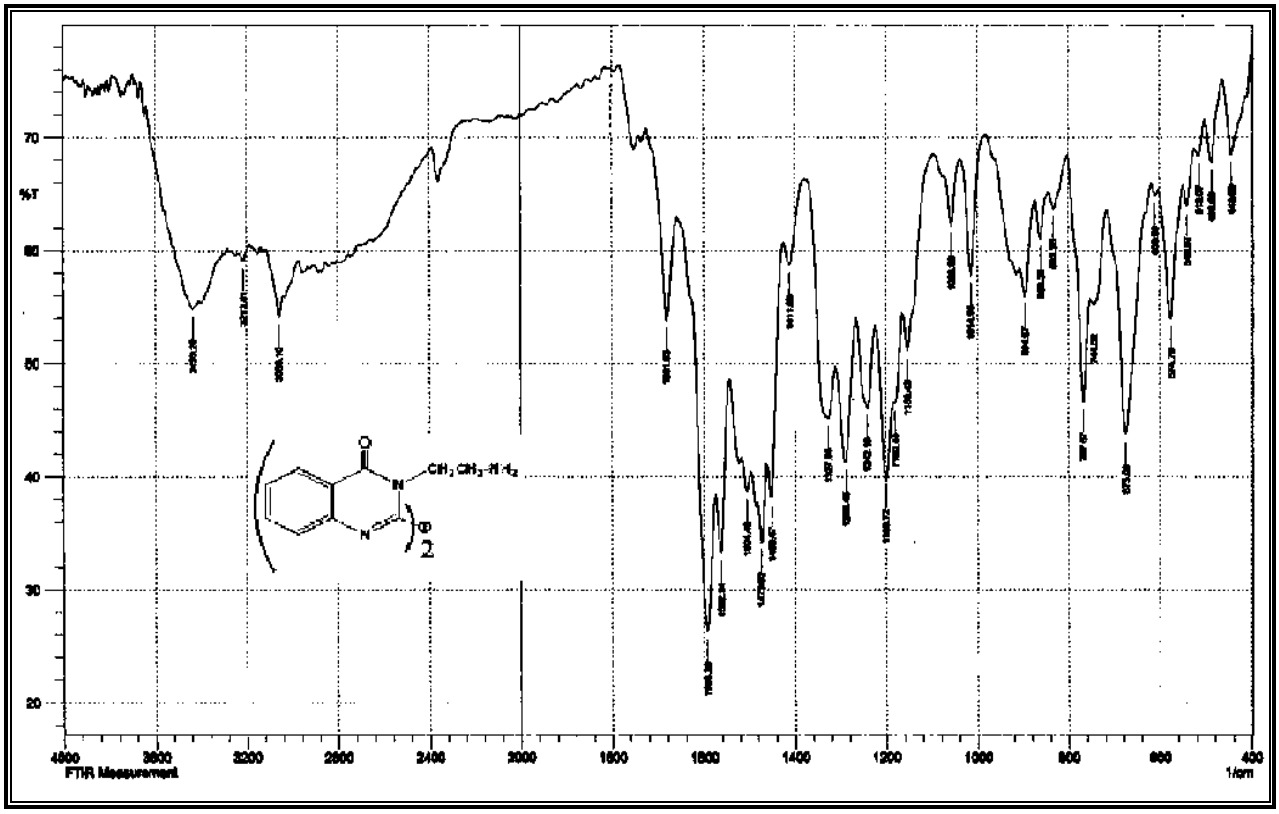


Fig (3-34). FT-IR spectrum analysis of compound [Vg]

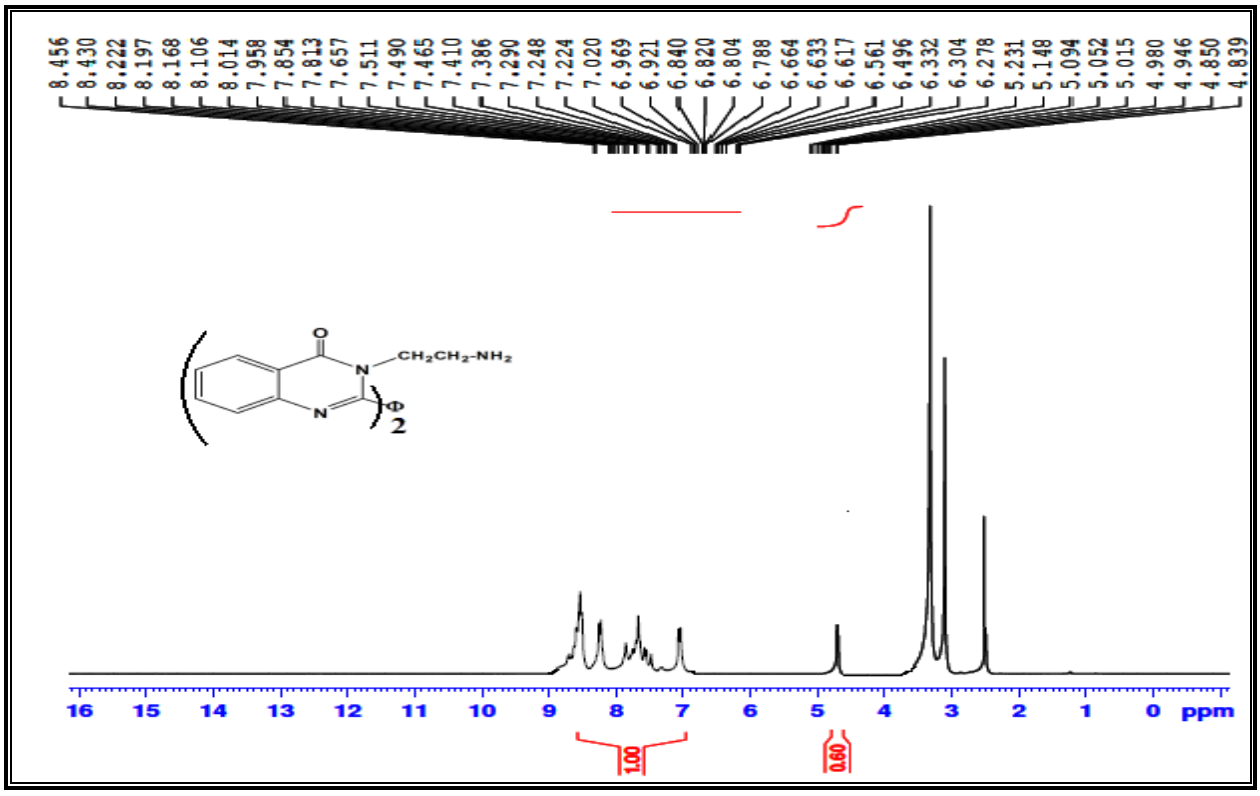


Fig (3-35). ^{1}H-NMR spectrum analysis of compound [Vg]

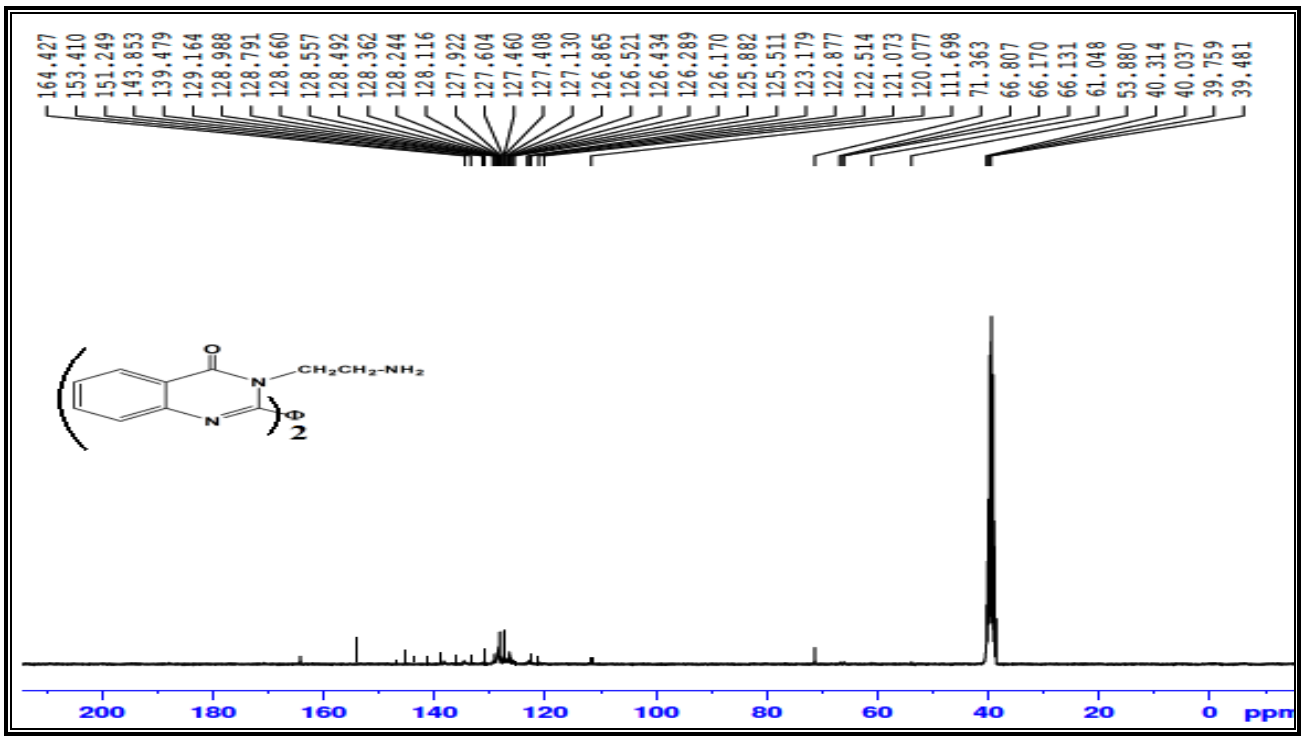


Fig (3-36). ^{13}C-NMR spectrum analysis of compound [Vg]

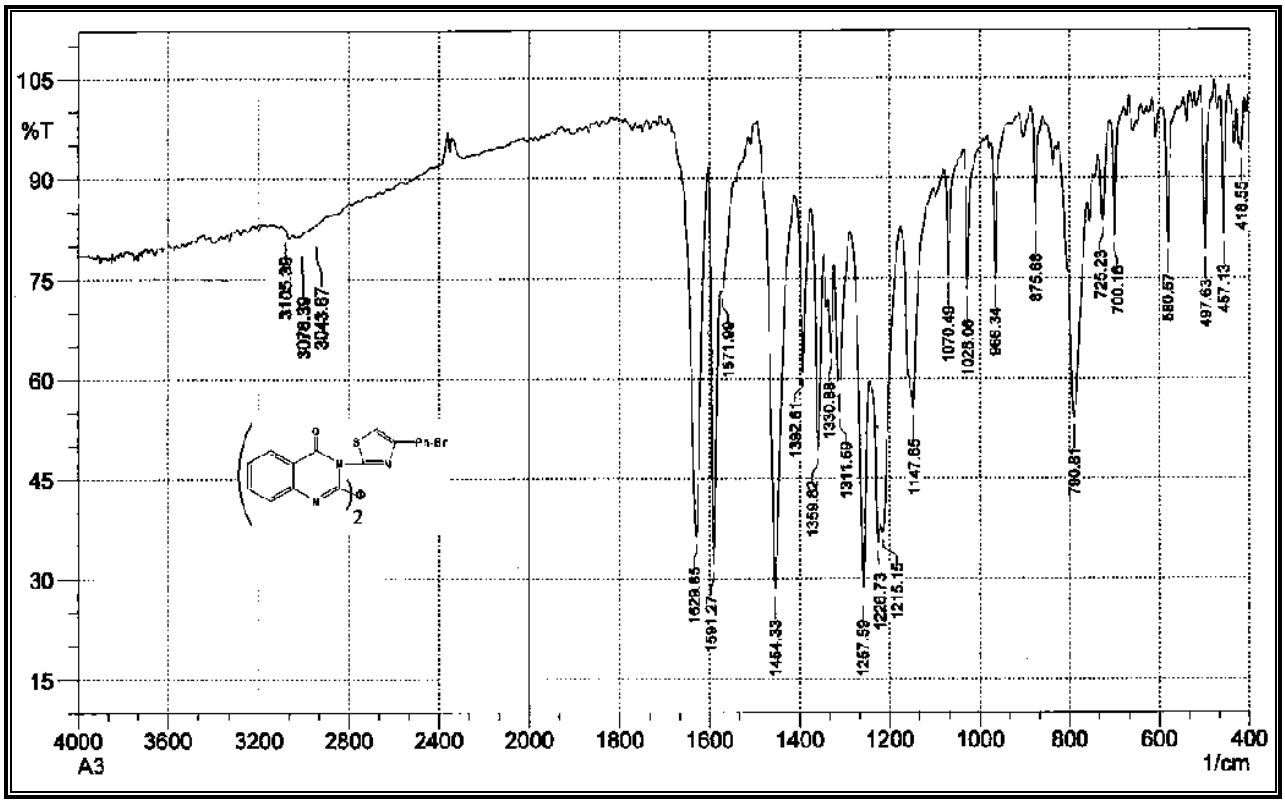


Fig (3-37). FT-IR spectrum analysis of compound [Vh]

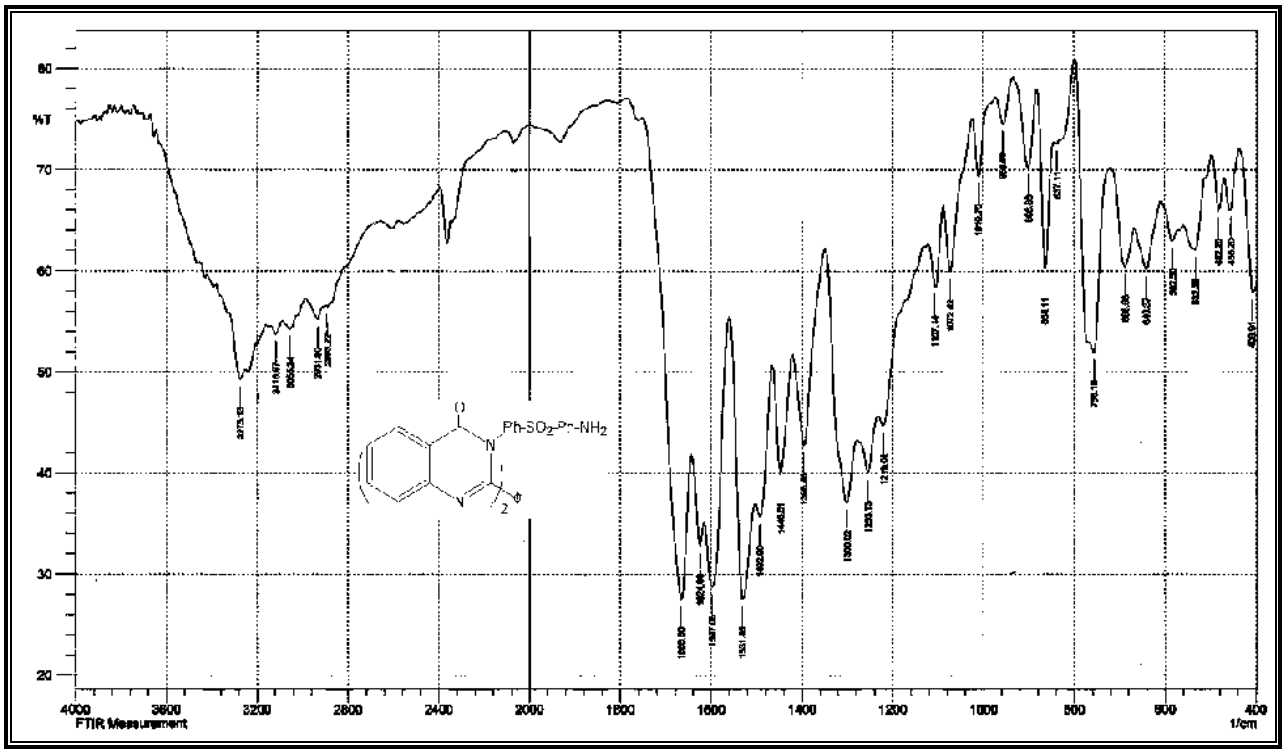


Fig (3-38). FT-IR spectrum analysis of compound [Vi]

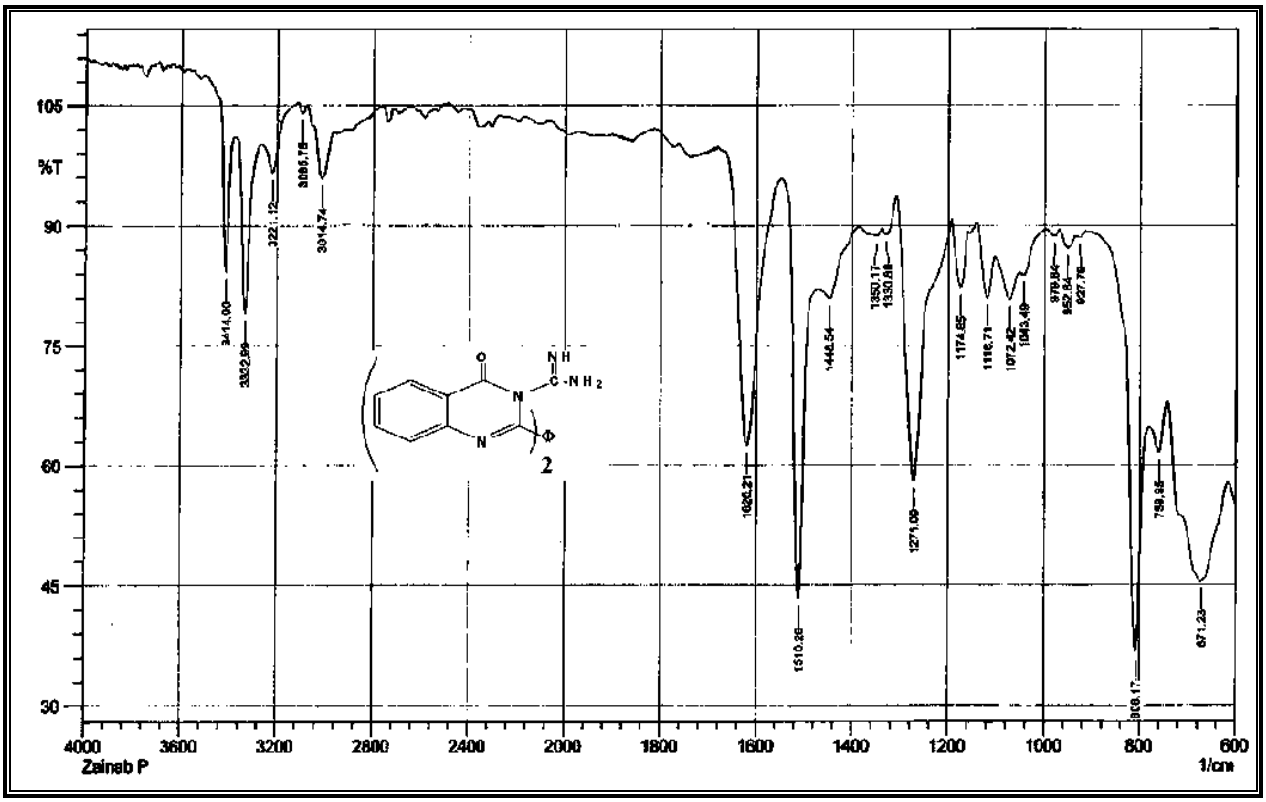


Fig (3-39). FT-IR spectrum analysis of compound [Vj]

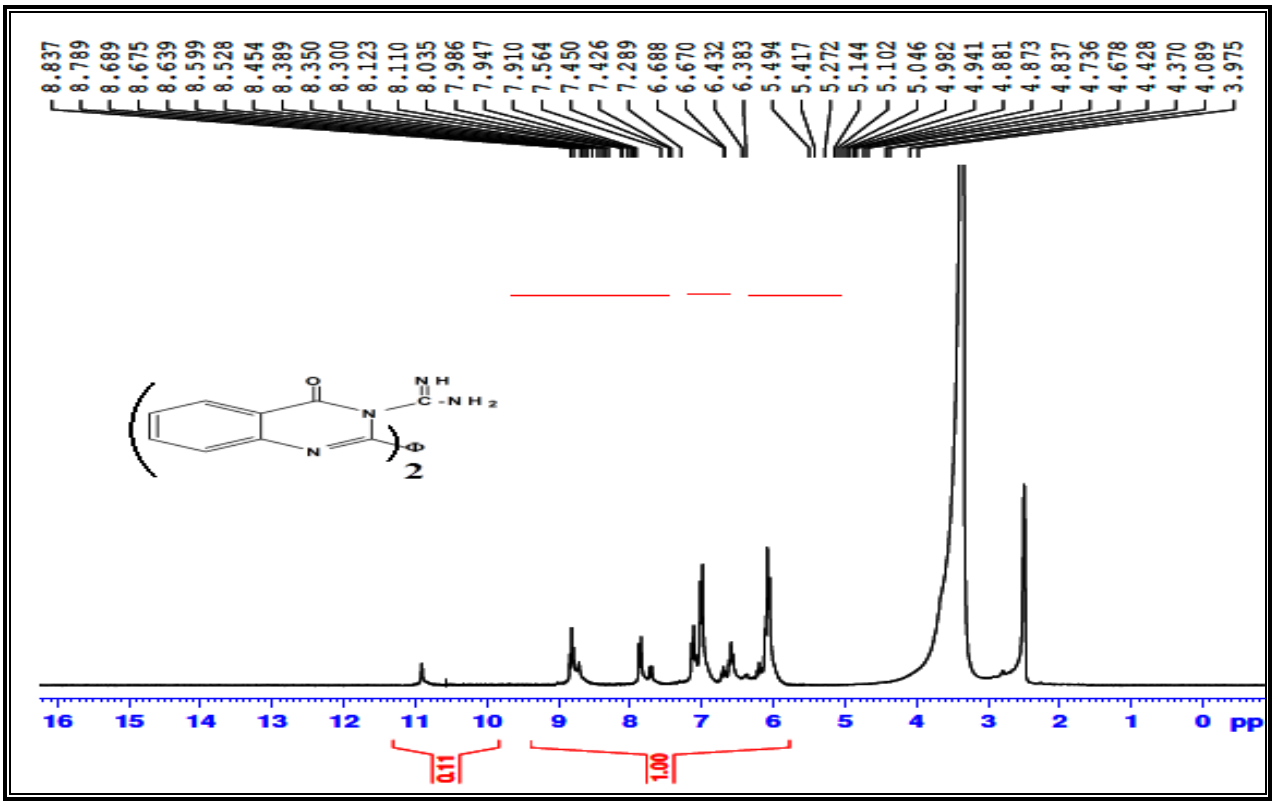


Fig (3-40). ^{1}H-NMR spectrum analysis of compound [Vj]

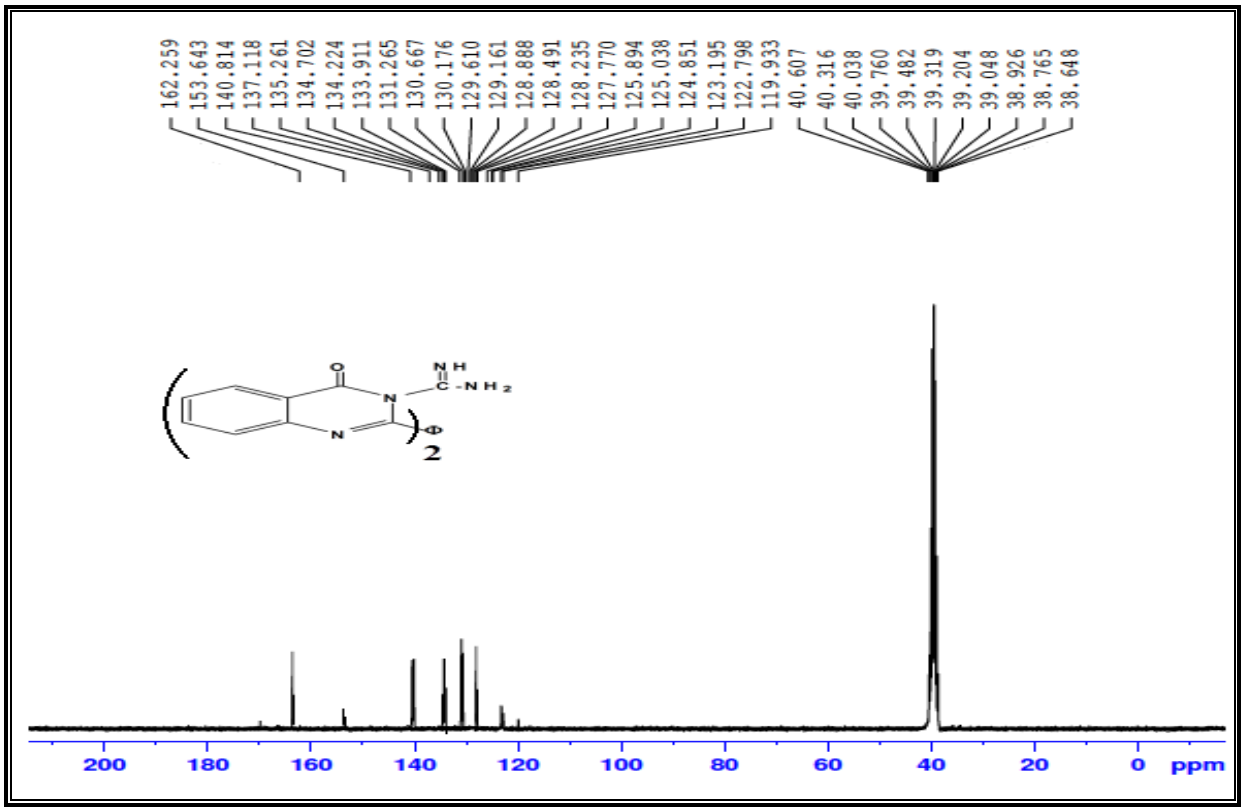


Fig (3-41). ^{13}C-NMR spectrum analysis of compound [Vj]

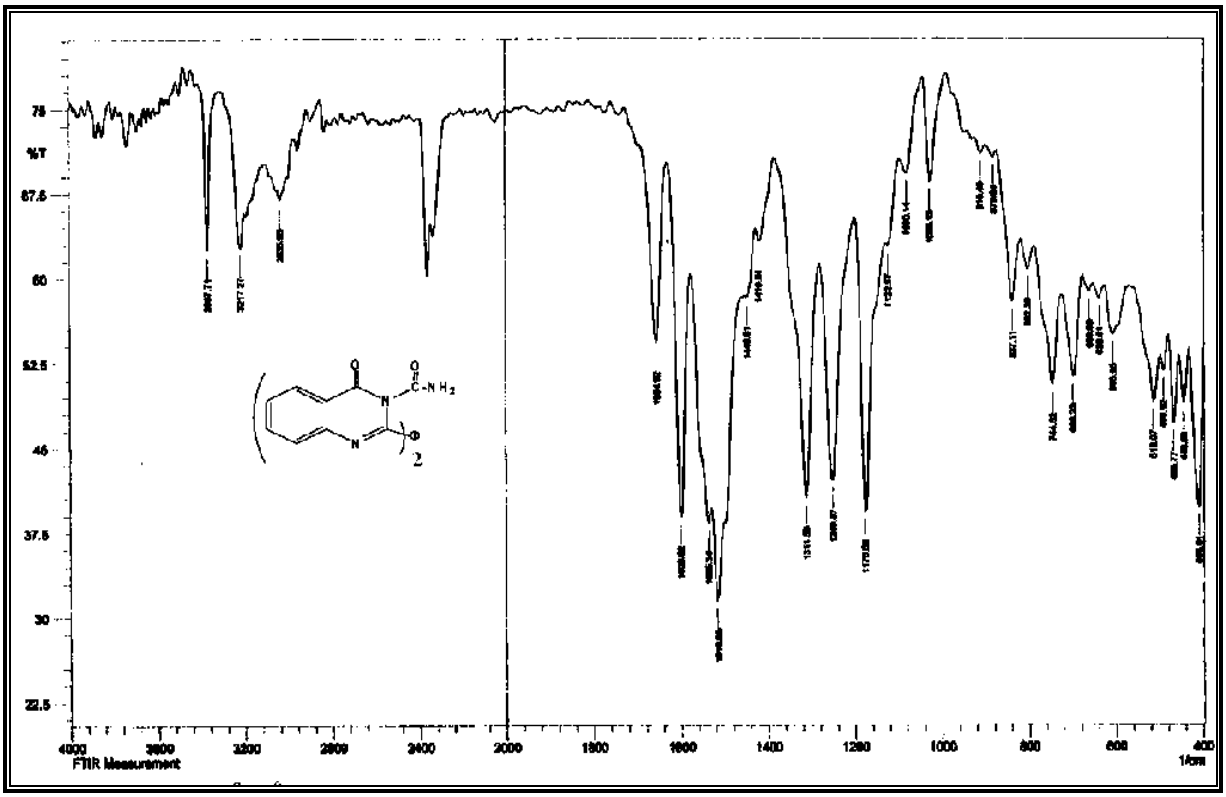


Fig (3-42). FT-IR spectrum analysis of compound [Vk]

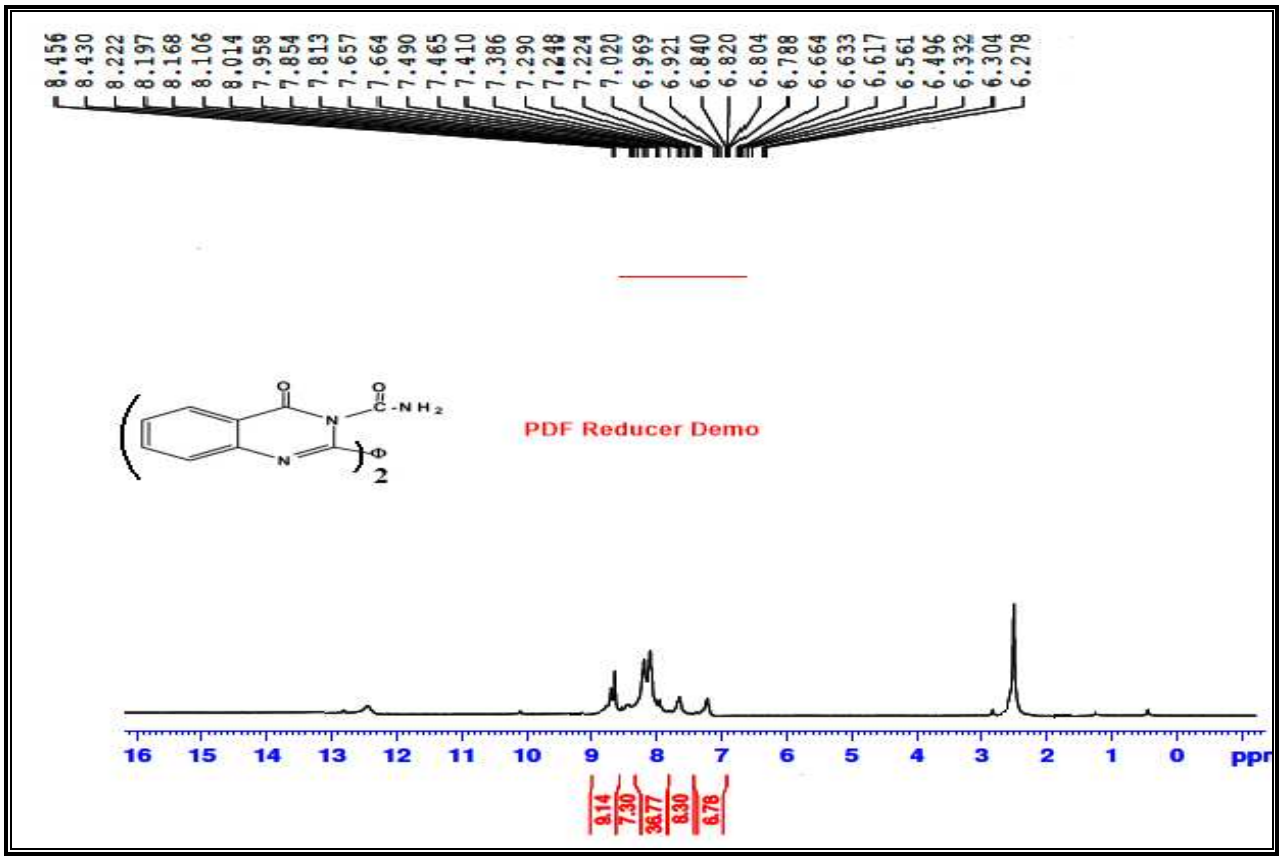


Fig (3-43). ^{1}H-NMR spectrum analysis of compound [Vk]

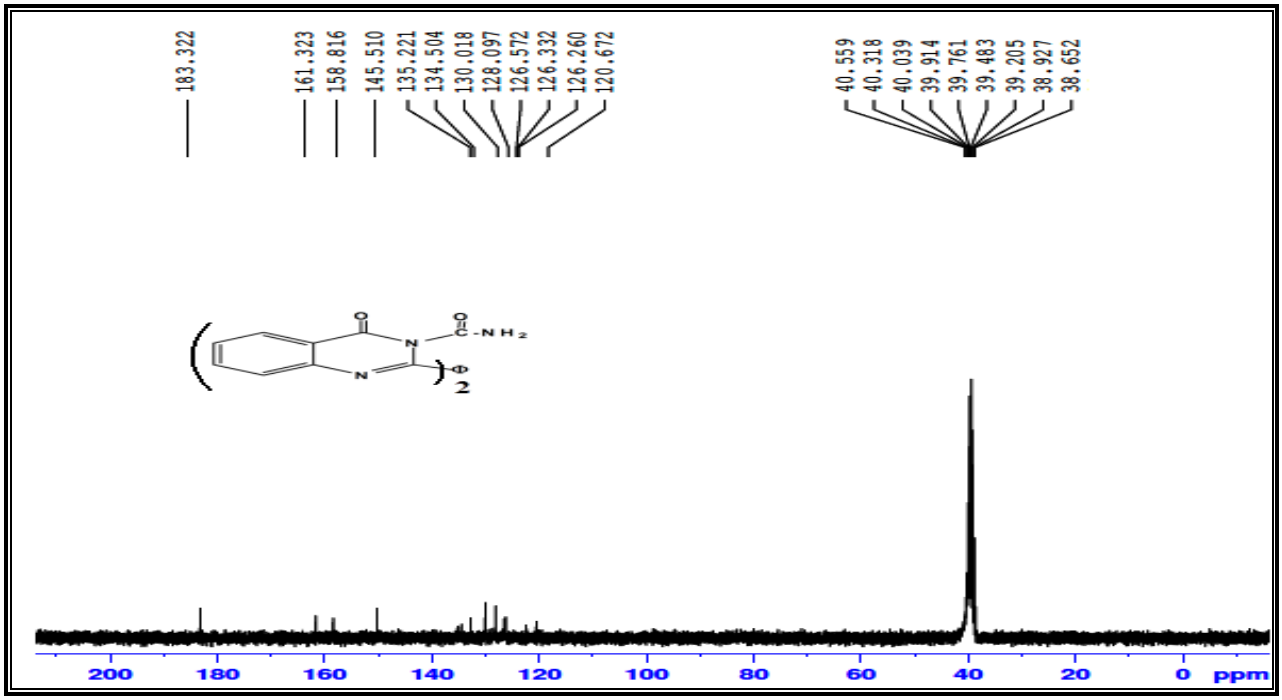


Fig (3-44). ^{13}C-NMR spectrum analysis of compound [Vk]

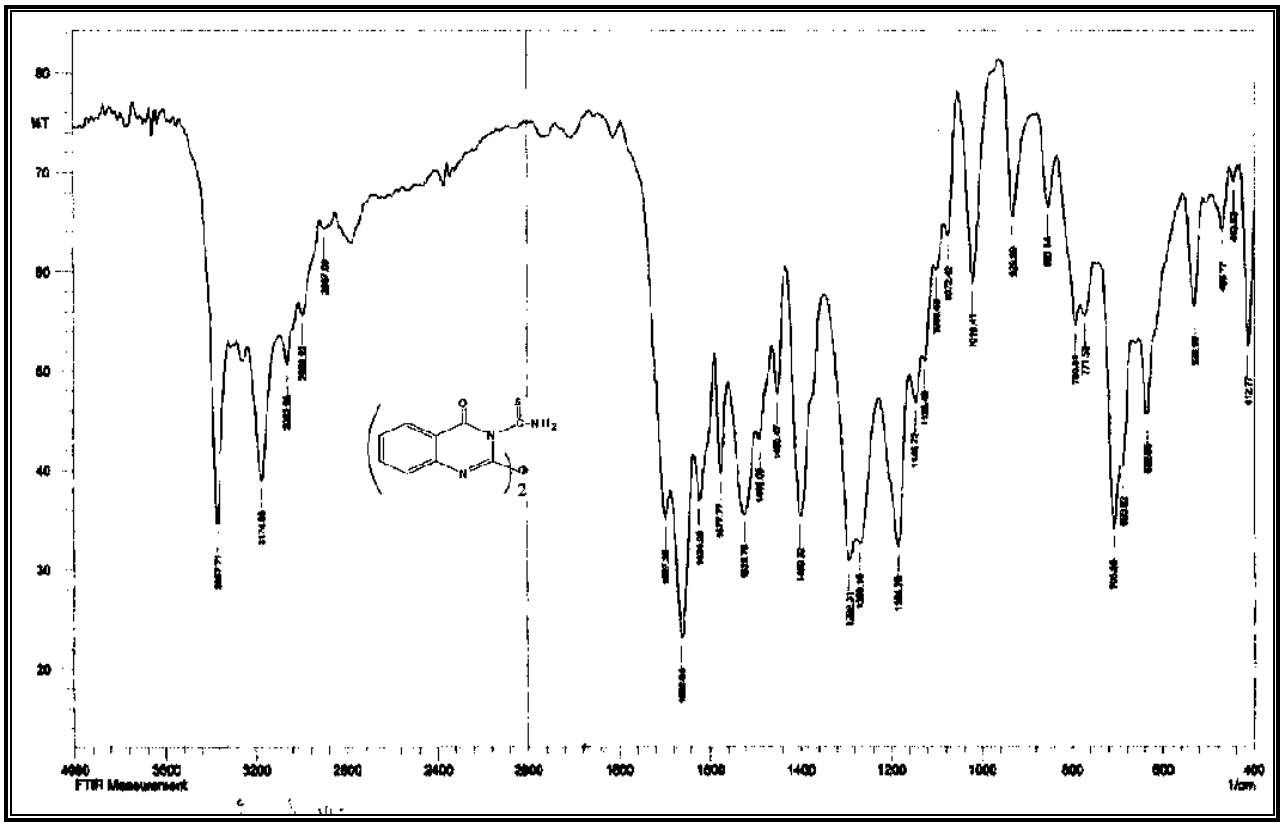


Fig (3-45). FT-IR spectrum analysis of compound [Vl]

