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science Ibn Al-Haitham
Department of Chemistry*



Synthesis, Characterization and Evaluation of Antimicrobial Agents of New Chalcones, Pyrimidine Derivatives at 2, 4, 6 Positions

A Thesis

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2017A.D.**

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

﴿ قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا إِلَّا مَا

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Dedication

To whom God has sent as a light in darkness and messenger to guide us...

Mohammed (May God pray upon him)

To My father and mother...

with my great love

To the soul of my sister (Nadia)

with mercy...

To my brothers... Mohamed & Omar...

To my Husband... Akram...

To the light of my eyes... my sons...

Mohamad and Hamzah...

with my great love... and respect

Israa

Acknowledgment

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My deep grateful thanks are due to Asst. Prof. Zianab Abdul Razzaq, 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 and my appreciation to the staff of Al-Rajaa office for typing and photocopying.

The researcher Israa

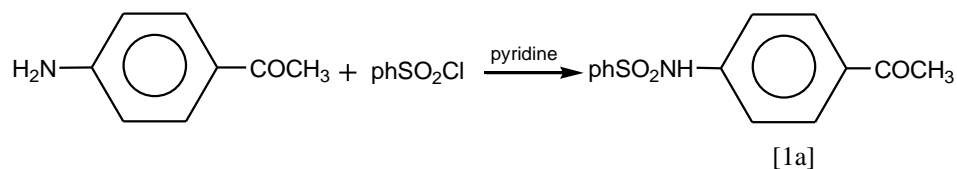
Abstract

Many researches in pyrimidine have interesting future in antimicrobial and pharmaceutical studies. For this purpose we design to synthesize compounds containing pyrimidines unit containing some effective biological active groups at positions-2,4 and 6, in order to increase the extension of its antimicrobial effect, like *p*-benzenesulphonamidophenyl, *p*-ureidophenyl, *p*(*N*-methylamino)phenylazophenyl *p*,*N*-phthalimidophenyl and *p*(*N*-phthalimido)benzamido-*N*'-phenyl groups at position-4, *p*-chlorophenyl and *p*-nitrophenyl groups at position-6, and oxo, imino, thioxo groups at position-2.

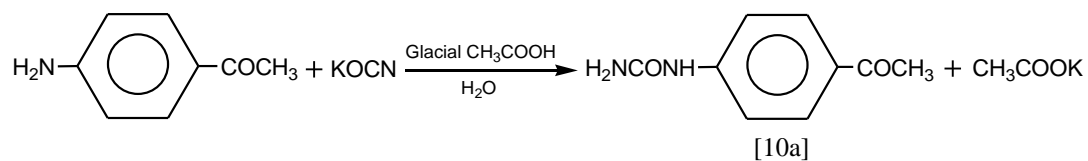
In order to build up such pyrimidines derivatives, the following steps are involved:

I. Synthesis of:

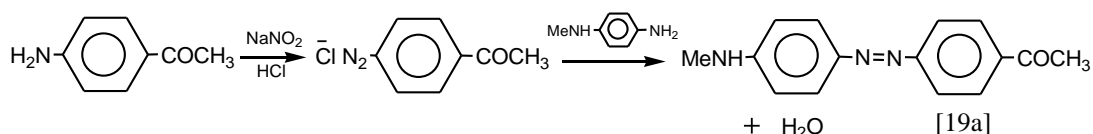
A- *p*-acetylphenylbenzenesulphonamide [1a], by condensation of benzenesulphonylchloride with *p*-aminoacetophenone in the presence of pyridine.



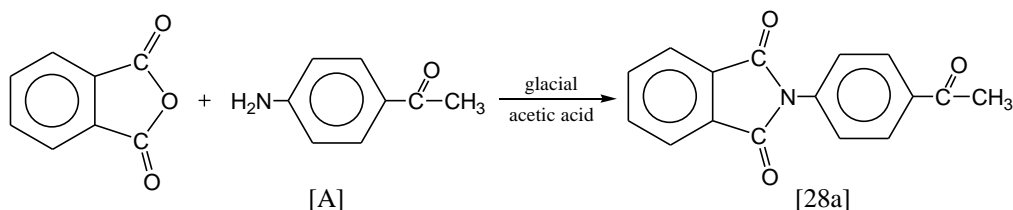
B- *p*-acetylphenylurea [10a], by reaction of potassium cyanate with *p*-aminoacetophenone, in water solution containing acetic acid.



C- *p*-acetyl-*p'*(*N*-methylamino)azobenzene [19a], by diazotization of *p*-aminoacetophenone with sodium nitrite in presence of hydrochloric acid, to give *p*-acetylphenyl diazonium salt, which was coupled with *p*(*N*-methylamino) aniline to give the titled compound.



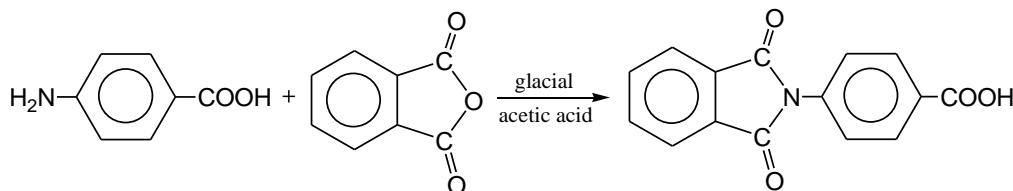
D- *N*-(4-acetyl)phenylphthalimide [28a], by reaction of *p*-aminoacetophenone with phthalic anhydride in the presence of glacial acetic acid.



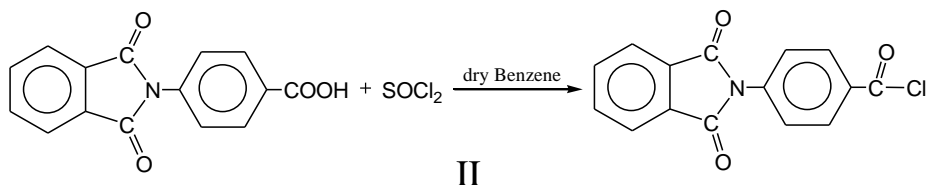
E- *N*(4-acetylphenyl)*p*-(*N*-phthalimido)benzamide [37a]

This compound was synthesized in three steps:

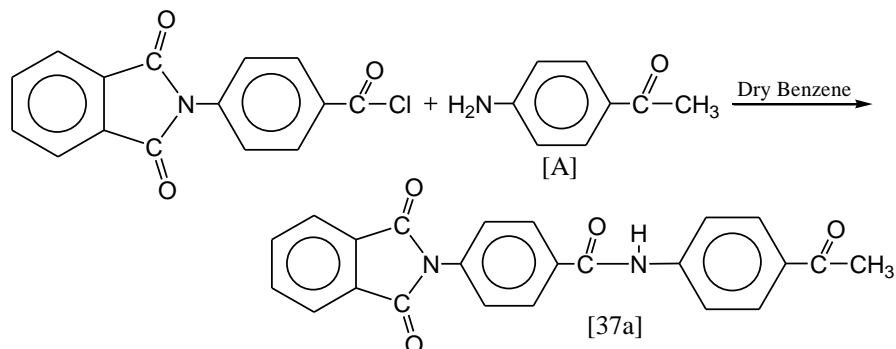
Step I. Synthesis of 4-*N*-phthalimidobenzoic acid, by reaction of phthalic anhydride with *p*-aminobenzoic acid in the presence of glacial acetic acid.



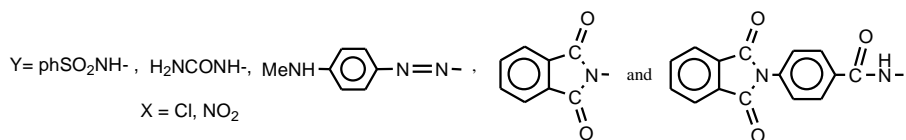
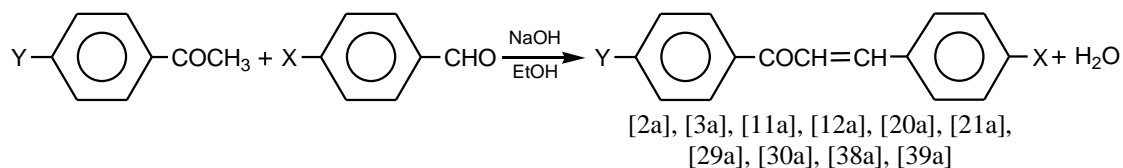
Step II. Synthesis of 4-*N*-phthalimidobenzoyl chloride, by reaction of 4-*N*-phthalimidobenzoic acid with thionyl chloride in dry benzene.



Step III. Synthesis of 4(4'-acetylphenylamido)phenyl phthalimide [37a], by reaction of 4-N-phthalimidobenzoyl chloride with *p*-aminoacetophenone in dry benzene.

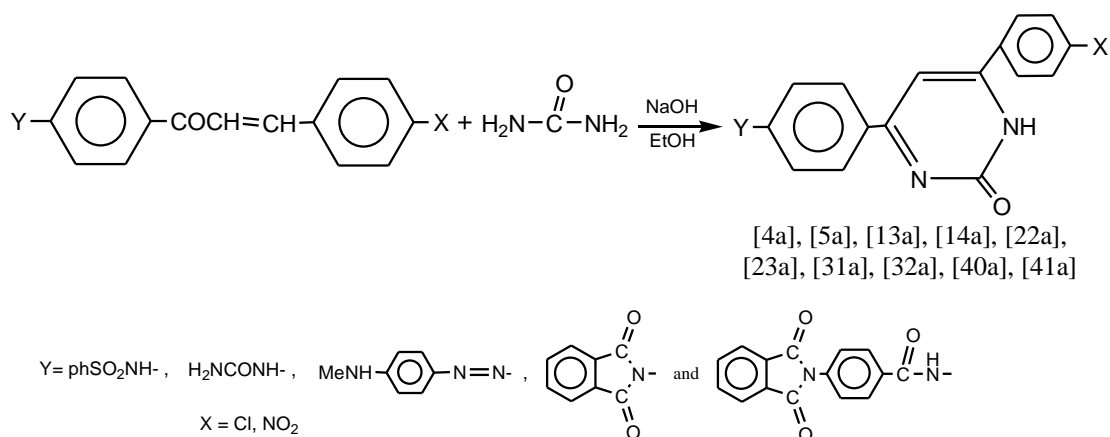


II. Chalconization processes, involve condensation of equimolar ratio of compounds [1a], [10a], [19a], [28a] and [37a] with *p*-chlorobenzaldehyde and *p*-nitrobenzaldehyde in the presence of sodium hydroxide to give *p*-substituted-1,3-diaryl-propene-2-one [2a], [3a], [11a], [12a], [20a], [21a], [29a], [30a] [38a] and [39a] as following scheme:

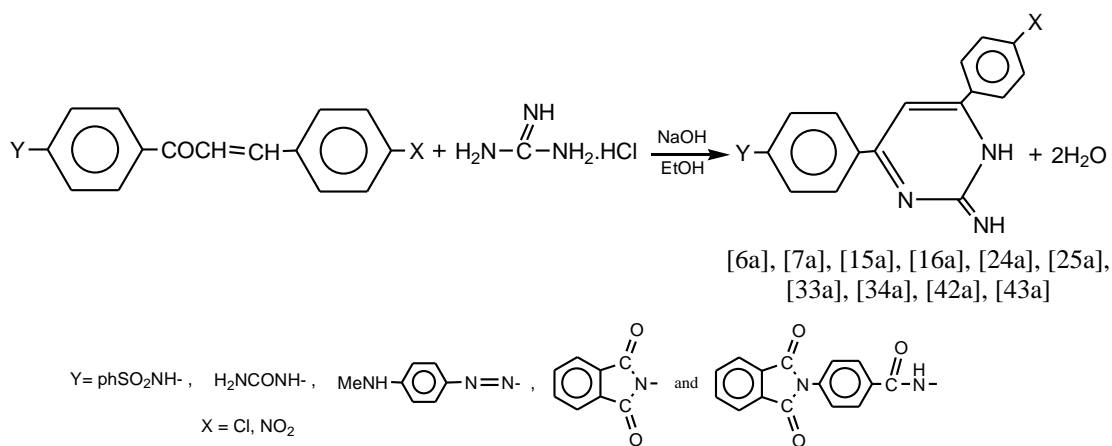


III. Synthesis of 2,4,6-substituted pyrimidines:

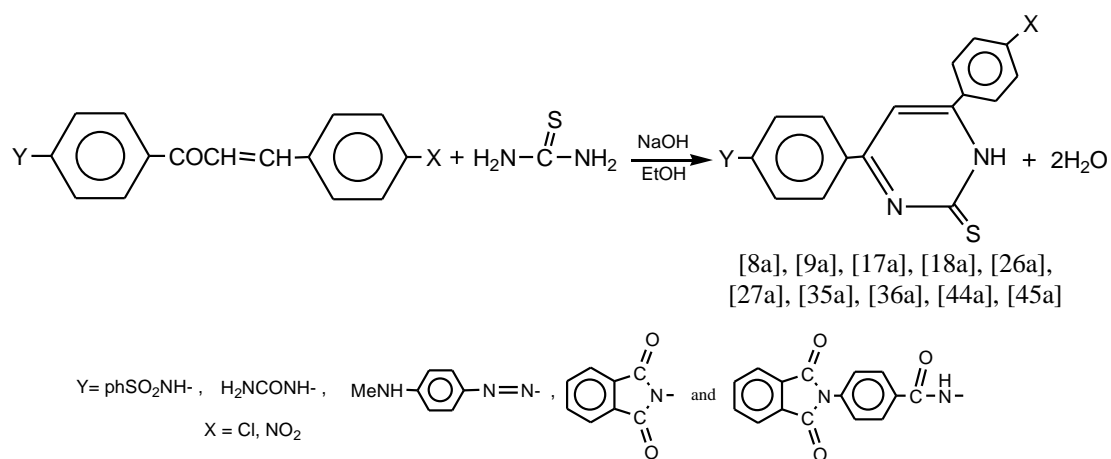
A- Condensation of equimolar ratio of following chalcones [2a], [3a], [11a], [12a], [20a], [21a], [29a], [30a], [38a] and [39a] with urea in the presence of sodium hydroxide, gave 4(*p*-substituted)-phenyl-6(*p*-substituted)-phenyl-2-oxo(1H) pyrimidines [4a], [5a], [13a], [14a], [22a], [23a], [31a], [32a], [40a] and [41a].