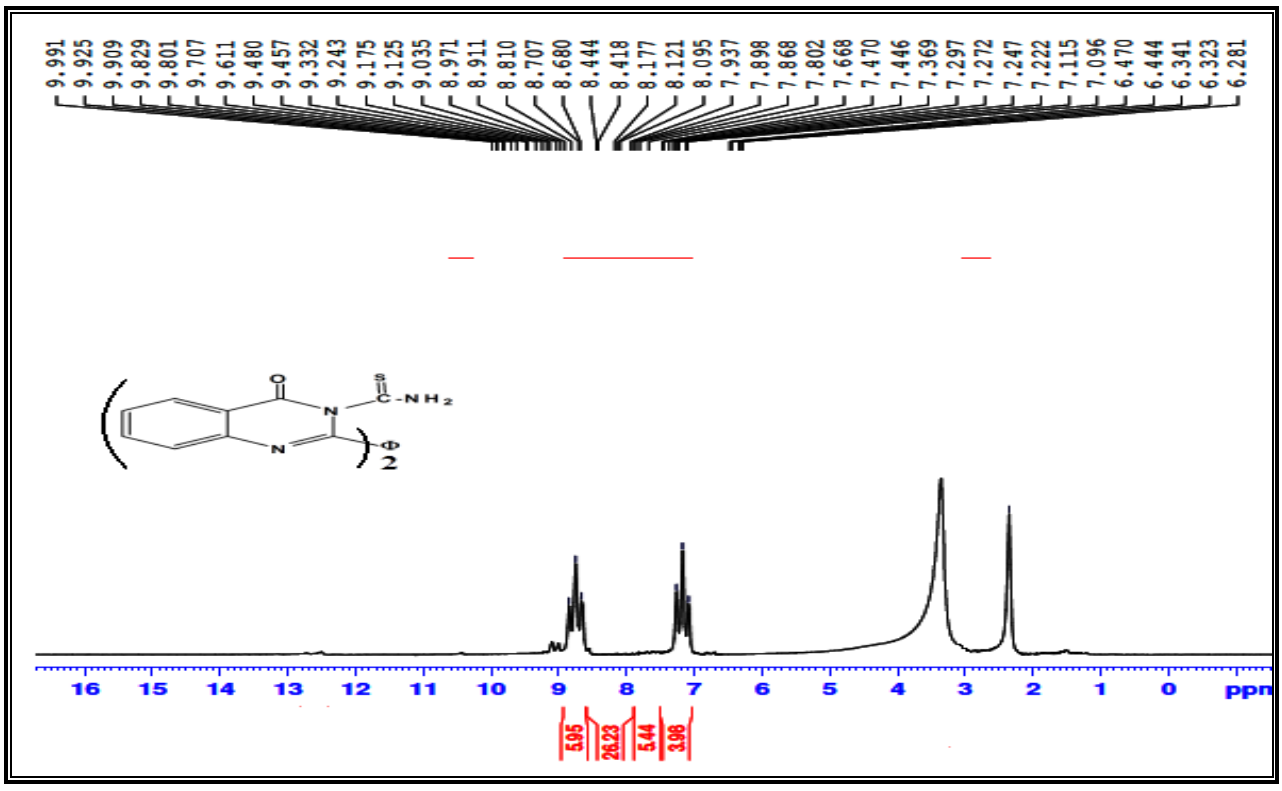


Fig (3-46). ^{1}H-NMR spectrum analysis of compound [Vl]

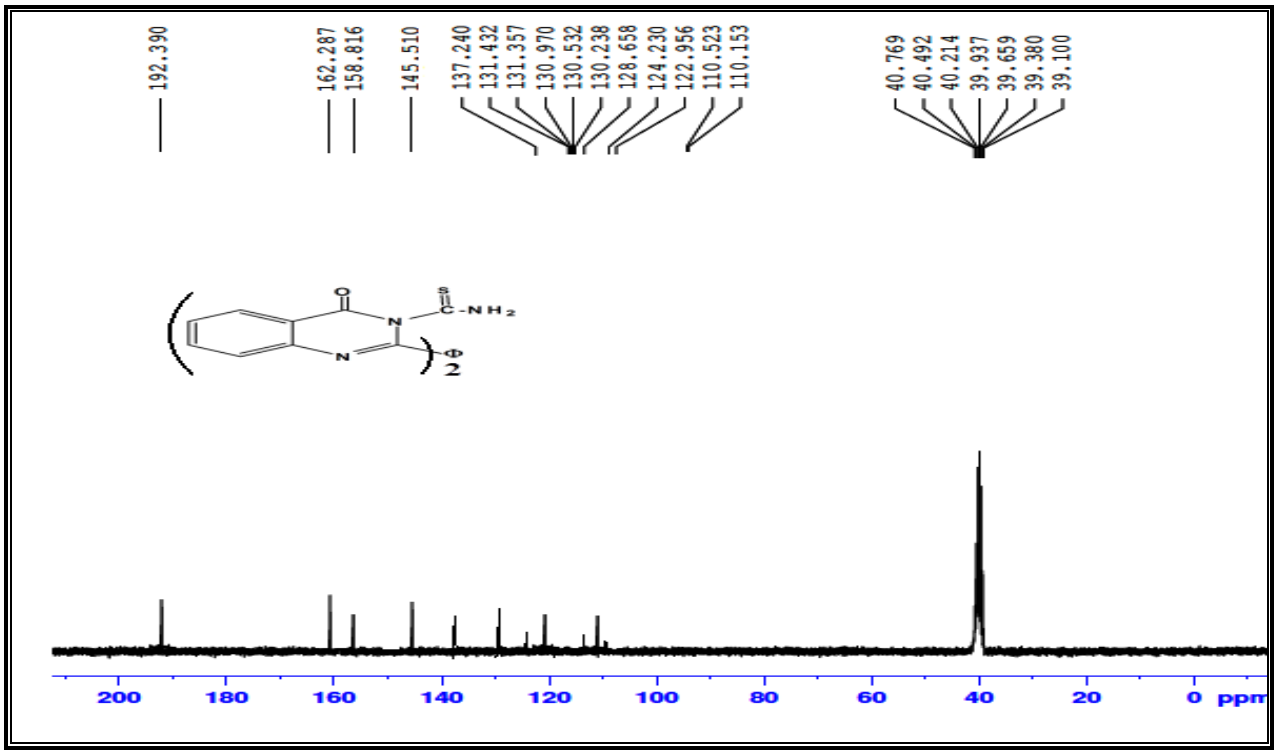


Fig (3-47). ^{13}C-NMR spectrum analysis of compound [Vl]

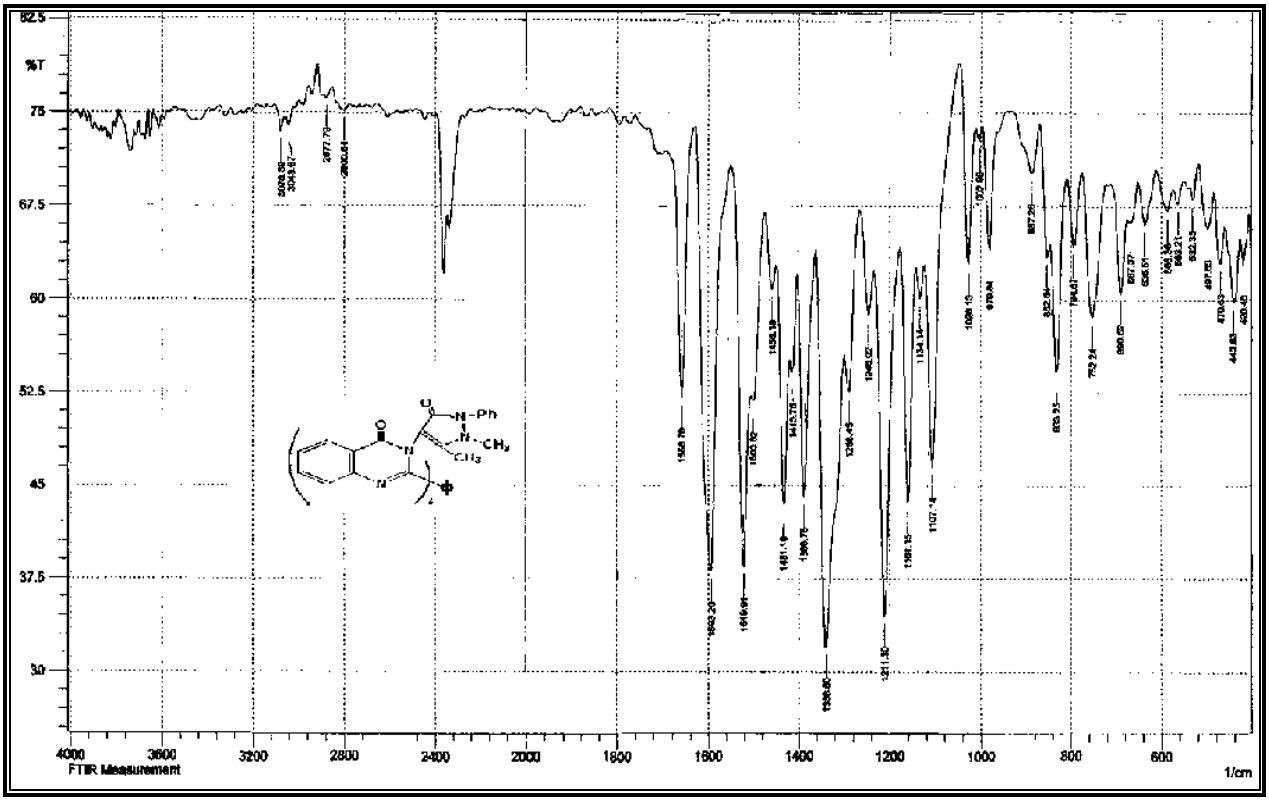


Fig (3-48). FT-IR spectrum analysis of compound [Vm]

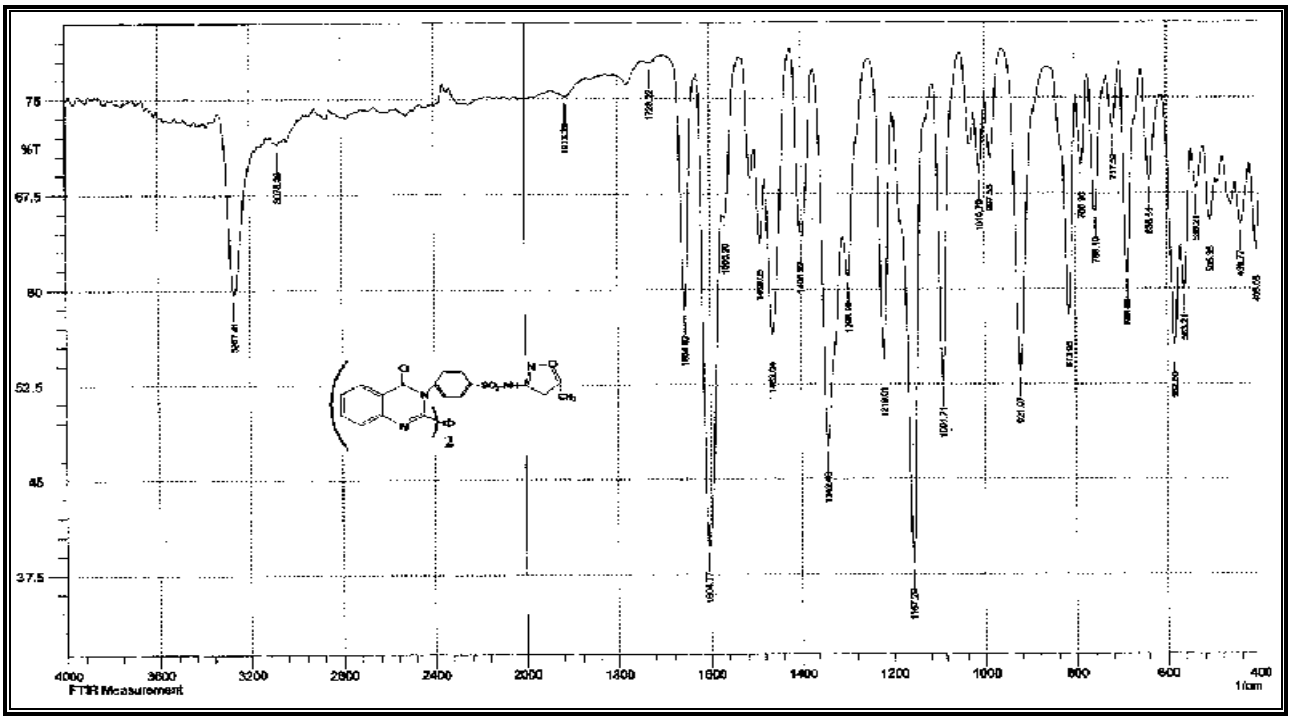


Fig (3-49). FT-IR spectrum analysis of compound [Vn]

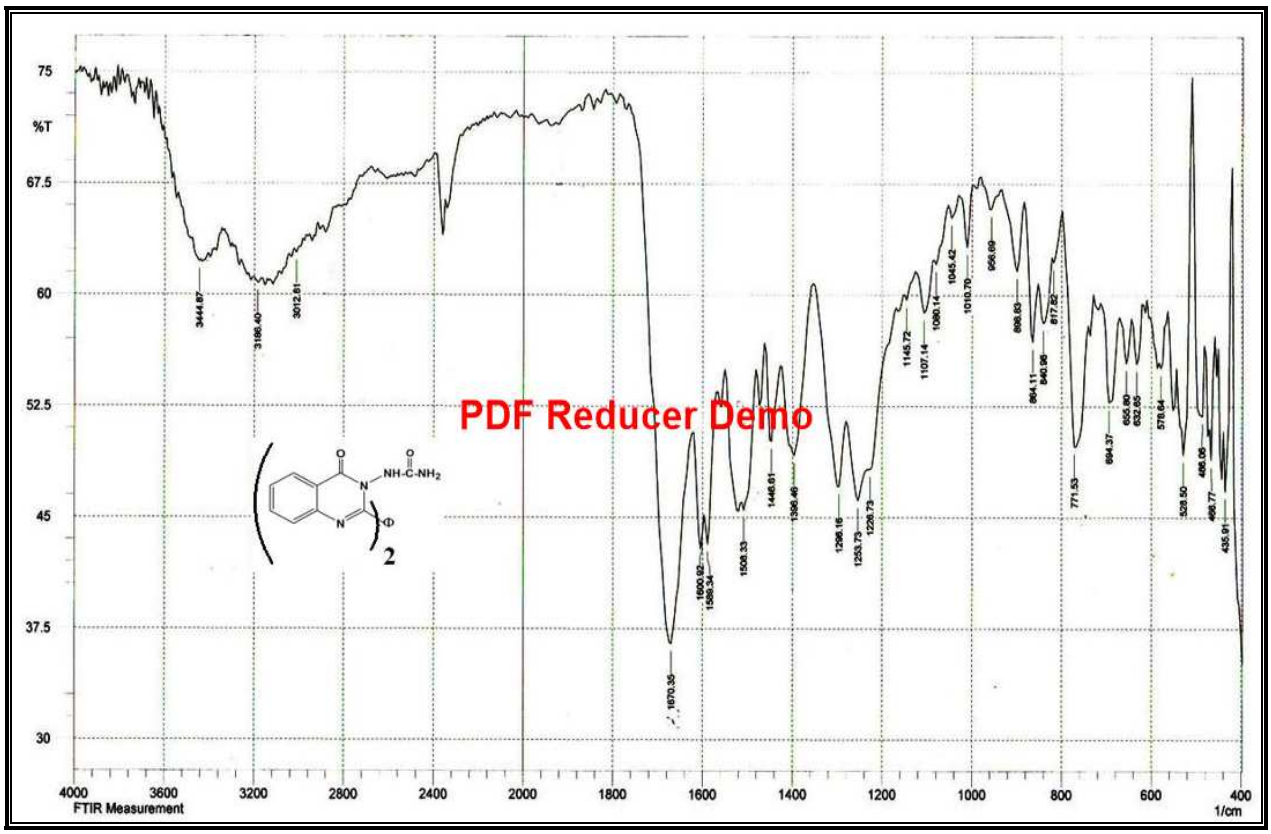


Fig (3-50). FT-IR spectrum analysis of compound [Vo]

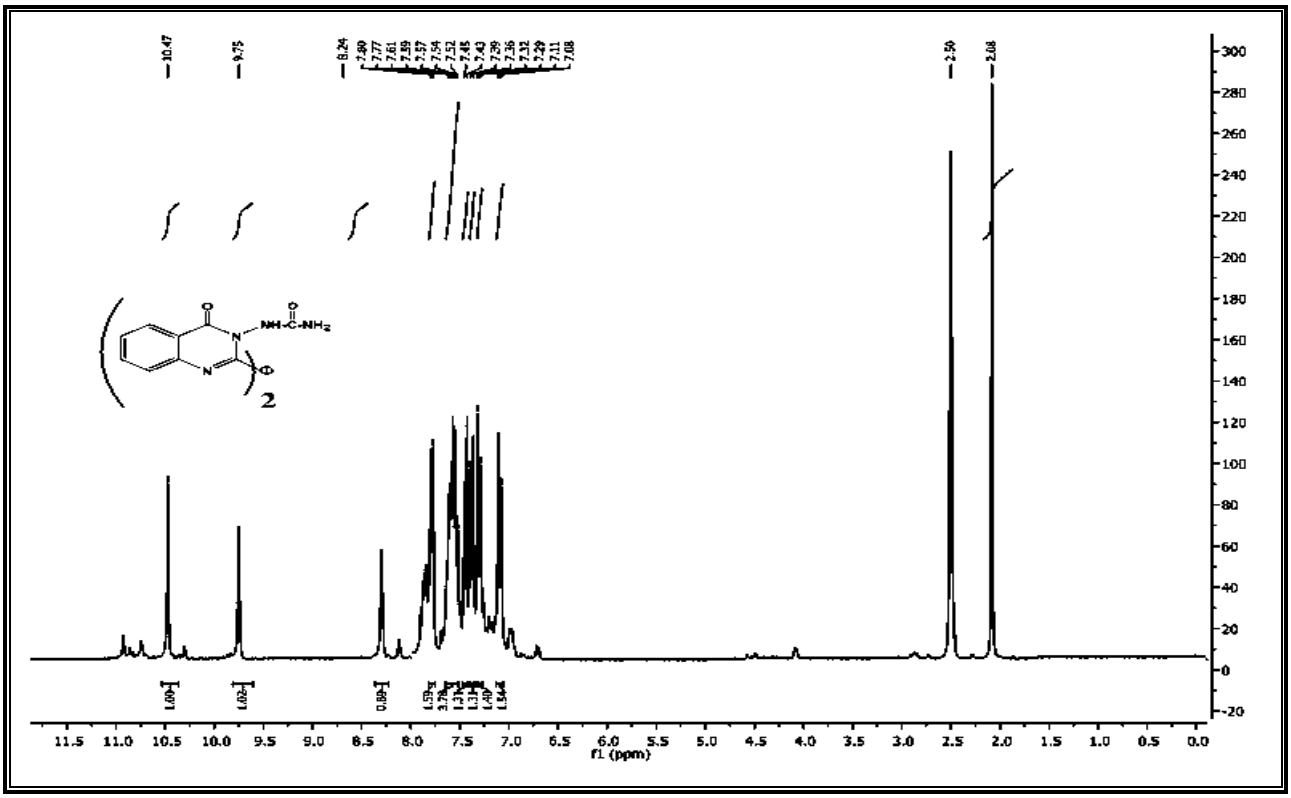


Fig (3-51). ^{1}H-NMR spectrum analysis of compound [Vo]

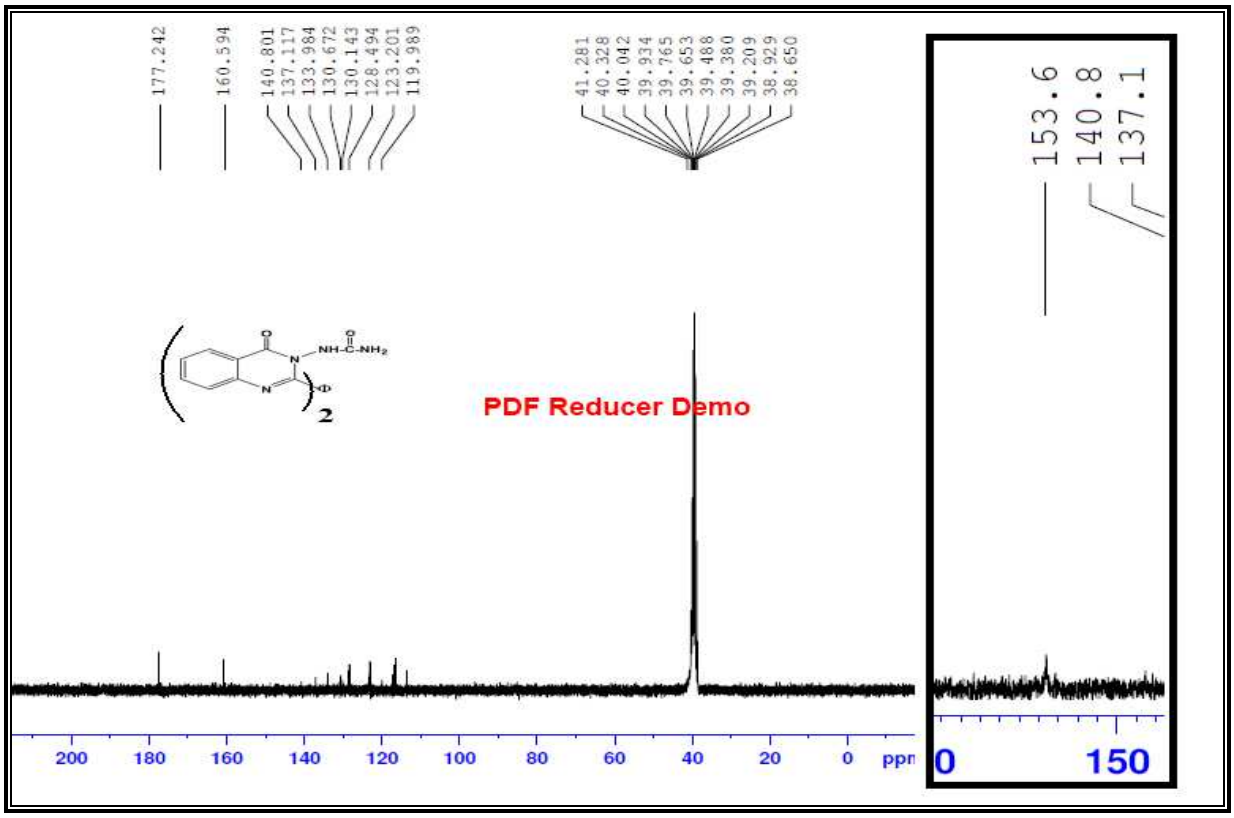


Fig (3-52). ^{13}C-NMR spectrum analysis of compound [Vo]

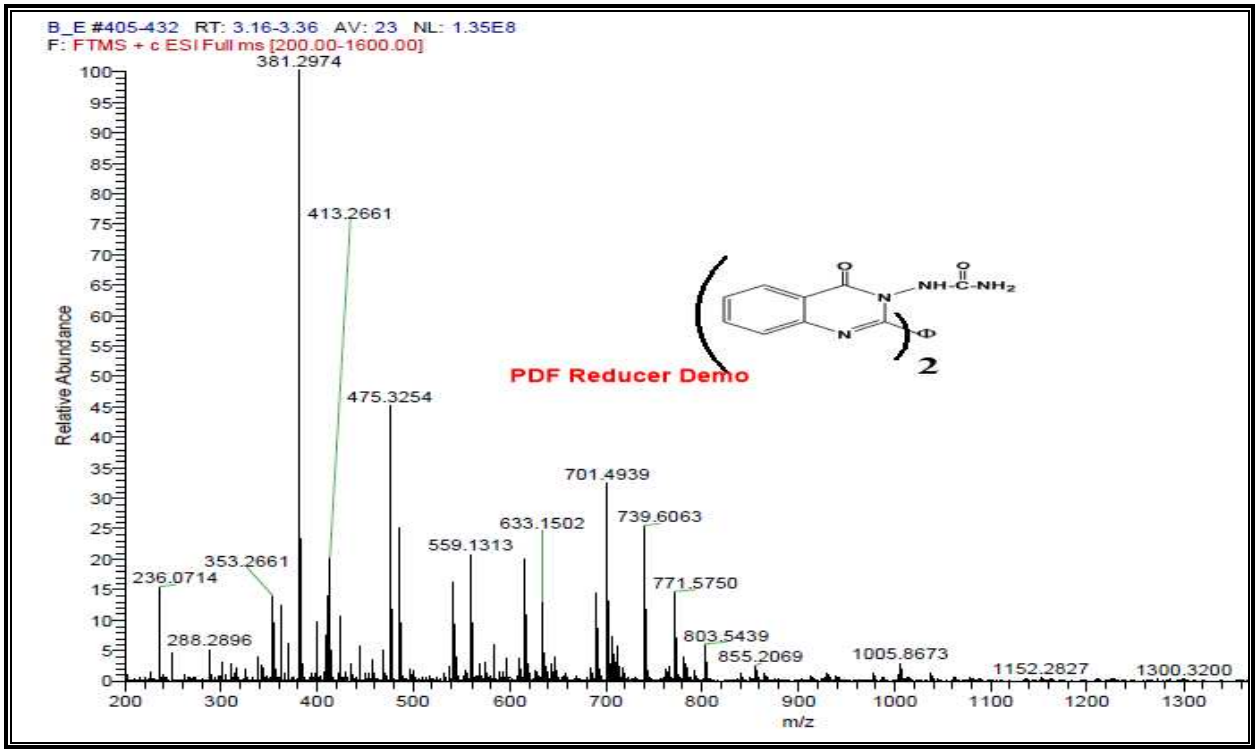


Fig (3-53). Mass spectrum analysis of compound [Vo]

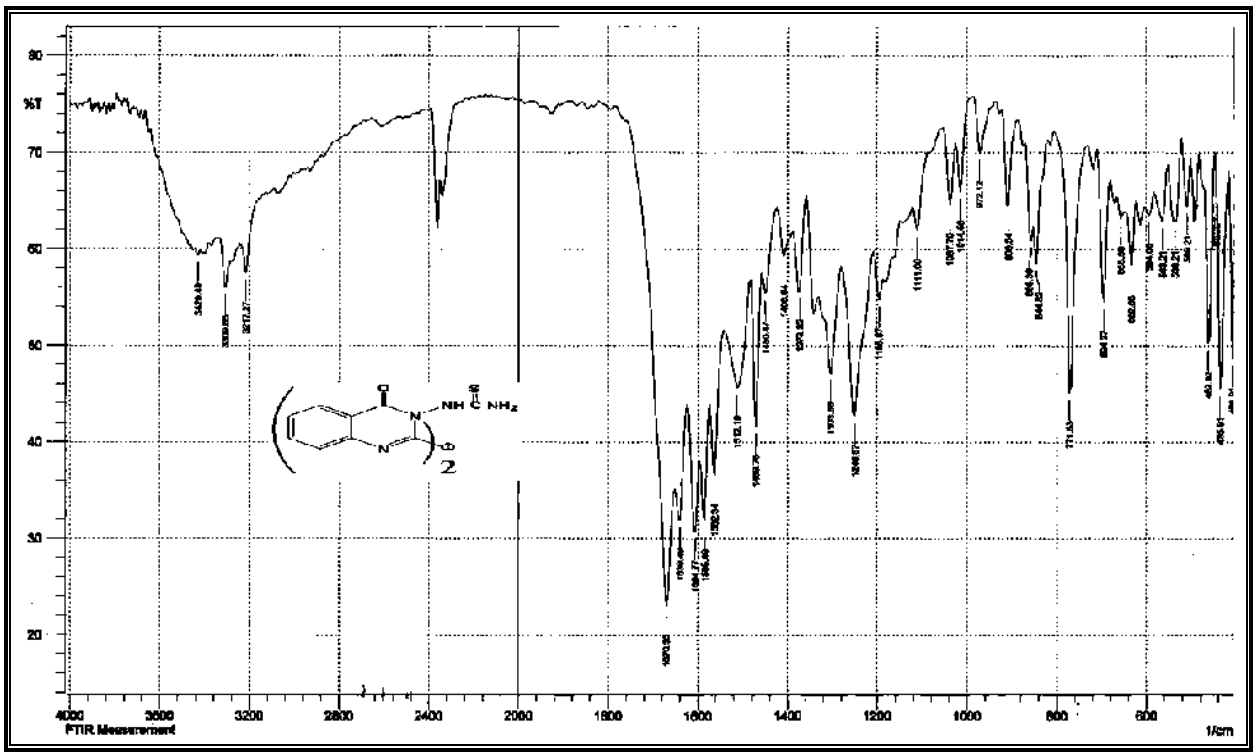


Fig (3-54). FT-IR spectrum analysis of compound [Vp]

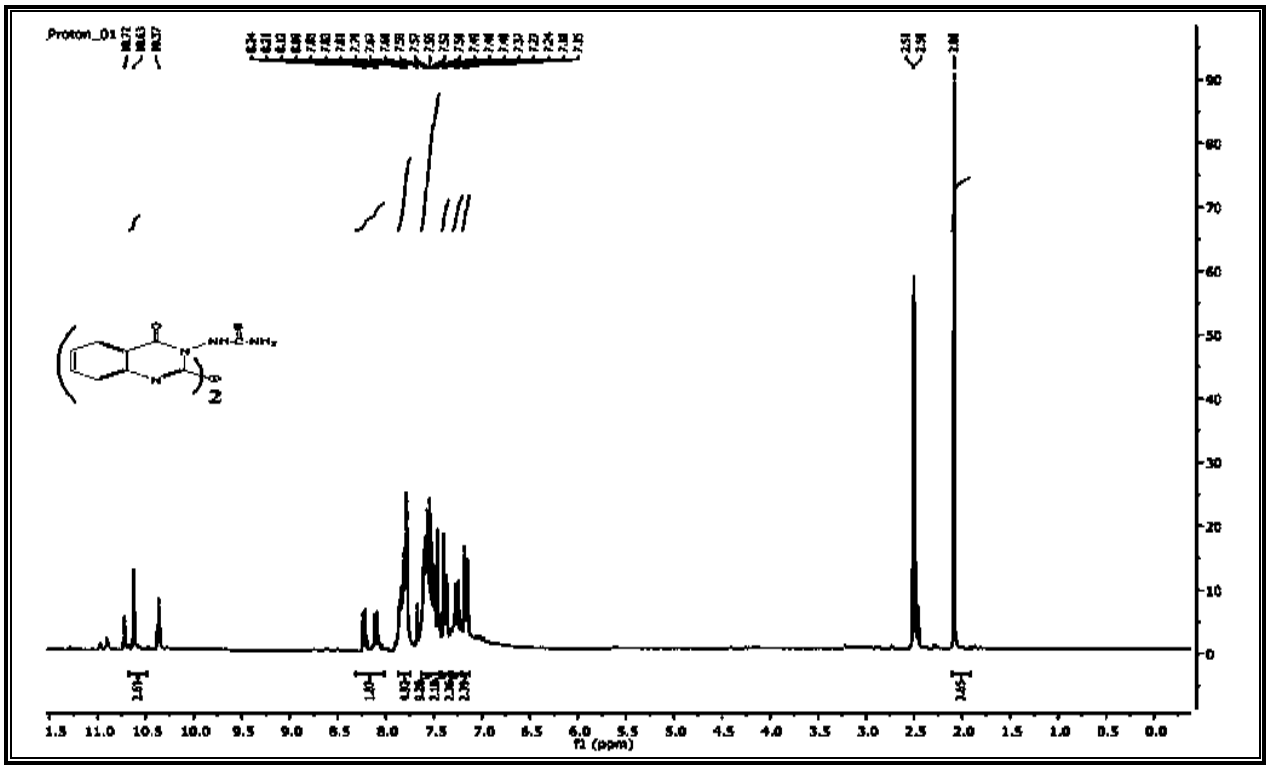


Fig (3-55). ^{1}H-NMR spectrum analysis of compound [Vp]

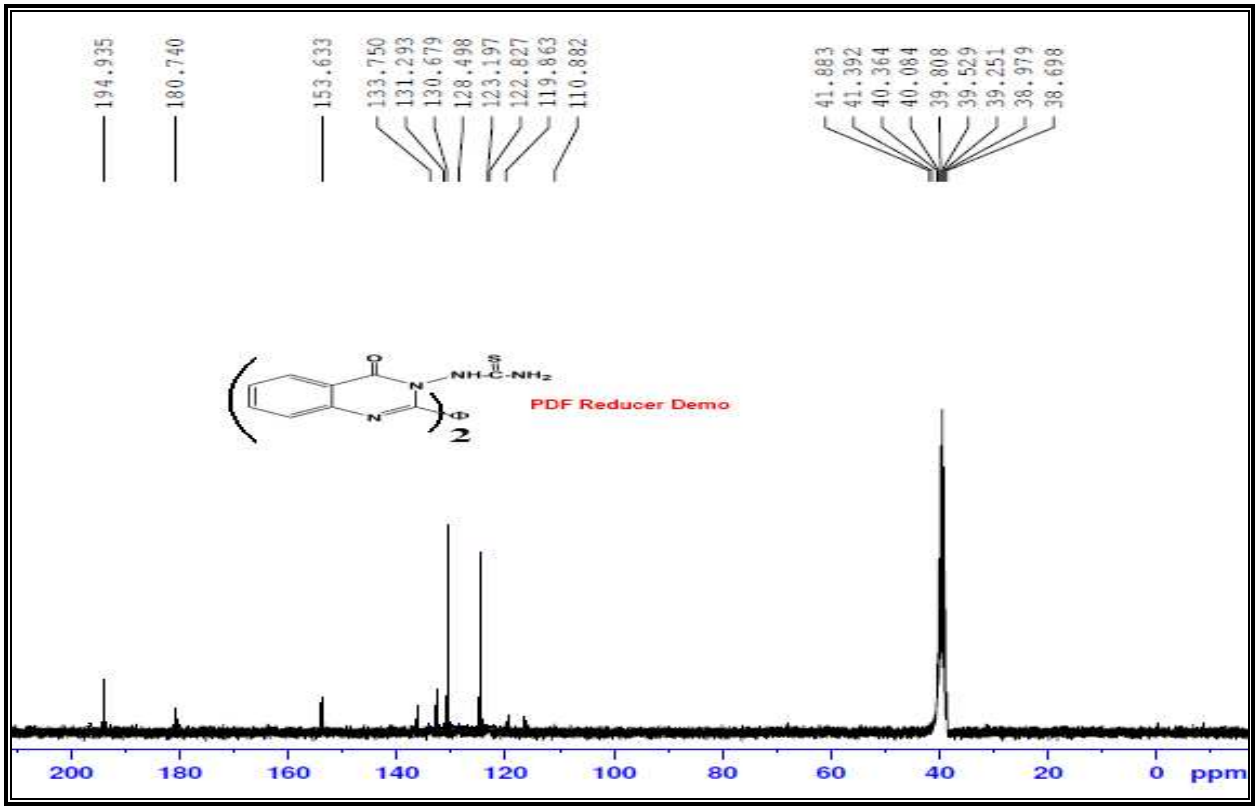


Fig (3-56). ^{13}C-NMR spectrum analysis of compound [Vp]

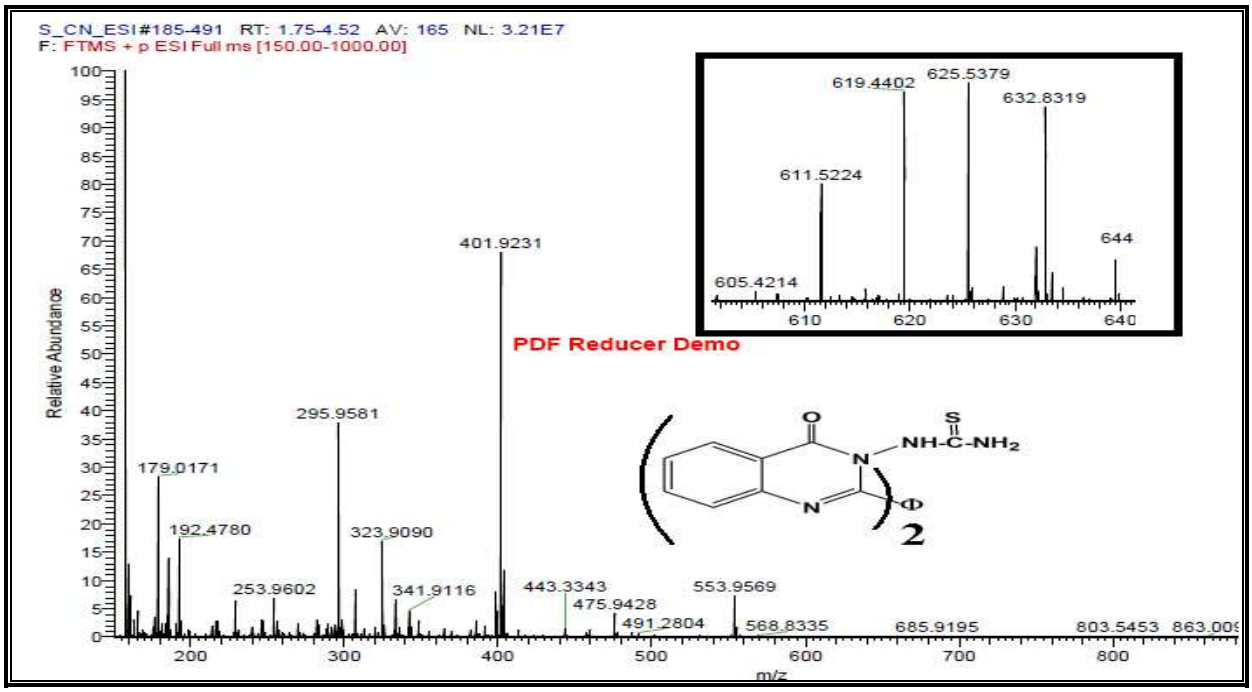


Fig (3-57). Mass spectrum analysis of compound [Vp]

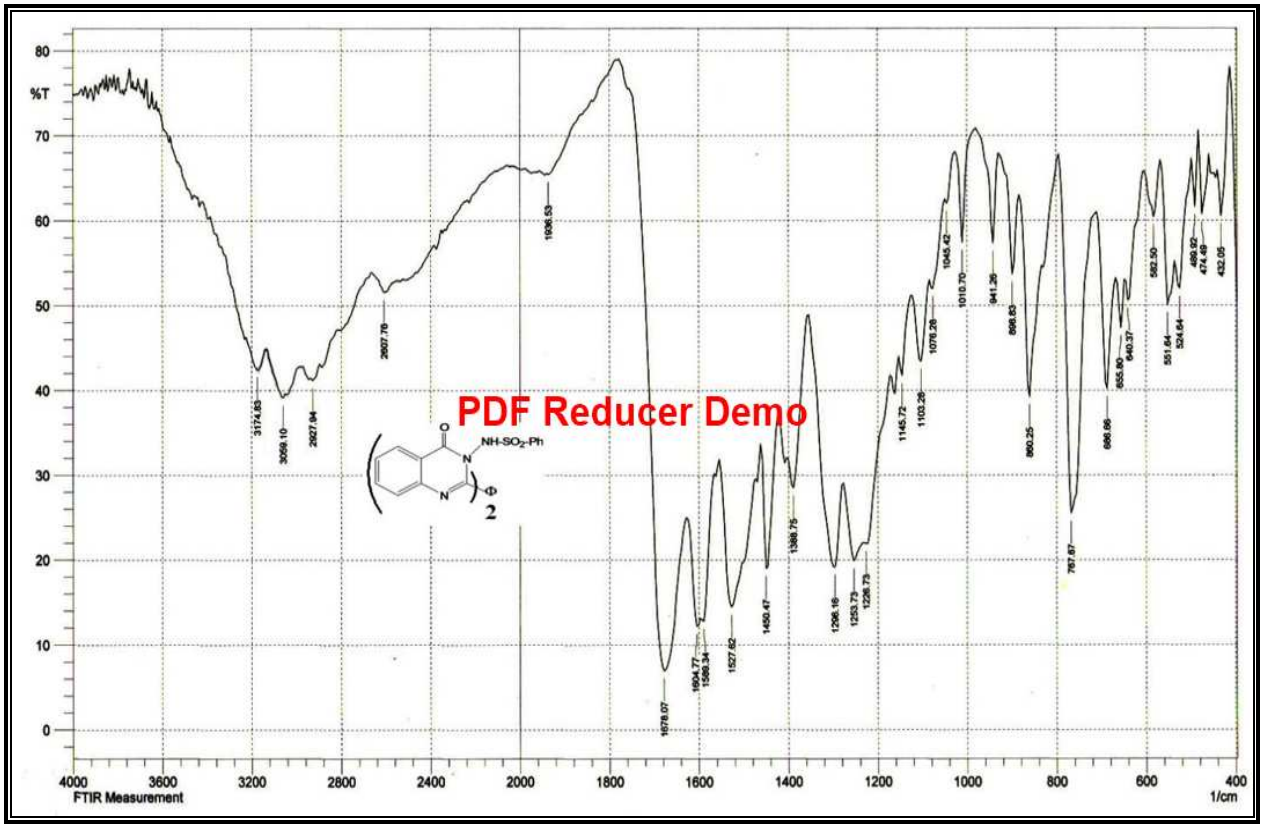


Fig (3-58). FT-IR spectrum analysis of compound [VIA]

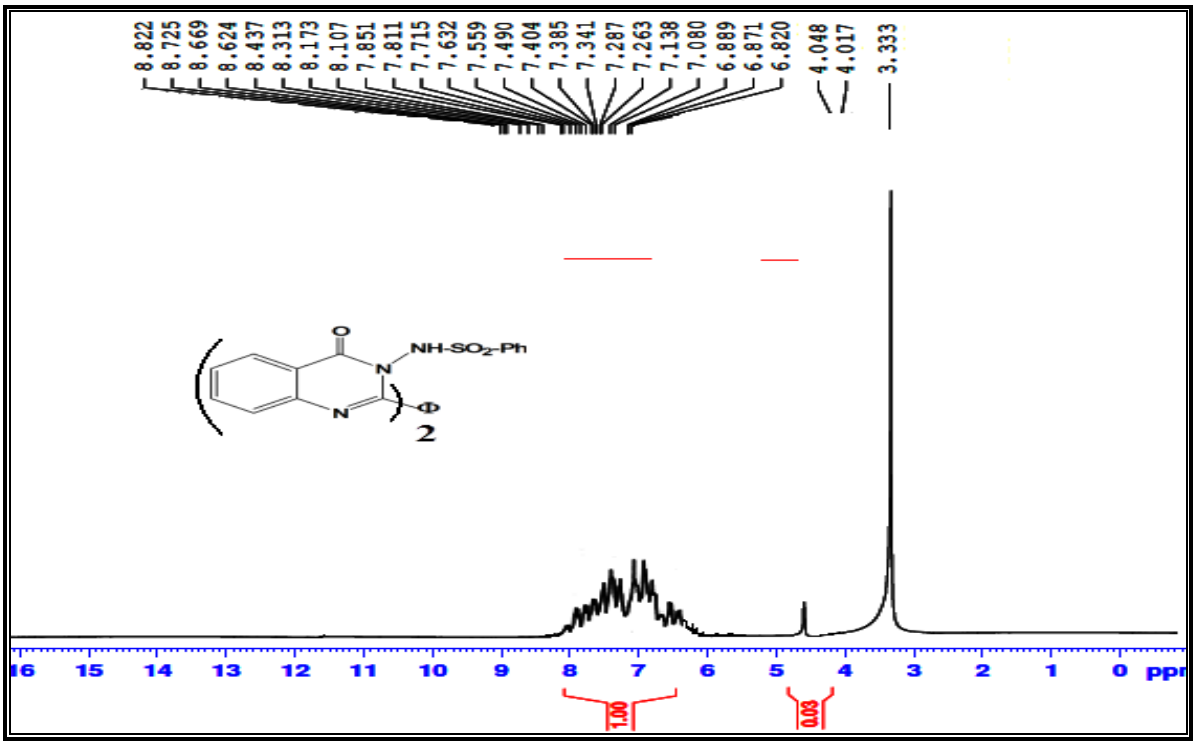


Fig (3-59). ^{1}H-NMR spectrum analysis of compound [VIA]

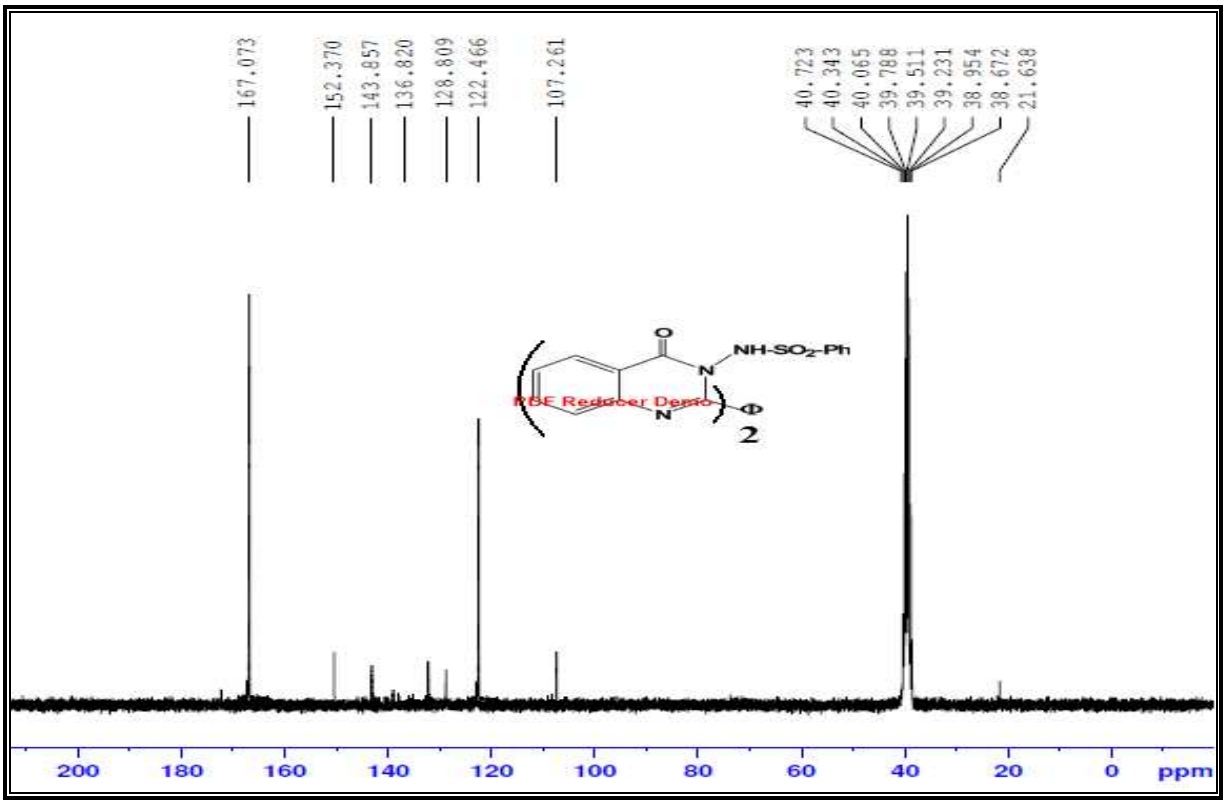


Fig (3-60). ^{13}C-NMR spectrum analysis of compound [VIA]

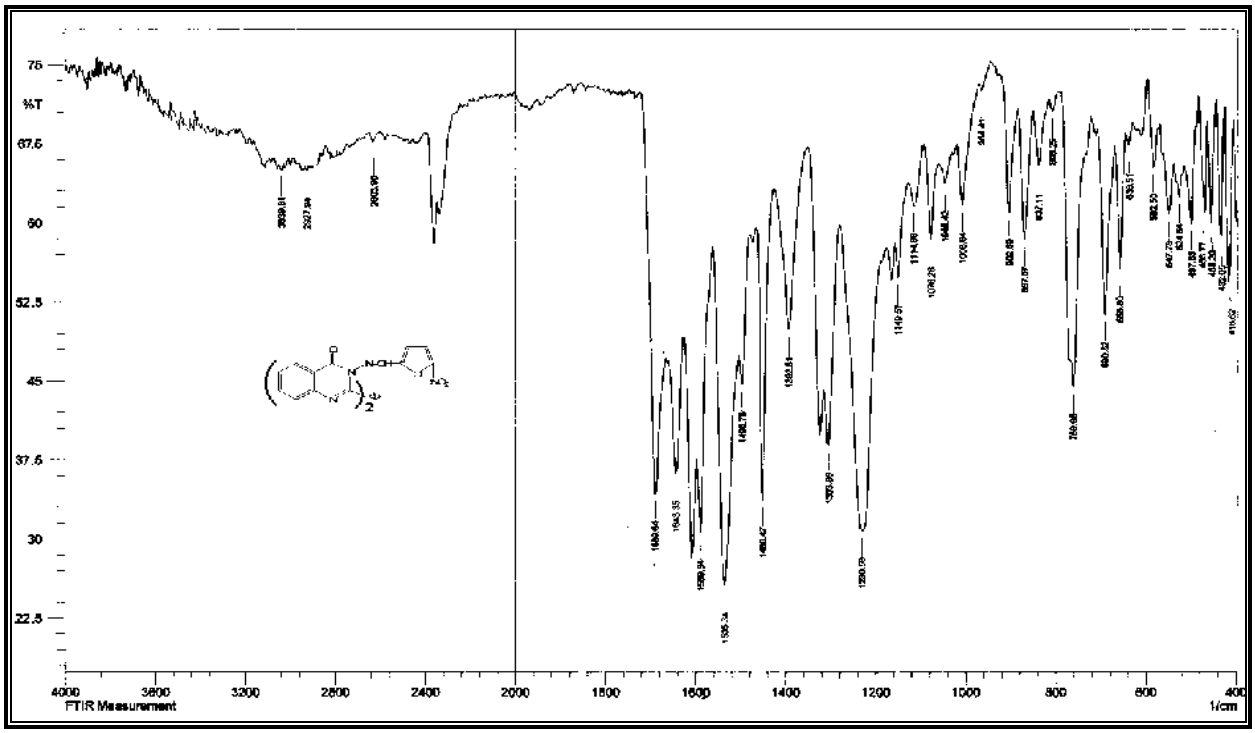


Fig (3-61). FT-IR spectrum analysis of compound [VIB]

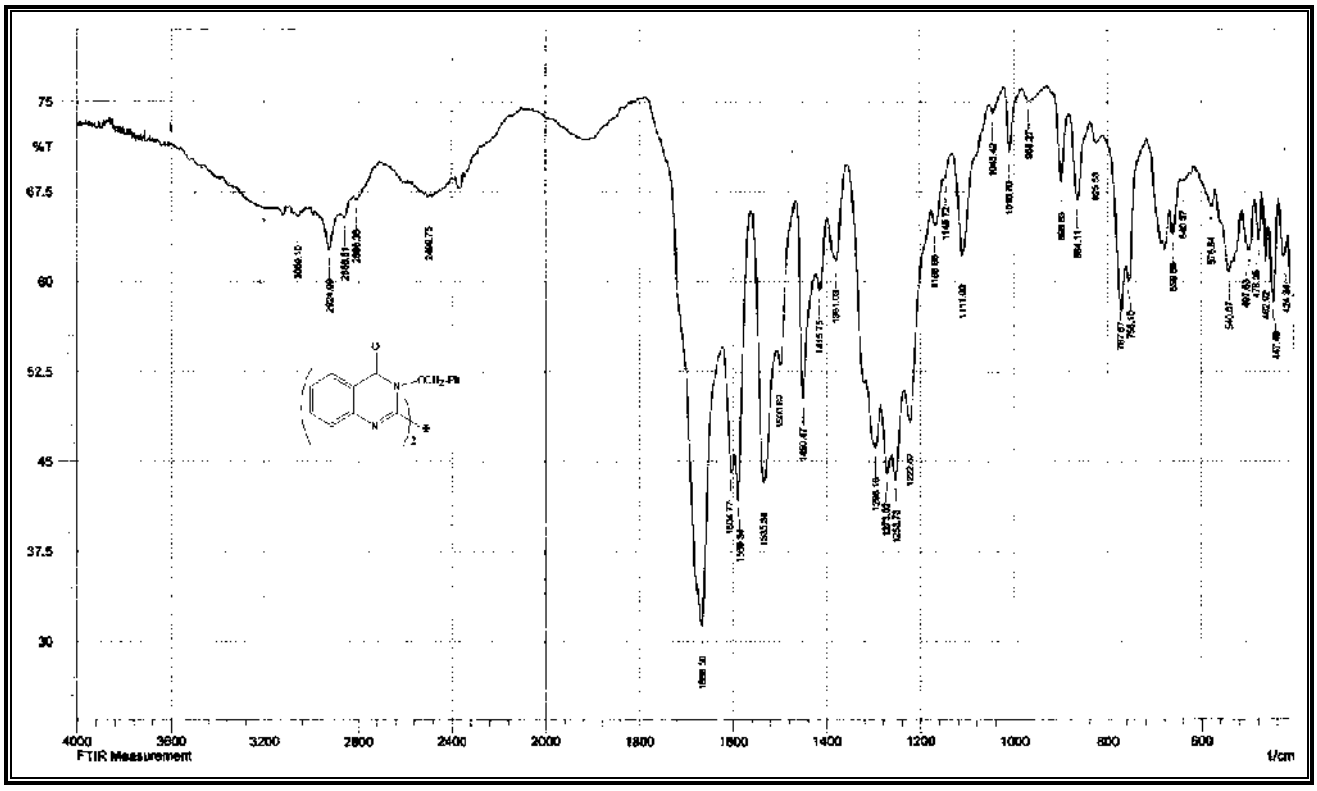


Fig (3-62). FT-IR spectrum analysis of compound [VIIA]

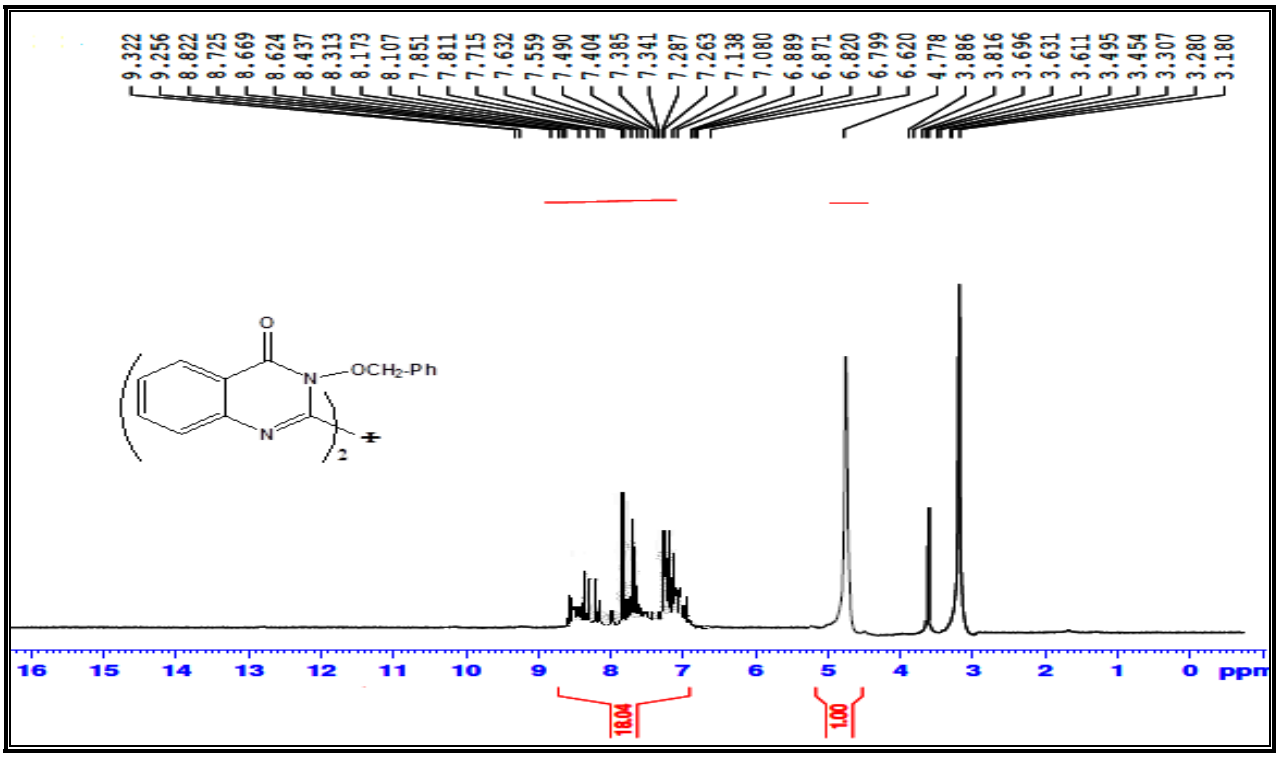


Fig (3-63). ^{1}H-NMR spectrum analysis of compound [VIIA]

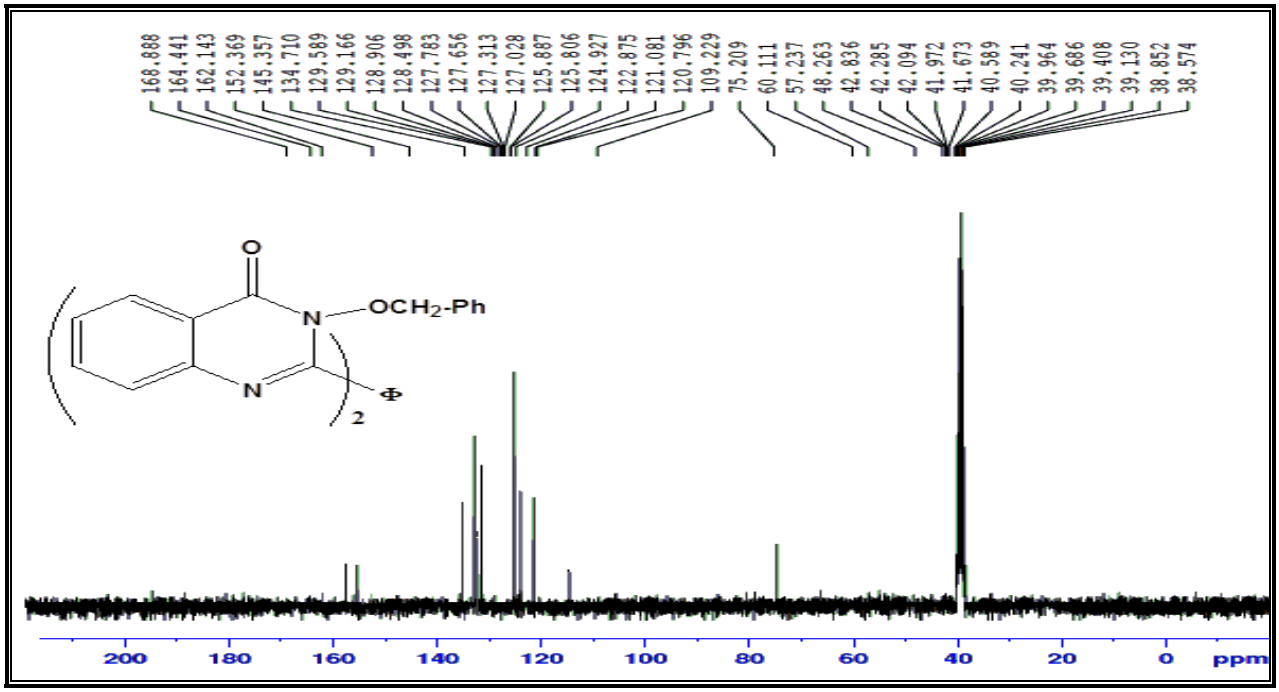


Fig (3-64). ^{13}C-NMR spectrum analysis of compound [VIIA]

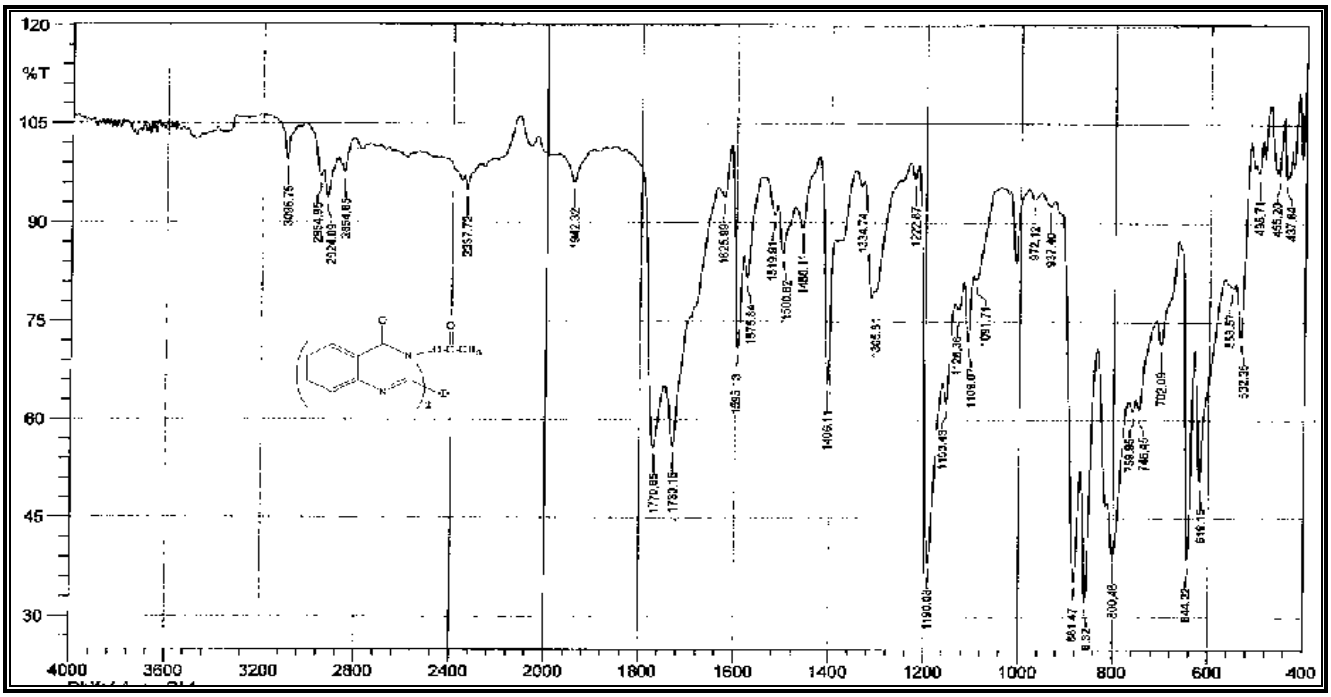


Fig (3-65). FT-IR spectrum analysis of compound [VIIB]

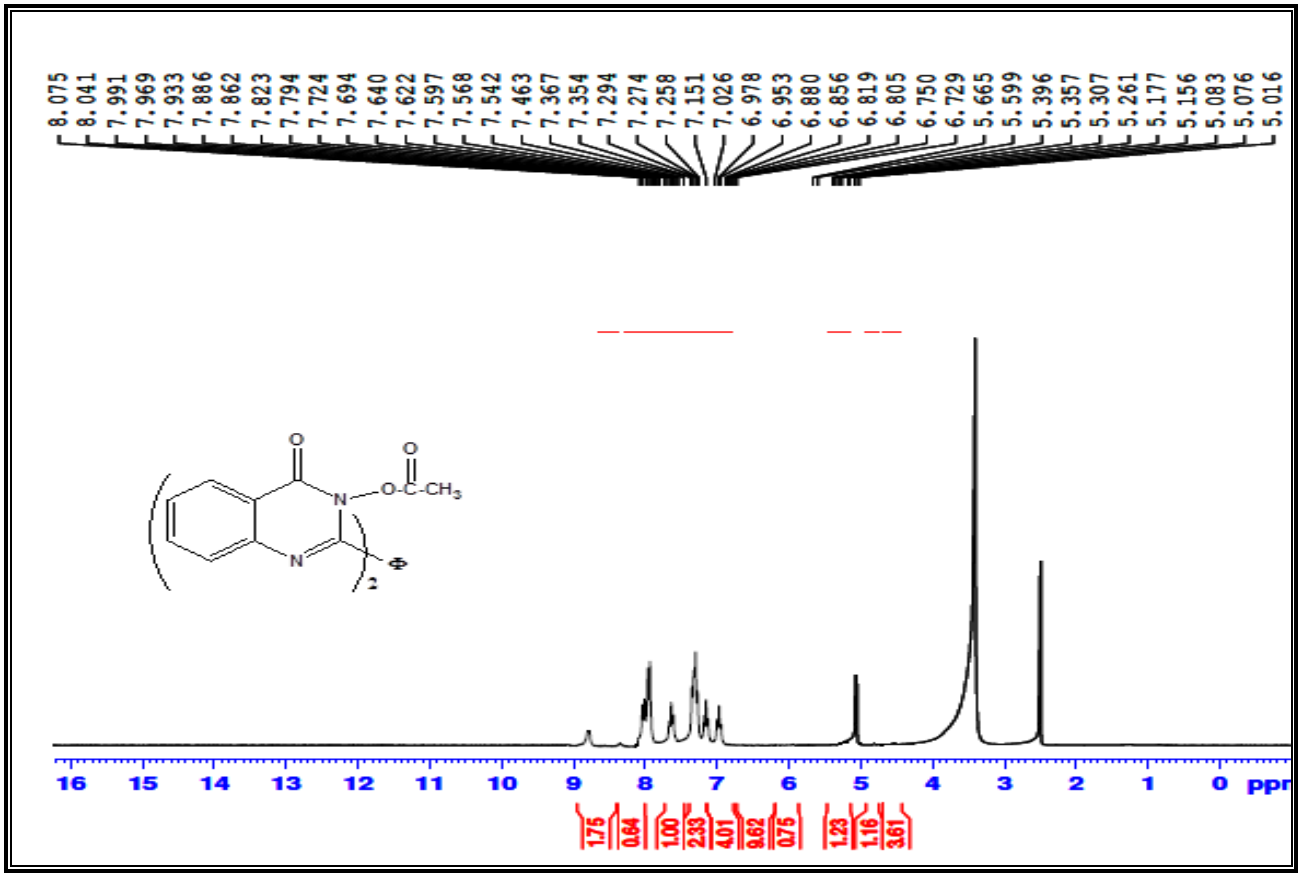


Fig (3-66). ^{1}H-NMR spectrum analysis of compound [VIIB]

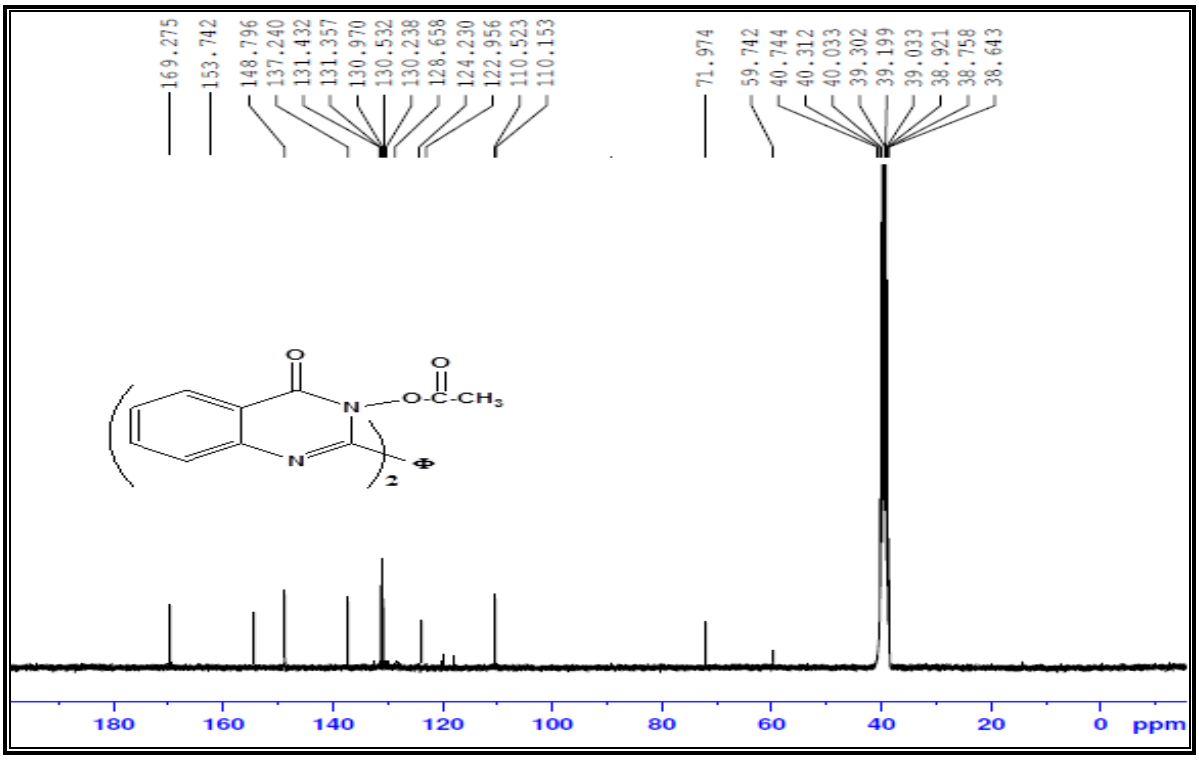


Fig (3-67). ^{13}C-NMR spectrum analysis of compound [VIIB]

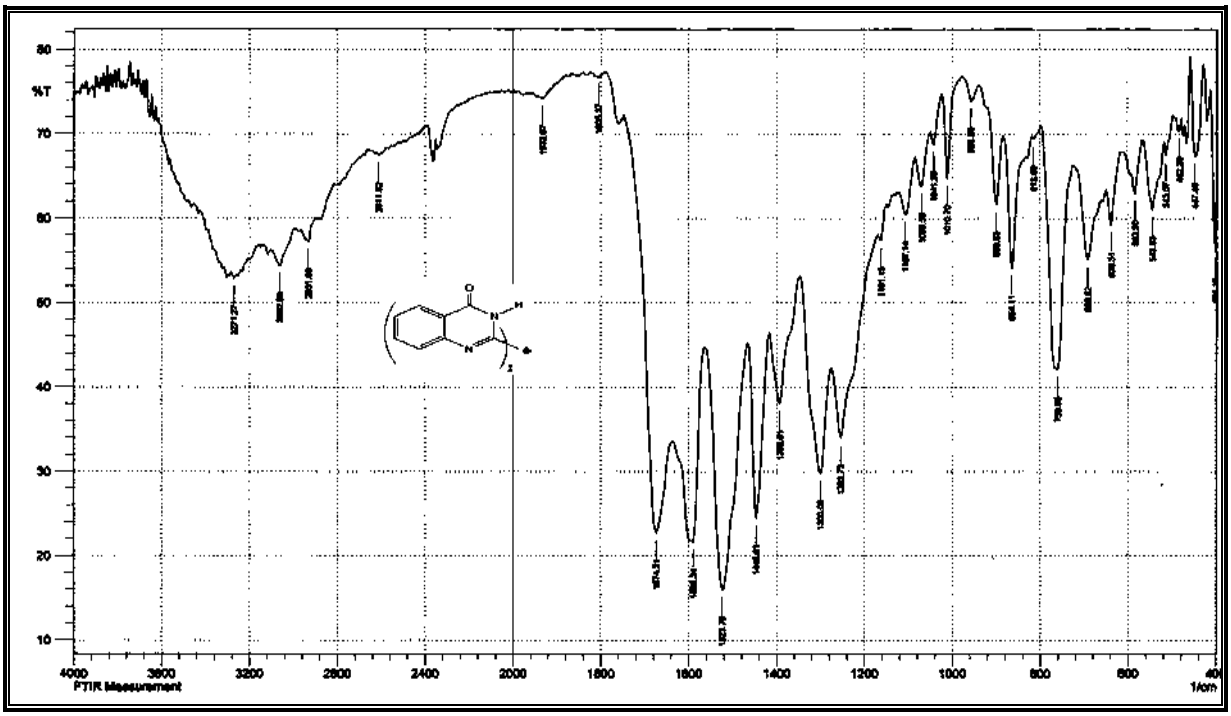


Fig (3-68). FT-IR spectrum analysis of compound [VIII]

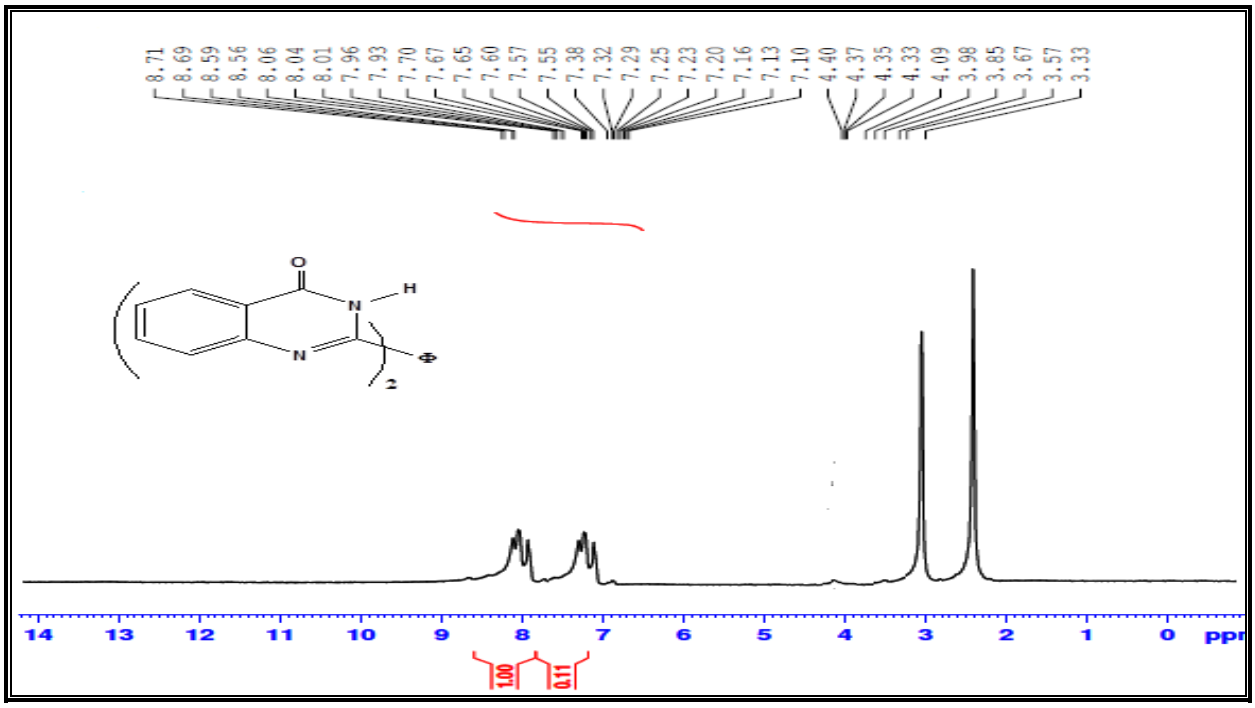


Fig (3-69). ^{1}H-NMR spectrum analysis of compound [VIII]

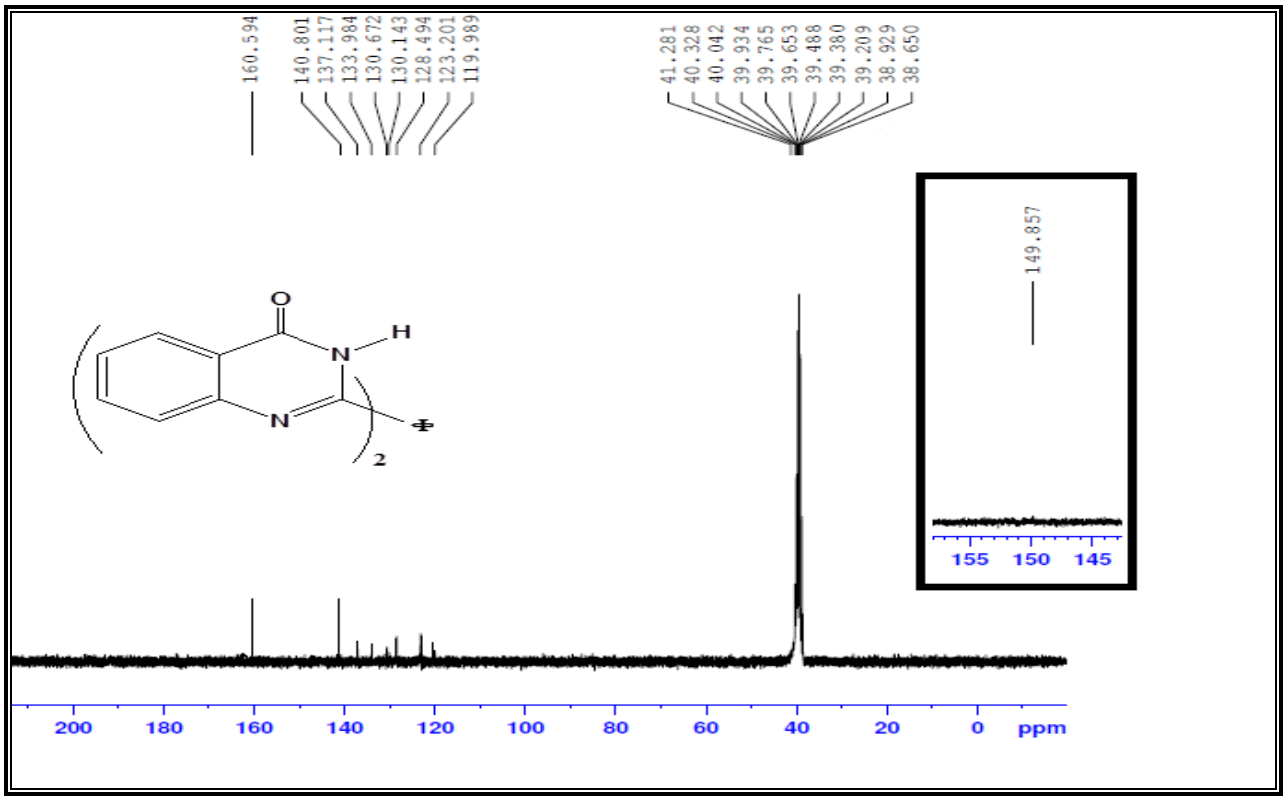


Fig (3-70). ^{13}C-NMR spectrum analysis of compound [VIII]