B- But condensation of equimolar ratio of following chalcones [2a], [3a], [11a], [12a], [20a], [21a], [29a], [30a], [38a] and [39a] with guanidine hydrochloride in the presence of double molar ratio of sodium hydroxide gave 4(*p*-substituted)phenyl-6-(*p*-substituted)-phenyl-2-imino (1H) pyrimidines [6a], [7a], [15a], [16a], [24a], [25a], [33a], [34a], [42a] and [43a].



C- Upon condensation of equimolar ratio of following chalcones [2a], [3a], [11a], [12a], [20a], [21a], [29a], [30a], [38a] and [39a] with thiourea in the presence of sodium hydroxide, gave 4(*p*-substituted)phenyl-6-(*p*-substituted)phenyl-2-thioxo(1H)-pyrimidines [8a], [9a], [17a], [18a], [26a], [27a], [35a], [36a], [44a] and [45a].



All new synthesized compounds [1a–45a], are characterized using various spectral analysis FTIR, ¹HNMR, ¹³C NMR and Mass measurements.

Antimicrobial activities of all types of synthesized compounds [1a–45a] and *p*-aminoacetophenone[A] were examined against Gram-Ve (*Serratia marcescens*, *pseudomonas aeruginosa*), Gram+Ve bacteria (*Staphylococcus aureus* and *streptococcus pyogenes*) and (*candida albicans*) fungi, in comparison with antimicrobial effect of known pharmaceutical antibiotics like Cephalexin, Amoxicillin, Tetracycline, Lincomycin and antifungal Nystatine and Flucanazole, results show:

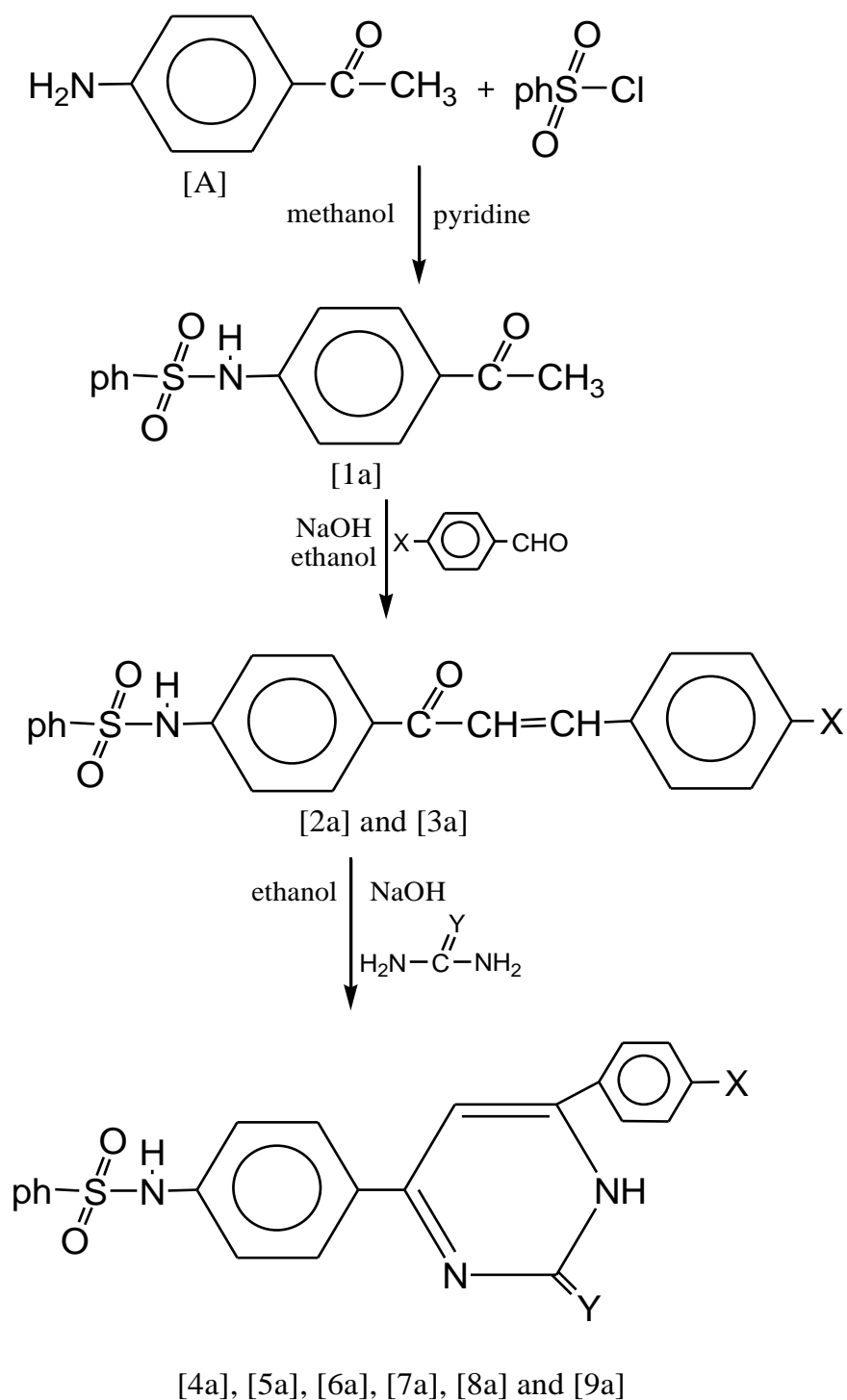
First: Synthesized *p*-substituted acetophenone [1a], [10a], [19a], [28a], [37a] and *p*-aminoacetophenone[A], showed good antimicrobial effect on (G–Ve) bacteria (*Serratia marcescens* and *pseudomonas aeruginosa*), better than used antibiotics and rank was [10a] > [1a] > [19a] > [A] > [28a], [37a].

Second: Synthesized chalcones also have much better effect than used antibiotics, but with small increasing effect that *p*-substituted acetophenones on (G–Ve) bacteria (*Serratia marcescens*

and *pseudomonas aeruginosa*), in the following rank [11a], [29a], [38a] > [2a], [20a], but in case of chalcone [21a] containing NO₂-group showed much better effect than others.

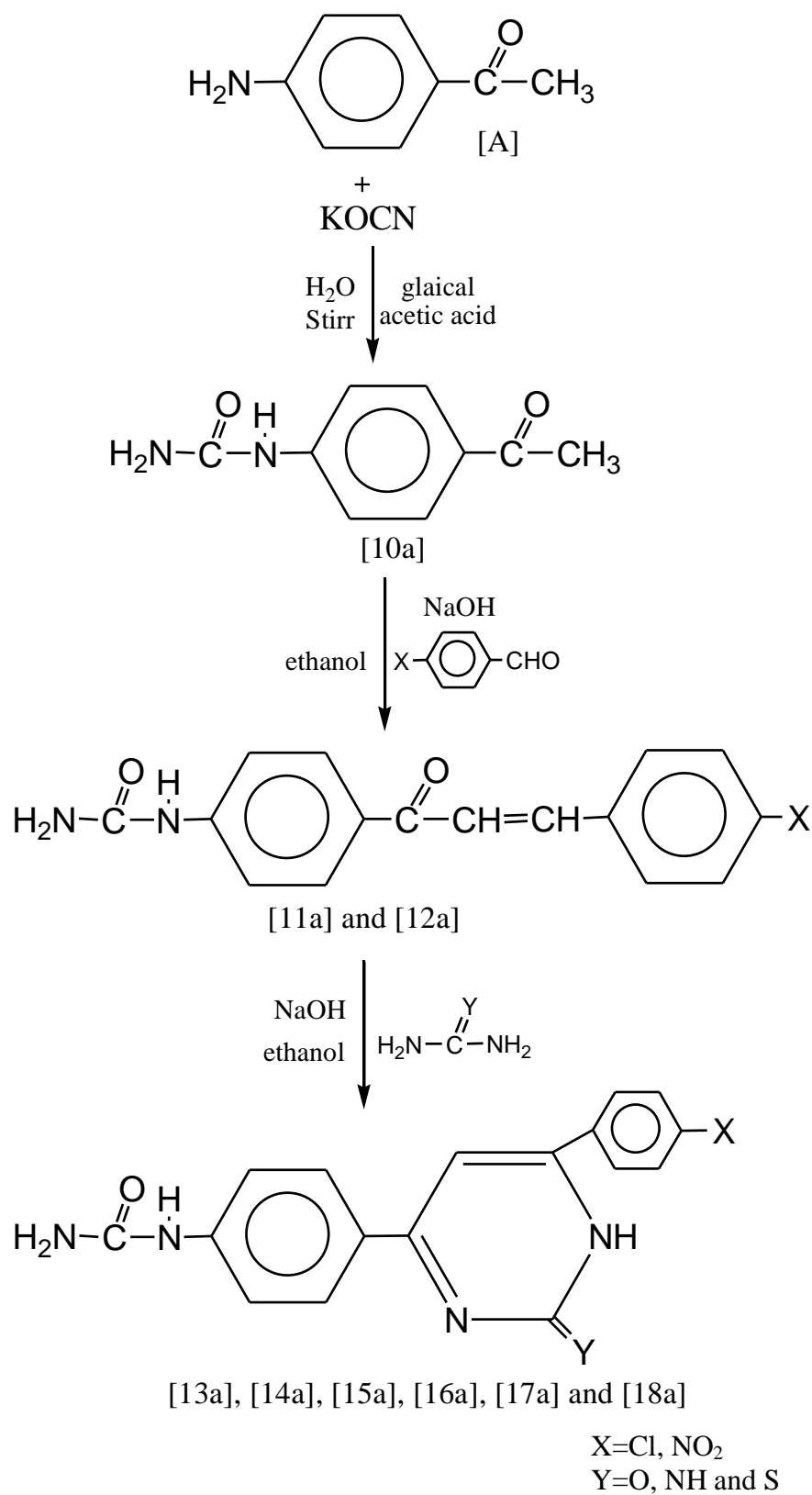
Third: All Synthesized pyrimidines [4a], [5a], [6a], [7a], [8a], [9a], [13a], [14a], [15a], [16a], [17a], [18], [22a], [23a], [24a], [25a], [26a], [27a], [31a], [32a], [33a], [34a], [35a], [36a], [40a], [41a], [42a], [43a], [44a] and [45a] showed good antimicrobial effect, but much better than antibiotics used in these studies, specially that containing, thioxo and imino groups at position-2.

Fourth: All Synthesized compounds, *p*-substituted acetophenones, chalcones and pyrimidines [1a–45a], showed very good inhibition effect on *candida albicans* fungi, specially, that chalcones [21a] and pyrimidine [22a] which contain azo group.