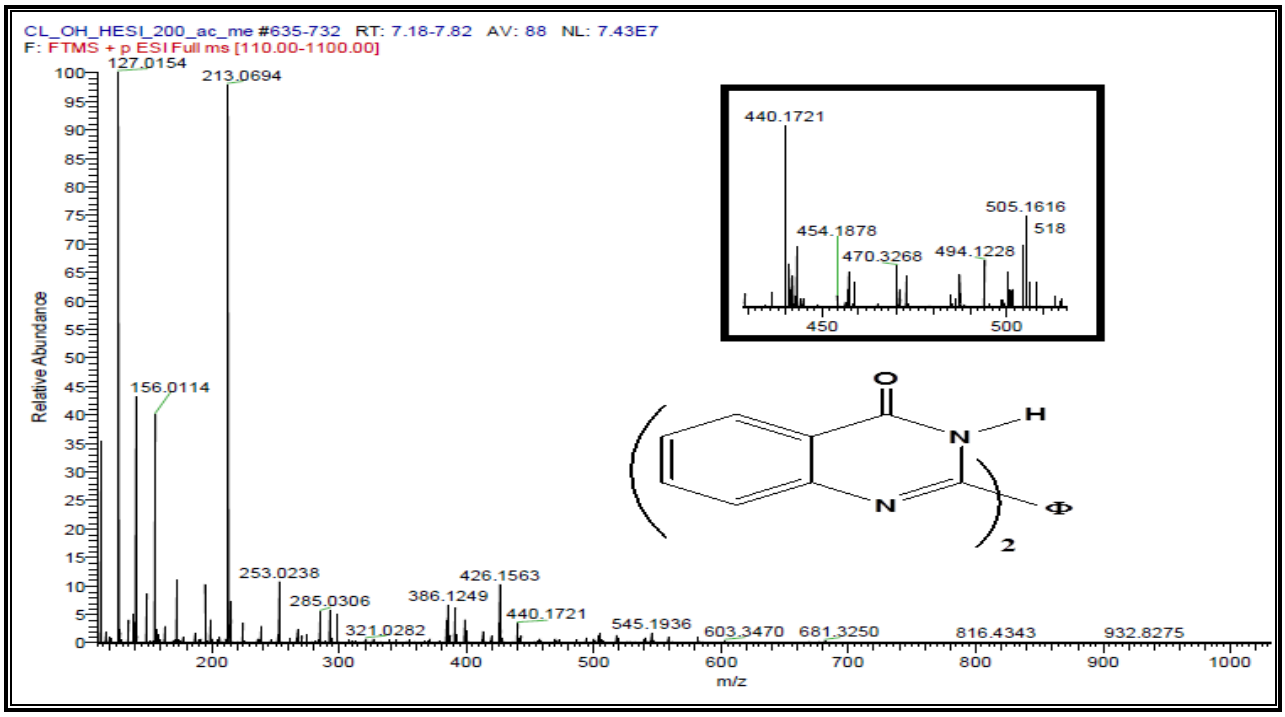


Fig (3-71). Mass spectrum analysis of compound [VIII]

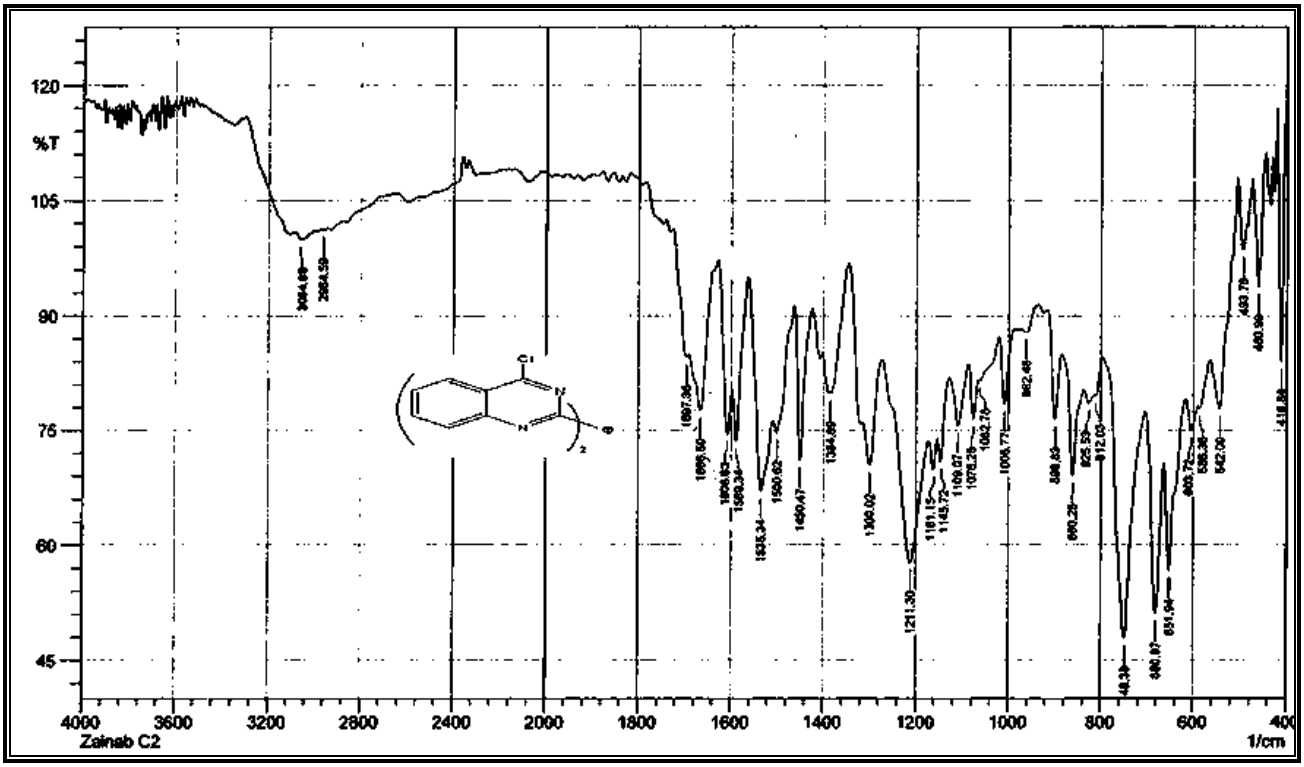


Fig (3-72). FT-IR spectrum analysis of compound [IX]

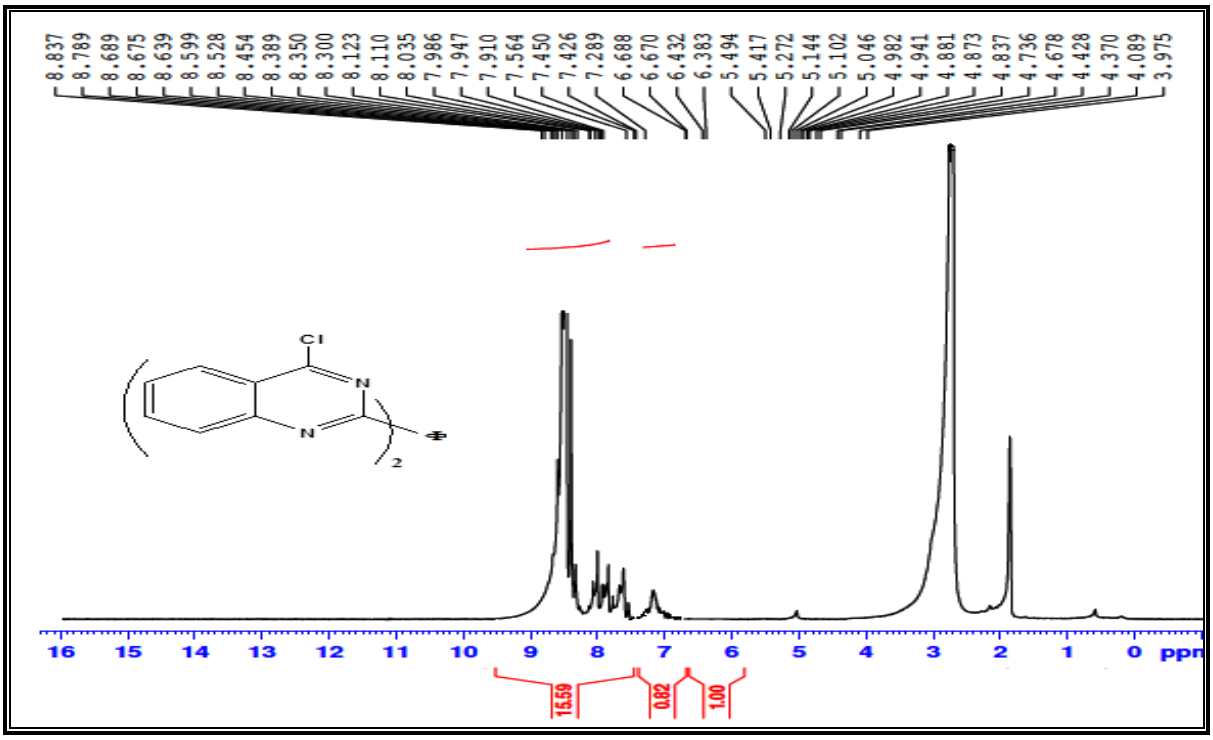


Fig (3-73). ^{1}H-NMR spectrum analysis of compound [IX]

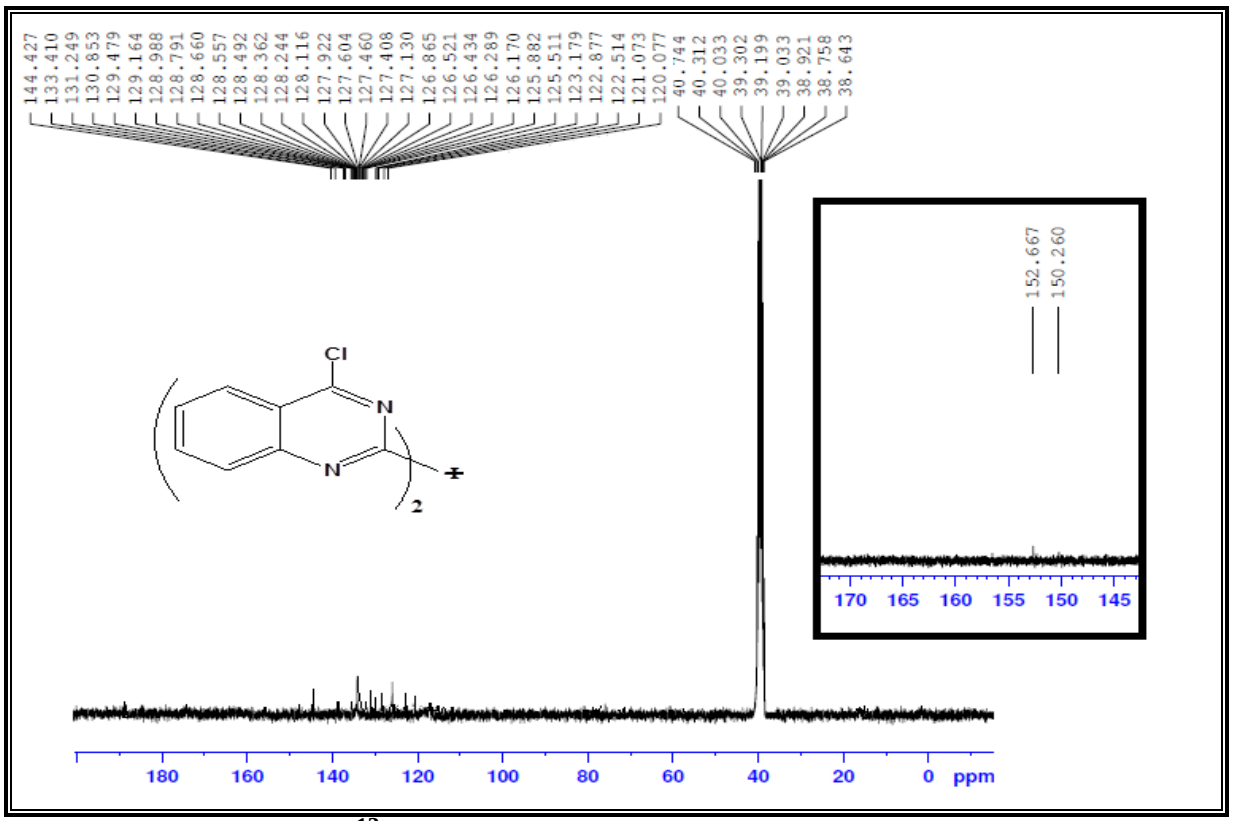


Fig (3-74). ^{13}C-NMR spectrum analysis of compound [IX]

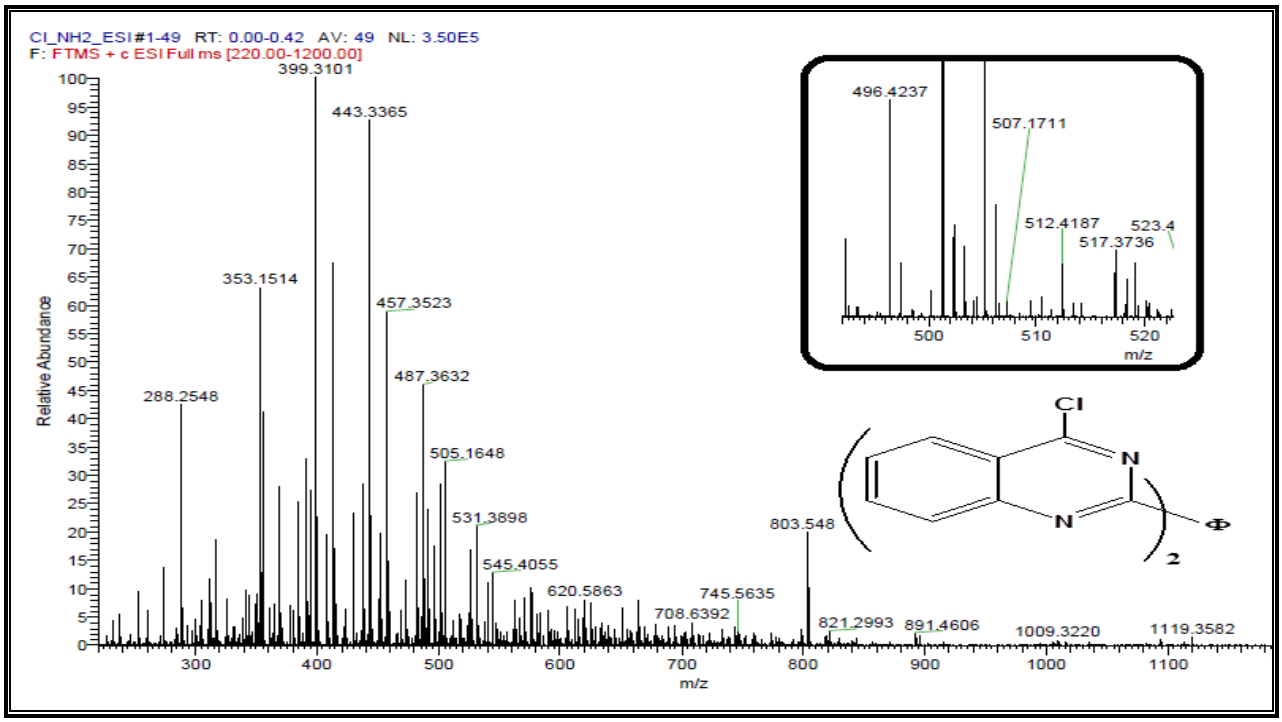


Fig (3-75). Mass spectrum analysis of compound [IX]

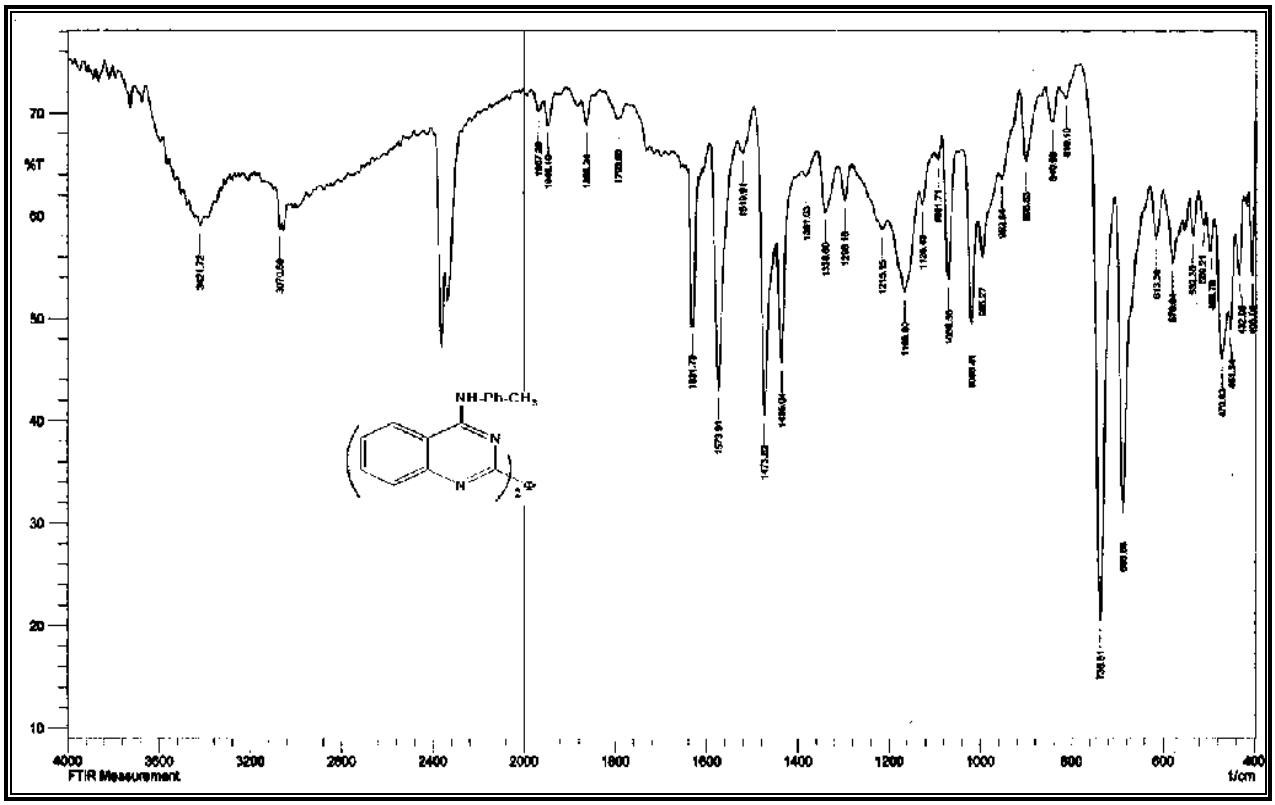


Fig (3-76). FT-IR spectrum analysis of compound [IXA]

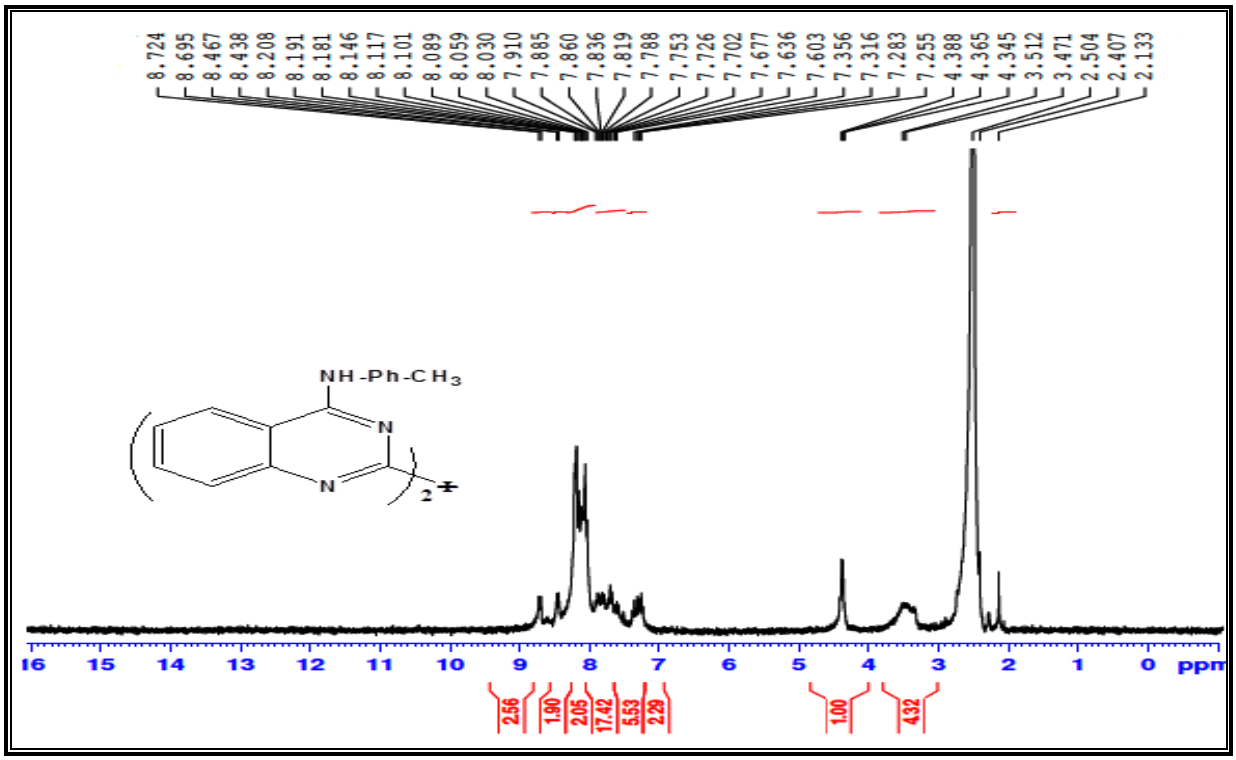


Fig (3-77). ^{1}H-NMR spectrum analysis of compound [IXA]

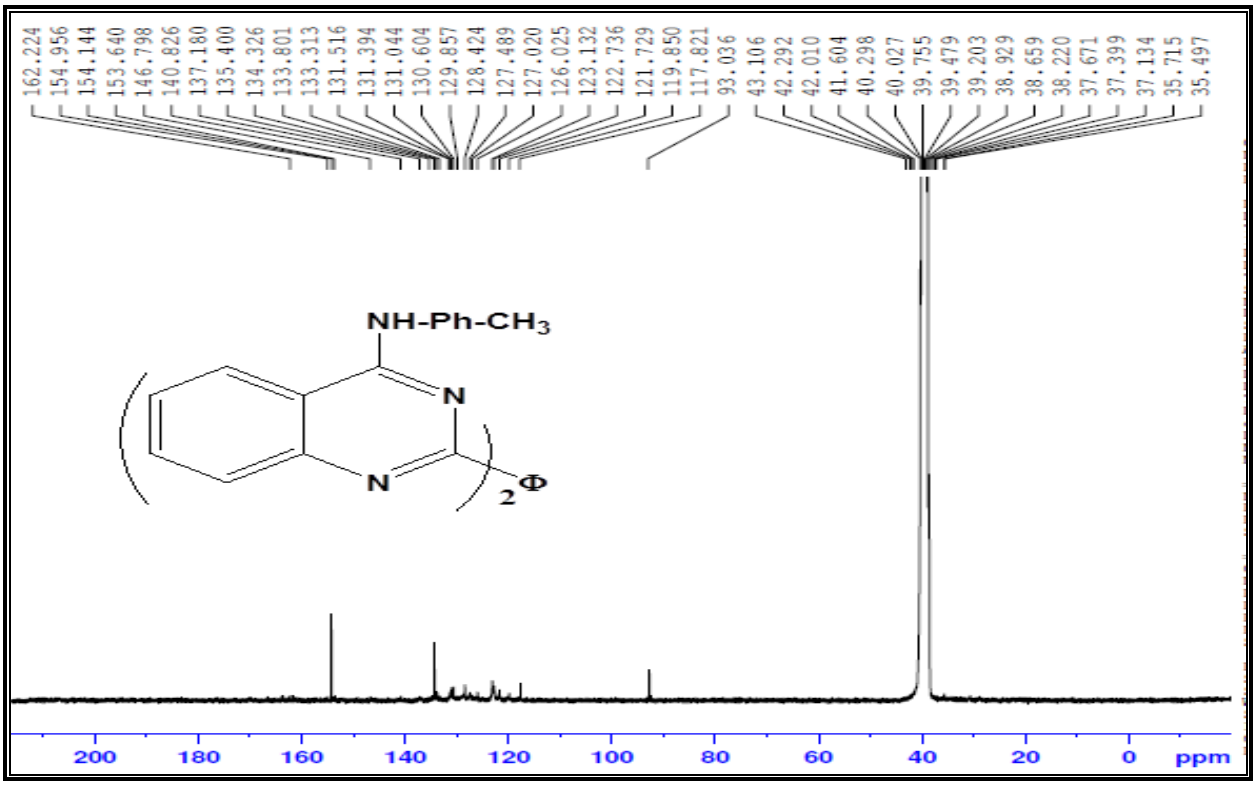


Fig (3-78). ^{13}C-NMR spectrum analysis of compound [IXA]

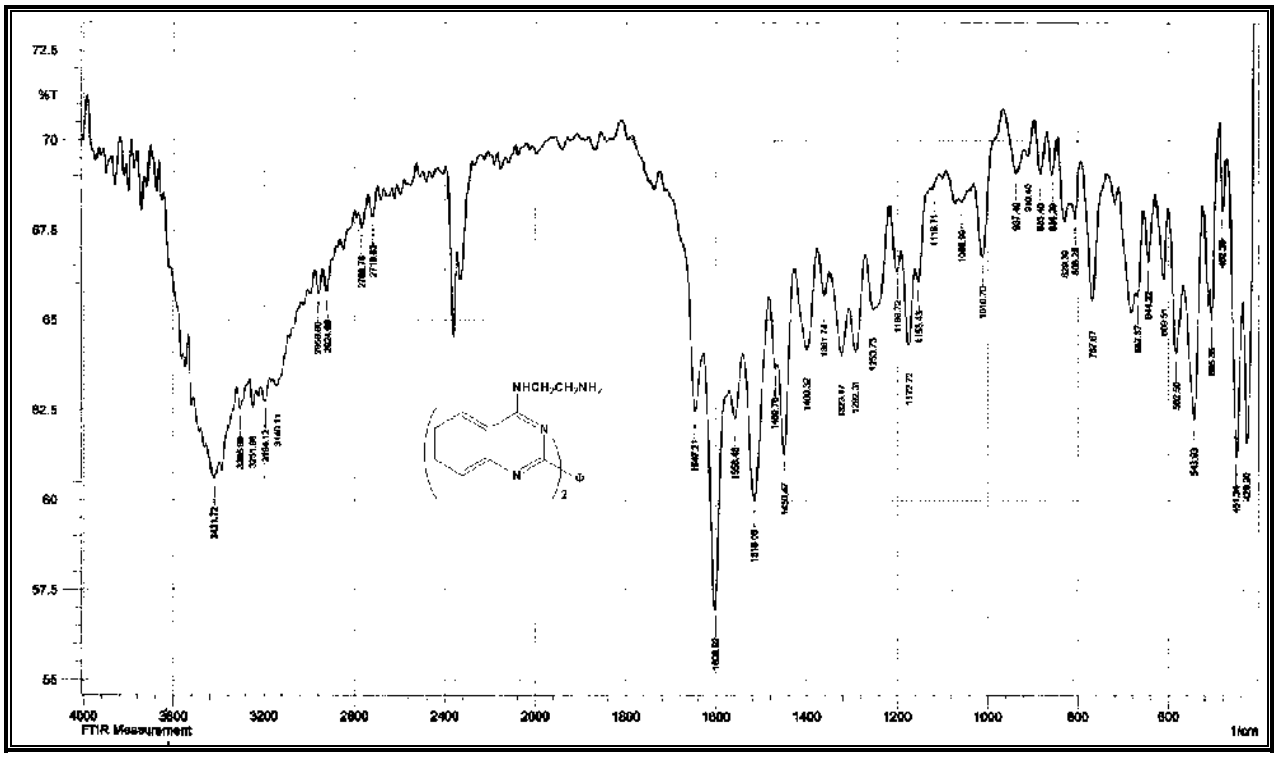


Fig (3-79). FT-IR spectrum analysis of compound [IXB]

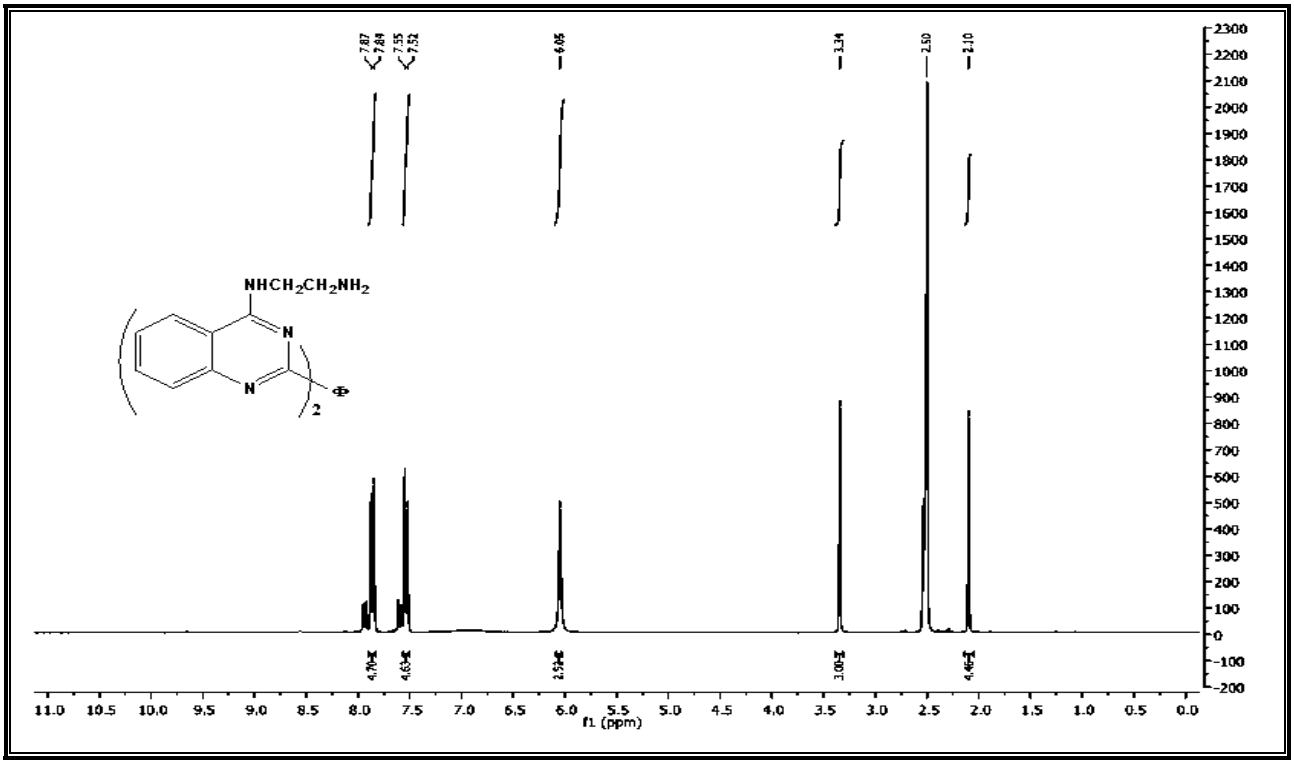


Fig (3-80). ^{1}H-NMR spectrum analysis of compound [IXB]

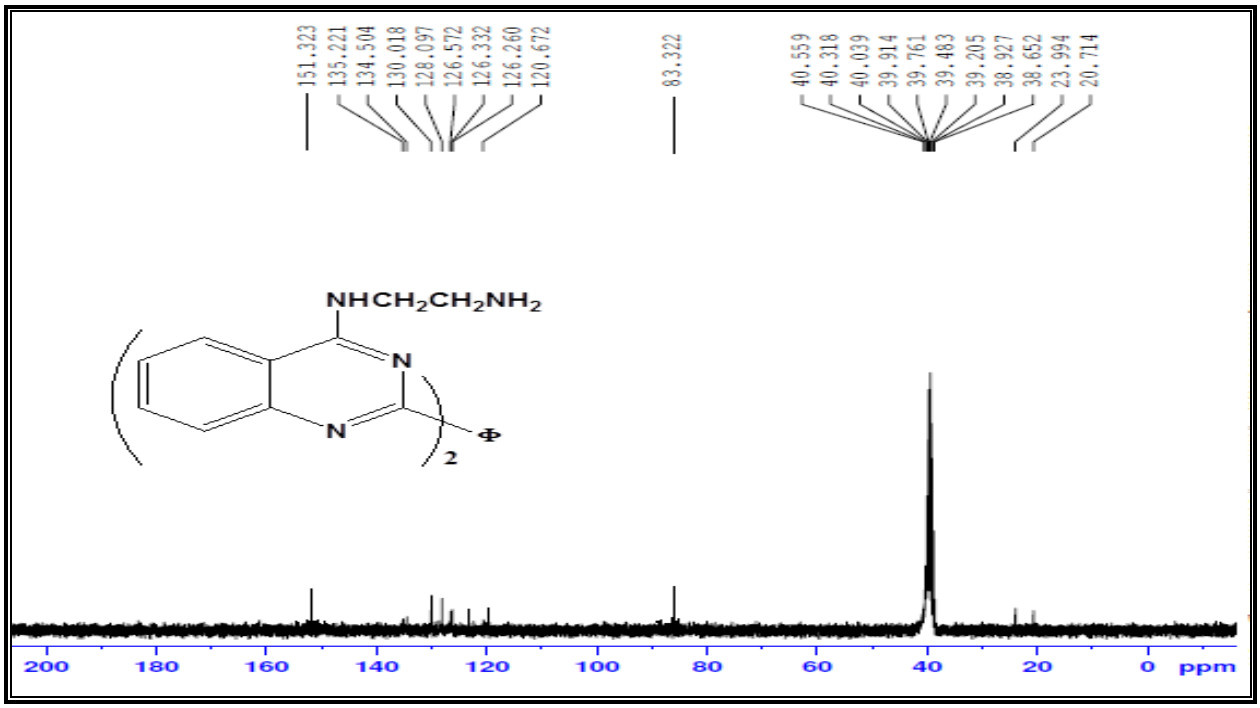


Fig (3-81). ^{13}C-NMR spectrum analysis of compound [IXB]

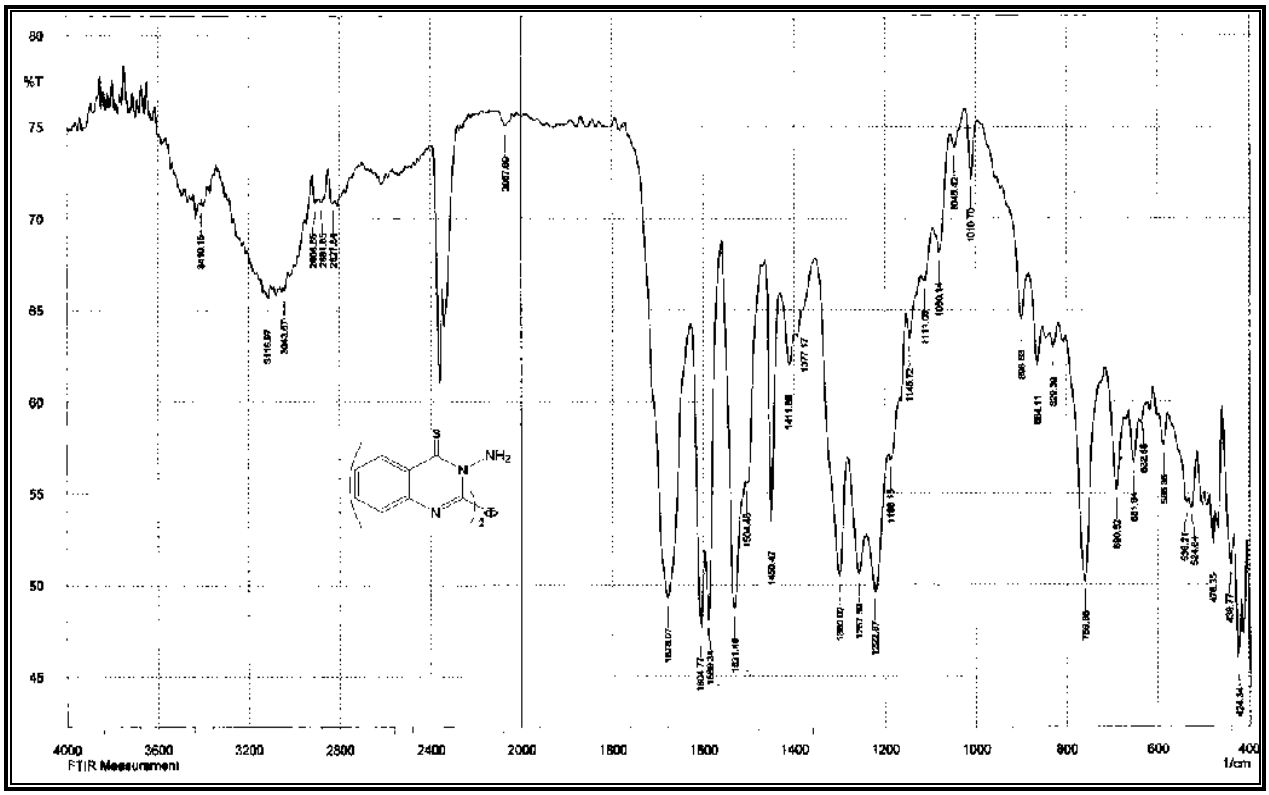


Fig (3-82). FTIR- spectrum analysis of compound [XA]