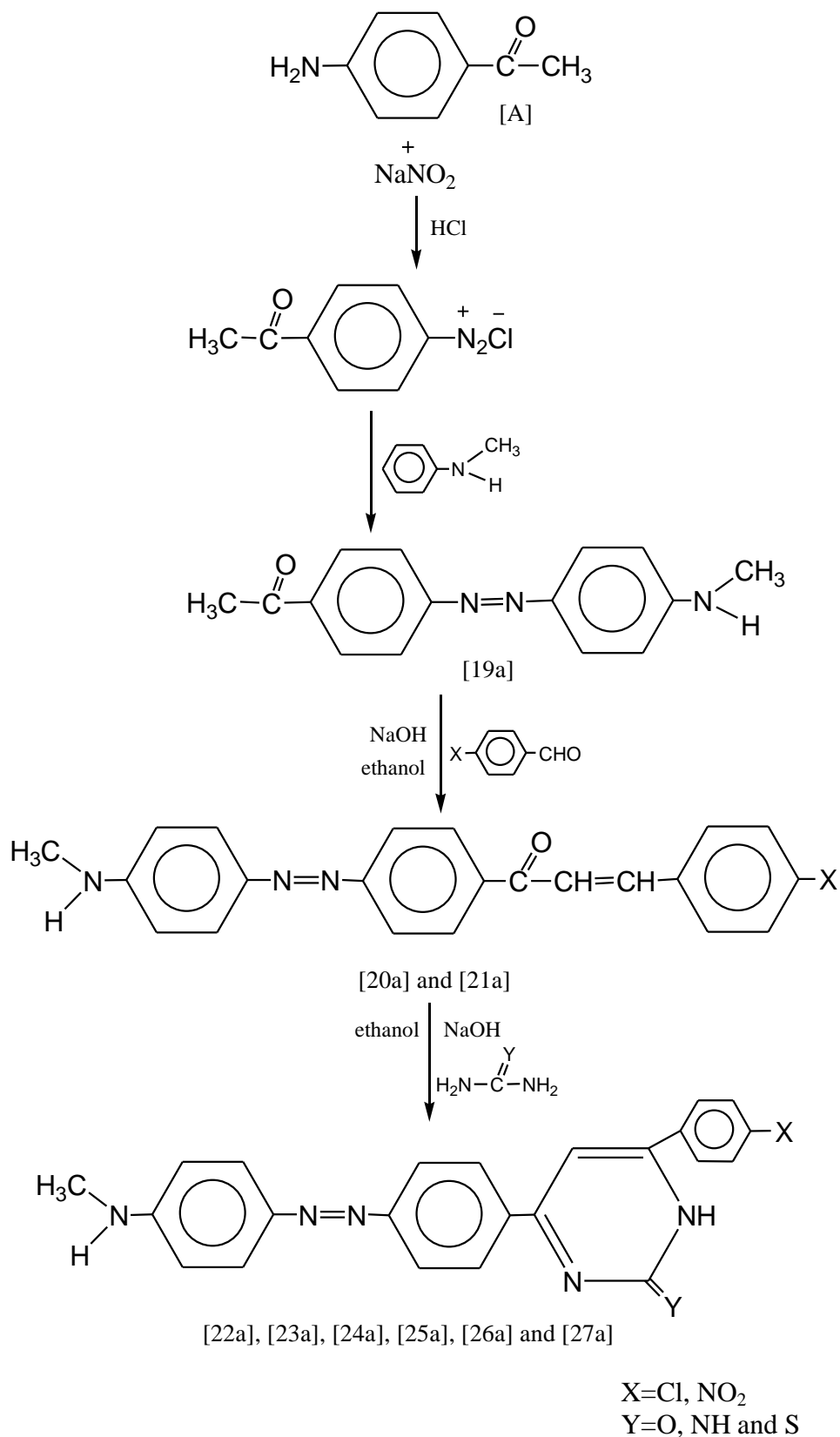


X=Cl, NO₂
Y=O, NH and S

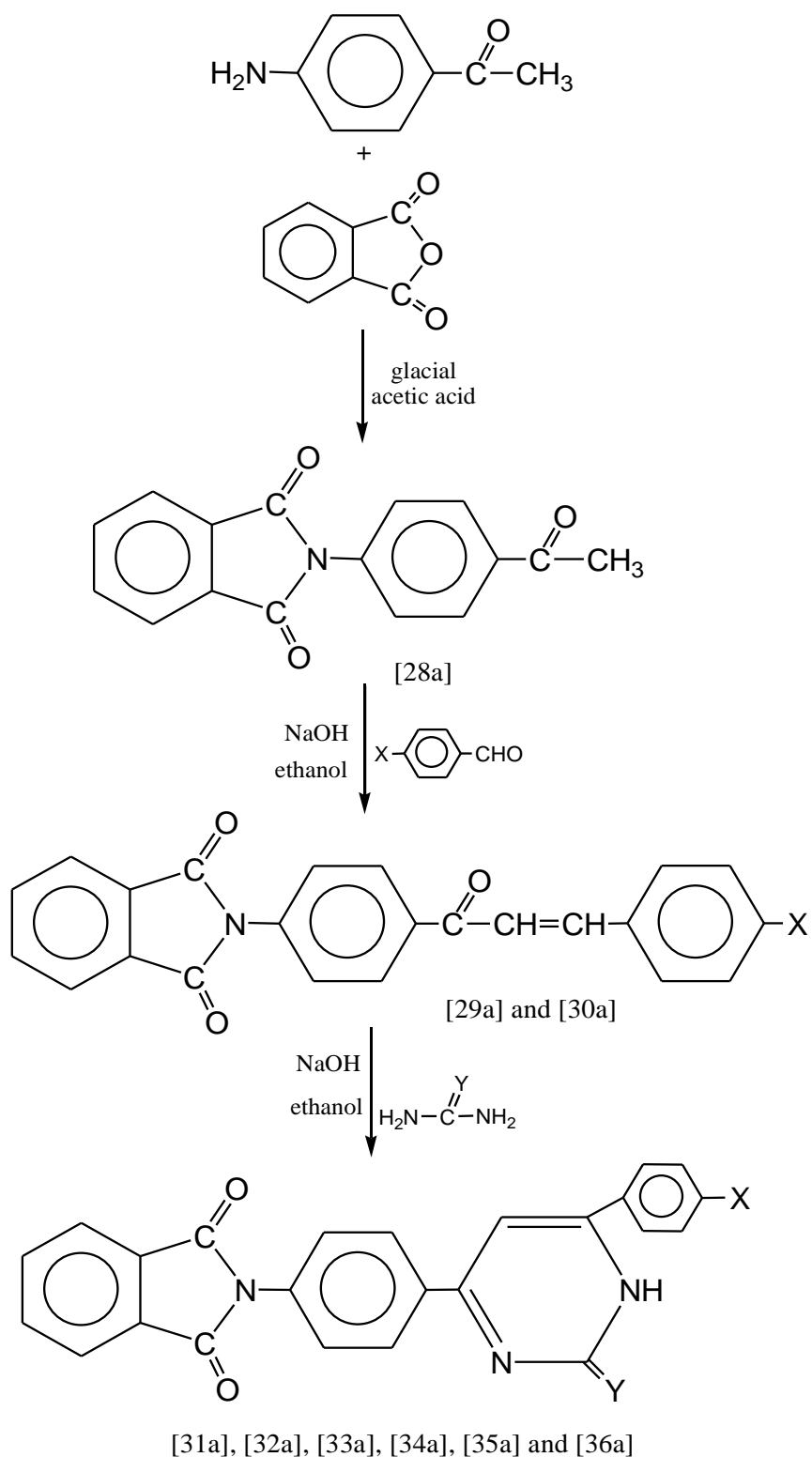
Scheme (1): Reactions of series One



Scheme (2): Reactions of series Two

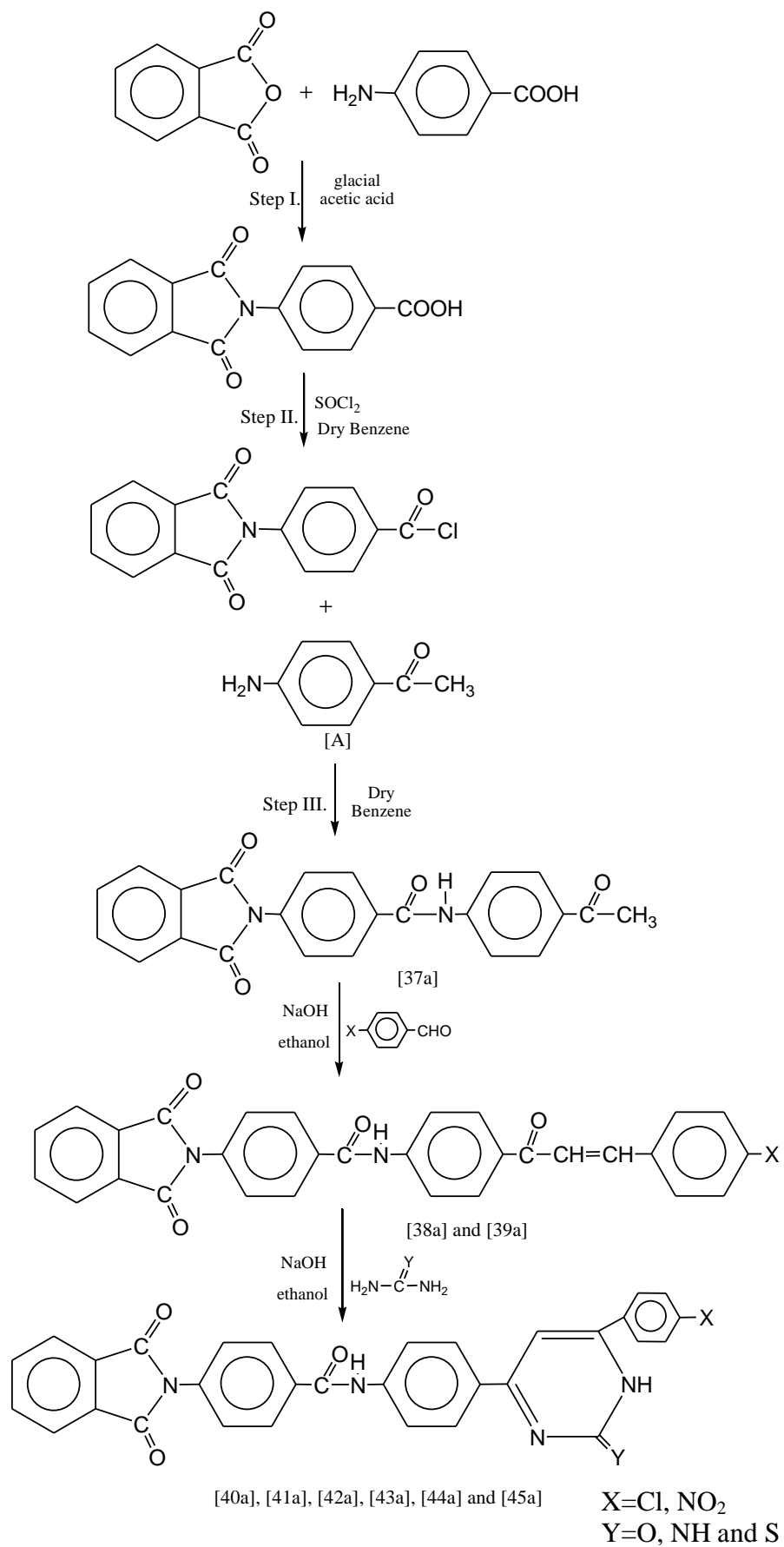


Scheme (3): Reactions of series Three



X=Cl, NO₂
Y=O, NH and S

Scheme (4): Reactions of series Four



Scheme (5): Reactions of series Five

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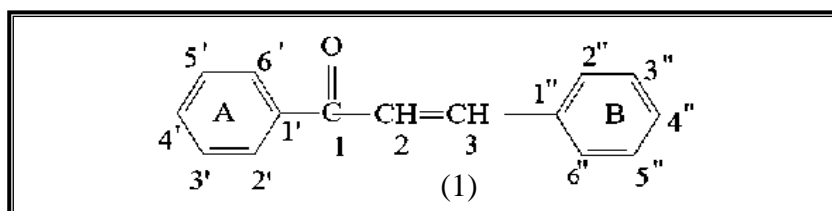
List of Abbreviations

A	p- aminoacetophenone
RT	Room temperature
PEG	Poly ethylene glycol
MIC	Minimum inhibition concentration
Alipha.	Aliphatic
Aroma.	Aromatic
DMF	Dimethyl formamide
DMSO	Dimethyl sulfoxide
RNA	Ribo nuclic acid
DNA	Deoxy ribonuclic acid
HIV	Humman immunodefciancy virus
¹³ C NMR	Carbon nuclear magnetic resonans
TLC	Thin layer chromatography
m.p	Melting point
Cepha.	Cephalexin
Amoxi.	Amoxiciline
Tetracy.	Tetracycline
Linco.	Lincomycine
EtOH	Ethanol
MeOH	Methanol

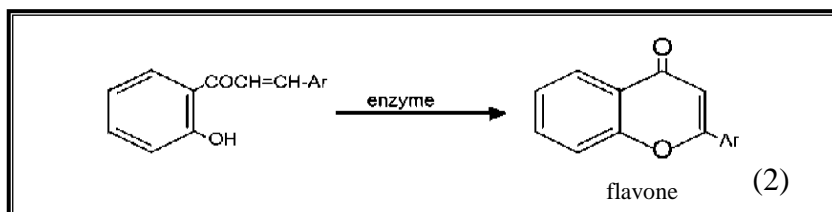
Chapter One
Introduction

1.1 Chalcone

Chalcones(1) are 1,3-diaryl-2-propene-1-one, they belong to flavonoid group compound. Chemically they consist of α,β -unsaturated carbonyl system ($-\text{C}=\text{C}-\text{C}=\text{O}$), in which the two aromatic rings substituents, join terminal carbons of α,β -unsaturated carbonyl system.



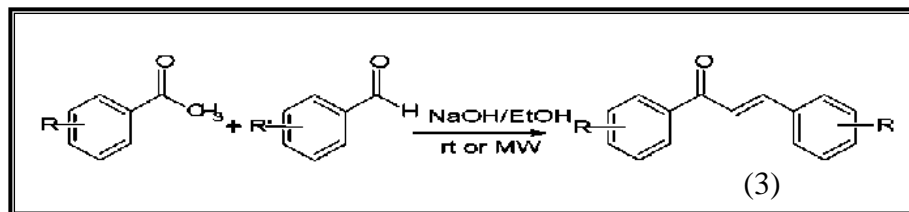
Chalcones are naturally occurring compounds, that are largely distributed in plants, fruits and vegetables. They are precursor in biosynthesis of flavone and anthocyanin, enzymatic cyclization of 6-hydroxy chalcones lead to the formation of flavones(2), flavonols, and isoflavones.



Traditionally chalcones can be synthesised by Claisen–Schmidt condensation of acetophenone or substituted acetophenones with aldehydes. The first condensation was reported by Kestanecki and he gave the name “Chalcones”^[1,2].

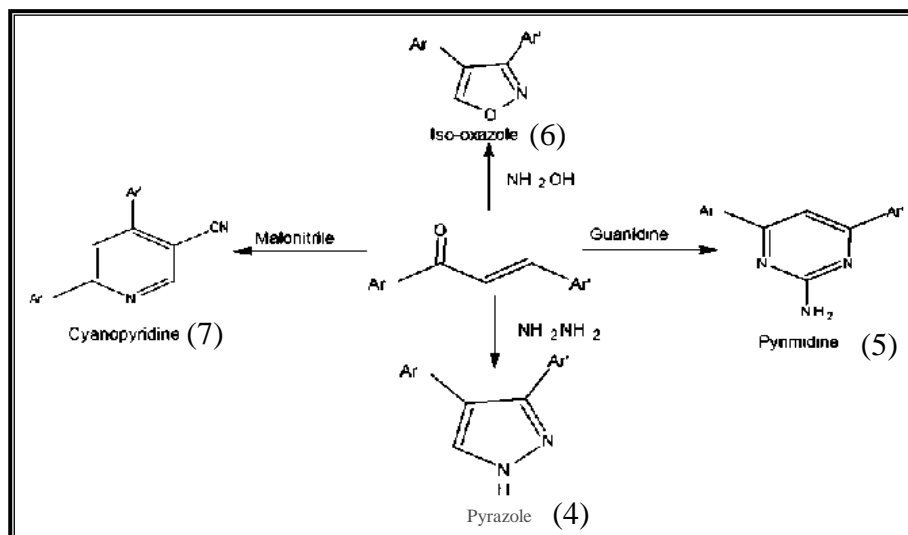
The reactions are generally base catalysed, acid catalysed, solid and resin supported, and microwave assisted versions are also reported. These reaction methodologies are associated with

drawbacks such as low yields, long reaction times, use of expensive reagent and catalysts etc...^[3].