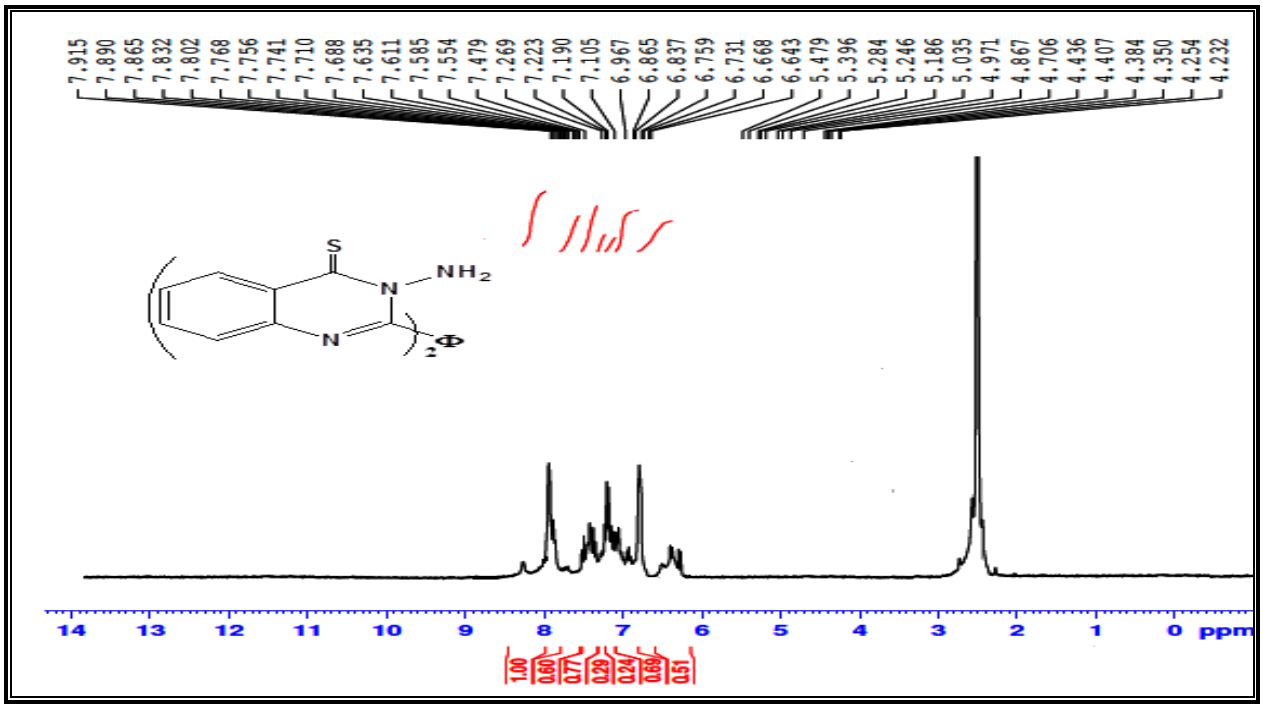


Fig (3-83). ^{1}H-NMR spectrum analysis of compound [XA]

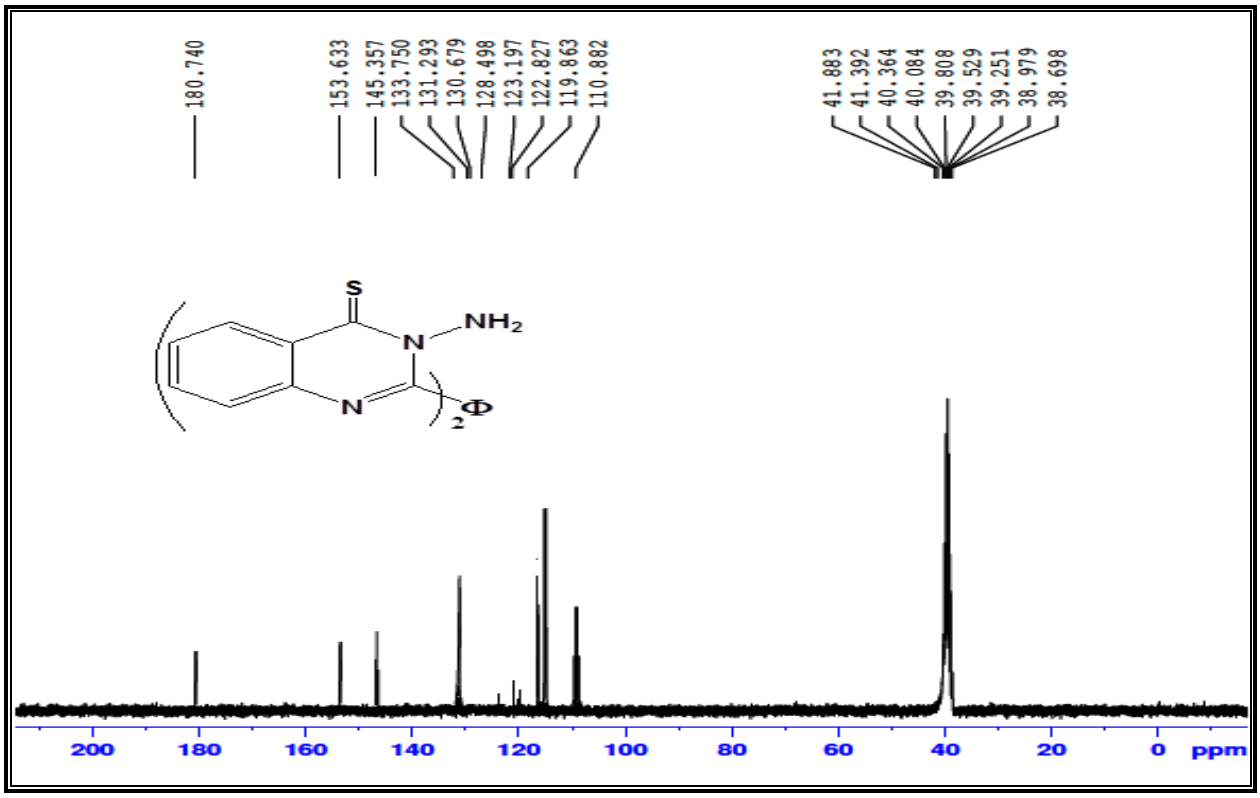


Fig (3-84). ^{13}C-NMR spectrum analysis of compound [XA]

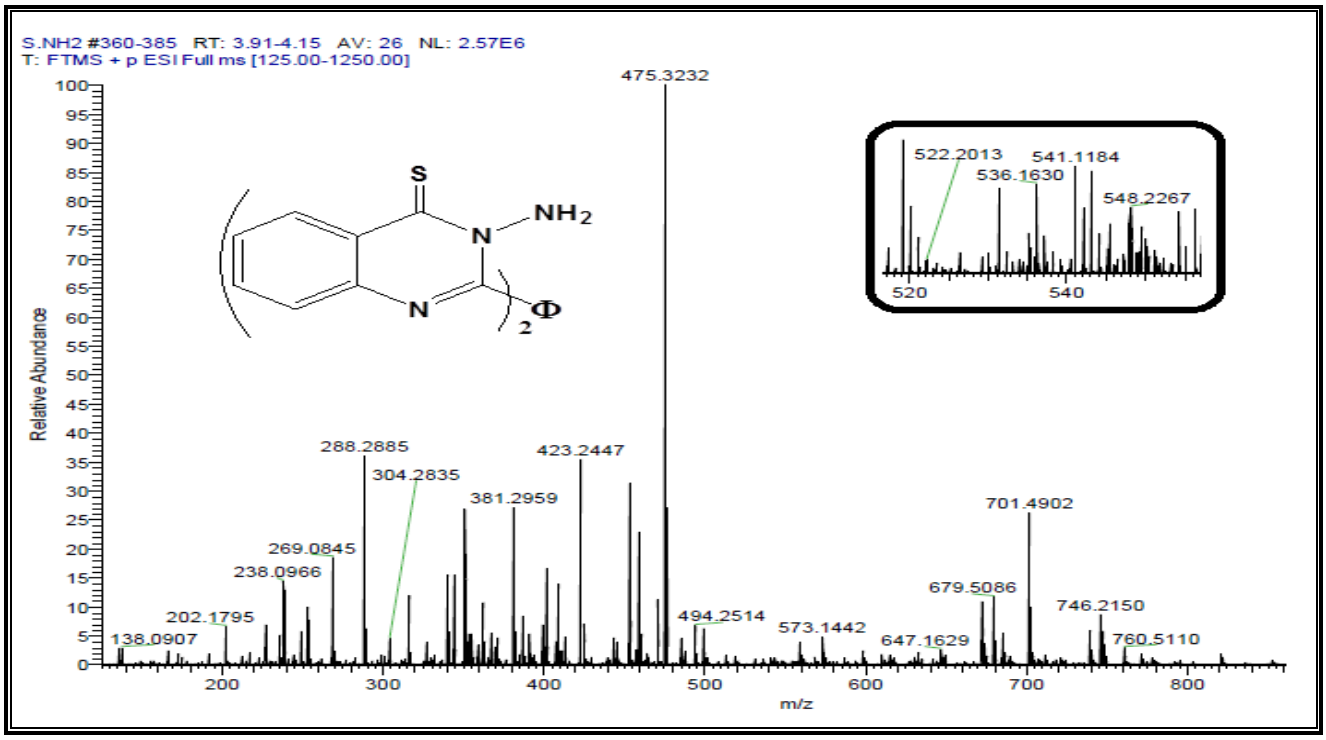


Fig (3-85). Mass spectrum analysis of compound [XA]

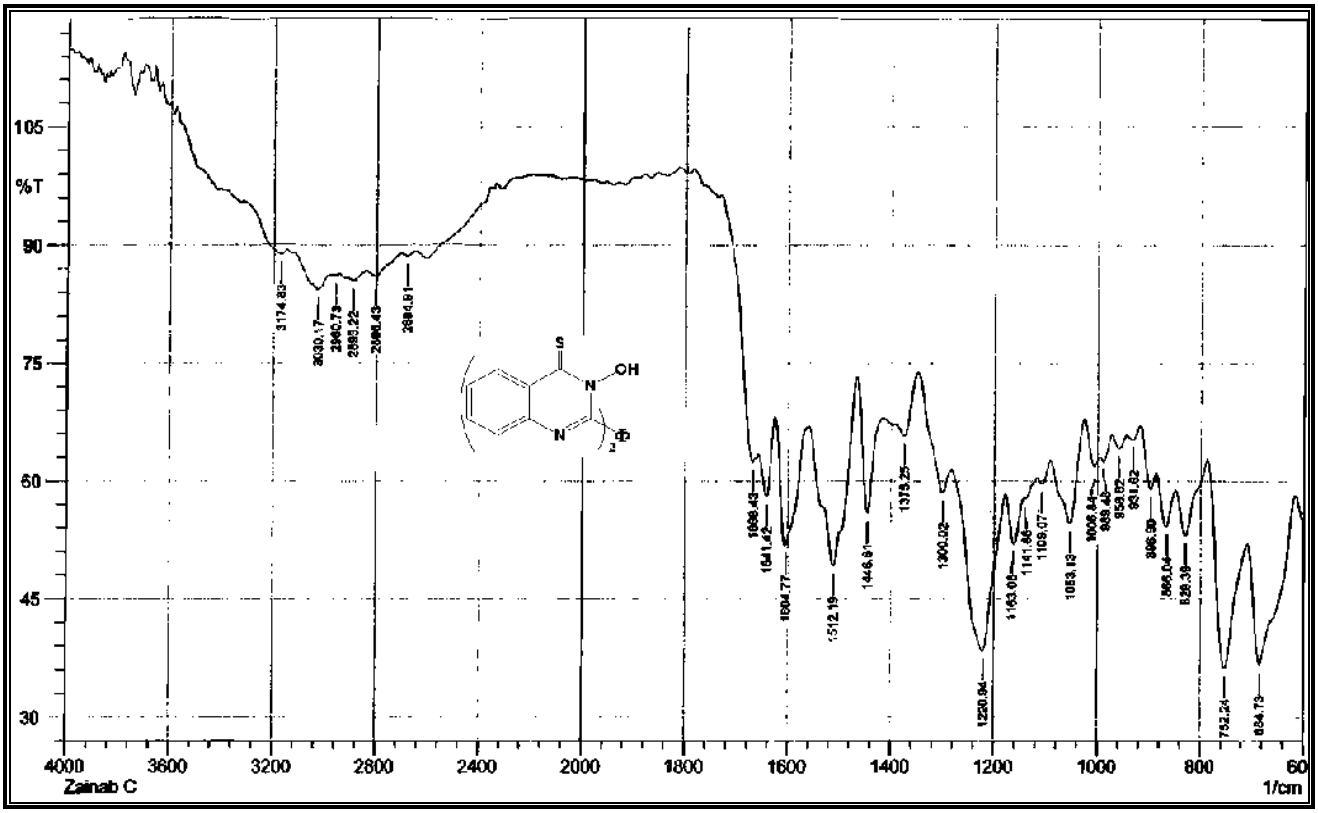


Fig (3-86). FT-IR spectrum analysis of compound [XB]

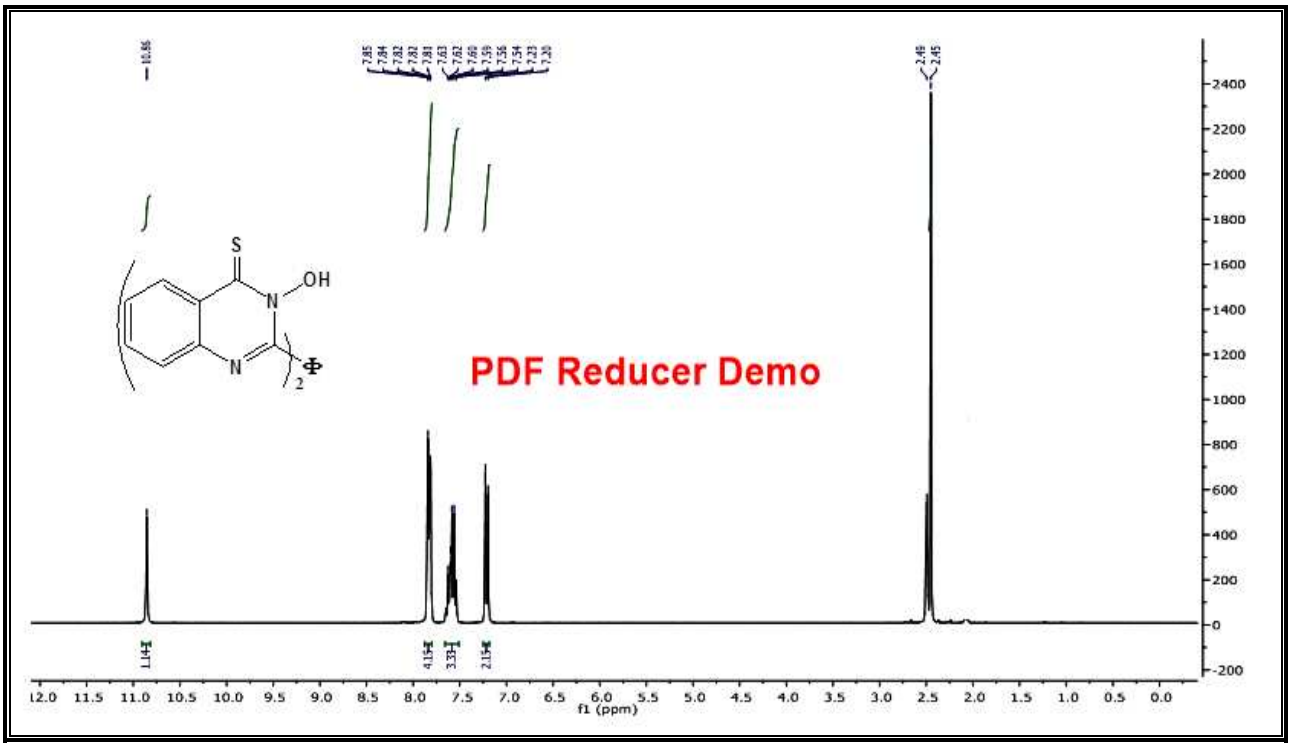


Fig (3-87). ^{1}H-NMR spectrum analysis of compound [XB]

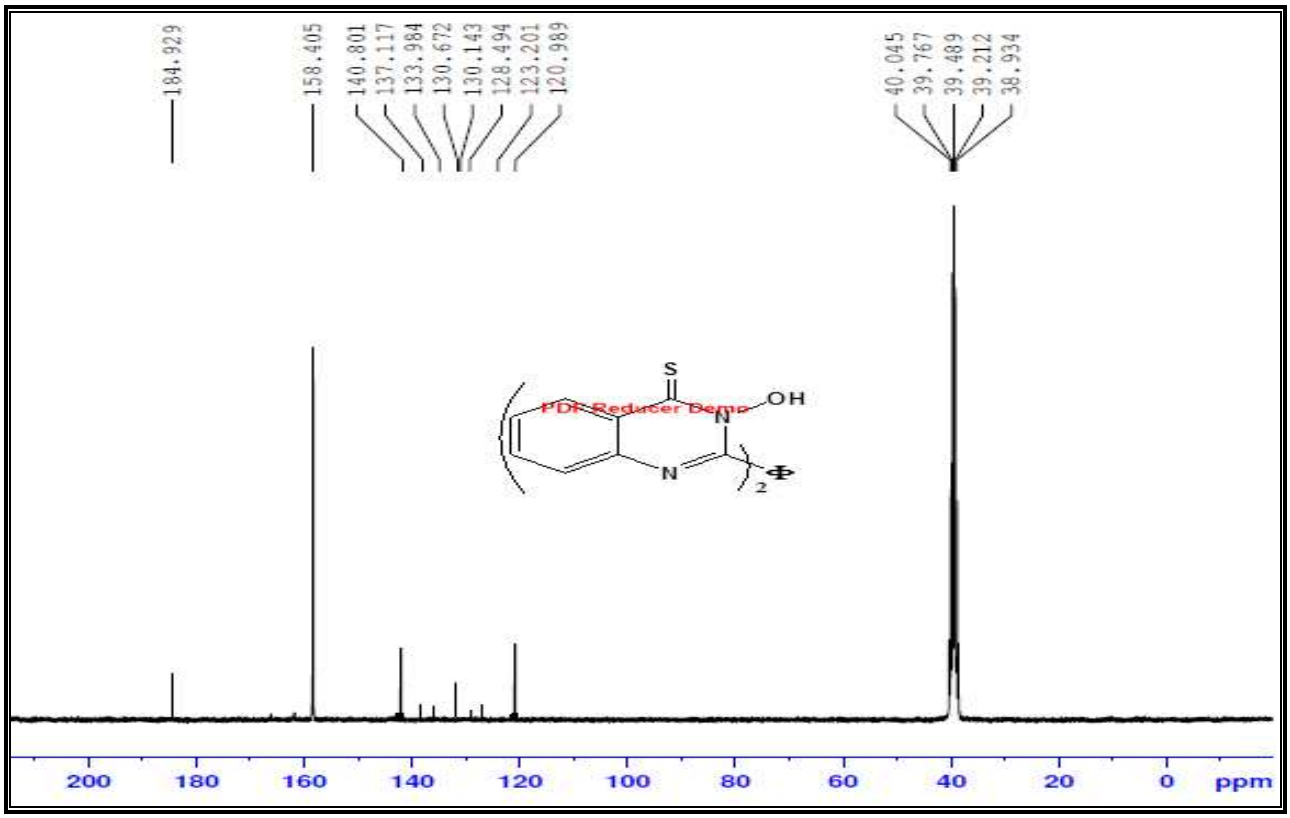


Fig (3-88). ^{13}C-NMR spectrum analysis of compound [XB]

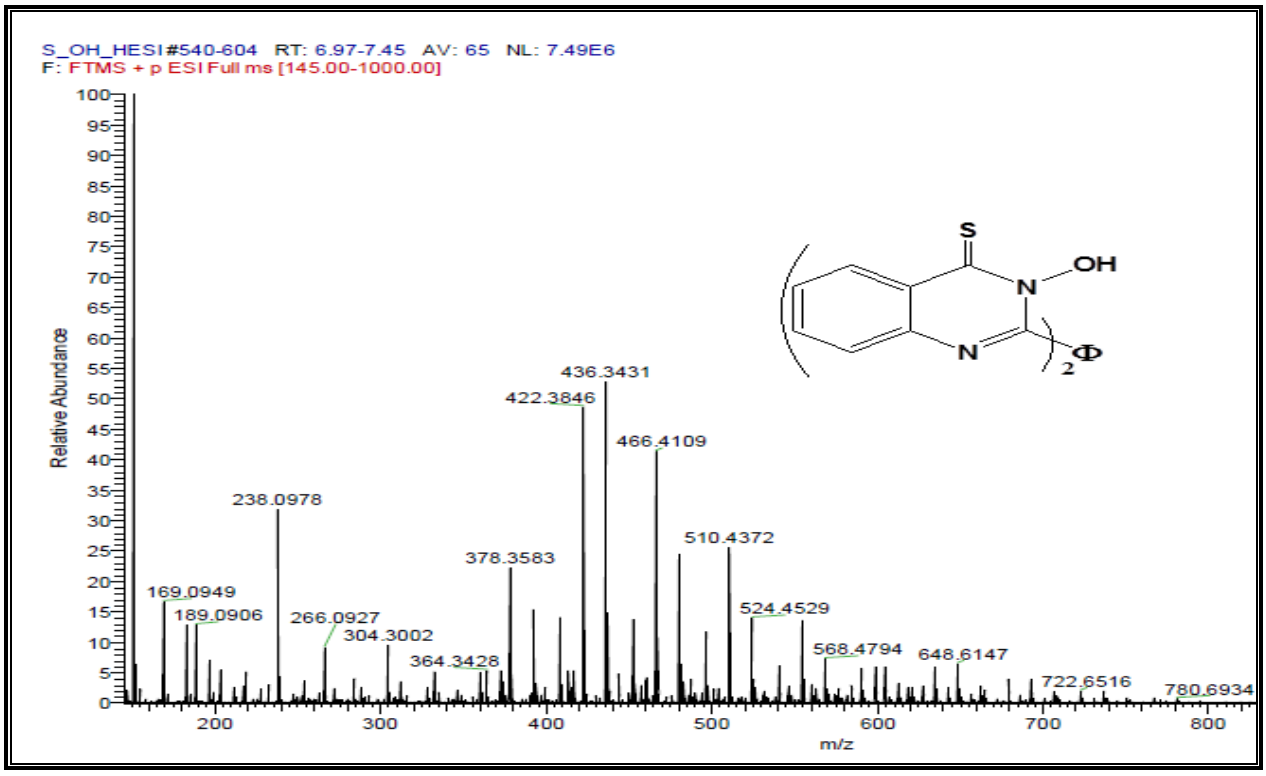


Fig (3-89). Mass spectrum analysis of compound [XB]

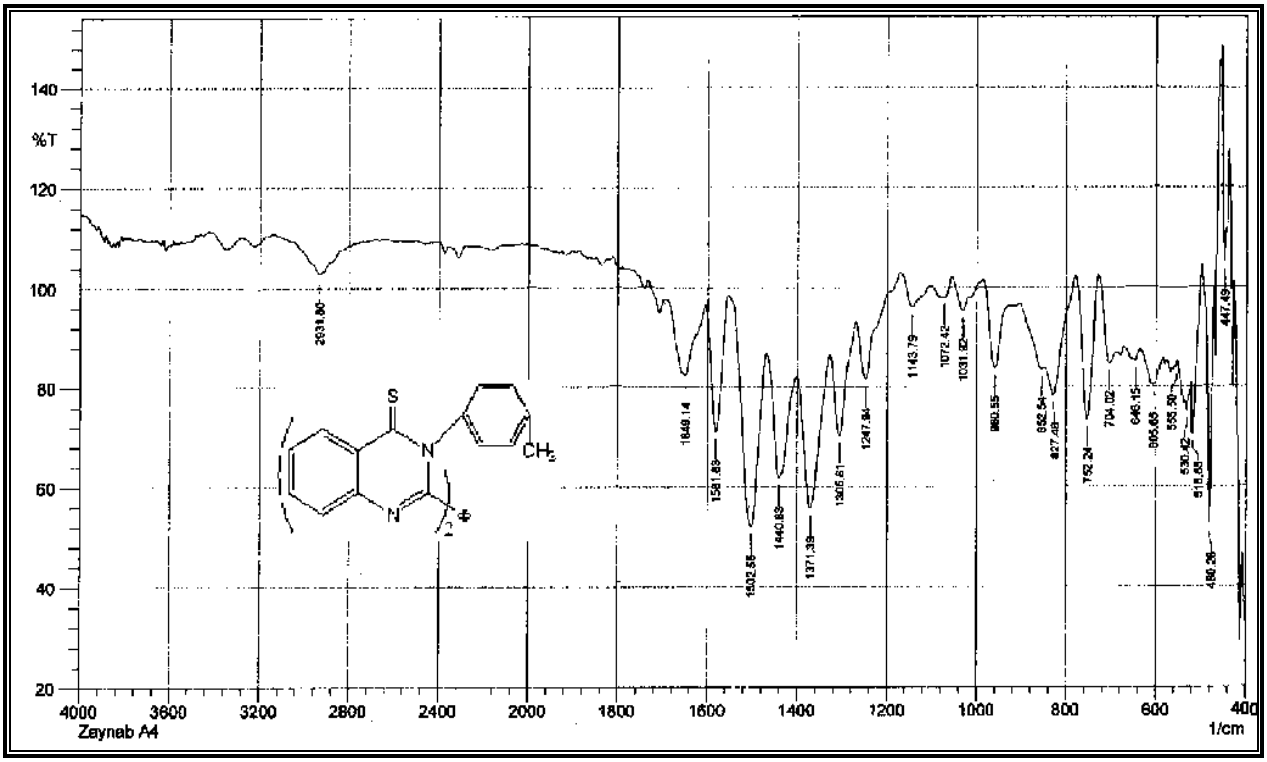


Fig (3-90). FT-IR spectrum analysis of compound [XC]

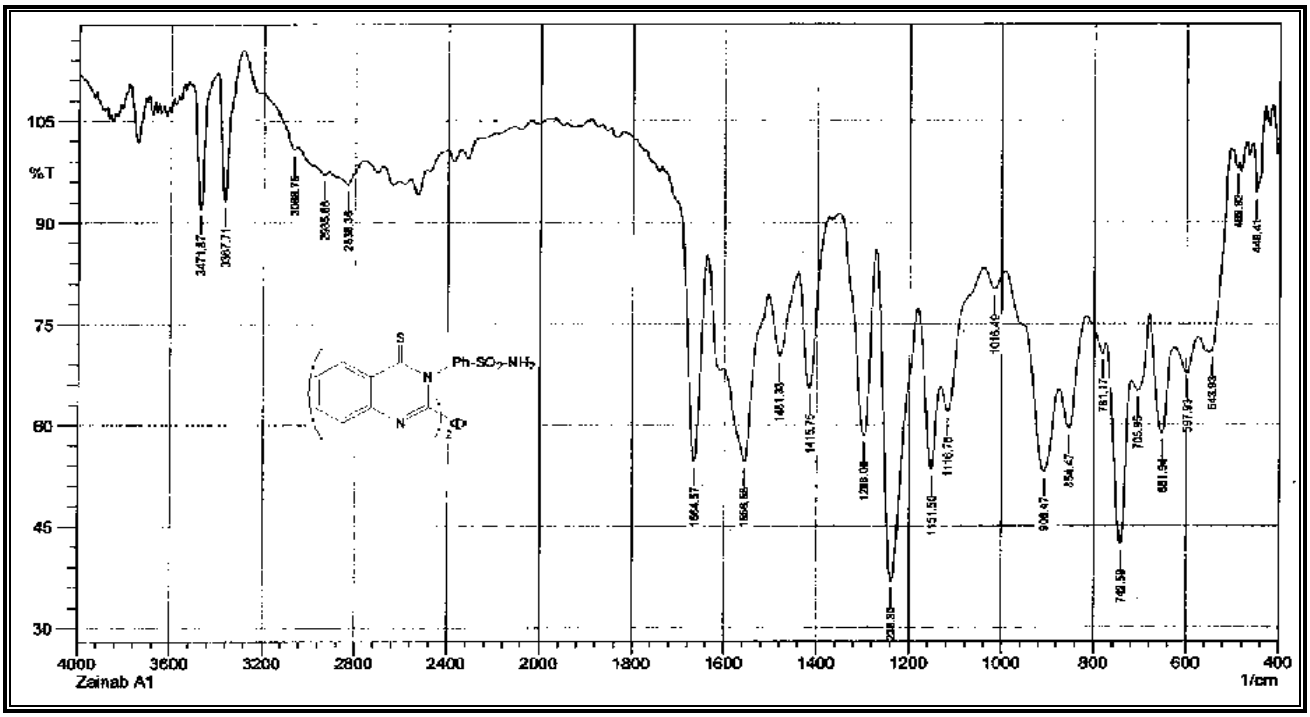


Fig (3-91). FT-IR spectrum analysis of compound [XD]

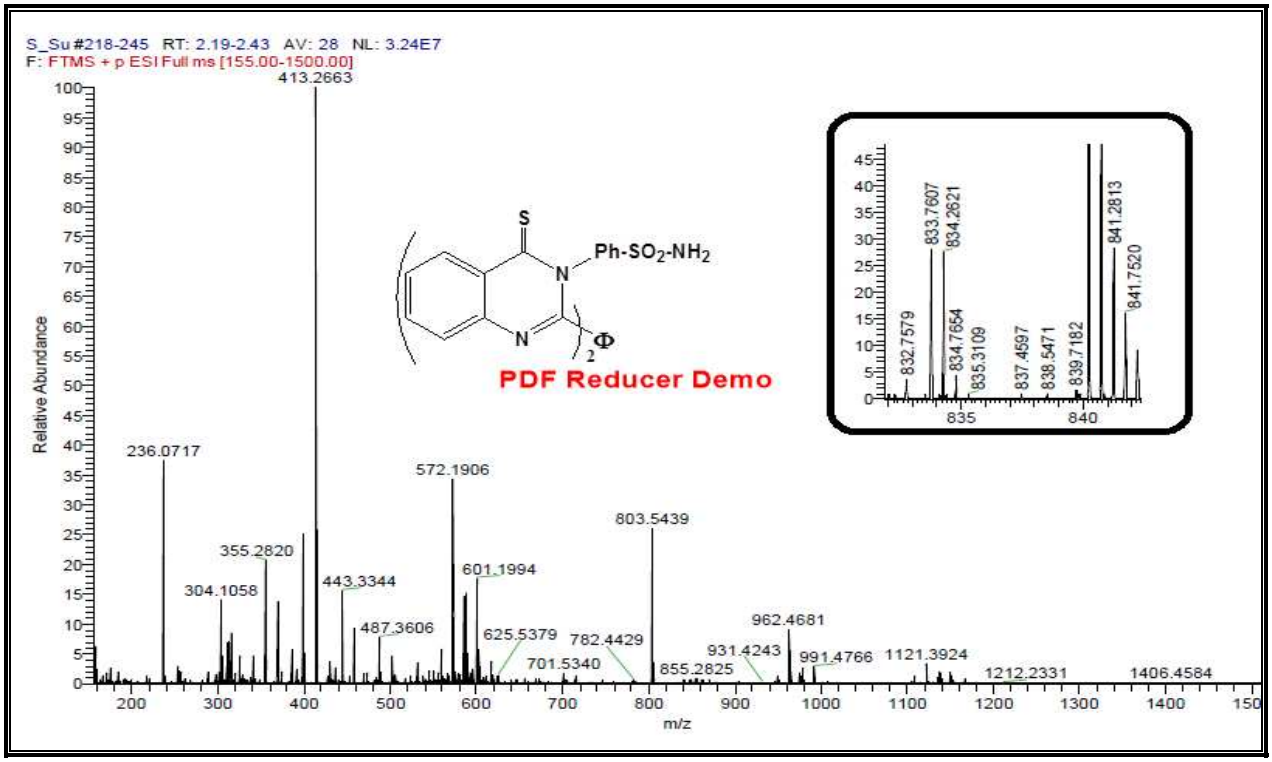


Fig (3-92). Mass spectrum analysis of compound [XD]

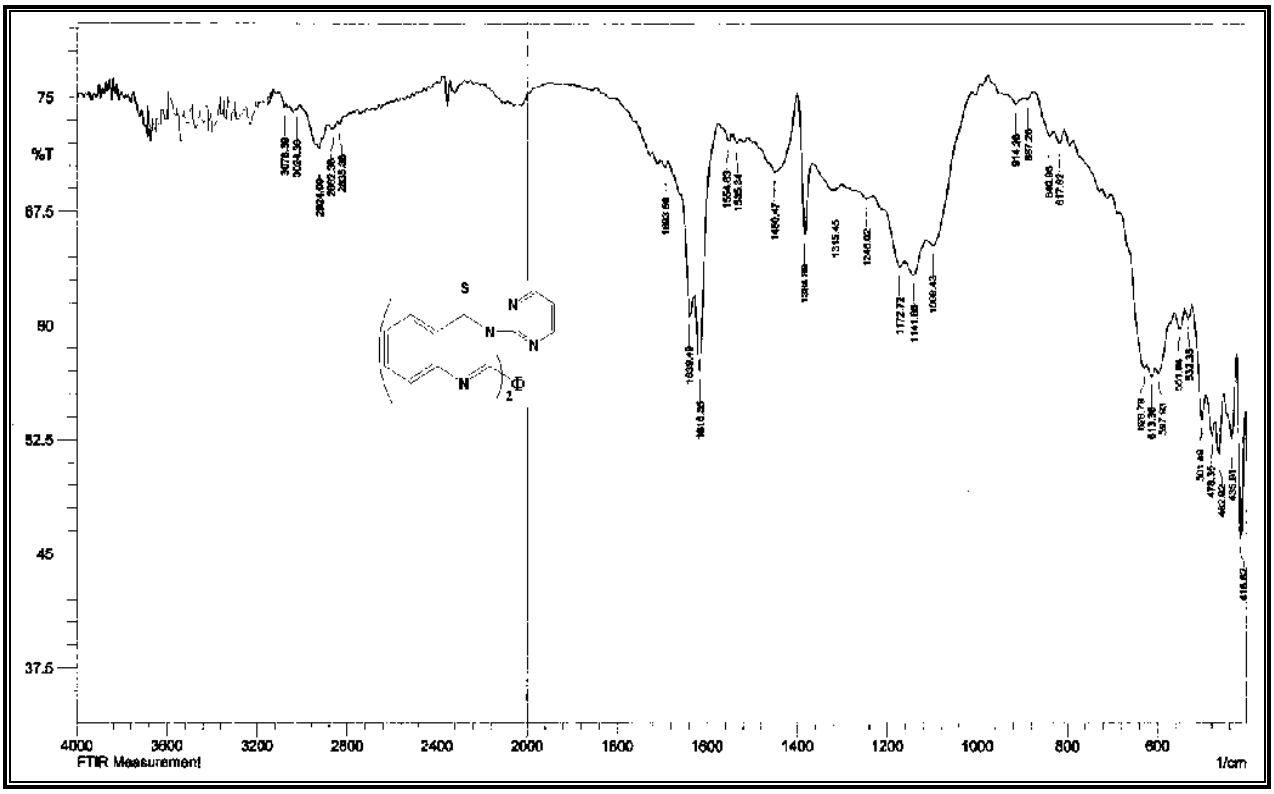


Fig (3-93). FT-IR spectrum analysis of compound [XE]

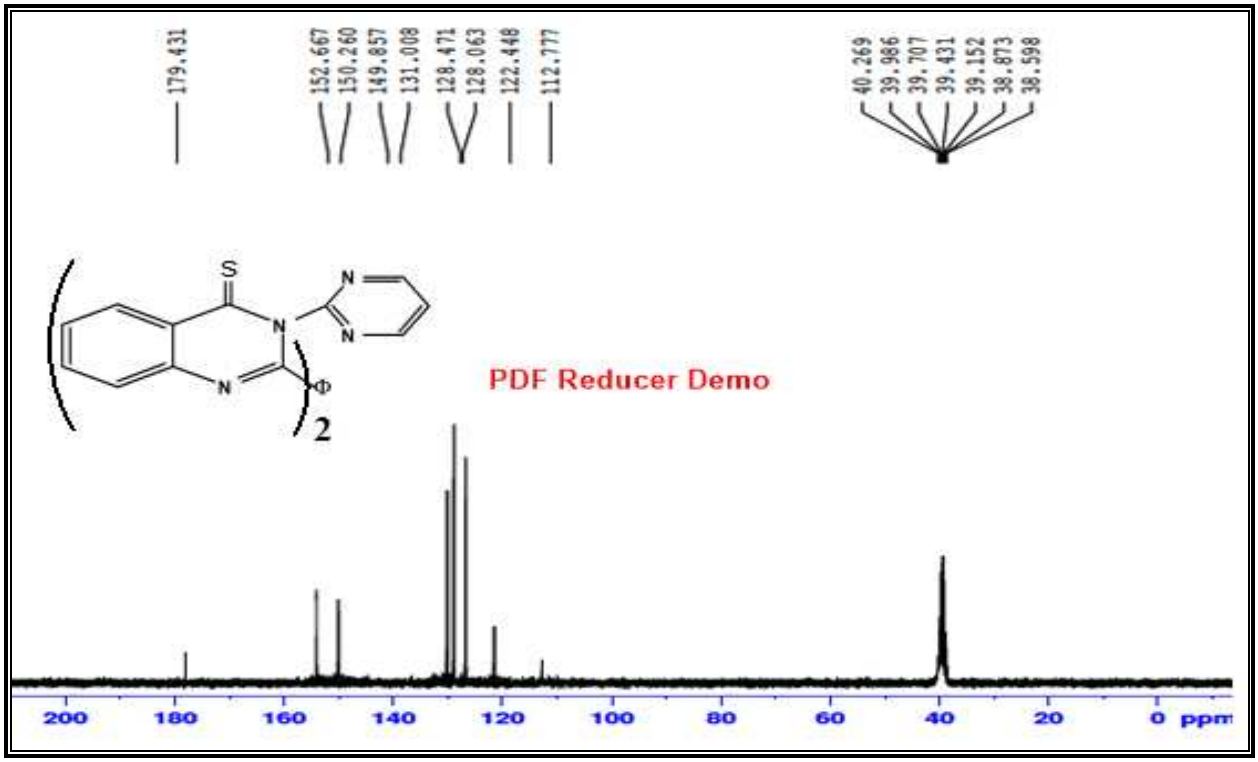


Fig (3-94). ^{13}C-NMR spectrum analysis of compound [XE]

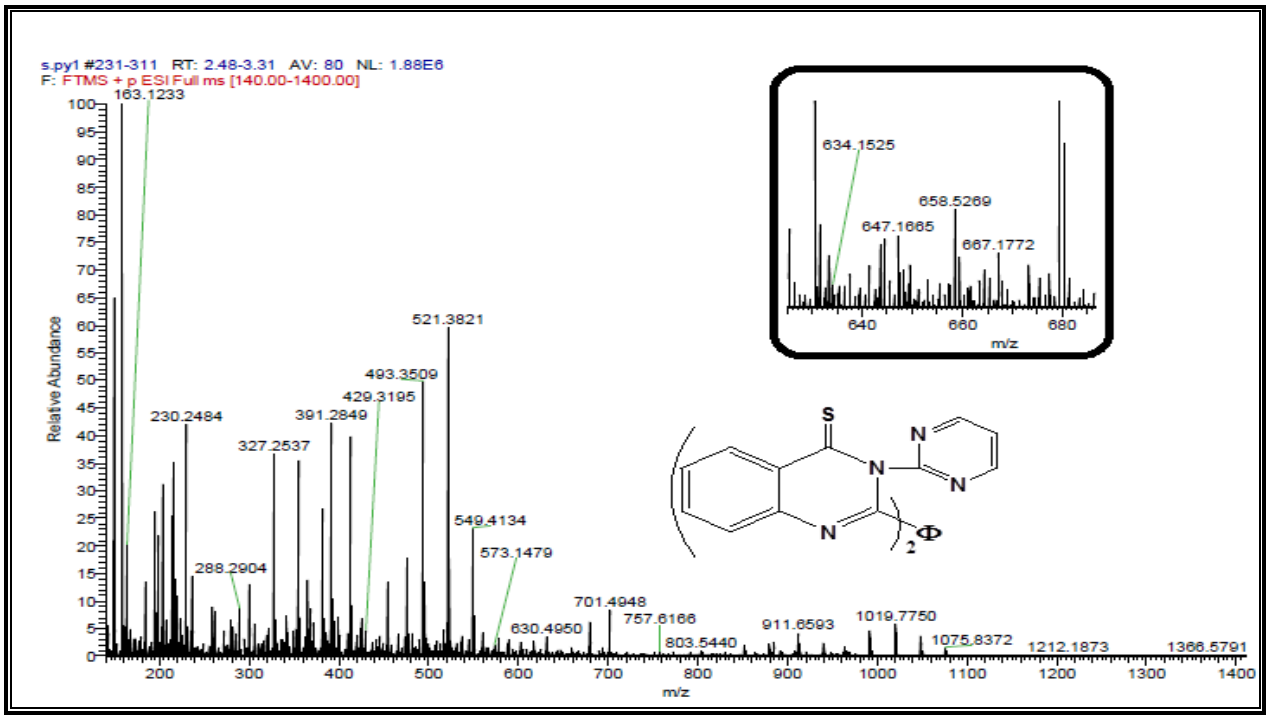


Fig (3-95). Mass spectrum analysis of compound [XE]