The chemistry of chalcones has been recognized as a significant field of study. An interesting feature of chalcones is that they serve as starting materials of the synthesis of various heterocyclic compounds such as pyrimidines pyrazolines, flavones, flavonals, aurones and benzoyl coumarones as well as contain compounds like deoxybenzoine an hydration which are of some therapeutic importance.

One of the important class of reactions which chalcones undergo are the ring closure reactions with hydrazine, guanidine, malonitrile, etc... affording heterocyclic derivatives such as pyrazole(4), pyrimidine(5), iso-oxazole(6), cyanopyridine(7) etc...^[4]. Then one functionality present in the chalcones provides an attractive site for 1,3-dinucleophiles affording such heterocyclic ring- systems^[5]. Such reactions are traditionally catalysed by ethanolic NaOH or ethanolic KOH solutions under reflux condition, but the use of other agents like piperidine is also reported^[6].

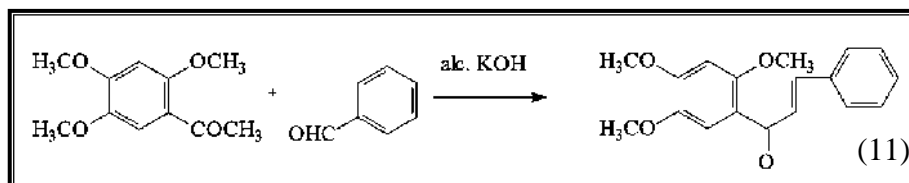


A number of chalcone derivatives is reported to inhibit several important enzymes of different cellular systems. Such enzymes include xanthine oxidase, aldose reductase, epoxide hydrolase, protein tyrosine kinase, quinone reductase, monoamine oxidase and lipoxygenase^[7-9].

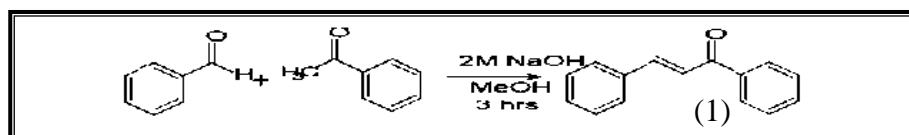
1.1.2. General methods of synthesis of chalcones

A variety of methods are available for synthesis of chalcones, but the most convenient method is that involving Claisen-Schmidt condensation of acetophenone, substituted acetophenone, or aromatic and heteroaromatic methyl ketones, with substituted aromatic aldehydes, in presence of alkali, alcoholic alkaline solution, at room temperature for 24 hours, grinding under conventional and thermal conditions, ultrasonic and microwave irradiation, zinc oxide support metal oxides, and PEG-400 support.

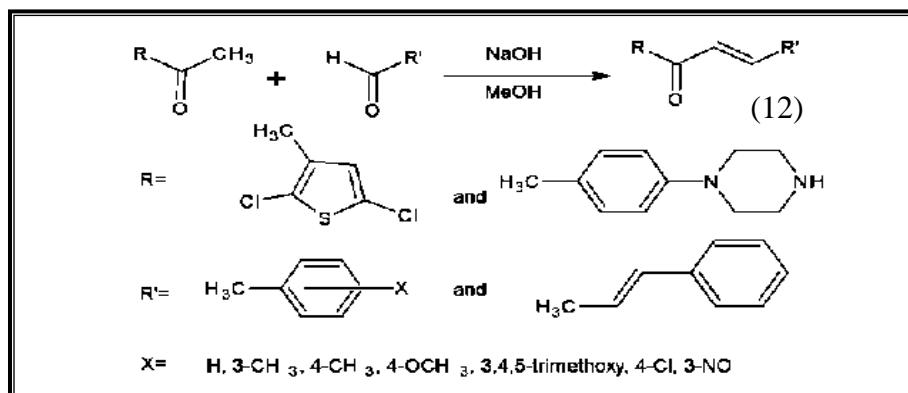
Reichel et al.,^[10] reported the synthesis of chalcone by reacting 2'-hydroxyacetophenone with benzaldehyde in the presence of 0.1 M NaOH to give the chalcone(8).



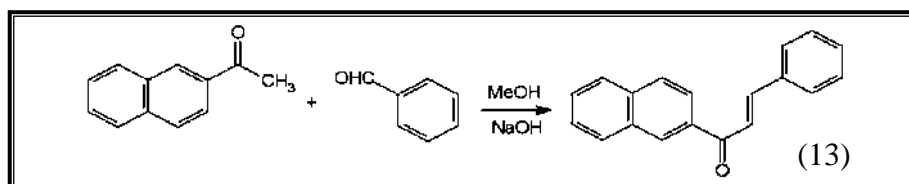
Sivakumar et.al.,^[14] reported the synthesis of α,β unsaturated ketones(1) from substituted aromatic aldehydes and acetophenone.



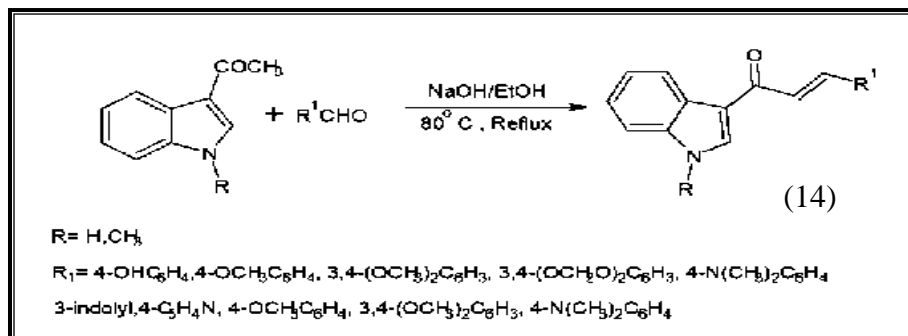
Tomar et.al.,^[15] prepared a series of substituted chalcones(12) by reacting 4'-piperazino acetophenone or 3-acetyl-2,5-dichlorothiophene and aromatic aldehyde.



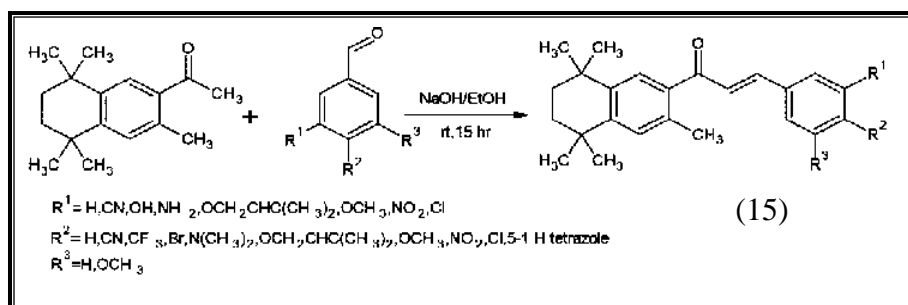
Deshpande et.al.,^[16] reported the condensation of 2-naphthylmethylketones with substituted arylaldehydes in the presence of NaOH under methanol as solvent gave the corresponding chalcones(13).



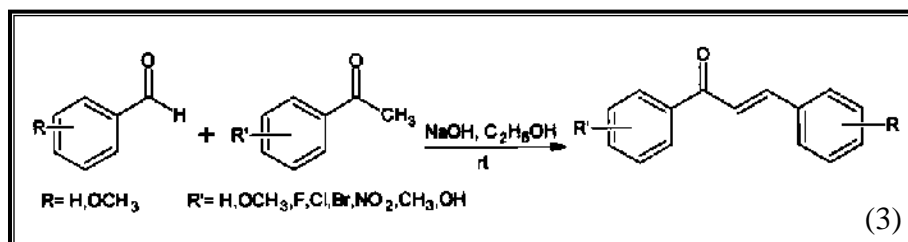
Kumar et.al.,^[17], synthesized indolyl chalcones(14) which were synthesized by reacting 3-acetylindole and appropriate aldehyde in presence of dilute sodium hydroxide under reflux.



Mizuno et.al.,^[18] synthesized retinoid-chalcone hybrids(15) by coupling acetophenone with different aldehydes using NaOH in ethanol.

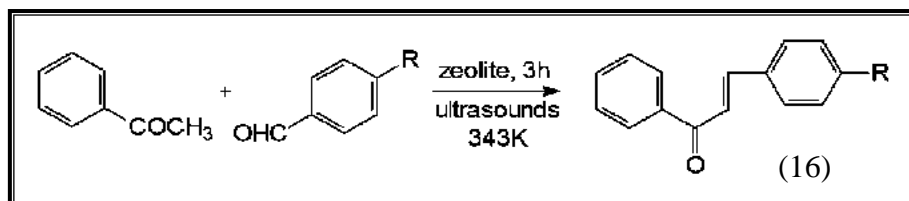


Bandgar et.al.,^[19], synthesized 3-(2,4-dimethoxy-phenyl)-1-phenyl-propenone(3) by reacting substituted 1-phenyl ethanone and 2,4-dimethoxy-benzaldehyde or 3,4,5 trimethoxybenzaldehyde using NaOH as catalyst.

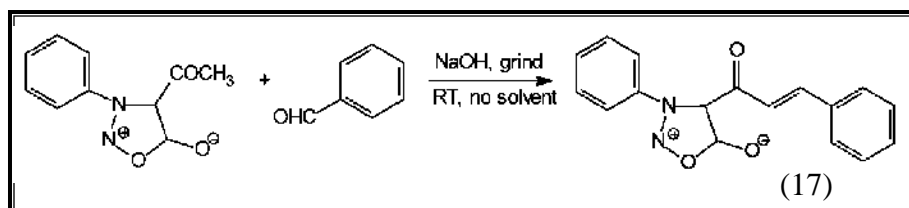


Elizabeth et.al.,^[20] reported the Claisen-Schmidt condensation between benzaldehyde and acetophenone by sonochemical and

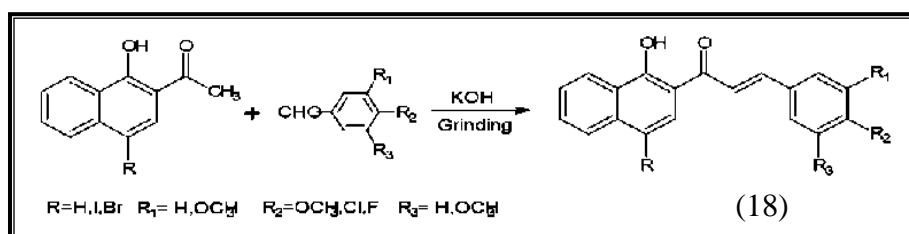
thermally activated reactions over zeolite as catalyst under solvent free conditions give chalcone(16).



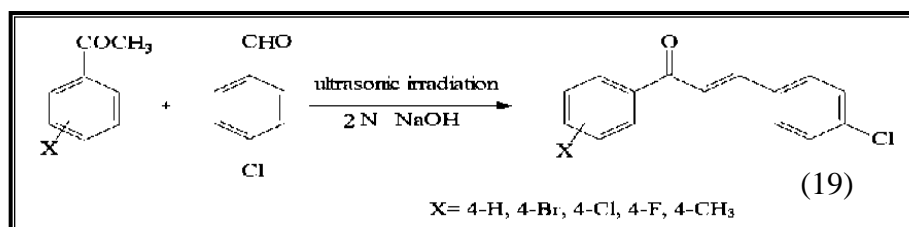
Bala Krishna and Gmesha^[21], reported the 4-Acetyl-3-aryl-syndones(17) when subjected to grinding with various arylaldehydes in the presence of a base catalyst under solvent free conditions yield syndonechalcones.



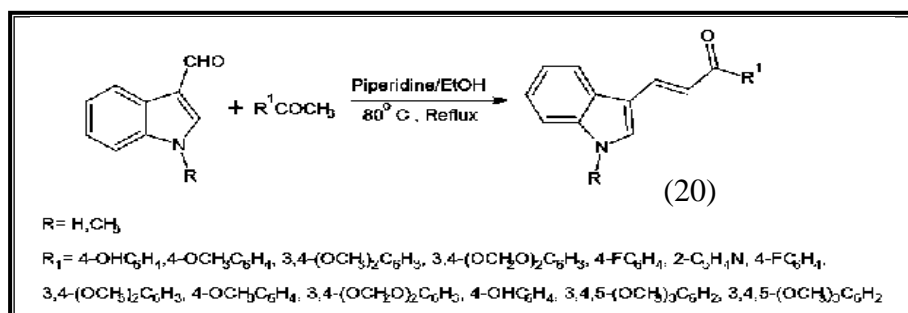
Zangade et.al.,^[22] synthesised some novel chalcones(18) by grinding substituted 2-acetyl-1-naphthol and substituted benzaldehydes in presence of potassium hydroxide.



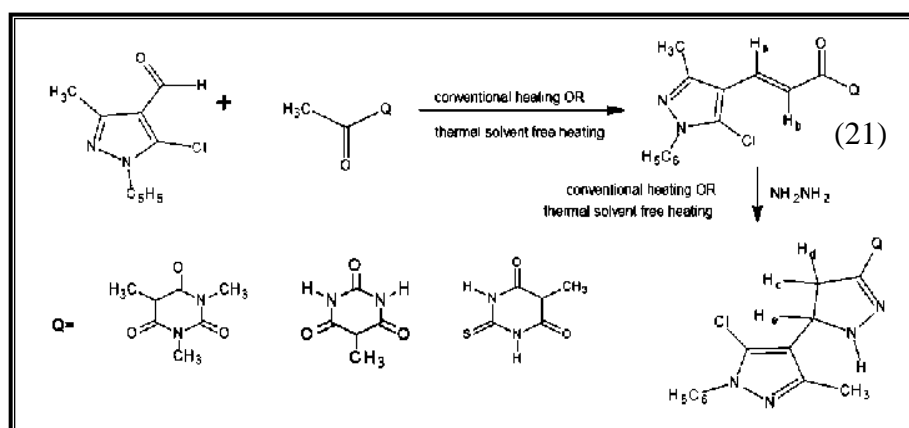
Gupta et.al.,^[23] reported an improved synthesis of chalcones(19) under ultrasonic irradiation and screened them for antimicrobial activity. Some of these compounds showed promising activity against *E. coli*, *S. aureus*, *C. albicans* and *A. niger*.



Kumar et.al.,^[17], synthesized indolyl chalcones(20) by reacting indol-3-carboxaldehyde and appropriate acetophenone in presence of piperidine under reflux.

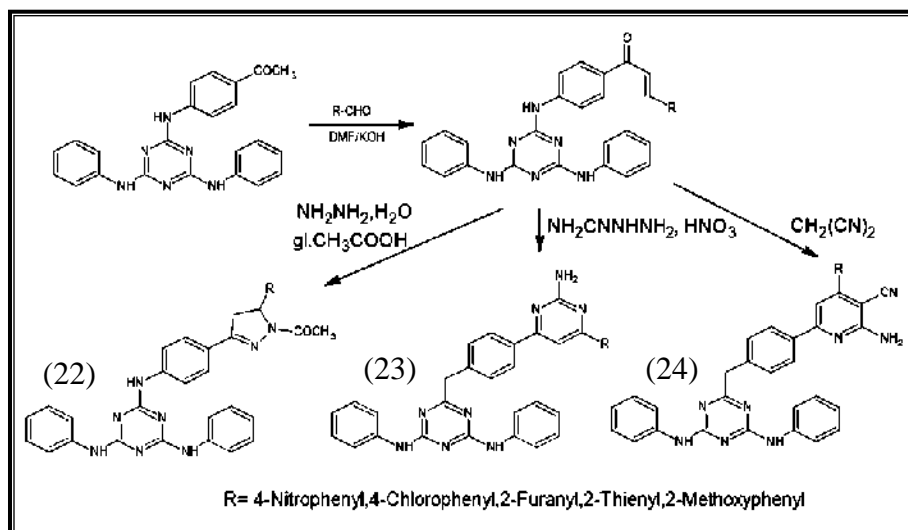


Siddiqui et.al.,^[24] synthesized heteroaryl chalcones(21) and their pyrazoline derivatives by reacting 5-chloro-3-methyl-1-phenyl pyrazole-4-carboxaldehyde and barbituric acid derivatives in both conventional and thermal solvent free conditions.

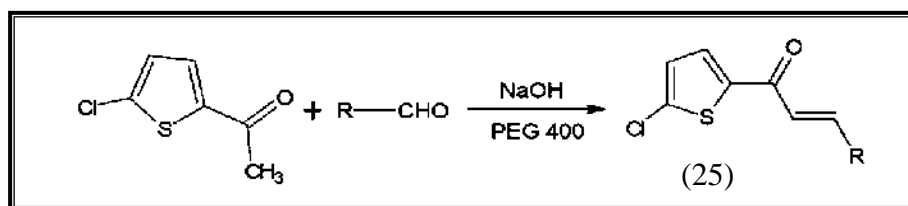


Solankee et.al.^[25], synthesized chalcones(22), (23) and (24) by condensation of ketones with various aldehydes in presence of DMF and KOH. These chalcones were further reacted with hydrazine

hydrate, guanidine nitrate, malononitrile to form acetylpyrazolines, aminopyrimidines and cyanopyridines respectively.



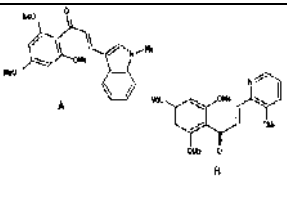
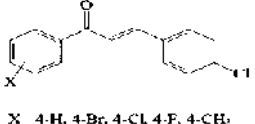
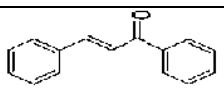
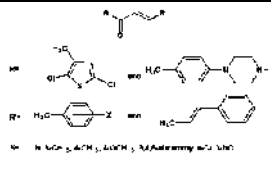
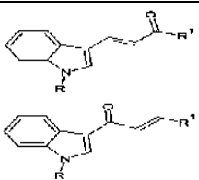
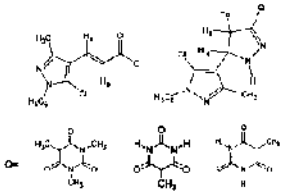
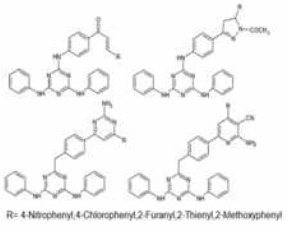
Lavania et.al.,^[26], synthesised substituted chalcone(25) by reacting 2-acetyl-5-chloro thiophene and aromatic aldehydes in the presence of sodium hydroxide, ethanol and PEG 400 acting as polymer support.



1.1.3. Biological activities

Chalcones and their heterocyclic derivatives were evaluated for several biological activities by various researchers. Here are presenting a list of few biological activities reported by the researchers on chalcones and their heterocyclic derivatives.

Table (1-1): Various pharmacological activities of chalcones

Author	Synthesized Compounds	Activity Studied	Cell lines/Animal model/Organisms/ Enzymes
Champelovier P. et.al., ^[11]		Anti-cancer	Human glioblastoma glioma-derived cell lines
Gupta et.al., ^[23]		Antimicrobial	<i>E.coli</i> , <i>S.aureus</i> , <i>C.albicans</i> and <i>A.niger</i>
Sivakumar PM et.al., ^[14]		Antimycobacterial	<i>M. tuberculosis</i>
Tomar V. et.al., ^[15]		Anti-microbial	<i>Staphylococcus aureus</i> , <i>Escherichia coli</i> , <i>Proteus vulgaris</i> , <i>Klebsiella pneumonia</i> , <i>Aspergillus fumigates</i> , <i>Candida albicans</i> , <i>Candida krusei</i> , <i>Candida glabrata</i>
Kumar D et.al., ^[17]		Anti-tumor	Epithelial, Pancreatic carcinoma, Androgenindependent Human prostatic Adenocarcinoma
Siddiqui ZN et.al., ^[24]		Anti-microbial	<i>Streptococcus pyogenes</i> (clinical isolate), <i>Staphylococcus aureus</i> (MRSA +Ve), <i>Pseudomonas aeruginosa</i> , <i>Klebsiella Pneumonia</i> (clinical isolate), <i>Escherichia coli</i> , <i>Candida albicans</i> , <i>Aspergillus fumigatus</i> , <i>Trichophyton mentagrophytes</i> , <i>Penicillium marneffe</i>
Solankee A et.al., ^[25]		Anti-microbial	<i>Bacillus cereus</i> , <i>Micrococcus flavus</i> , <i>Staphylococcus aureus</i> , <i>Escherichia coli</i> , <i>Pseudomonas aeruginosa</i> , <i>Enterobacter cloacae</i> , <i>Salmonella typhimurium</i> , <i>Listeria monocytogenes</i>

1.1.4. Therapeutic potential of chalcones

Chalcone is a unique template that is associated with several biological activities and is well known intermediates for synthesizing various heterocyclic compounds^[27]. They are secondary metabolites of terrestrial plants, precursors for the biosynthesis of flavonoids. The introduction of a halogen into the benzenoid part of these α,β -unsaturated ketones enhances their biological activity^[28].

Chalcones and their derivatives, whether synthetic or naturally occurring are an interesting and significant group of molecules as they possess a wide range of pharmacological activities such as anti-inflammatory, anti-microbial, anti-fungal, anti-bacterial, anti-oxidant, cytotoxic, antitumor, anticancer, antimitotic, anti-leishmanial, anti-malarial, antitubercular, antiviral^[29-43] insecticidal, anti-mutagenic^[44,45], anti-HIV^[46,47]. Analgesic, antiulcerative, antileishmanial, antiprotozoal, antihistaminic, antifedent, immunomodulatory, anticonvulsant, antihyperglycemic, antihyperlipidemic and antiplatelet activities^[48,49].

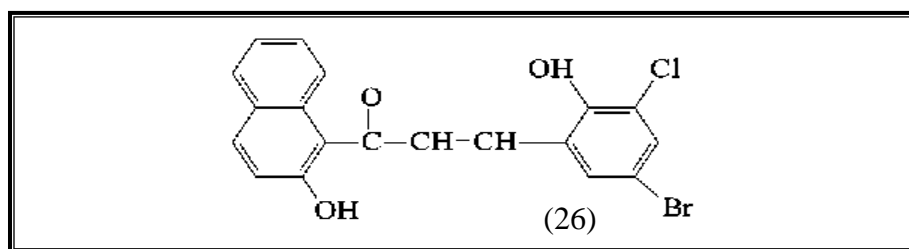
Chalcones are valuable intermediates in the synthesis of many active pharmaceutical drugs like biosynthesis of flavonoids^[50,51] and Auwers synthesis of flavones^[52].

Thus chalcones continue to attract considerable scientific attention because of their association with a variety of biological activities. Given below is a brief account of various modifications reported on chalcones, which resulted in a variety of biological and pharmacological activities.

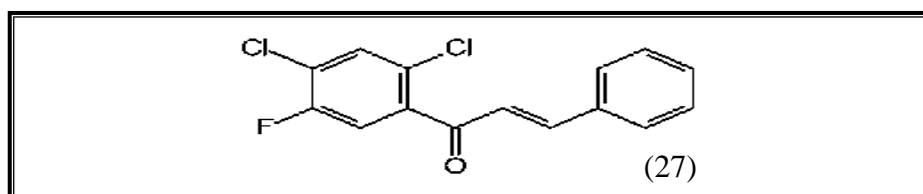
1.1.5. Antimicrobial activity

The antimicrobial activity of chalcones is being increasingly documented. Many research groups either isolated or synthesized chalcones that possess antimicrobial activity. The presence of a reactive α,β -unsaturated keto function in chalcones was found to undergo conjugate addition with a nucleophilic group like a thiol group in an essential protein, thus partly contributing for their antimicrobial activity, which may be altered depending on the type and position of the substituents on the aromatic rings.

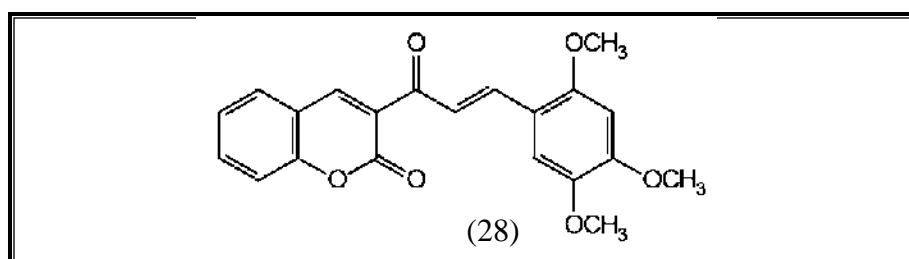
Prasad et.al.,^[53] synthesized a chalcone(26) having a naphthalene moiety on one side and an aryl moiety having substituents on the other side, which showed significant antifungal activity against *A.niger* and *Rhizopus oryzae*. This compound can also be considered to provide optimal hydrophilic and hydrophobic properties as evidenced by hydroxyl groups and the halogens.



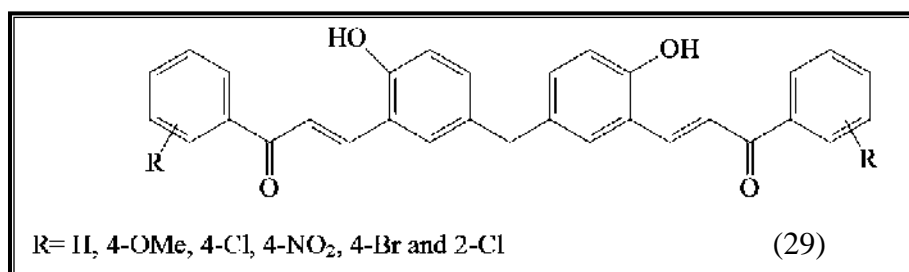
Karthikeyan et.al.,^[54] synthesized 3-aryl-1-(2,4-dichloro-5-fluorophenyl)-2-propen-1-ones(27) showing antimicrobial activity, again consistent with the observations that the halogens possess favorable lipophilic character required for antimicrobial activity.



Prasad et.al.,^[55] synthesized 3-[1-oxo-3-(2,4,5-trimethoxyphenyl)-2-propenyl]-2H-1-benzopyran-2-ones(28) that showed significant antimicrobial activity against *B.subtilis*, *B.pumilis* and *E.coli* when tested at a concentration of 1000 µg/ml. The study revealed the importance of electron releasing groups such as hydroxyl and methoxyl groups in enhancing the activity. Chalcones with halogen substituents like bromine and chlorine contributed favorably to the antifungal activity.

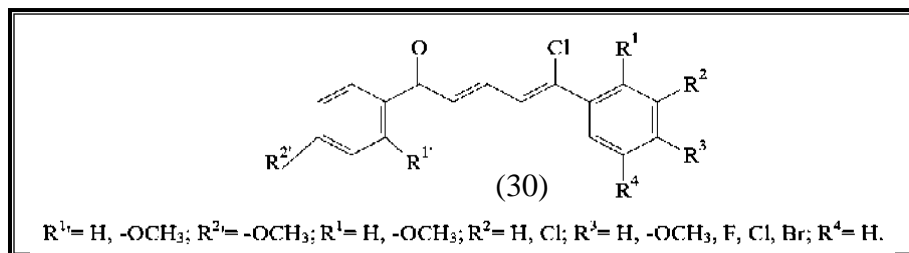


Reddy et.al.,^[56] synthesized some novel bis-chalcones(29) and evaluated for their antimicrobial activity. The results proved that the presence of methoxy/chloro groups on the phenyl ring was essential for antibacterial activity. The activity was found to be maximum when the methoxy group present at 4th position. These compounds were also highly active against *C. albicans*.