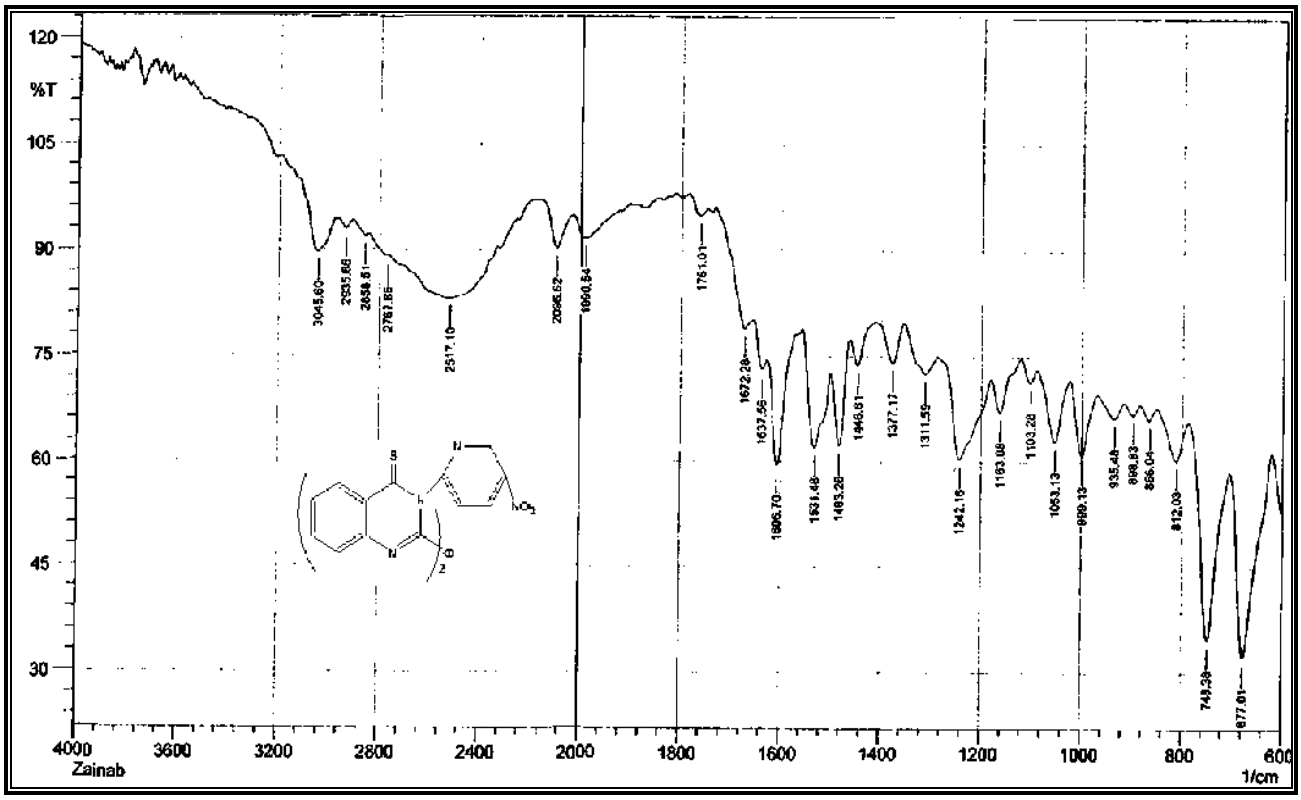


Fig (3-96). FT-IR spectrum analysis of compound [XF]

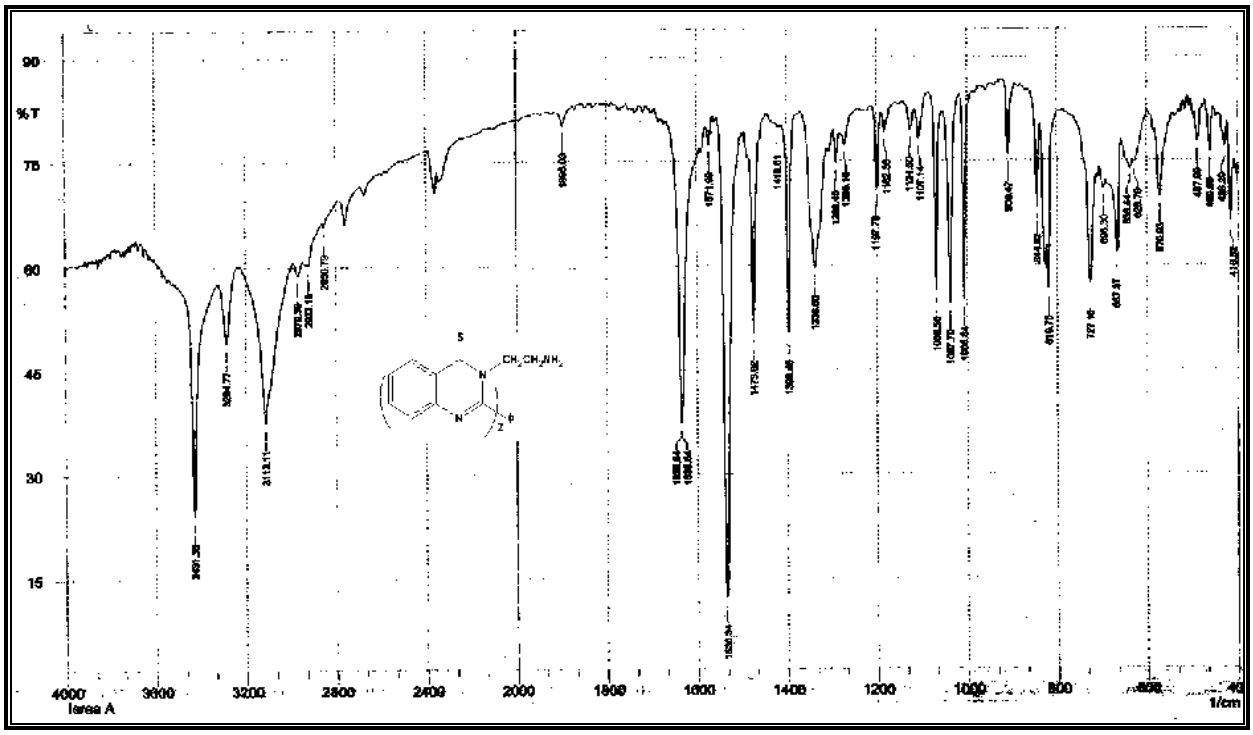


Fig (3-97). FT-IR spectrum analysis of compound [XG]

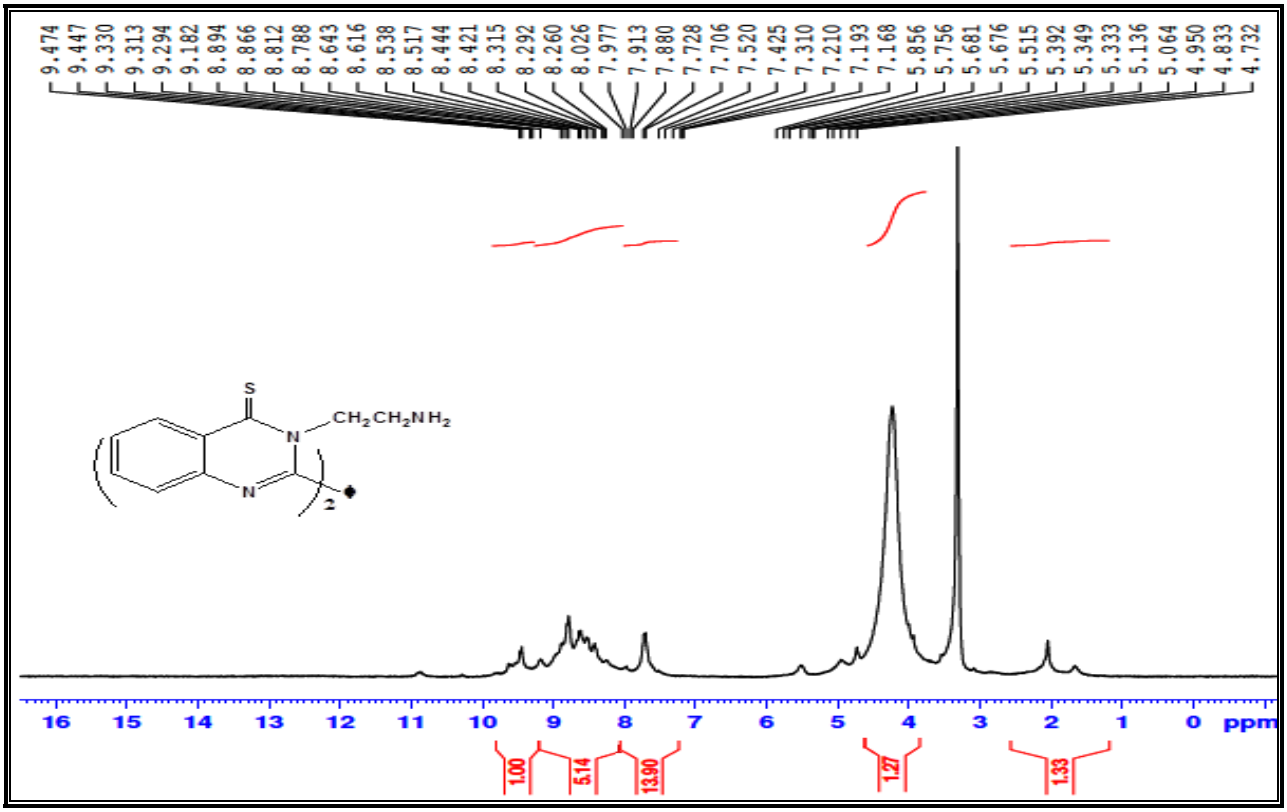


Fig (3-98). ^{1}H-NMR spectrum analysis of compound [XG]

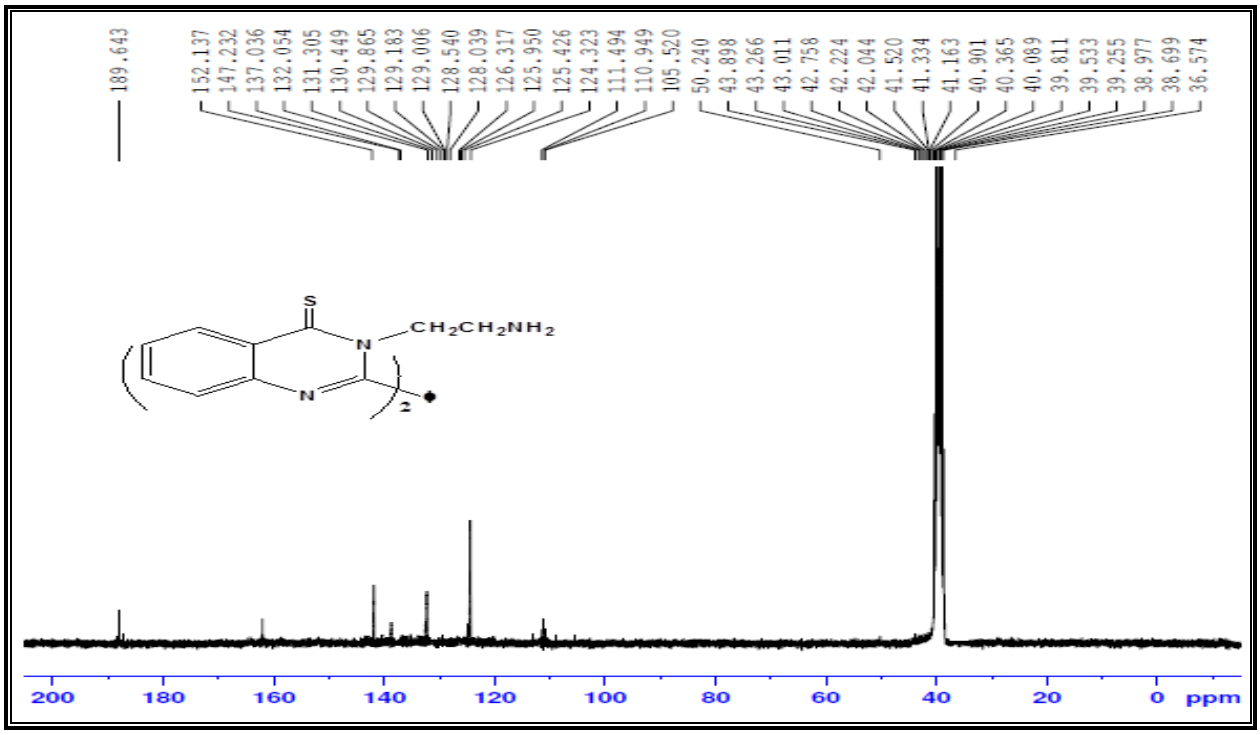


Fig (3-99). ^{13}C-NMR spectrum analysis of compound [XG]

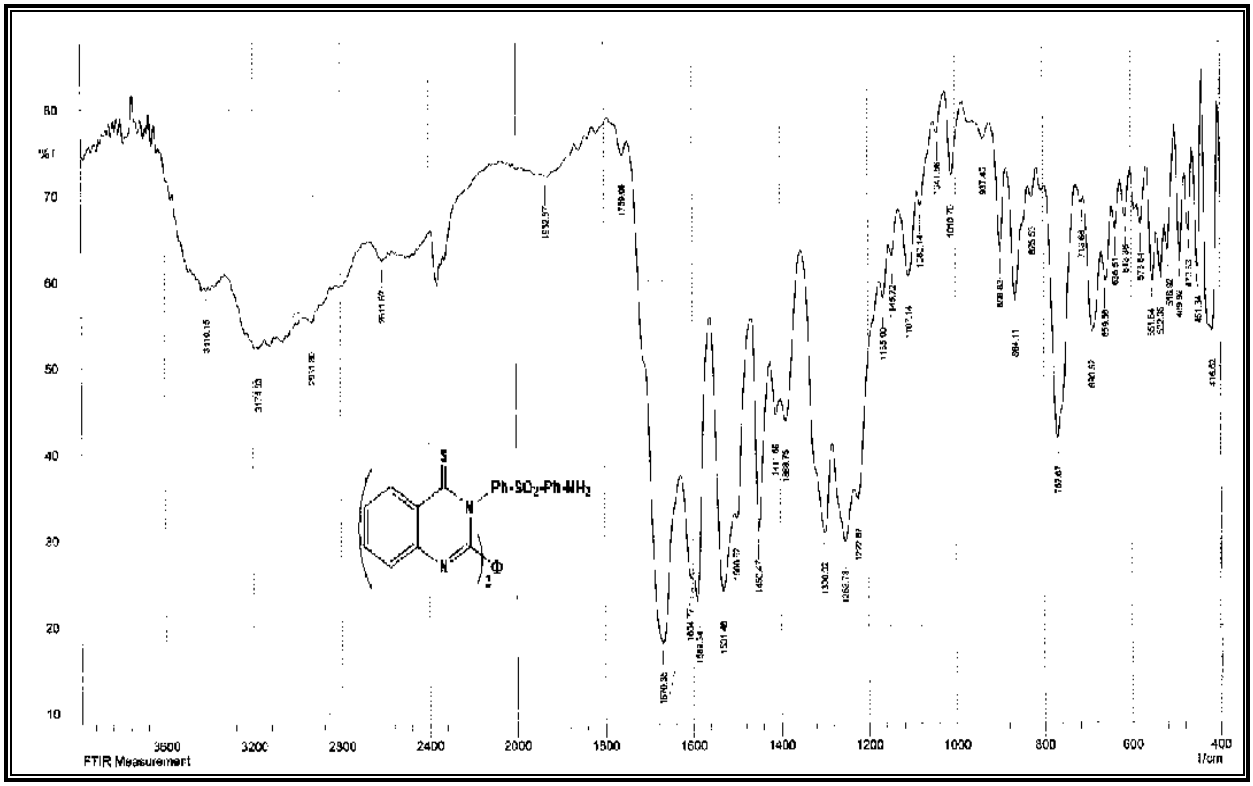


Fig (3-100). FT-IR spectrum analysis of compound [XI]

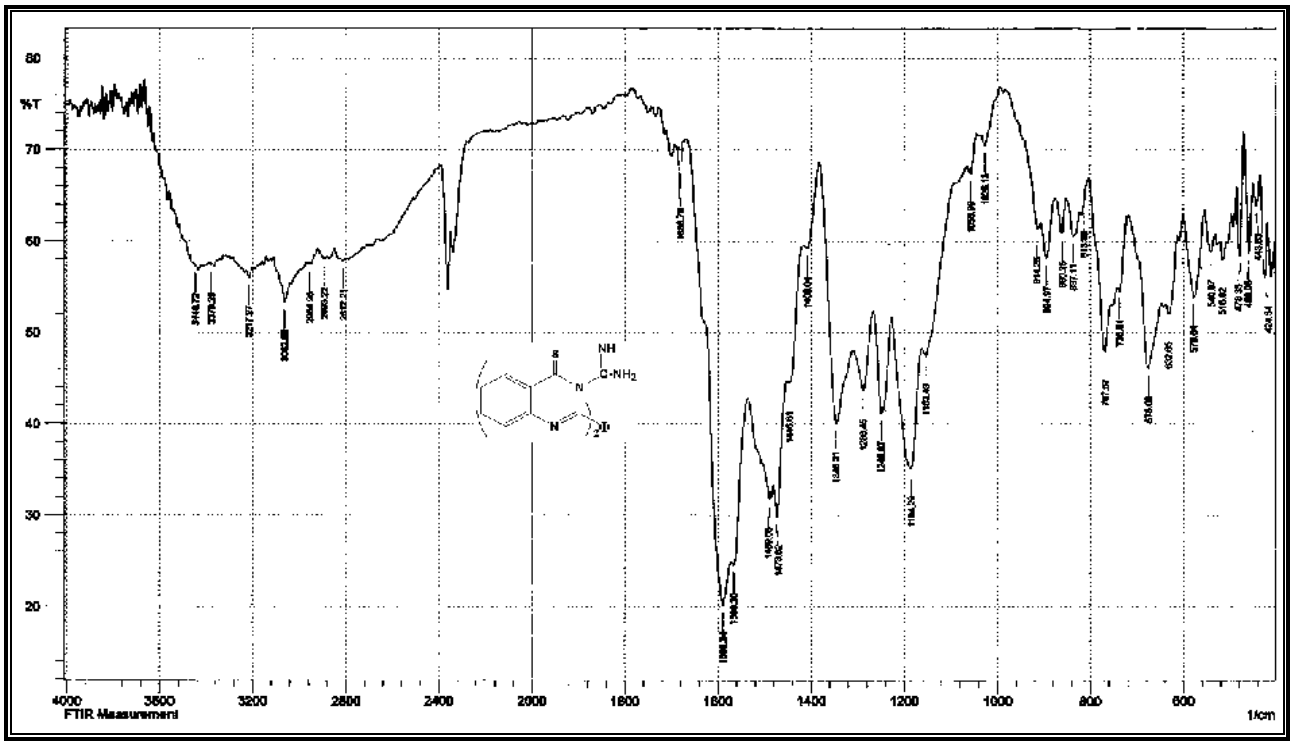


Fig (3-101). FT-IR spectrum analysis of compound [XJ]

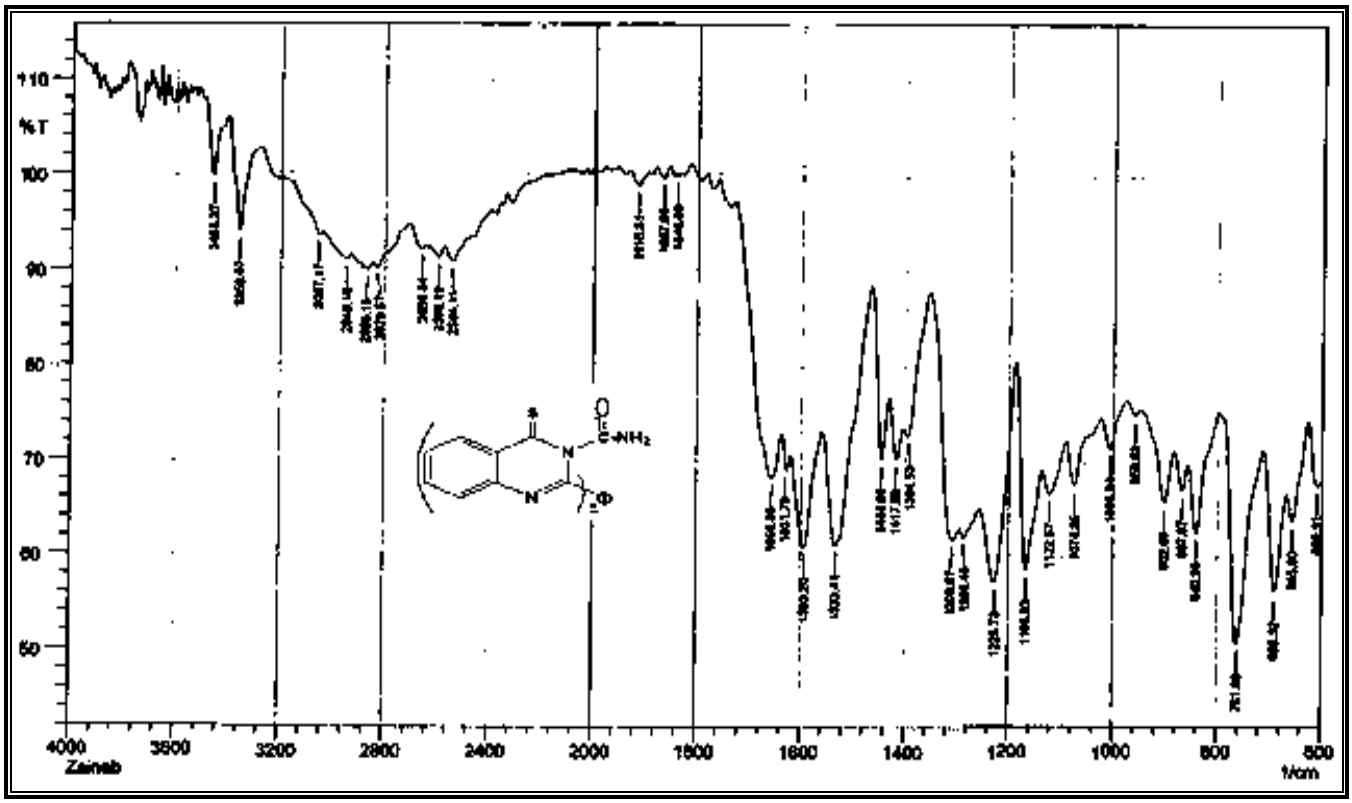


Fig (3-102). FT-IR spectrum analysis of compound [XK]

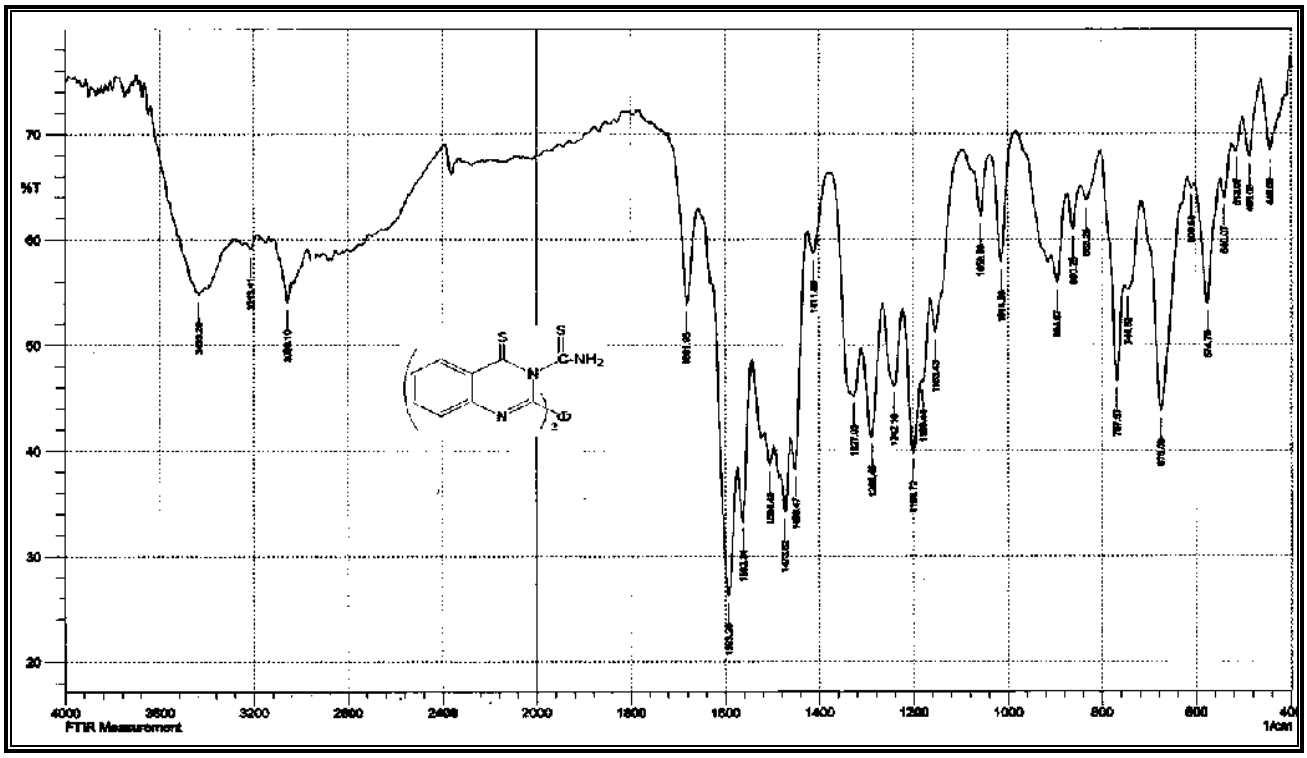


Fig (3-103). FT-IR spectrum analysis of compound [XL]

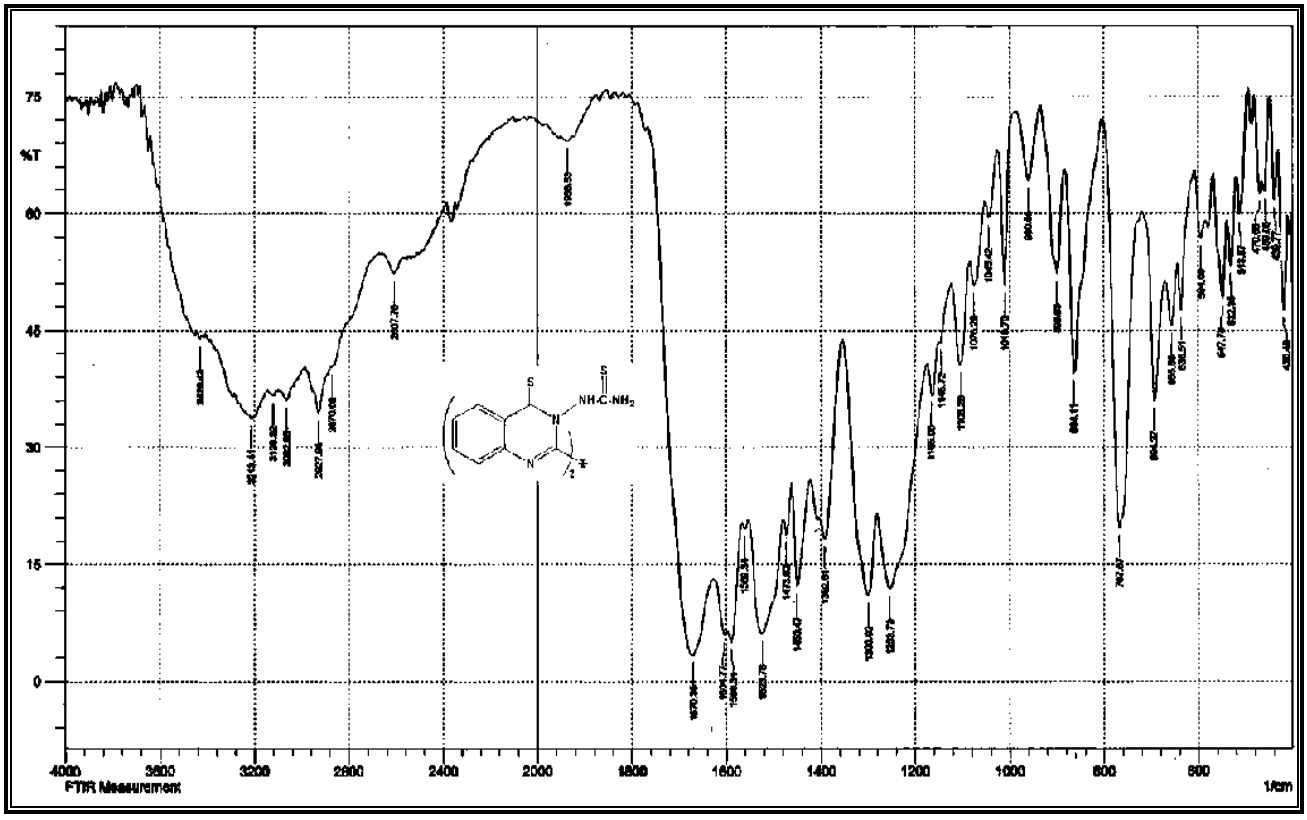


Fig (3-104). FT-IR spectrum analysis of compound [XP]

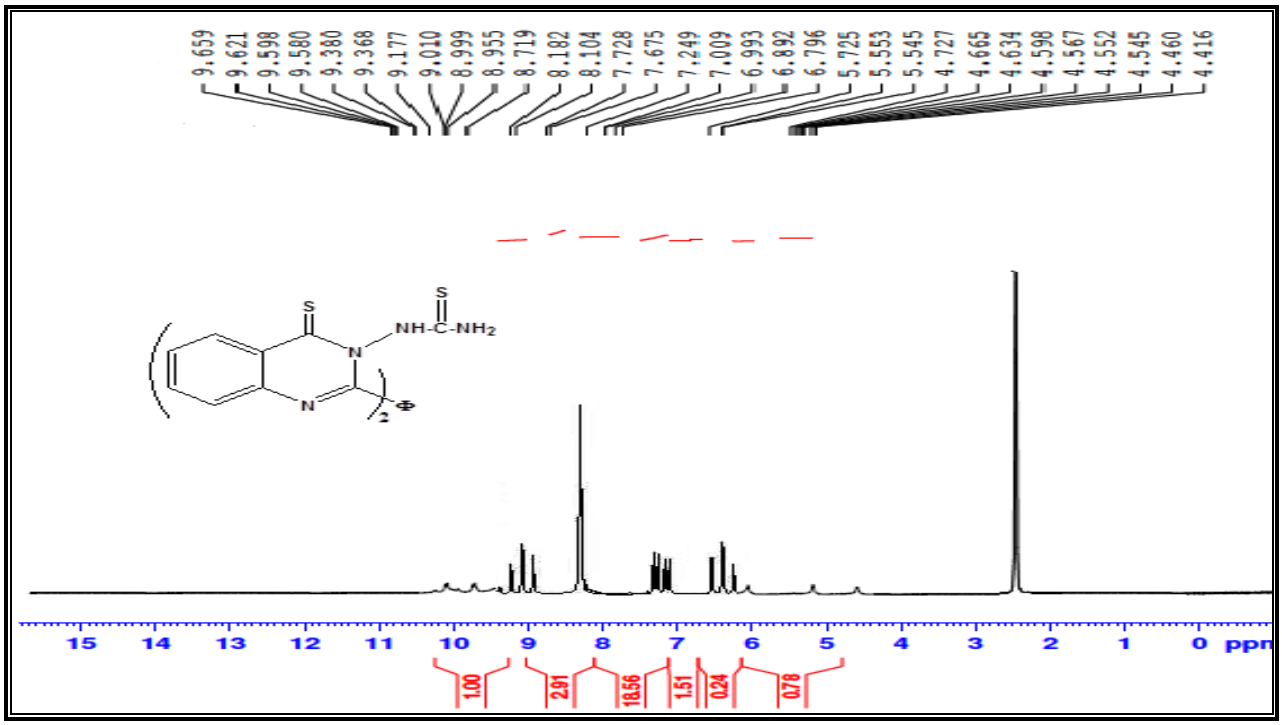


Fig (3-105). ^{1}H-NMR spectrum analysis of compound [XP]

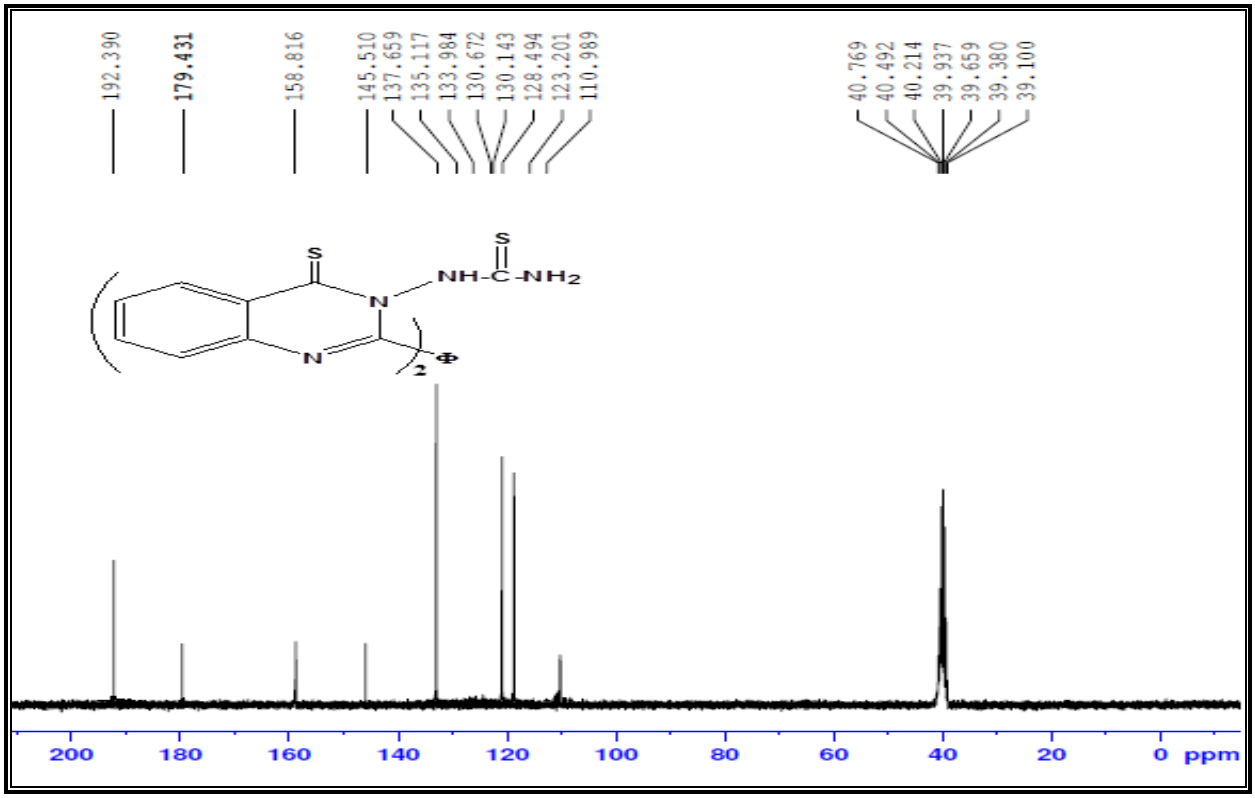


Fig (3-106). ^{13}C-NMR spectrum analysis of compound [XP]

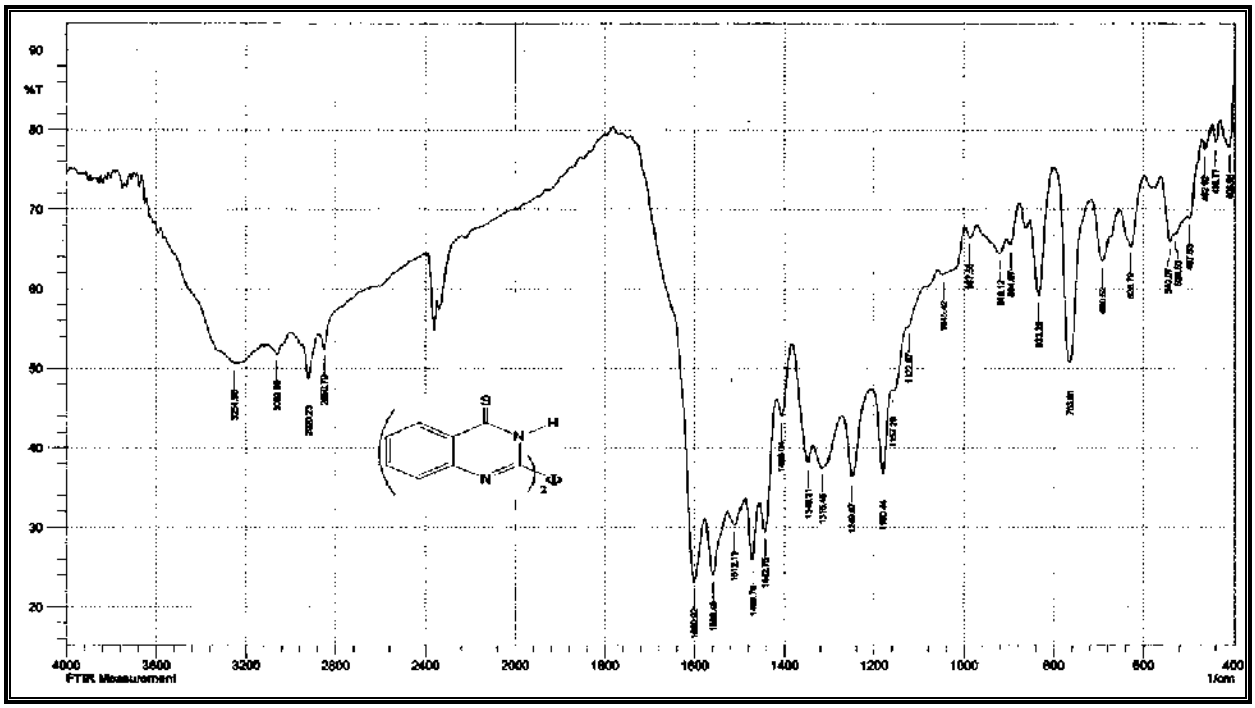


Fig (3-107). FT-IR spectrum analysis of compound [XI']

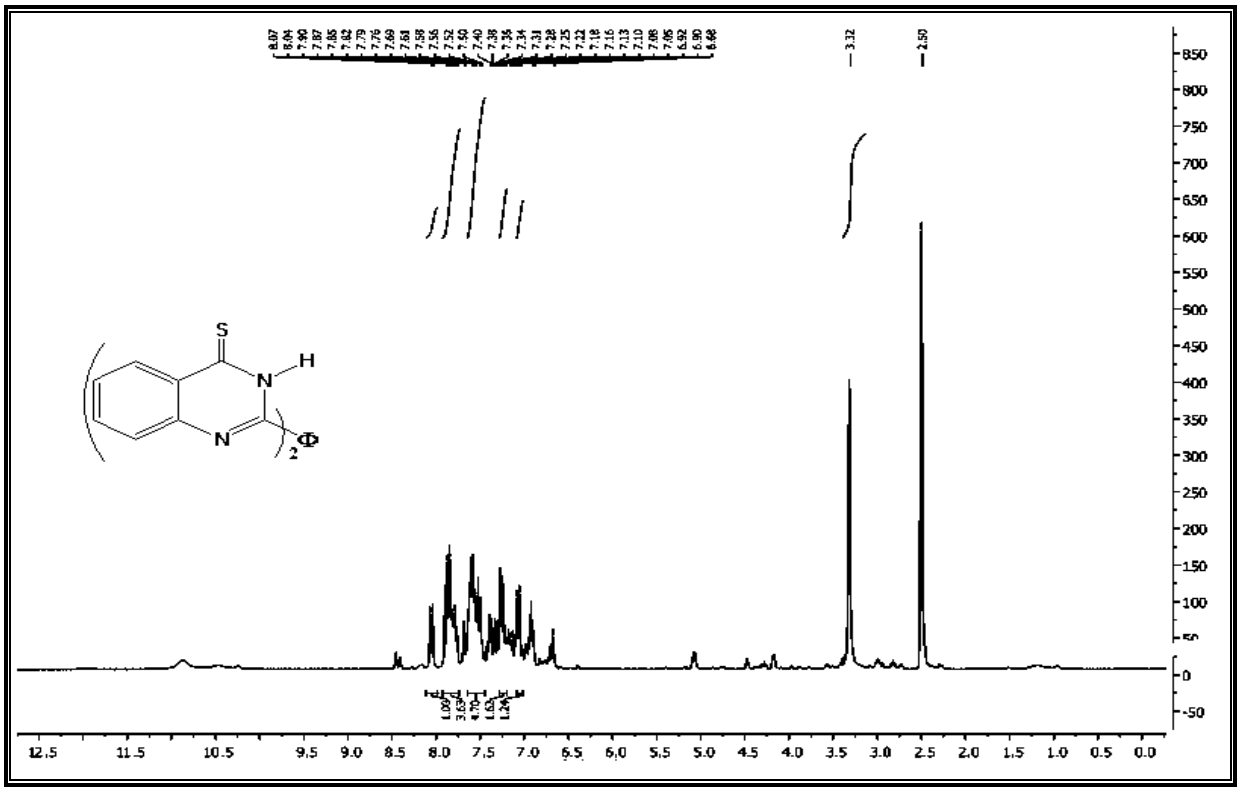


Fig (3-108). ^{1}H-NMR spectrum analysis of compound [XI']

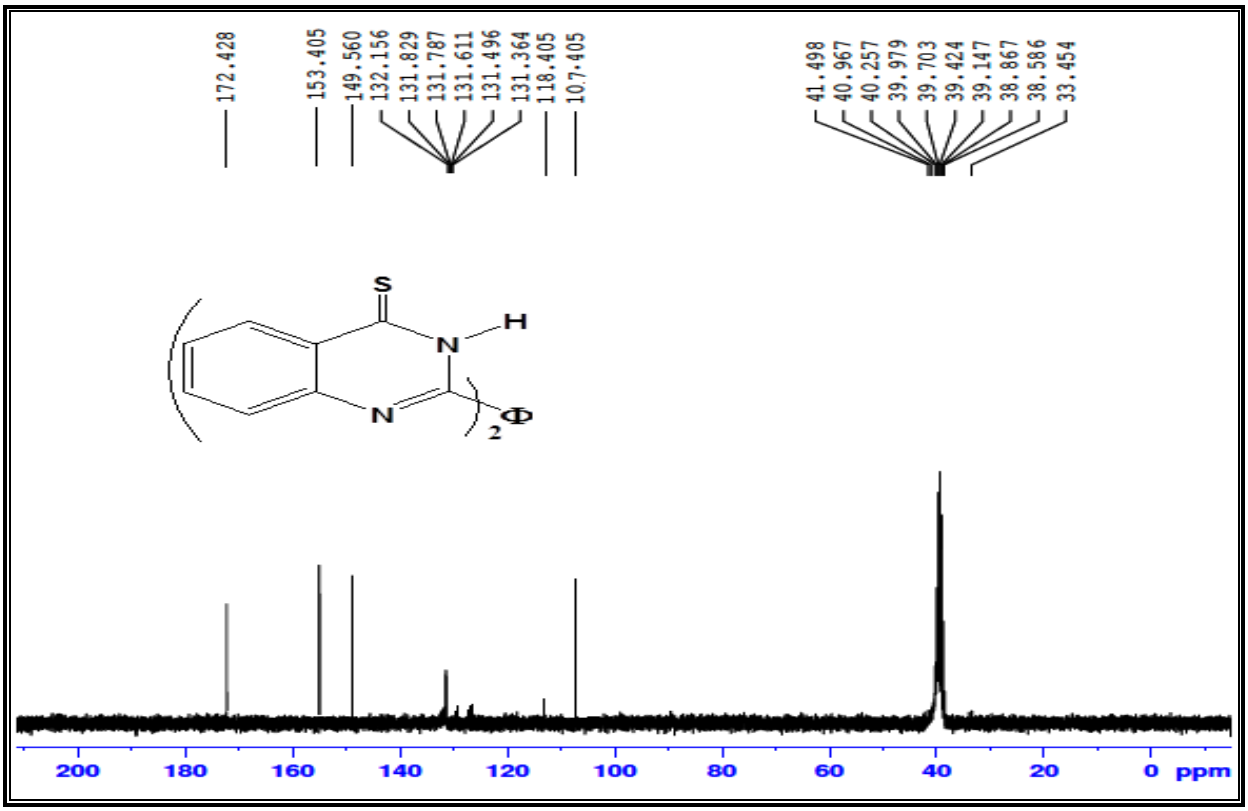


Fig (3-109). ^{13}C-NMR spectrum analysis of compound [XI']

Chapter Four
Antimicrobial Activity

4. Antimicrobial evaluation:

Agar well diffusion method[172-175] was used to detect antimicrobial activity, for the synthesized compounds. Compounds were tested for their antibacterial with Gram –Ve (*Escherichia coli, Klebsiella pneumonia*) and Gram +Ve (*Staphylococcus aurous, Bacillus*), antifungal with (*Aspergillus flavs, Penecillium*).

The antimicrobial activity of synthesized compounds [I-XI'] were compared with standard antibiotics Cephalexin, Amoxicillin, Tetracycline, Lincomycin, Nystatine and Fluconazole, which considered popular for treatment of diseases caused by those six pathogenic species.

4.1. Bacterial and fungal cultures:

Four species of pathogenic Bactria used in this study as tested organisms. These are *Escherichia coli, Klebsiella pneumonia* (Gram negative) and *Staphylococcus aurous, Bacillus* (Gram positive). Fungal used (*Aspergillus flavs, Penecillium*). These bacterial and fungal species were obtained from the Central Environmental Laboratory at Baghdad University.

4.2. Determination of antimicrobial activity:

Fresh bacterial cultures suspension equivalent of 0.5 tube McFarland turbidity standards (10^8 cfu/µl) (Colony forming unit/ml) and incubated at 37°C for 24 - 48hrs, were spread on Muller- Hinton agar plates in case of bacteria and spread on Sabouraud Dextrose agar plates in case of fungi using sterile cotton swabs. Wells of 8mm diameter were cut in solidified agar and filled with 30µl of each concentration.

Concentrations of 4mg/ml (w/v) of each compound were prepared by Dimethyl Sulfoxide (DMSO) solvent. The plates were incubated aerobically at 37°C for 24- 48 hours. Then inhibition zones diameter (mm) around wells were

measured by role. All testes were applied as duplicate. "To ensure that the solvent had no effect on the bacterial and fungi growth, a control was performed with the test medium supplemented with DMSO at the same dilutions as used in the experiments, and it was observed that DMSO had no effect on the microorganisms in the concentrations studied. The results obtained from antimicrobial susceptibility testing are depicted in Table (4-1).

4.3. Drugs and antibiotics sensitivity test:

Antibiotic susceptibility of *(Escherichia coli, Klebsiella pneumonia*), and (*Staphylococcus aurous, Bacillus)*, were determined also by the agar well diffusion method. Antibiotics solutions were prepared by using DMSO. These antibiotics with their respective concentrations are Cephalexin, Amoxicillin, Tetracycline and Lincomycin (4mg/ml) (w/v).

Drugs susceptibility of fungi (*Aspergillus flavs, Penecillium*), were determined also by the agar well diffusion method. Drugs solutions were prepared by using DMSO. These drugs with their respective concentrations are Nystatine and Fluconazole (1.25mg/ml) (w/v).

4.2. Antimicrobial activity:

In the last three decades, quinazolin and quinazolinone derivatives, are considered as an important class of chemical, for synthesis of various pharmacological and biological utilized molecules [176-186].

Quinazolin and quinazolinone, are one of most active types of heterocyclic compounds, which have a broad spectrum of pharmacological and biological activities, such as antibacterial, antifungal, anti-microbial, anti-cancer, anti-tumor, anti-HIV, anti-oxidant, anti-hypertension, anti-inflammatory, anticonvulsant and anti-analgesic.[187-199]

For this purpose, we design to synthesize many of di[3-substituted quinazolin, quinazolin-4-one and quinazolin-4-thion-2-yl] moieties, substituted at (p,p')-positions of bridged azobenzene molecule, via synthesized di(3,1-benzoxazin-4-one) moiety, substituted at (p,p')-position, of bridged azobenene molecule (scheme 3-1).

Many classes of synthesized compounds namely, azobenzen-p,p'-di[3-substituted-4(3H)quinazolinone-2-yl] [Va-Vq], azobenzen-p,p'-di[3,N-substituted-4(3H)quinazolinone-2-yl] [VIA,VIB], azobenzen-p,p'-di[3,O-substituted-4-(3H)quinazolinone-2-yl] [VIIA,VIIB], azobenzen-p,p´-di[3-hydro-4(3H)quinazolinone-2-yl] [VIII], azobenzen-p,p'-di[4-chloro-quinazolinone-2-yl] [IX], azobenzen-p,p'-di[4-substituted-quinazolinone-2-yl] [IXA, IXB], and azobenzen-p,p'-di[3-substituted-4(3H)quinazolinthione-2-yl] [X(A, B, C, D, E, F, G, I, J, K, L, P), XI'], were examined as antibacterial agents against *Staphylococcus aurous, Bacillus* gm (+ ve) bacteria and *Escherichia coli, Klesbsiella pneumonia* gm (- ve) bacteria, in comparison with the effect of Cephalexin, Amoxicillin, Tetracycline and Lincomycin antibiotics. Also these classes of synthesized compound, were examined as antifungal agents against *Aspergillus flavs* and *Peneicllium* fungi, in comparison with the effect of Nystatine and Fluconazole antifungal treatments, results were given in Table (4-1).

According to the results given in Table (4-1), we would deduce the following observation:-

In general most of synthesized compounds [I – XI'], were found to have a broad extended effect as antibacterial agents, against gm (+ ve), *Staphyloccus aureus, Bacillus* bacteria, and gm (- ve), *Escharictia coli, Klesbsiella penumoniae* bacteria. Also most compounds (I – XI'), were found to acts as antifungal agents, against Aspergillus flavs and Peneicllium fungi, as in following details :-

First: All synthesized [IV – XI'] compounds, were found to have a broadening antibacterial effect, against gm (+ ve) *Bacillus* bacteria, specially azobenzen-p,p'-di[3-substituted-4(3H)quinazolinone-2-yl] [V(a, b, h, i), VIIA, VIII], azobenzen-p,p'-di[4-substituted-quinazolin-2-yl] [IXA, IXB], and azobenzen-p,p'-di[3-substituted-4(3H)quinazolin-thione-2-yl] [X(A, P, I, K), XI'], which have very broadening antibacterial effect on *Bacillus* bacteria, in comparison with effect of Cephalexin, Amoxicillin, Tetracycline and Lincomycin antibiotics.

Second: All synthesized [IV – XI'] compounds, were found to have moderate to higher antibacterial effect, against gm (+ ve) *Staphylococcus aurous* bacteria, specially azobenzen-p,p'-di[3,1-benzoaxazin-4-one-2-yl] [IV], azobenzen-p,p'-di[3-substituted-4(3H)quinazolinone-2-yl] [V(a, b, c, d)], and azobenzen-p,p'-di[3-hydro-4(3H)quinazolin-thione-2-yl] [XI'], as well as compound [I, II, III], which gave a broadening antibacterial effect bacteria, in comparison with effect of Cephalexin, Amoxicillin, and Tetracycline antibiotics.

Third: Many of synthesized [IV – XI'] compounds, were found to have good to excellent antibacterial effect against gm (- ve) *Escherichia coli* bacteria, specially azobenzen-p,p'-di[3-substituted-4(3H)-quinazolinone-2-yl] [VIA, VIIB], which showed a broadening antibacterial effect on *Escherichia coli* bacteria, in comparison with effect of Tetracycline and Lincomycin antibiotics.

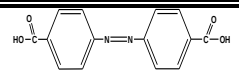
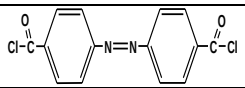
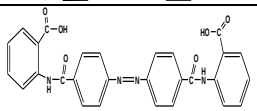
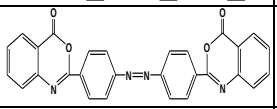
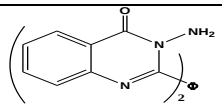
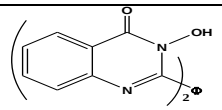
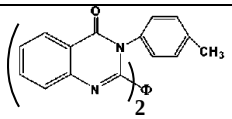
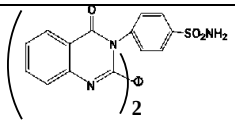
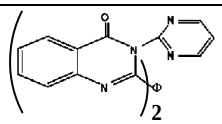
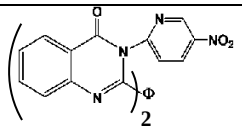
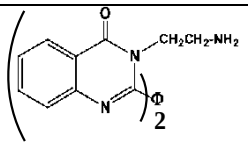
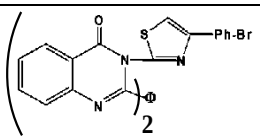
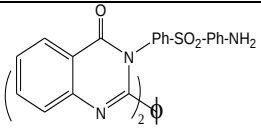
Fourth: Many of synthesized [IV – XI'] compounds, were found to have good to excellent antibacterial effect against gm (-ve) *Klebsiella* bacteria, specially azobenzen-p,p'-di[3-substituted-4(3H)quinazolinone-2-yl] [V(a, d, h, i)], azobenzen-p,p'-di[4-substituted-quinazolinone-2-yl] [IXB], and azobenzen-p,p'-di[3-substituted-4(3H)-quinazolinone-2-yl] [XI, XP, XI'], which showed good antibacterial effect in comparison with effect of Tetracycline antibiotics.

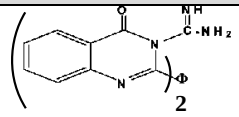
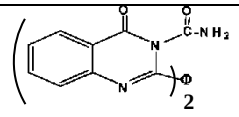
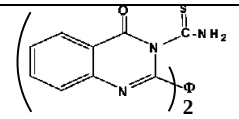
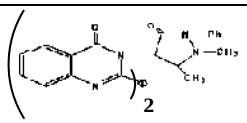
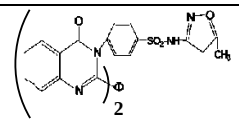
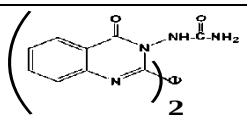
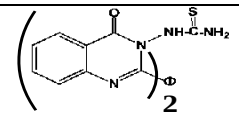
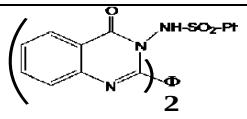
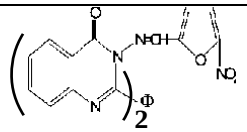
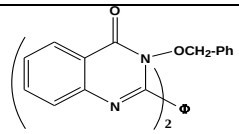
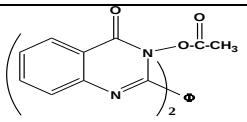
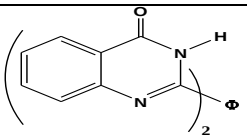
Fifth: Some of synthesized [IV – XI'] compounds, were found to have moderate to excellent antifungal results against *Aspergillus flavs* fungi, specially azobenzen-p,p'-di[3,1-benzoaxzin-4-one-2-yl] [IV], azobenzen-p,p'-di[3-substituted-(3H)quinazolinone-2-yl] [V(a, d, i, l, n, o, p), VIII], azobenzen-p,p -di[4-substituted-quinazolinone-2-yl] [IX, IXA, IXB], and azobenzen-p,p'-di[3-substituted-4(3H)quinazolin-thione-2-yl] [X(A, B, C, D, F, G, J, K, L)], in comparison with the effect of Nystatin and Fluconazole antifungal treatments.

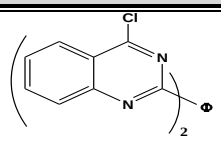
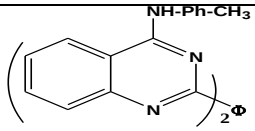
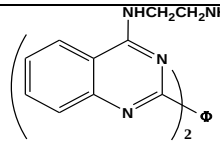
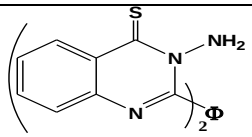
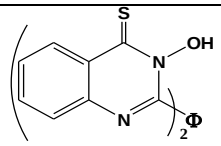
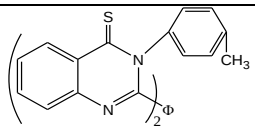
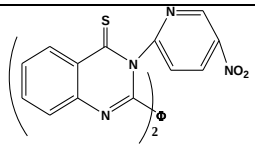
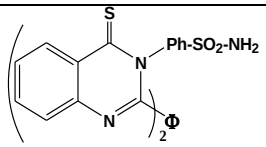
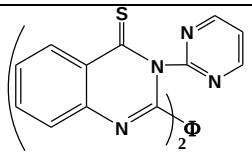
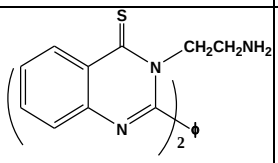
Sixth: Also some of synthesized [IV – XI'] compounds, were found to have moderate to excellent antifungal results, against *Penecillium* fungi, specially azobenzen-p,p -di[3-subsitituted-4(3H)quinazolinone-2-yl] [V(c, d, h, i), VIII], azobenzen-p,p'-di[4-substituted-(3H)quinazolinone-2-yl] [IX], and azobenzen-p,p'-di[3-substituted-4(3H)quinazolin-thione-2-yl] [X(G, J, K, L)], in comparison with the effect of Nystatin and Fluconazole antifungal treatments.

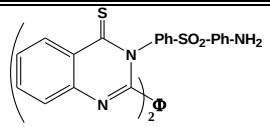
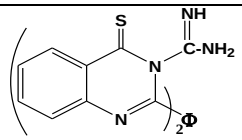
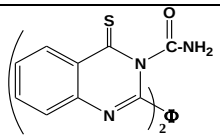
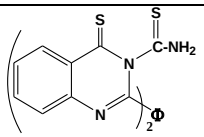
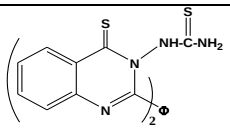
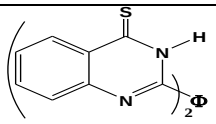
Seventh: Synthesized compounds, azobenzen-p,p'-dicarboxylic acid[I], azobenzen-p,p'-diacid chloride [II], and azobenzen-p,p'-[(dibenzoic acid-2-yl)-dicarbxamide] [III], were found to give moderate to excellent gm(+ve, and –ve) antibacterial results, against *Staphylococcus aurous, Bacillus, and Escherichia coli, Kelebsiella pneumonia* bacteria respectively, in comparison to the effect of Cephalexin, Amoxicillin, Tetracycline and Lincomycin antibiotics. Also they found to give good results against *Aspergillus flavs* and *Penecillium* fungi, in comparison with the effect of Fluconazole antifungal treatments.

Table (4-1): Antimicrobial activity of compounds [I – IX']

Comp No.	Structure	Mean of Inhibition zone Diameter (mm)					
		Staphylococcus aurous	*Bacillus*	*Escherichia coli*	*Klebsiella pneumonia*	*Aspergillus flavs*	*Peneicllium*
I		18	9	16	10	8	10
II		24	-	14	12	11	12
III		16	9	18	8	13	12
IV		22	-	16	10	13	10
Va		20	17	8	12	12	-
Vb		23	30	8	10	11	13
Vc		17	-	-	11	8	16
Vd		20	9	8	12	11	25
Ve		8	-	8	8	10	12
Vf		9	13	8	8	9	12
Vg		8	8	8	8	-	-
Vh		16	15	15	15	11	28
Vi		**8**	**15**	**8**	**15**	**15**	**16**

Comp No.	Structure	Mean of Inhibition zone Diameter (mm)					
		Staphylococcus aurous	Bacillus	Escherichia coli	Klebsiella pneumonia	Aspergillus flavs	Peneicillium
Vj		**8**	**11**	**10**	**10**	-	-
Vk		**8**	**8**	-	**8**	-	-
Vl		8	13	10	9	12	9
Vm		8	15	9	8	-	-
Vn		8	8	8	9	14	9
Vo		8	14	8	8	12	-
Vp		8	11	8	9	12	-
VIA		15	14	14	10	10	12
VIB		8	13	31	8	11	10
VIIA		9	17	15	10	11	14
VIIB		15	-	23	8	9	10
VIII		20	18	14	11	20	17

Comp No.	Structure	Mean of Inhibition zone Diameter (mm)					
		Staphylococcus aurous	Bacillus	Escherichia coli	Klebsiella pneumonia	Aspergillus flavs	Peneicllium
IX		10	8	8	9	13	17
IXA		12	16	12	11	14	10
IXB		12	18	12	12	13	10
XA		10	20	10	10	13	10
XB		9	10	18	8	14	9
XC		10	12	10	8	15	8
XD		10	9	13	8	14	8
XE		12	9	12	8	10	9
XF		15	13	8	-	13	12
XG		15	9	8	-	12	16

Comp No.	Structure	Mean of Inhibition zone Diameter (mm)					
		Staphylococcus aureus	Bacillus	Escherichia coli	Klebsiella pneumonia	Aspergillus flavs	Peneicllium
XI		15	13	8	-	11	13
XJ		15	-	16	11	12	16
XK		12	12	10	10	21	15
XL		11	10	10	12	14	15
XP		10	10	9	12	11	-
XI'		17	13	8	14	10	-

Drugs	**Mean of Inhibition zone Diameter (mm)**					
	Staphylococcus aureus	***bacillus***	***Escherichia coli***	***Klebsiella pneumonia***	***Aspergillus flavs***	***perecillium***
Cephalexin	18	5	-	-	-	-
Amoxicillin	12	7	-	-	-	-
Tetracycline	17	-	30	12	-	-
Lincomycine	-	-	22	20	-	-
Nystatine	-	-	-	-	17	20
Fluconazole	-	-	-	-	12	15
Dimethyl sulphoxide	0.0	0.0	0.0	0.0	0.0	0.0

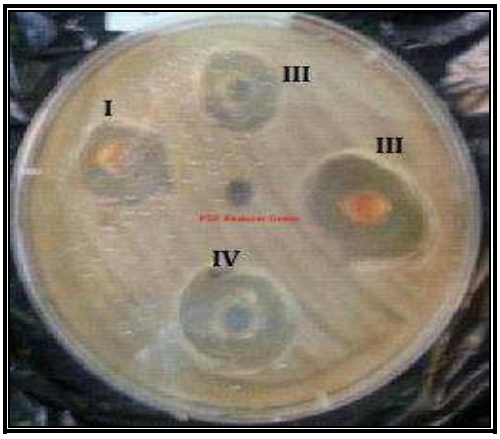


Figure (4-1): The antibacterial activity of compounds [I,II,III and IV] against *Staphylococcus aurous*

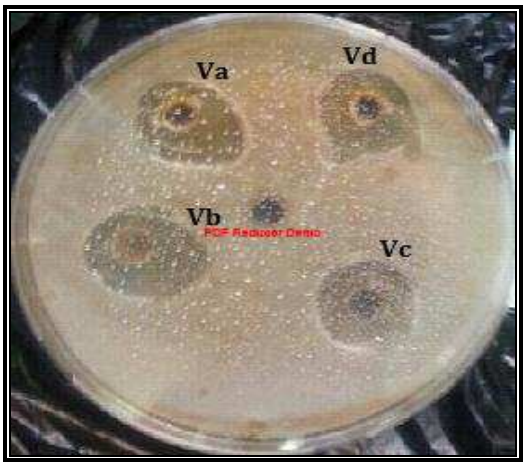


Figure (4-2): The antibacterial activity of compounds [Va, Vb, Vc and Vd] against *Staphylococcus aurous*

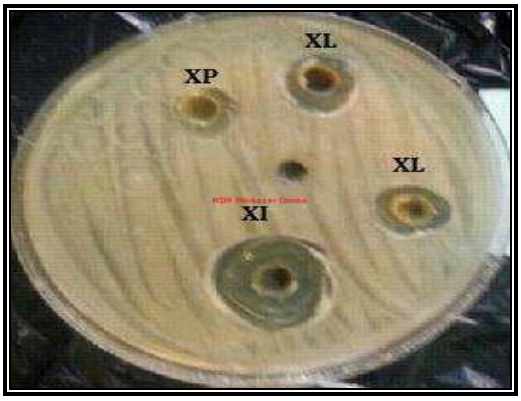


Figure (4-3): The antibacterial activity of compounds [XP, XL, XK and XI] against *Staphylococcus aureus*

Figure (4-4): The antibacterial activity of compounds [Va, Vb, Vc, and Vd] against *Bacillus*

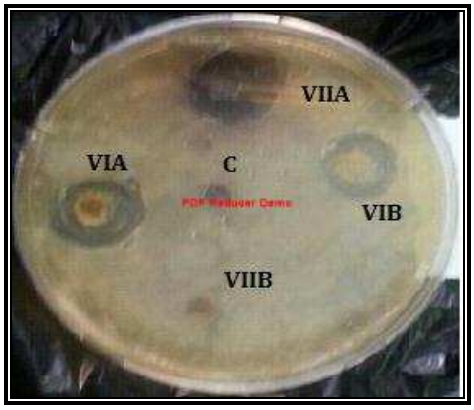


Figure (4-5): The antibacterial activity of compounds [VI(A,B) and VII(A,B)] against *Bacillus*

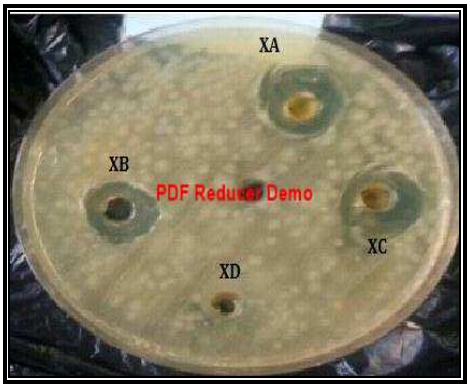


Figure (4-6): The antibacterial activity of compounds [X(A,B,C, and D] against *Bacillus*

Figure (4-7): The antibacterial activity of compounds [VIII, XI and XI] against *Bacillus*

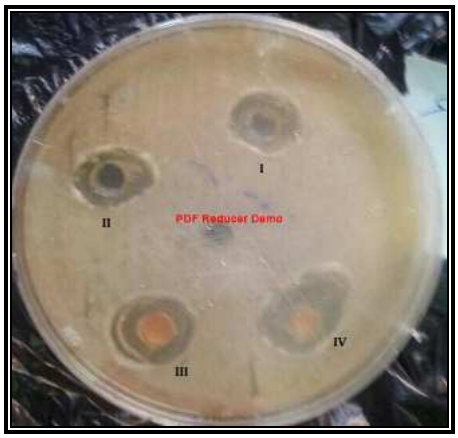


Figure (4-8): The antibacterial activity of compounds [I, II,III, and IV] against *Escherichia coli*

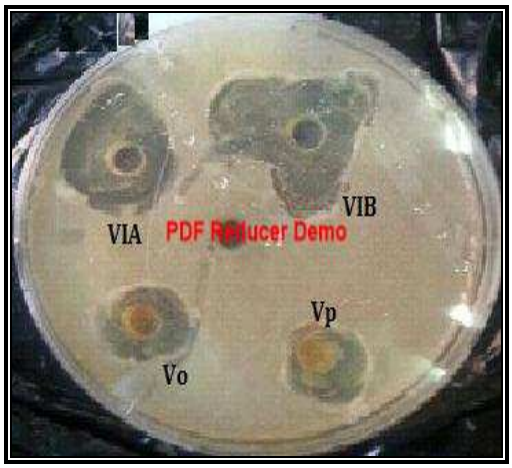


Figure (4-9): The antibacterial activity of compounds [VIA, VIB, Vo and Vp] against *Escherichia coli*

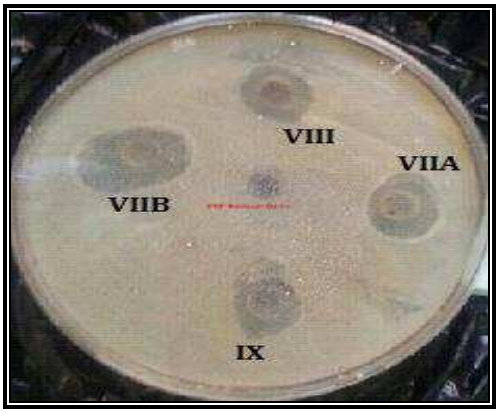


Figure (4-10): The antibacterial activity of compounds [VIII, VIIA,VIIB and IX] against *Escherichia coli*

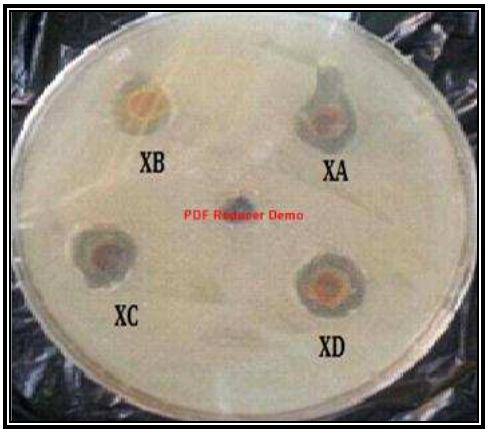


Figure (4-11): The antibacterial activity of compounds [XA, XB, XC and XD] against *Escherichia coli*

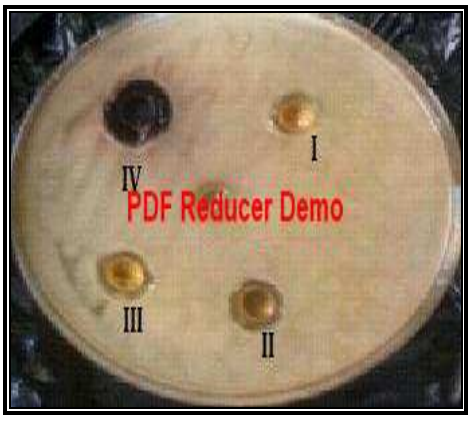


Figure (4-12): The antibacterial activity of compounds [I, II, III and IV] against *Klebsiella pneumonia*

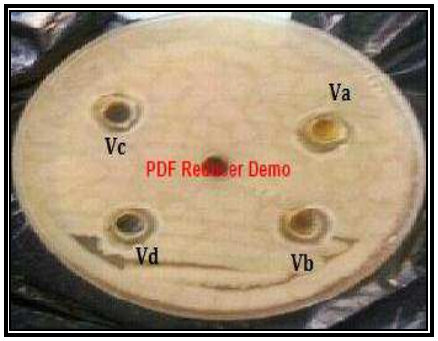


Figure (4-13): The antibacterial activity of compounds [Va, Vb, Vc and Vd] against *Klebsiella pneumonia*

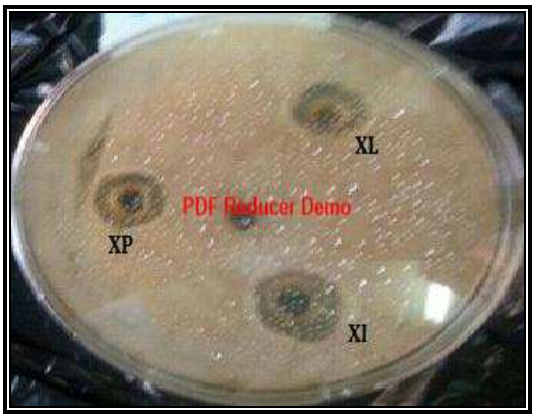


Figure (4-14): The antibacterial activity of compounds [XL, XP and XI´] against *Klebsiella pneumonia*

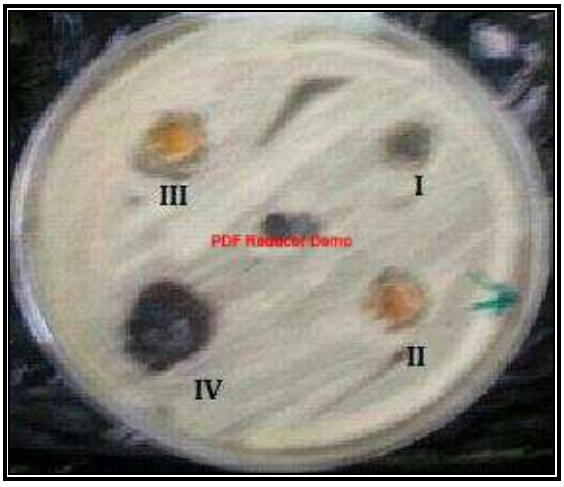


Figure (4-15): The antifungal activity of compounds [I, II, III and IV] against *Asergillus flavs*

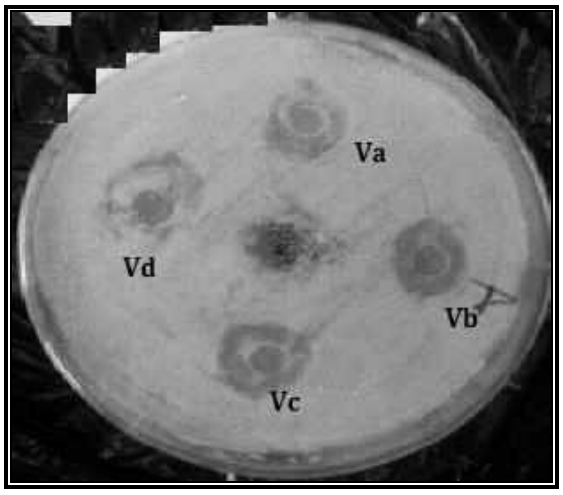


Figure (4-16): The antifungal activity of compounds [Va, Vb, Vc and Vd] against *Asergillus flavs*

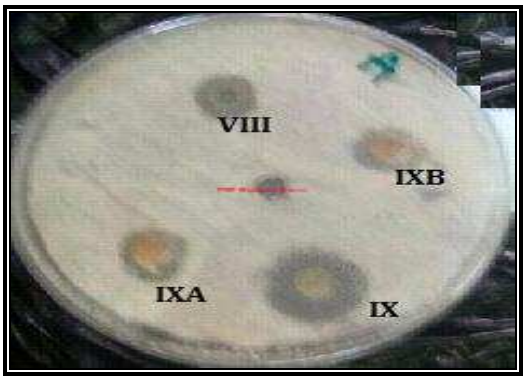


Figure (4-17): The antifungal activity of compounds [VIII, IX, IXA and IXB] against *Asergillus flavs*

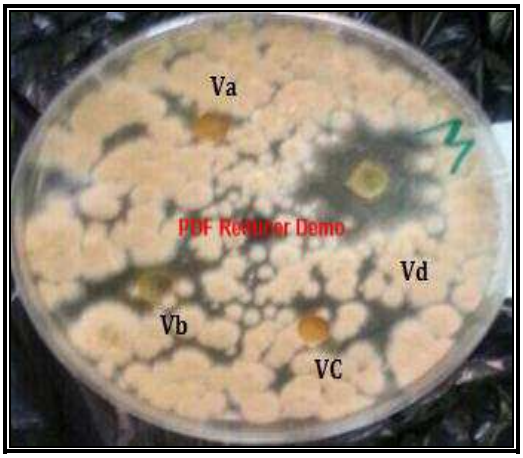


Figure (4-18): The antifungal activity of compounds [Va, Vb, Vc and Vd] against *Peneicillium*

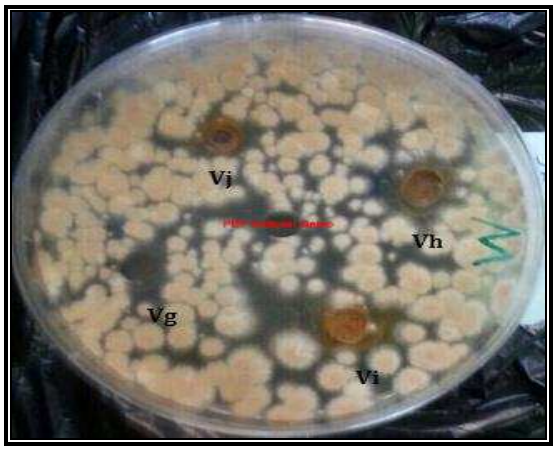


Figure (4-19): The antifungal activity of compounds [Vh, Vi, Vg and Vj] against *Peneicillium*

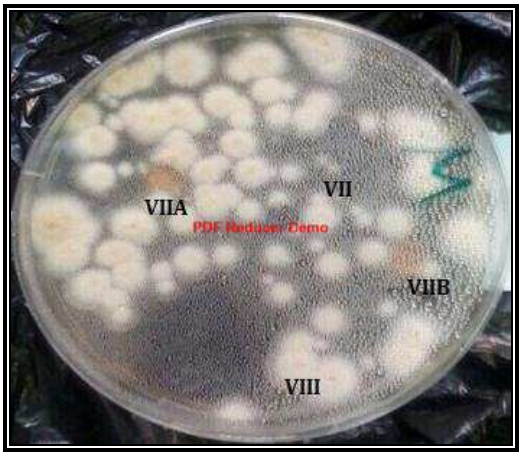


Figure (4-20): The antifungal activity of compounds [VII, VIIA, VIIB and VIII] against *Peneicillium*

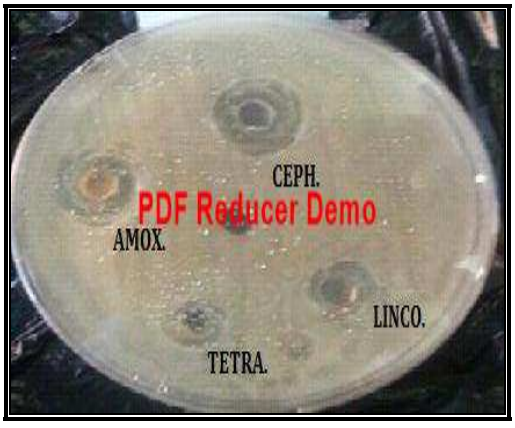


Figure (4-21): The antibacterial activity of drugs [cephalexin, amoxicillin, tetracycline and lincomycine] against *Staphylococcus aurous*

Figure (4-22): The antibacterial activity of drugs [cephalexin, amoxicillin, tetracycline and lincomycine] against *Bacillus*

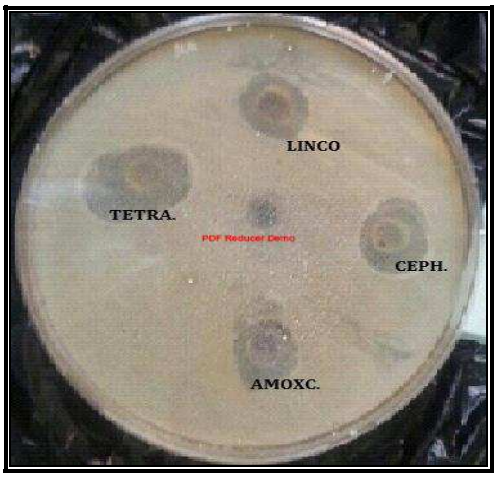


Figure (4-23): The antibacterial activity of drugs [cephalexin, amoxicillin, tetracycline and lincomycine] against *Escherichia coli*

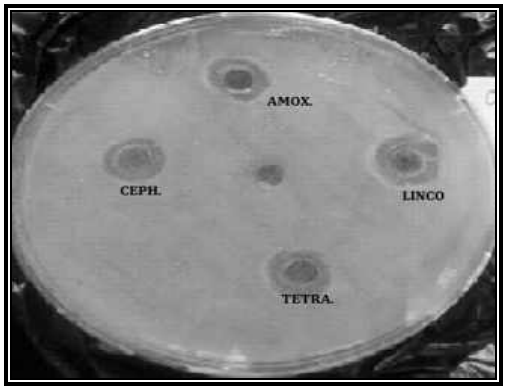


Figure (4-24): The antibacterial activity of drugs [Cephalexin, Amoxicillin, Tetracyclin and Lincomycine] against *Klebsiella pneumonia*

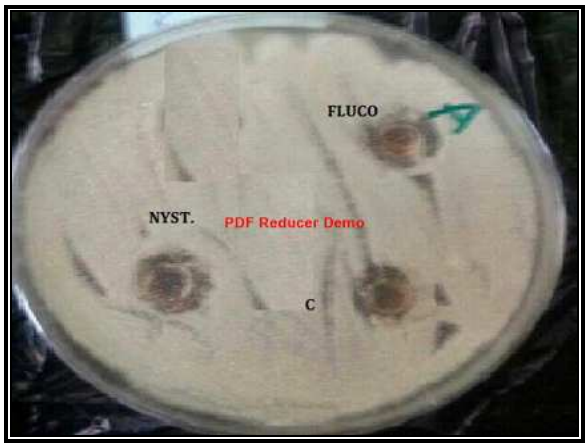


Figure (4-25): The antifungal activity of drugs

[Nystatine and Fluconazole] against *AsperglLius flavs*

Figure (4-26): The antifungal activity of drugs

[Nystatine and Fluconazole] against *Peneicillium*

Conclusions:

Because of the importance of quinazolin, quinazolinone and quinazolin-thion and its derivatives in the field of antimicrobial studies.