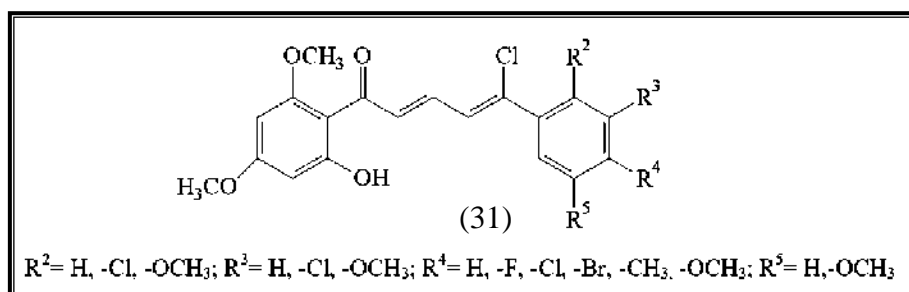


Bandgar et.al.,^[57] synthesized some β-chlorovinyl chalcones(30) by Claisen-Schmidt condensation reaction and the compounds were screened for their antimicrobial activity. It was observed that the compounds having bromo, chloro, methoxy and

fluoro substituents enhanced the antimicrobial activity with MIC values ranging from 50-100 $\mu\text{g/mL}$ against selected pathogenic bacteria and fungi.

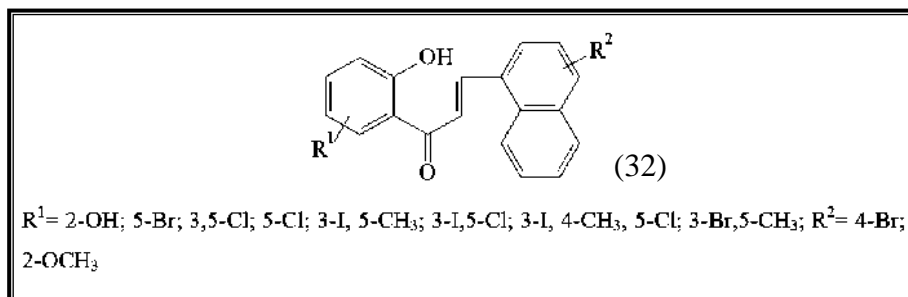


Bandgar et.al.,^[58] also reported in another study that the chalcones(31) having 2- chlorophenyl, 4-chlorophenyl, 4-fluorophenyl and 2,4-dichlorophenyl moieties showed maximum antibacterial activity against *Bacillus subtilis*, *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumoniae* and *Pseudomonas vulgaris*. It was also found that the compounds having 4-bromophenyl, 4-fluorophenyl and 2,4-dichlorophenyl moieties contributed favourably to the antifungal activity against *Aspergillus fumigatus*, *Aspergillus niger*, *Trichoderma viridie*, *Candida albicans* and *Penicillium chrysogenum*.

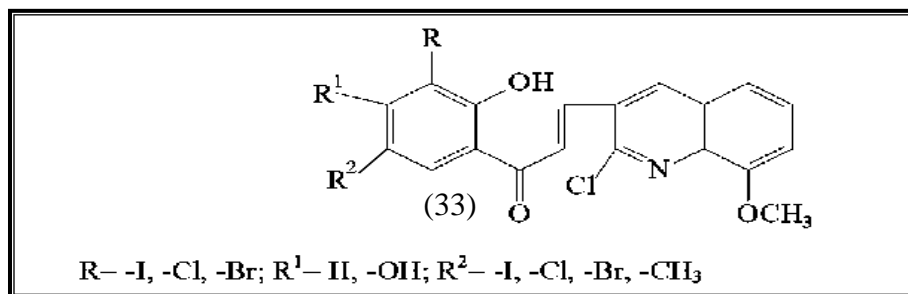


Vibhute et.al.,^[59] reported the synthesis of some new chalcones(32) containing substituted naphthalene nucleus. These compounds when screened for antibacterial activity revealed that the

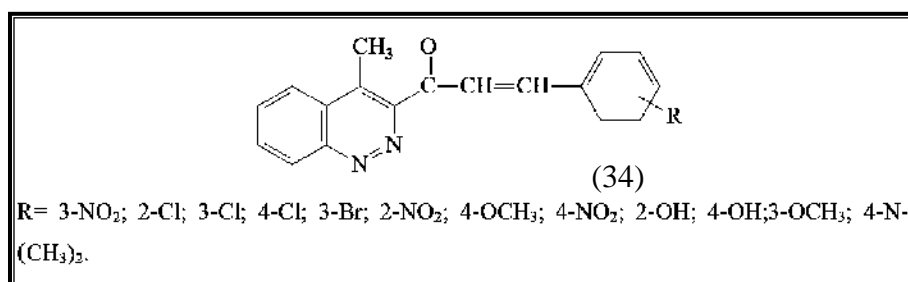
compounds with chloro substituents possessed remarkable inhibition against *E. coli*.



Vibhute et.al.,^[60] also synthesized some new chalcones(33) having a 2-chloro-8-methoxyquinolinyl moiety and evaluated their antibacterial activity against *Xanthomonas citri*, *Erwinia carotovora*, *E.coli* and *B. subtilis*. The compounds having 2'-hydroxy-3'-iodo-5'-chlorophenyl and 2'-hydroxy-3'-chloro-5'-iodophenyl moieties showed significant activity which is more than that of the ampicillin used as the standard.



Gautam et.al.,^[61] reported the synthesis of some new cinnoline based chalcones(34) which were evaluated for antimicrobial activity. The cinnoline system was found to contribute favourably to antibacterial activity against *E.coli*.



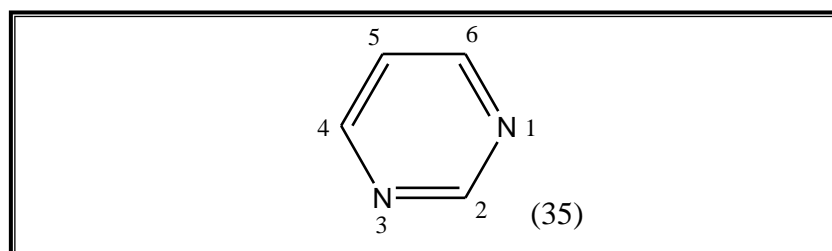
1.2. Pyrimidines

Pyrimidine(35) is 1,3-diazines heterocyclic compounds, colourless compound. It is weakly basic, as compared to pyridine or imidazole. The decrease in its basicity is due to the electron-withdrawing effect of the second nitrogen atom present in the ring. Moreover, the addition of proton does not increase the probability for mesomerism and hence the resonance energy^[62].

Pyrimidine is the most important member of all the diazine as this heterocyclic ring system occurs widely in living organisms. Purine, uric acid, alkoxan, barbituric acid, and also in agricultural chemical, as succuful treatment of various diseases.

Pyrimidines and their derivatives considered to be important for drugs, they have many biological activities, such as antimicrobial, antitumor, antifungal, anticancer, antiviral, antibacterial, antioxidant, antiallergic and antidepressant, antimalarial activities.

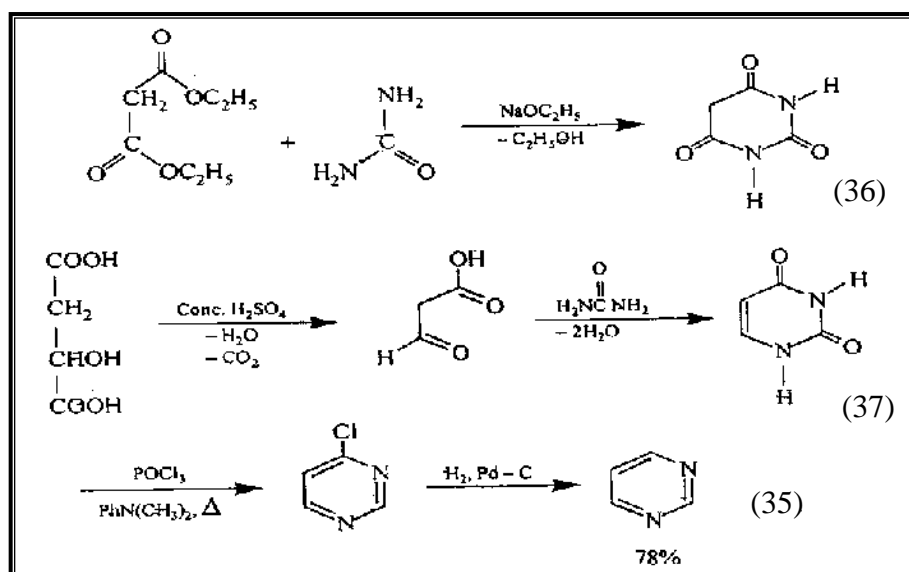
The chemistry of pyrimidine has been widely studied, its was first isolated by Gabriel and Colman. Since pyrimidine is symmetrical about the line passing C₂ and C₅, position C₄ and C₆ are equivalent and so are N-1 and N-3^[63-65].



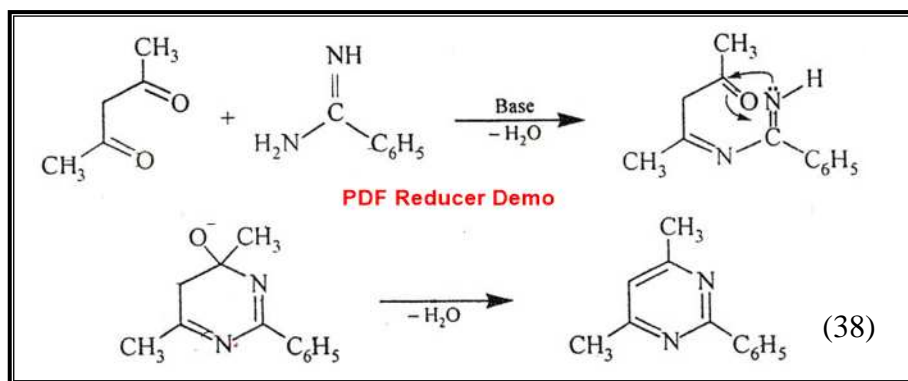
1.2.1 Synthetic Methods

Pyrimidines have been prepared by number of methods but the most important are those in which the ring is formed from two fragments which contribute the C-C-C and N-C-N atoms respectively.

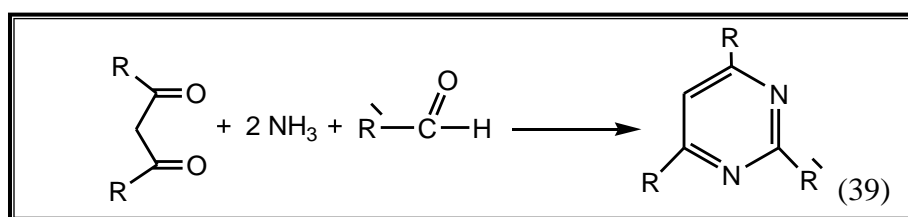
1. From Malonic Esters or Malonic acid with urea: A simple synthesis^[66,67] of pyrimidine ring involves a condensation of malonic ester and urea in the presence of a base to yield barbituric acid(36). A modification of this method consists of using substituted malonic ester. Beside malonic esters, a series of other compounds such as β - keto acid or ester β -diketones may be employed. Uracil(37), for instance, is obtained from α -formylacetic acid produced *in situ* by decarboxylation of malic acid with conc. Sulfuric acid and reaction of the β -keto acid with urea. Uracil can be converted to pyrimidine(35) in the following steps:



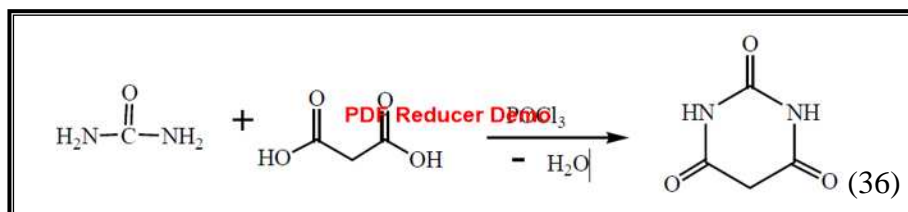
Urea may be replaced by amidine, guanidine or thiourea and condensed with 1,3-diketone. Thus acetylacetone on reaction with benzamidine give 4,6-dimethyl-2-phenylpyrimidine(38).



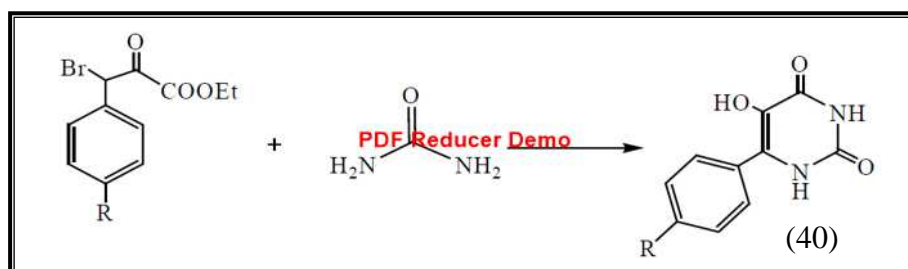
A 1,3-diketone may be condensed with an aldehyde and ammonia to furnish pyrimidine(39)^[68].