I- We design to synthesize many compounds containing di[(3-substituted) quinazolin, quinzolinone and quinazolin-thion-2-yl] moieties, substituted at (p,p')-position of bridged azobenzene molecule derivatives.

II- Antimicrobial examination study of those synthesized quinazolin, quinazolinone and quinazolinthion derivatives, showed good to extended effect as antibacterial and antifungal, much more better than those common pharmaceutical antibiotics Cephalexin, Amoxicillin, Tetracycline, Lincomycine and antifungal Nystatine, Fluconazole treatments, on (Gram –Ve) (Escherichia coli, Klebsiella pneumonia), and (Staphylococcus aurous, Bacillus) bacteria, (Gram +Ve) bacteria and (Aspergillums flavs, Penecillium) fungi.

Future Works:

A- From all synthesized compounds can be:

1- Synthesis and characterization of new of quinazolin derivatives.

2- Synthesis and characterization of new of quinazolinone derivatives.

3- Synthesis and characterization of new of quinazolin-thion derivatives.

B- From all synthesized compounds can be:

1-Synthesis and characterization of new ligands and its complexes for some of these compounds.

2- Synthesis and characterization of new polymers by reaction these compounds with commercial polymers.

3- Study examined microbial activity of these compounds.

References

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2. **Nesterova, N.A., Kovalenko, S.I., Karpenkos, O.V., and Belenichev, Ukr. Farmatsevtichnii Zhurnal (kiev), (2004),** "Synthesis of Some New 4-(3H)-quinazoline Analogs as Potential Antioxidant Agents" 1, 5.
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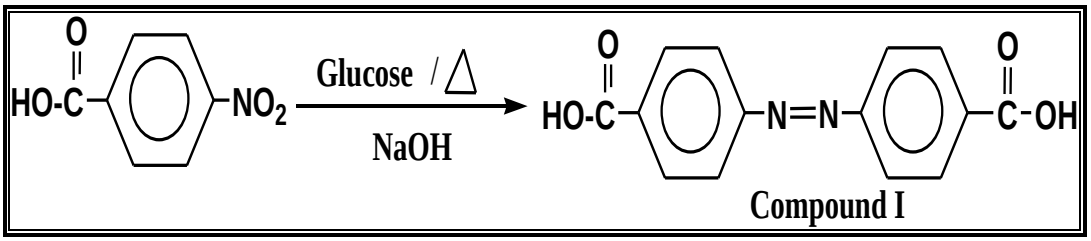
الخلاصة

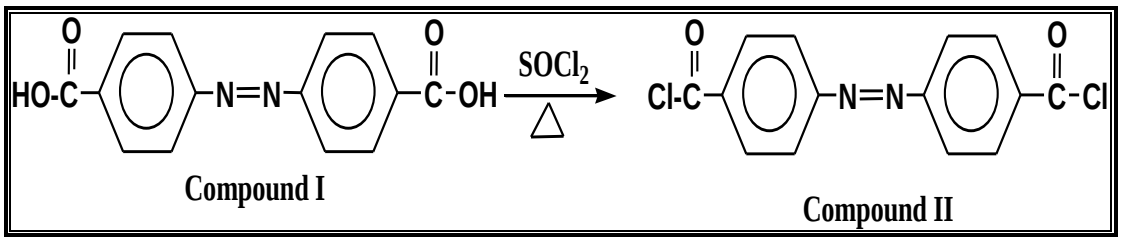
في السنوات الأخيرة العديد من الأبحاث في مجال مشتقات البنزوكسازين، الكوينازولين، الكوينازولينون والكوينازولين ثايون، نالت الاهتمام نظرا لفعاليتها البيولوجية واهميتها الدوائية. في ضوء هذه الاسباب قمنا بتصميم لتخليق العديد من المركبات التي تحتوي وحدات ثنائي (3- معوض) البنزوكسازين، الكوينازولين، الكوينازولينون والكوينازولين ثايون-2 يل معوضه بالموقع بارا،بارا بجزئية الازوبنزين الجسرية، عن طريق تخليق وحدة ثنائي (1,3- بنزوكسازين-4-اون-2يل) معوضه بالوقع بارا،بارا بجزئية الازوبنزين الجسرية. وفقا لمسارات التخليق التالية:-

1- تخليق الازوبنزين-بارا،بارا-ثنائي حامض كربوكسيل [I]:



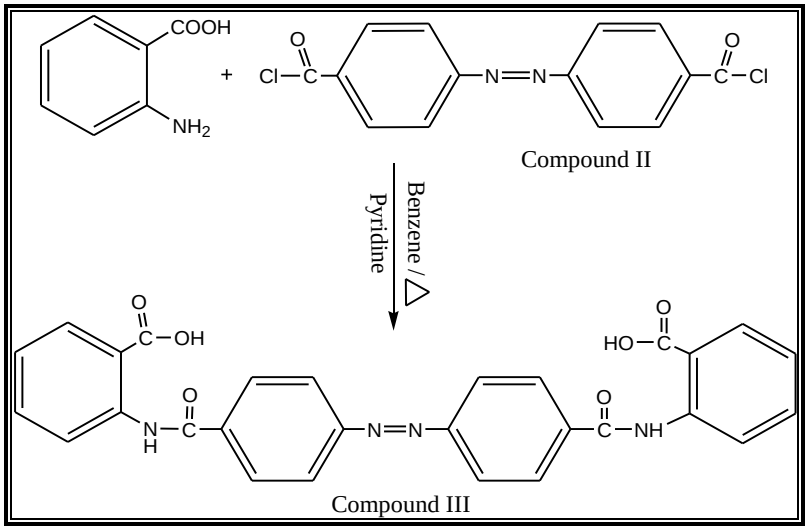
تم تحضير هذا المركب في وسط قاعدي، بتفاعل اختزال - تكثيف حامض البارا- نايترو بنزويك وبوجود الكلوكوز، والذي شخص بالتحليل الدقيق للعناصر وطيف الأشعة تحت الحمراء.

2- تخليق الازوبنزين بارا،بارا- ثنائي كلوريد حامض البنزويك [II]:



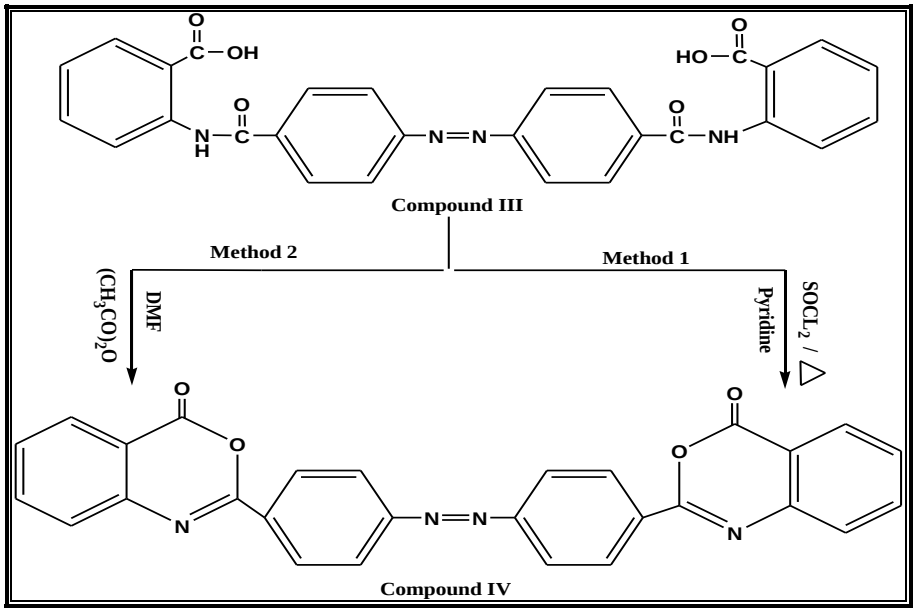
عند معاملة المركب [I] مع زيادة من كلوريد الثايونيل بوجود البريدين نحصل على المركب [II] والذي شخص بواسطة التحليل الدقيق للعناصر وطيف الاشعة تحت الحمراء وطيف الرنين النووي المغناطسي (البروتوني والكربوني) وطيف الكتلة.

3- تخليــق الازوبنــزين-بــارا،بــارا-(ثنــائي حــامض البنزويــك-2-يــل) ثنــائي كاربوكسامايد [III]:



عند تكثيف الازوبنزين-بارا،بارا-ثنائي كلوريد حامض كاربوكسيل [II] مع حامض الانثرانلك بنسب مولية (2:1) بوجود البيريدين نحصل على الازوبنزين - بارا،بارا- ثنائي[(حامض البنزويك-2-يل) ثنائي كاربوكسامايد] [III]، والذي شخص بواسطة التحليل الدقيق للعناصر وطيف الاشعة تحت الحمراء وطيف الرنين النووي المغناطسي (البروتوني والكربوني) وطيف الكتلة.

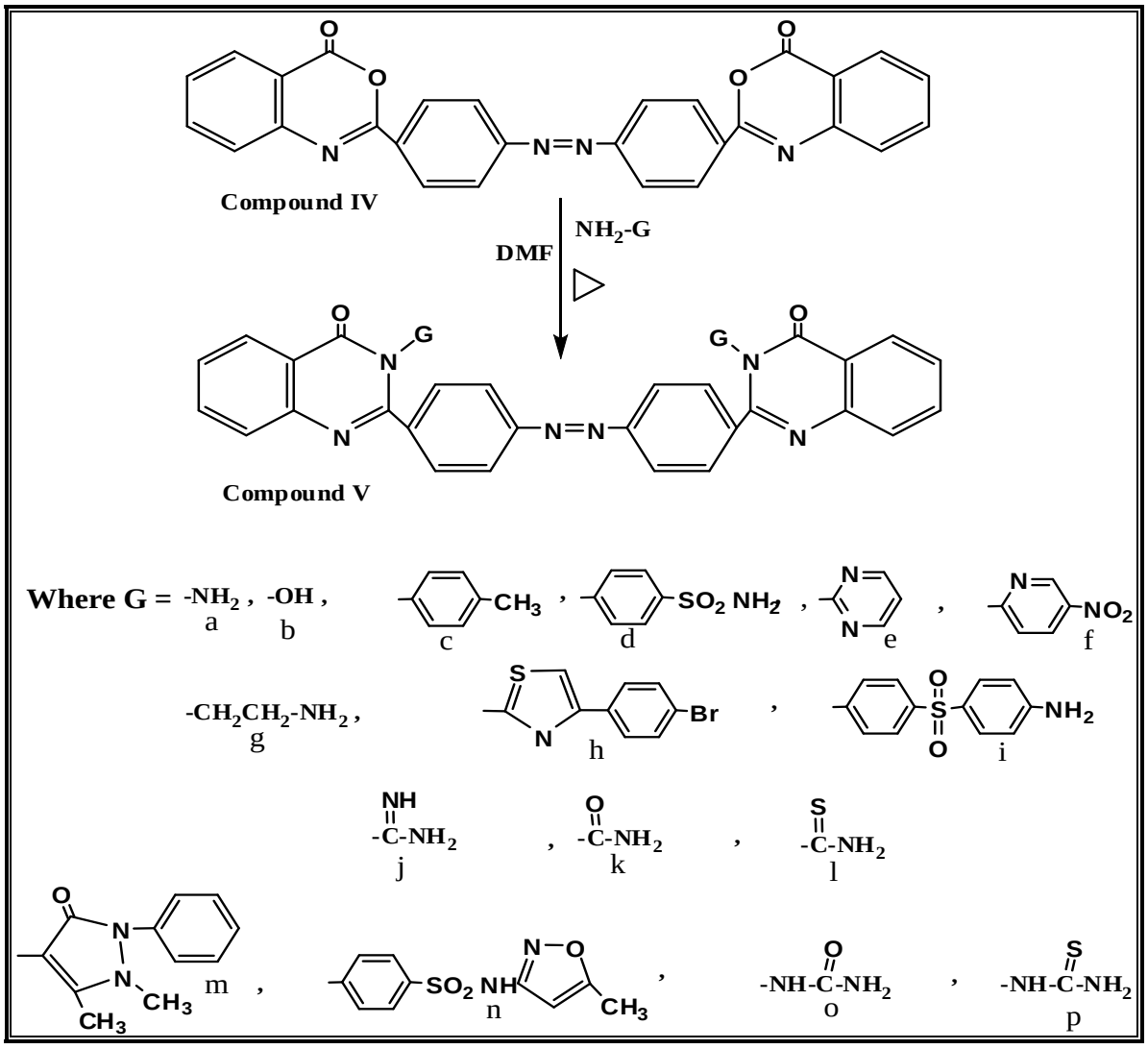
4. تخليق الازوبنزين-بارا،بارا-ثنائي(1,3-بنزوكسازين-4-ون-2-يل) [IV]:



خلق هذا المركب بطريقتين، اما عن طريق تسخين الازوبنزين-بارا،بارا-(ثنائي حامض البنزوك-2-يل)ثنائي كاربوكسامايد [III]، مع زيادة من كلوريد الثايونيل بوجود البريدين، او مع زيادة من انهدريد الخليك بوجود ثنائي مثيل فورماميد، والذي شخص بواسطة درجة الانصهار، ومزج الناتجين معا المحضران بالطريقتين وقياس درجة الانصهار لهما، شخص المركب بواسطة التحليل الدقيق للعناصر وطيف الاشعة تحت الحمراء وطيف الرنين النووي المغناطسي (البروتوني والكربوني) وطيف الكتلة.

*** السلسلة الاولى:**

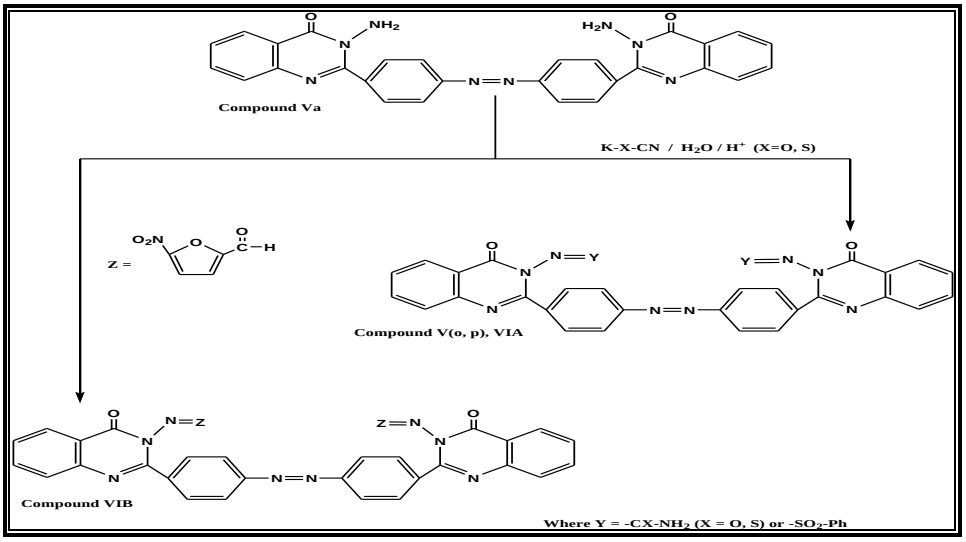
5- تخليق الازوبنزين-بارا،بارا-ثنائي[(3-معوض-4(H3) كوينازولينون-2-يل)] [V]:



تم تخليق هذه المركبات عن طريق تسخين الازوبنزين-بارا،بارا-ثنائي(1,3-بنزوكسازين-4-ون-2-يل) [VI]، مع وحدات الامين بنسب مولية (2:1)، مثل الهيدرازين المائي، الهيدروكسيل امين، الكواندين، اليوريا، ثايويوريا، سيميكاربازيد، ثايوسيميكاربازيد والامينات الاليفاتية. مركبات الازوبنزين-بارا،بارا-ثنائي[(3-معوض)-4(H3) كوينازولينون-2-يل] [V(a-p)] ، شخصت بتحليل طيف الاشعة تحت الحمراء، والعديد منها شخص بواسطة طيف الرنين النووي المغناطيسي البروتوني والكربوني، والبعض منها بواسطة طيف الكتلة.

***السلسلة الثانية:**

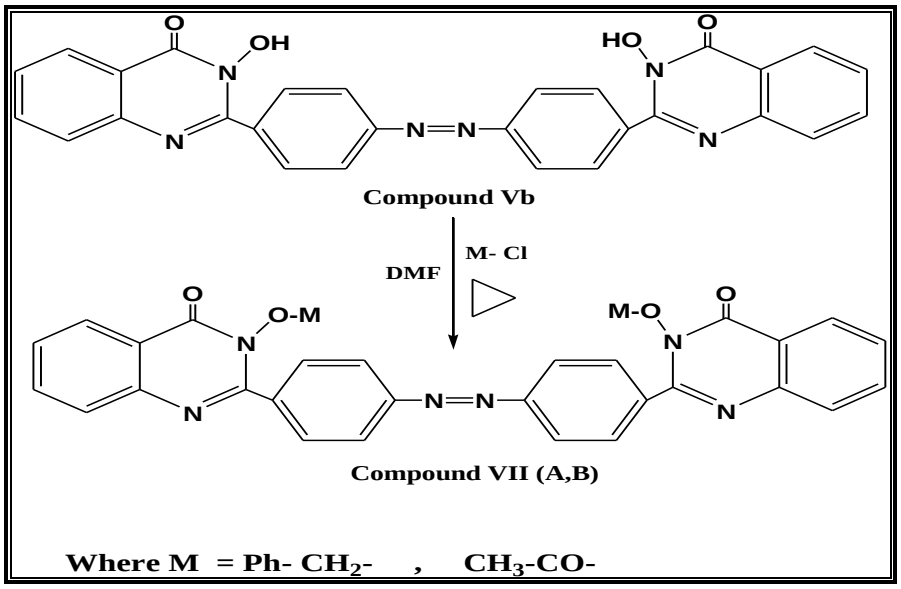
6-تخليق الازوبنزين-بارا،بارا-ثنائي [(3،N-معوض-4-(H3)كوينازولينون-2-يل)] [V(o, p), VIA, VIB]



عند تكثيف الازوبنزين-بارا،بارا-ثنائي[(3-امينو)-4(H3) كيونازولين-2-يل] [Va] ، مع سيانات البوتاسيوم او الثايوسيانات، كلوريد بنزين سلفونيل و4-نايترو فورفورال بنسب مولية (1:2) لتعطي المركبات [V(o, p), VIA, VIB] على التوالي. شخصت المركبات[V(o, p)] بواسطة درجة الانصهار، ودرجة الانصهار المختلطة، مع المركبات المحضرة بتكثيف الازوبنزين-بارا،بارا-ثنائي(1,3-بنزوكسزين-4-ون-2-يل) [VI]، مع السميكاربازايد والثايوسميكاربازايد بنسب مولية (1:2) على التوالي، وتطابق اطياف الأشعة تحت الحمراء لهذه المركبات المحضرة بالطريقتين، بينما شخصت المركبات[VIA, VIB] بطيف الاشعة تحت الحمراء، طيف الرنين النووي المغناطسي البروتوني والكربوني، وطيف الكتلة.

* السلسلة الثالثة:

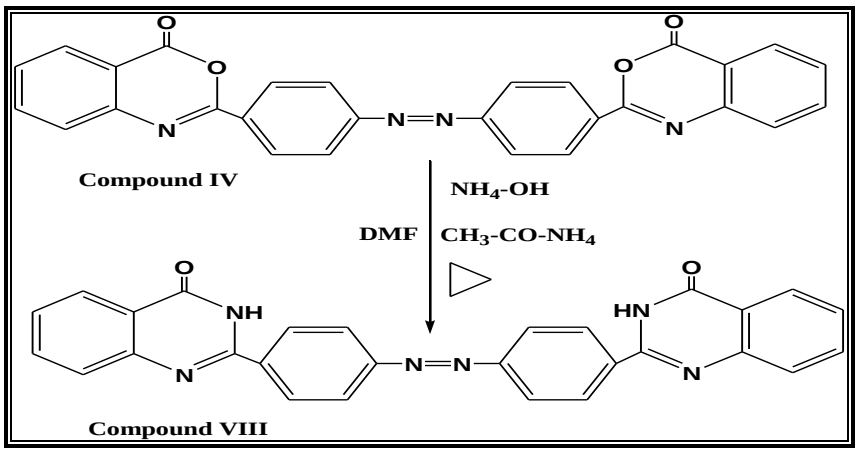
7- تخليـق الازوبنــزين-بــارا،بــارا-ثنــائي[(3،O-معـوض-4(H3) كوينــازولينون-2-يــل)] [VIIA,VIIB]:



عند تكثيف الازوبنزين-بارا،بارا-ثنائي(3-هيدروكسي-4(H3)كوينـازولينون-2-يل) [Vb]، مع كلوريـد البنزيـل او كلوريـد الاسـيل بنسـب موليـة (2:1)، تعطـي المركبـات [VIIA,VIIB] علـى التـوالي. والتـي شخصـت بطيـف الأشـعة تحـت الحمـراء، وطيـف الـرنين النـووي المغناطيسـي البروتوني والكربوني.

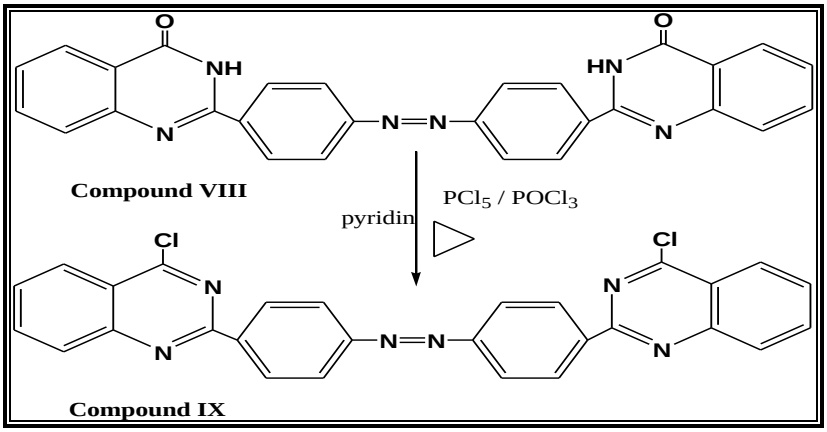
*السلسلة الرابعة:

8-تخليق الازوبنزين-بارا،بارا-ثنائي[(3-هايدرو-4-كوينازولينون-2-يل)] [VIII]



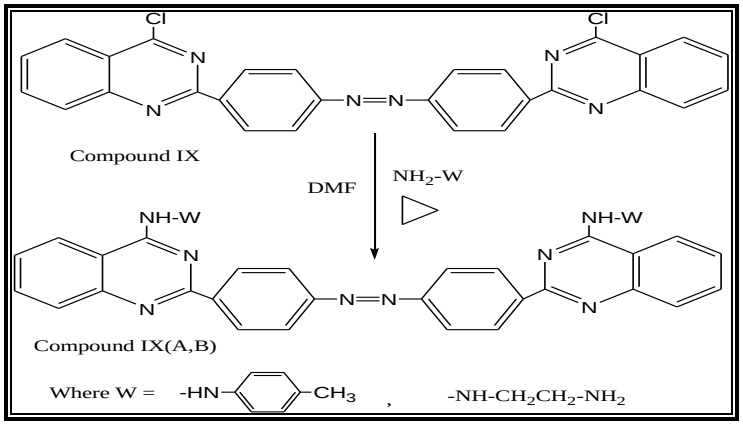
عند تكثيف الازوبنزين-بارا،بارا-ثنائي(1,3-بنزوكسازين-4-ون-2-يل) [VI] ، مع زيادة من الامونيا واسيتات الامونيا في مذيب ثنائي مثيل فورماميد، بنسب مولية (2:1)، تعطي المركب الازوبنزين-بارا،بارا-ثنائي[3-هايدرو-4(H3)-كوينازولينون-2-يل] [VIII]، والذي شخص بطيف الأشعة تحت الحمراء، طيف الرنين النووي المغناطيسي البروتوني والكربوني وطيف الكتلة.

9- تخليق الازوبنزين-بارا،بارا-ثنائي[(4-كلورو-كوينازولين-2-يل)] [IX]:



عند تكثيف الازوبنزين-بارا،بارا-ثنائي(3-هايدرو-4(H3)-كوينازولينون-2-يل) [VIII]، مع خماسي كلوريد الفسفور بوجود ثلاثي كلوريد اوكسي الفسفور، بنسب مولية (2:1)، نحصل على المركب الازوبنزين-بارا،بارا-ثنائي[4-كلورو-كوينازولين-2يل] [IX]، والذي شخص بطيف الأشعة تحت الحمراء، طيف الر نين النووي المغناطيسي البروتوني والكربوني، وطيف الكتلة.

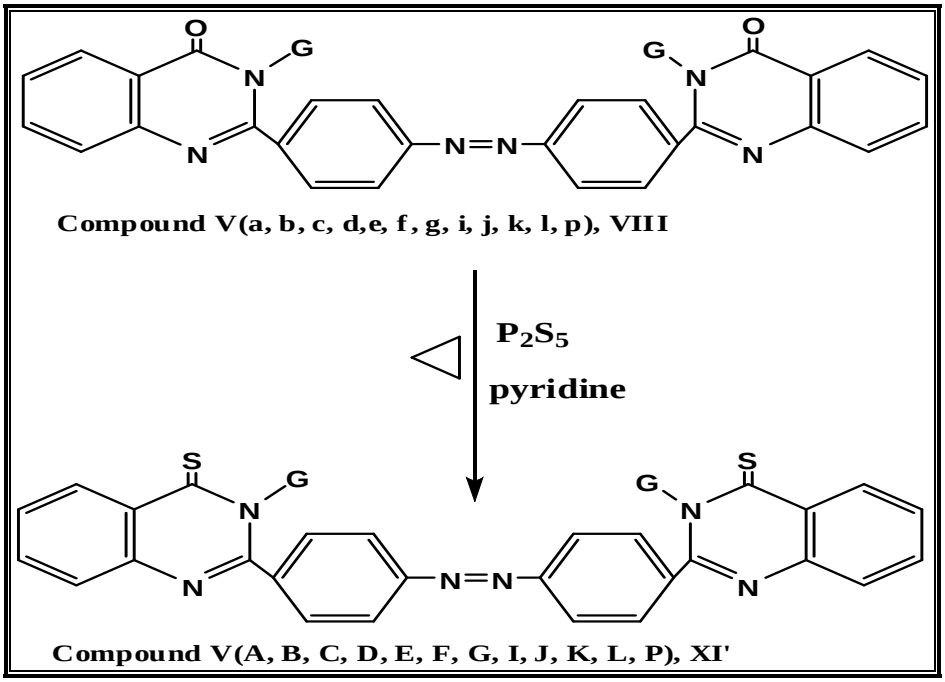
10- تخليق الازوبنزين-بارا،بارا-ثنائي[(4-معوض-كوينازولين-2يل)] [IX(A, B)]:



ان استبدال الكلورين في الازوبنزين-بارا،بارا-ثنائي(4-كلورو-كوينازولين-2-يل) [IX] مع بارا-تولودين او الاثلين ثنائي الامين بنسب مولية (2:1)، نحصل على المركبات الازوبنزين-بارا،بارا-ثنائي(4،-تولودينو-كيونازولين--2يل] [IXA] و الازوبنزين-بارا،بارا-ثنائي(4،ن-امينو اثيل امين-كوينازولين-2-يل] [IXB]، واللذان شخصا بواسطة طيف الأشعة تحت الحمراء، وطيف الرنين النووي المغناطيسي البروتوني والكربوني.

***السلسلة الخامسة:**

11- تخليق الازوبنزين-بارا،بارا-ثنائي[(3-معوض-4(H3)كوينازولين ثايون-2-يل)´IX , P,L, I, A-G)X]:



عند تسخين بعض مركبات الازوبنزين-بارا،بارا-ثنائي[3-معوض-4(H3) كوينازولينون-2-يل] [V(a-g), i-l, p), VIII]، مع زيادة من خماسي كبريتيد الفسفور بوجود البريدين، نحصل على مركبات الازوبنزين-بارا،بارا-ثنائي(3-معوض-4(H3)كوينازولين-ثايون-2-يل) ,I-L, A-G)X] [´XI ,P), هذه المركبات شخصت بطيف الأشعة تحت الحمراء، وقسم منها شخص بطيف الرنين النووي المغناطيسي البروتوني والكربوني، وقسم اخر [X(A, B, E, F)] شخص بطيف الكتلة.

دراسة المضادات الجرثومية:

بالنظر إلى أهمية مشتقات الكوينازولين في المجالين الدوائي والبيولوجي، فإن العديد من أنواع المركبات المحضرة ذات وحدات ثنائي (3- و 4-معوض) كوينازولين، كوينازولينون، كوينازولين ثايون-2-يل)، معوض بالموقع بارا،بارا-بجسر الازوبنزين. تم اختبار سلوك المضاد الجرثومي لهذه المركبات ضد غرام(+) من بكتريا المكورات العنقودية الذهبية، العصيات. وضد غرام(-) من بكتريا القولون والالتهاب الرئوي. واختبرت هذه المركبات ايضا ضد نوعين من الفطريات اسبرجليس فلافس والبنسلنيوم، بالمقارنة مع بعض المضادات الحيوية المعروفه كالسيفالكسين، الاموكسيسيلين،التتراسايكلين والليفوكومايسين. والمركبات الدوائية المضادة للفطريات كالنيستاتين والفلاكونازول على التوالي. وبصفة عامة وجد ان اغلب المركبات المخلقة لها تأثير واسع كمضاد جرثومي ضد غرام (+) بكتريا المكورات العنقودية والعصيات. وضد غرام (-) من بكتريا القولون والالتهاب الرئوي. وكذلك ضد انواع الفطريات الاسبرجلس والبنسيلينوم، وحسب التفاصيل التالية:

* **اولا:** المركبات من انواع الازوبنزين-بارا،بارا-ثنائي(3-معوض-4(H3) كوينازولينون-2-يل) [V(a,b,h,i), VIIA,VIIB] ، الازوبنزين-بارا،بارا-ثنائي(4-معوض-(H3)كوينازولين-2-يل)، الازوبنزين-بارا،بارا-ثنائي(3-معوض-4(H3) كوينازولين ثايون-2-يل)، لها تأثير واسع كمضاد جرثومي ضد غرام(+) من بكتريا العصيات بالمقارنة مع تأثير المضاد الحيوي كالسيفاكسيلين، الاموكسيسلين، والتتراسايكلين.

* **ثانيا:** المركبات من انواع الازوبنزين-بارا،بارا-ثنائي(1,3-بنزوكسازين-4-ون-2-يل) [IV]، الازوبنزين-بارا،بارا-ثنائي(3-معوض-4(H3) كوينازولينون-2-يل) [V(a,b ,c,d)]، و الازوبنزين-بارا،بارا-ثنائي(3-معوض-4(H3) كوينازولين ثايون-2-يل) [XI]، لها تأثير واسع كمضاد جرثومي ضد غرام(+) من بكتريا المكورات بالمقارنة مع تأثير المضاد الحيوي كالسيفاكسيلين، الاموكسيسلين، والتتراسايكلين.

* **ثالثا:** المركبات من انواع الازوبنزين-بارا،بارا-ثنائي(3-معوض-4(H3) كوينازولينون-2-يل) [VIA, VIIB]، لها تأثير واسع كمضاد جرثومي ضد بكتريا القالون بالمقارنة مع تأثير المضاد الحيوي التتراسايكلين والليفوكومايسين.

* **رابعا:** المركبات من انواع الازوبنزين-بارا،بارا-ثنائي(3-معوض-4(H3) كوينازولينون-2-يل) [V(a,d,h,i)], الازوبنزين-بارا،بارا-ثنائي(4-معوض-(H3) كوينازولينون-2-يل) [IXA,IXB]، والازوبنزين-بارا،بارا-ثنائي(3-معوض-4(H3) كوينازولين ثايون-2-يل) [X(I,P), XI´]، لها تأثير جيد كمضاد جرثومي ضد غرام(-) من بكتريا الالتهاب الرئوي بالمقارنة مع تأثير المضاد الحيوي التتراسايكلين.

* **خامسا:** المركبات من انواع الازوبنزين-بارا،بارا-ثنائي(1,3-بنزوكسازين-4-اون-2-يل) [VI]، الازوبنزين-بارا،بارا-ثنائي(3-معوض-4(H3) كوينازولينون-2-يل) [V(a,d,I,l,n,o,p), VIII]، والازوبنزين-بارا،بارا-ثنائي(4-معوض-كوينازولين-2-يل) [IX, IXA,IXB]، و الازوبنزين-بارا،بارا-ثنائي(3-معوض-4(H3) كوينازولين ثايون-2-يل) [X(A,B,C,D,F,G,J,K,L)]، لها تأثير متوسط الى ممتاز كمضاد جرثومي ضد فطر الاسبرجلس فلافس بالمقارنة مع تأثير المضاد الحيوي النستاتين والفلاكونوزول.

* **سادسا:** المركبات من انواع الازوبنزين-بارا،بارا-ثنائي(3-معوض-4(H3) كوينازولينون-2-يل) [V(c,d,h,i), VIII]، الازوبنزين-بارا،بارا-ثنائي(4-معوض-كوينازولين-2-يل) [IX]، و الازوبنزين-بارا،بارا-ثنائي(3-معوض-4(H3) كوينازولين ثايون-2-يل) [(G,J,K,L)]، لها تأثير متوسط الى ممتاز كمضاد جرثومي ضد فطر البنسيليوم بالمقارنة مع تأثير المضاد الحيوي النستاتين والفلاكونوزول.

* **سابعا:** المركبات من انواع الازوبنزين-بارا،بارا-ثنائي حامض البنزوك [I]، الازوبنزين-بارا،بار-ثنائي كلوريد حامض البنزوك [II]، الازوبنزين-بارا،بارا-(ثنائي حامض البنزوك-2-يل)-ثنائي كاربوكسامايد [III]، لها تأثير متوسط الى ممتاز ضد غرام(+)، غرام(-)، من بكتريا المكورات العنقودية الذهبية، العصيات، وبكتريا القولون والالتهاب الرئوي على التوالي، بالمقارنة مع تأثير المضاد الحيوي السيفاكسيلين، الاموكسيسيلين، التتراسايكلين واللينوكومايسين. وكذلك تأثير جيد ضد فطر الاسبرجلس فلافس والبنسيلنيوم بالمقارنة مع المضاد الحيوي النستاتين والفلاكونوزول.

جمهورية العراق
وزارة التعليم العالي والبحث العلمي
جامعة بغداد
كلية التربية/ ابن الهيثم للعلوم الصرفة والتطبيقية
قسم الكيمياء

تصميم، تخليق، تشخيص، ودراسة الفعالية الجرثومية لمشتقات [أزوبنزن- بارا، بارا'- ثنائي (3- معوض 4(H3) كوينازولين 4- ون، 4- ثايون و 4- معوض كوينازولين-2- يل] الجديدة المحضرة من المركب الجديد أزوبنزن- بارا، بارا'-ثنائي (1،3- بنزوكسازين-4- ون-2- يل)

أطروحة مقدمة إلى

مجلس كلية التربية– ابن الهيثم للعلوم الصرفة والتطبيقية– جامعة بغداد

وهي جزء من متطلبات نيل درجة الدكتوراه فلسفة في علوم الكيمياء

من قبل

زينب عبد الرزاق جبارة ابو رغيف

ماجستير علوم كيمياء– 2002 – جامعة بغداد

بإشراف

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1438هـ 2017 م