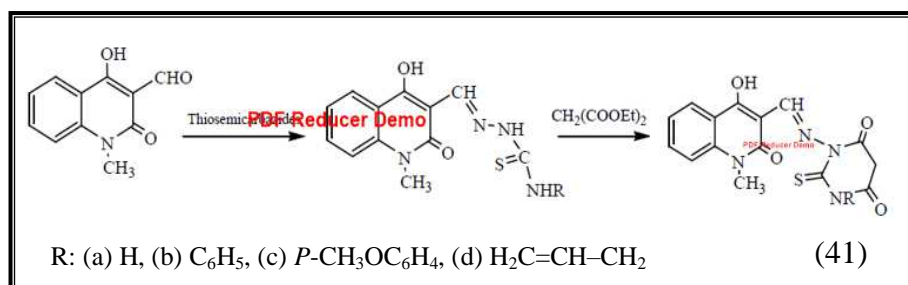
Grimaux^[69] reported the preparation of barbituric acid(36) from urea and malonic acid in the presence of phosphorus oxychloride.



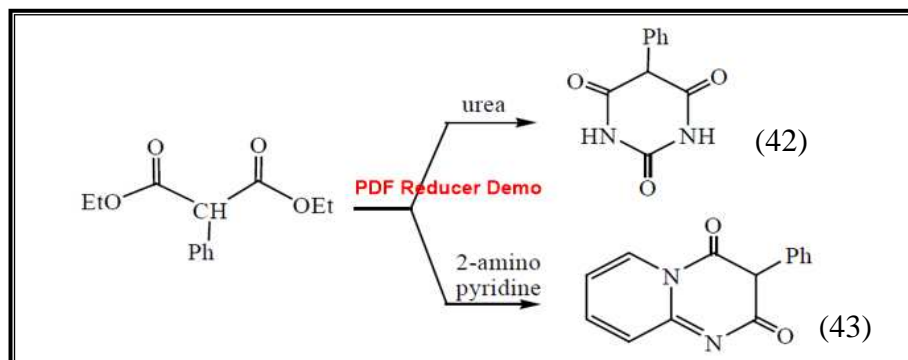
Andereichikov et.al.,^[70] reported the synthesis of uracil derivatives(40) by the reaction of aryl substituted bromopyruvate esters with urea.



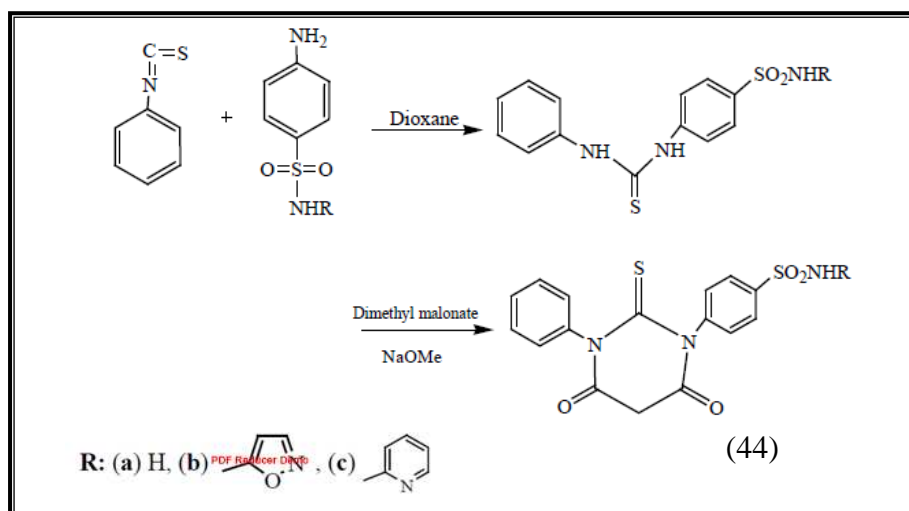
Mohamed^[71] reported the reaction of 1,2-dihydro-4-hydroxy-1-methyl-2-oxoquinoline-3-carbaldehyde with thiosemicarbazides to yield desired thiosemicarbazones. These thiosemicarbazones then reacted with diethyl malonate which resulted into corresponding pyrimidine derivatives(41) in good yields.



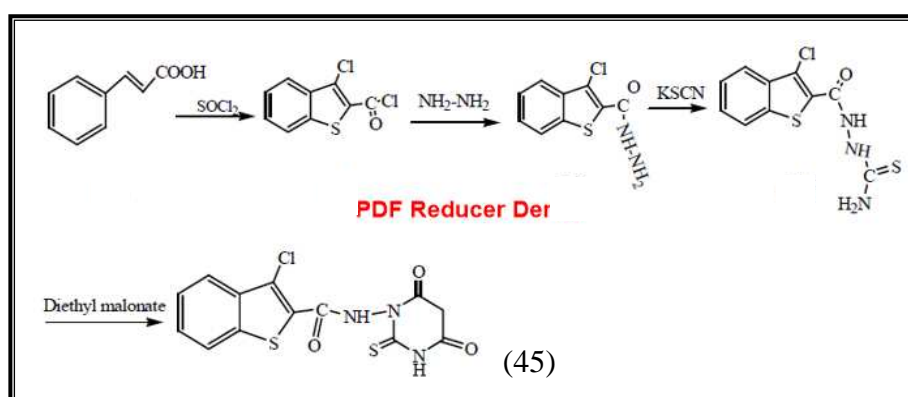
Stadlbauer et.al.,^[72] reported the reaction of diethyl malonate with urea and 2-aminopyridine which gave barbituric acid derivative(42) and pyrido[1,2-*a*]pyrimidine-2,4-dione derivative(43), respectively in better yields.



Bawazir et.al.,^[73] reported the reaction of phenylthiocyanate with sulfa drugs in 1,4-dioxane that yielded *N,N'*-disubstituted thiourea derivatives which, on reaction with dimethyl malonate in presence of sodium methoxide provided corresponding 1,3-disubstituted thiobarbituric acid derivatives(44).

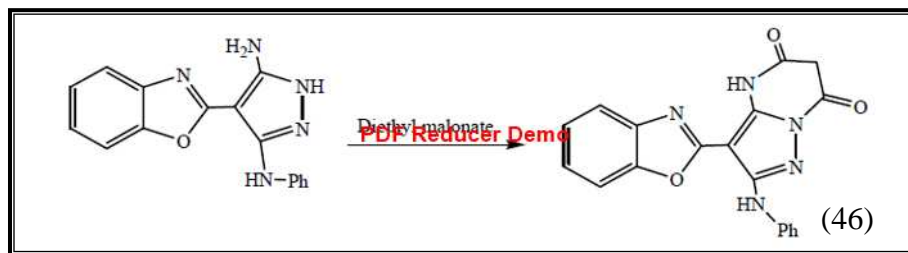


Naganagowda et.al.,^[74] reported the synthesis of 3-chloro-1-benzothiophene-2-carbonylchloride from cinnamic acid. The compound reacted with hydrazine and gave 3-chloro-1-benzo[*b*]thiophene-2-carboxylic acid hydrazide, which on reaction with potassium thiocyanate provided 2-[(3-chloro-1-benzo[*b*]thiophen-2-yl)carbonyl]hydrazine carbothioamide which on reaction with diethyl malonate yielded 3-chloro-N(4,6-dioxo-2-thioxo-tetrahydropyrimidin-1(2H)-yl)-1-benzothiophene-2-arboxamide(45).

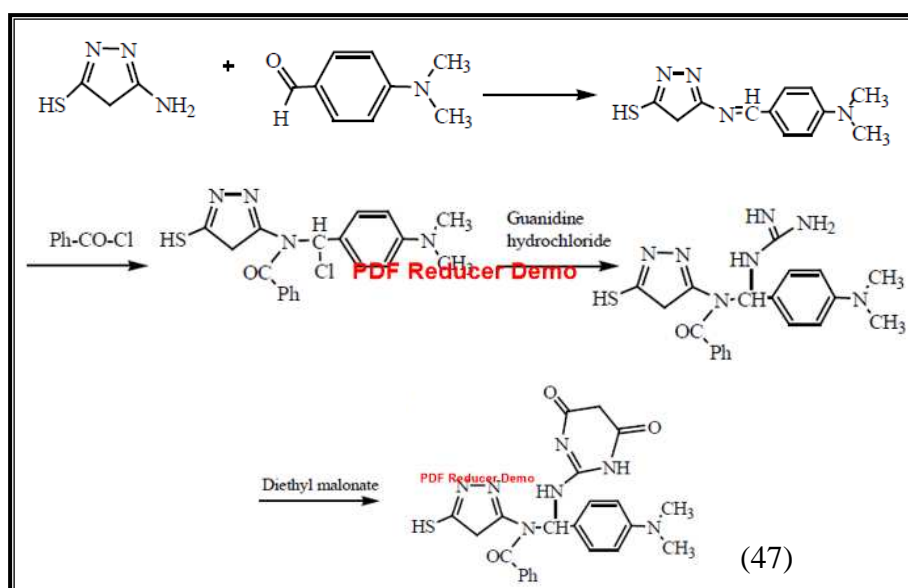


Wahab and Mohamed^[75] reported the reaction of N-[3-amino-4-(benzoxazol-2-yl)pyrazol-5-yl]phenylamine with diethyl malonate

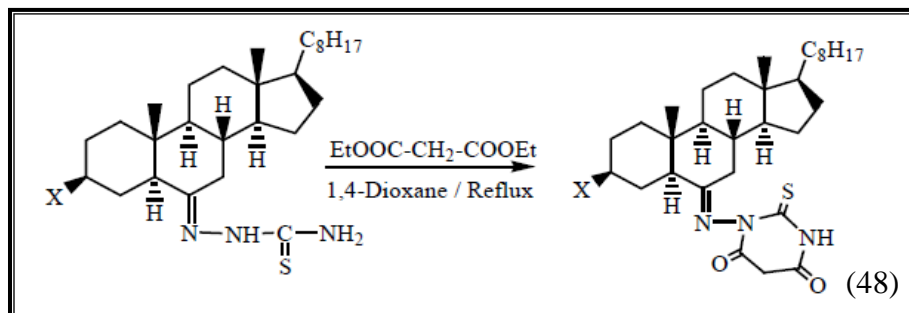
which provided 3-benzoxazol-2-yl-2-phenylamino-4H-pyrazolo[1,5-*a*]pyrimidine-5,7-dione(46) in 80 % yield.



Essa et.al.,^[76] reported the reaction of 5-amino-3-mercaptopyrazole with 4-dimethylaminobenzaldehyde which gave 5-(4'-dimethylamino) benzylidene)amino-3-mercaptopyrazole. This compound on react with benzoyl chloride gave 5-(4'-dimethylamino) chlorobenzylidene)-N-(benzoyl)amino-3-mercaptopyrazole. This compound reacted with guanidine hydrochloride and yielded 5-((4'-dimethylamino)-benzylidene)-N-(benzoyl)-N-(guanidino))-amino-3-mercaptopyrazole which later on reaction with diethyl malonate gave 5-((4'dimethylamino)benzylidene)-N-(benzoyl)(4,6-dioxotetrahydropyrimidin-2-ylamino)methyl)-} amino-3-mercaptopyrazol(47).

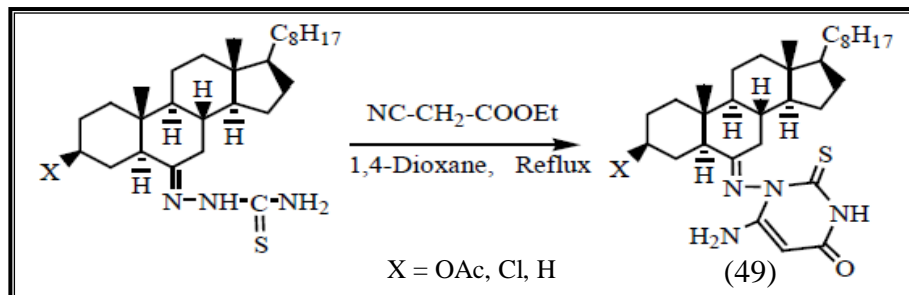


Shamsuzzaman et.al.,^[77] reported the reaction of steroidal thiosemicarbazones with diethyl malonate that provided steroidal pyrimidinones(48) in better yields.

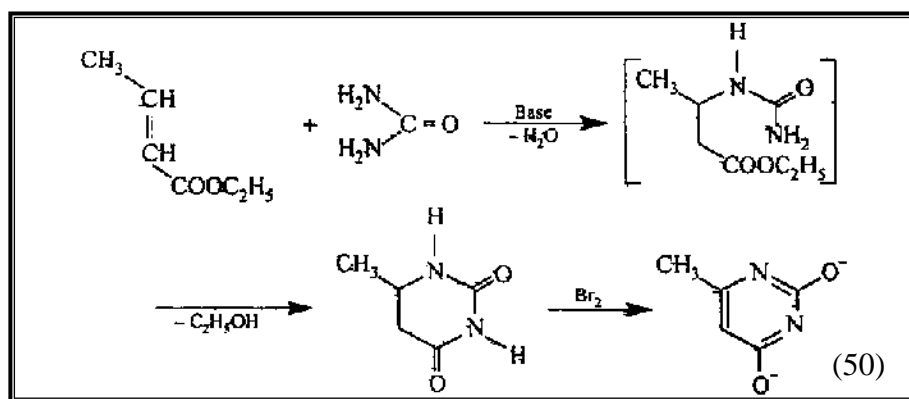


2. From ethyl cyanoacetate with thiosemicarbazones:

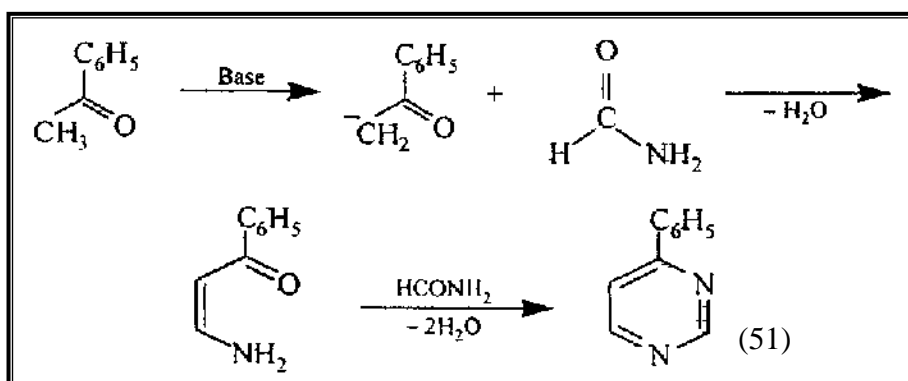
Shamsuzzaman et.al.,^[78] also reported another set of reaction in which steroidal thiosemicarbazones reacted with ethylcyanoacetate and yielded differently substituted steroidal pyrimidines(49) in sufficient amounts.



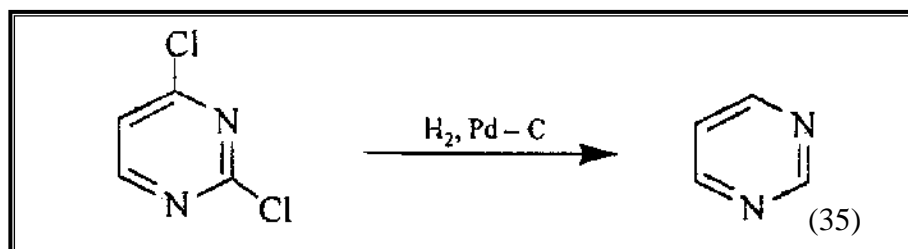
3. **From ethyl crotonate:** Another useful method involves the condensation of amidines or urea with unsaturated compounds such as ethyl crotonate in the presence of a base. A dihydropyrimidine is the initial product which is readily oxidized to the corresponding pyrimidine(50)^[65].



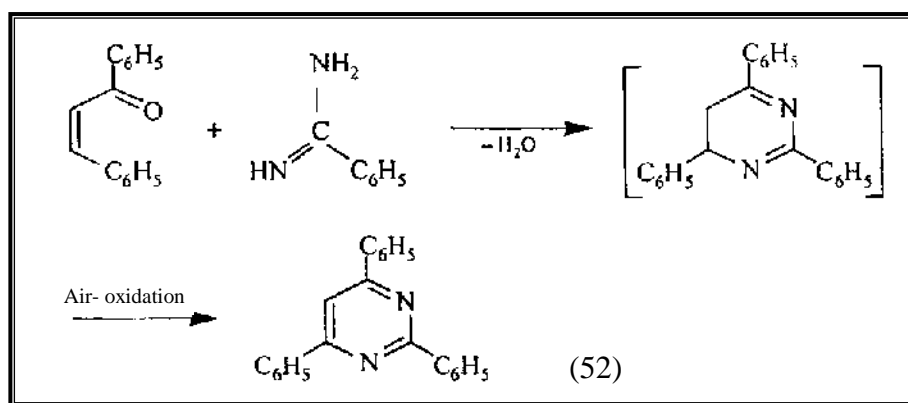
4. Formamide reacts with compounds containing active methylene group^[79] in a way to form β -enaminoketones. With excess formamide, the β -enaminoketones cyclizes to form pyrimidine. Acetophenone, for instance, reacts with formamide to yield 4-phenylpyrimidine(51). A closely related procedure involves the reaction of β -diketones with an excess of formamide^[80].



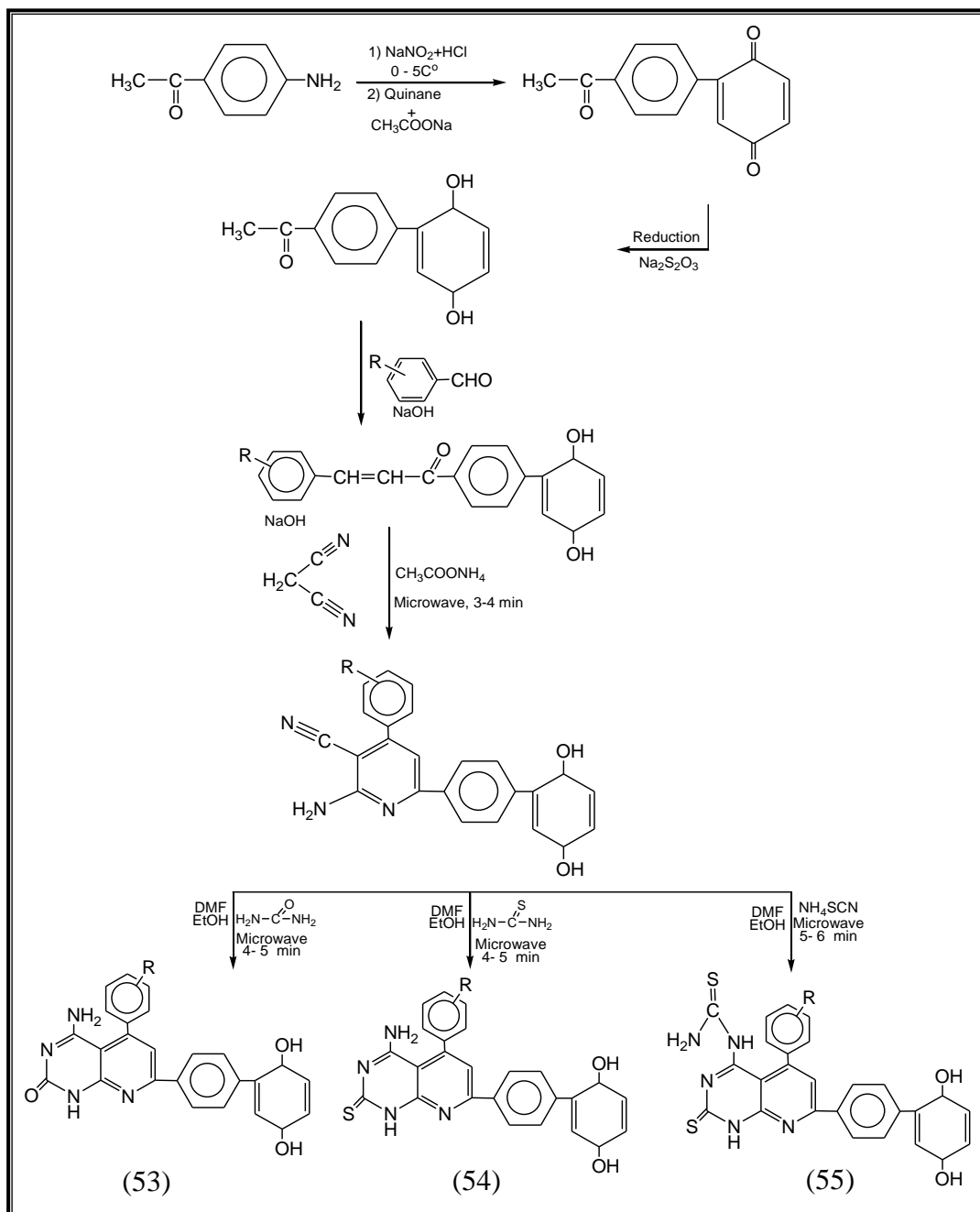
5. Pyrimidine(35) itself can be obtained by the decarboxylation^[81] of pyrimidine-4,6-dicarboxylic acid or by the dechlorination of 2,4-dichloropyrimidine as shown in the following equation.



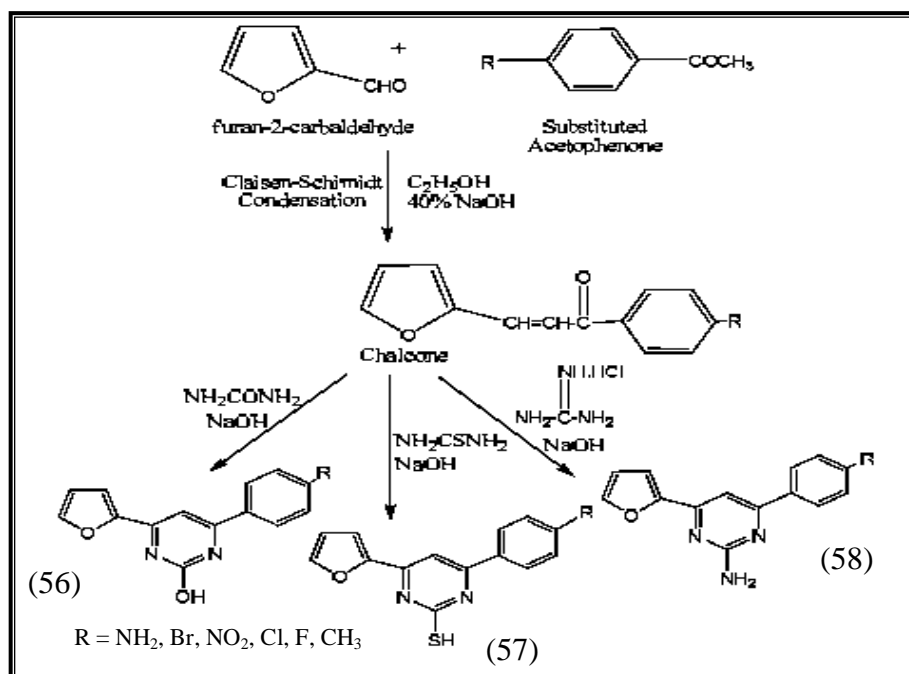
6. **From α , β -unsaturated ketones:** An interesting reaction of simple α , β -unsaturated ketone chalcones with amidine to give pyrimidines, has been reported^[82]. The initial product of this reaction is probably a dihydropyrimidine which is readily oxidized by a stream of air to the corresponding pyrimidine. Benzamidine and β -benzoylstyrene furnish 2,4,6-triphenylpyrimidine(52).



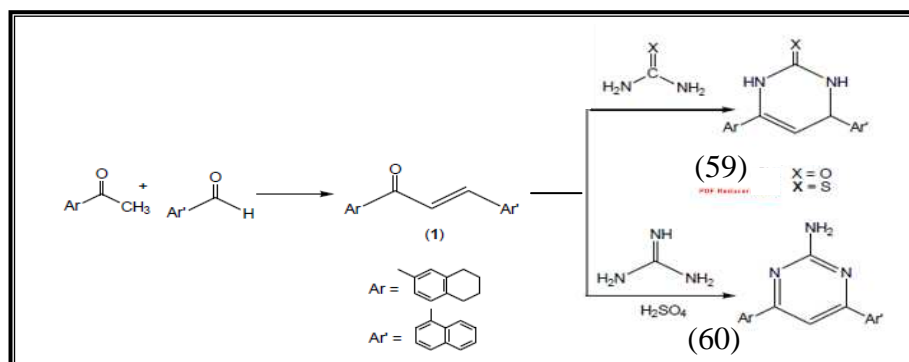
Patel et.al.,^[83] reported the synthesis of a Series of Pyrido[2,3-d]Pyrimidine Derivatives(53), (54) and (55) from the reaction of 2-amino-6-[4'-(2'',5'' dihydroxyphenyl)phenyl]-4-(substitutedphenyl) pyridine-3-carbonitrile with urea, thiourea and ammonium thiocyanate respectively. These compounds have been screened for their antibacterial and antifungal activities against different microorganisms.



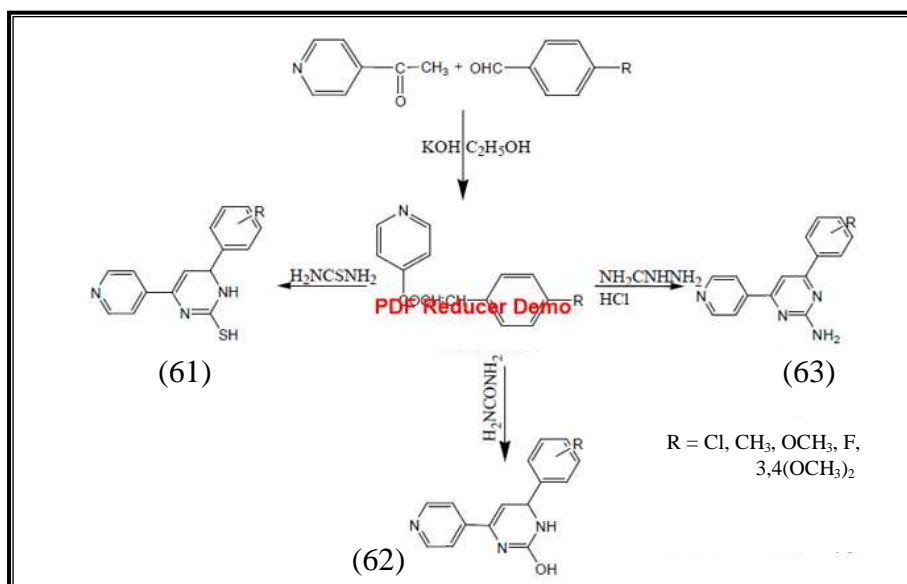
Joshi et.al.,^[84] reported various pyrimidine derivatives (56), (57) and (58), prepared by reaction of Chalcone with urea, thiourea and guandine HCl in ethanolic sodium hydroxide. The synthesized selected compounds were evaluated for their anti-inflammatory and analgesic activity.



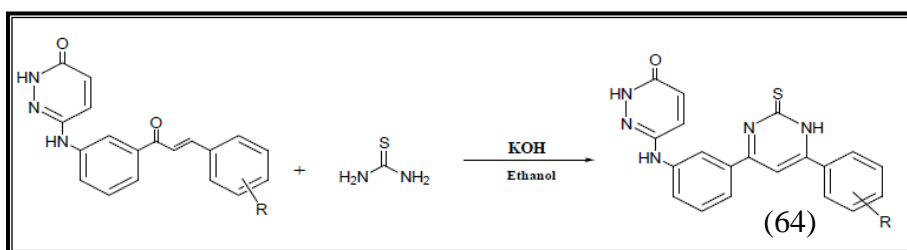
Gouhar and Youns^[85], reported the synthesis of pyrimidines(59) and (60) by the aldol condensation of 2-acetyl (5,6,7,8-tetrahydro-naphthalene) with 1-naphthaldehyde afforded chalcone derivative that is considered as an excellent starting material for the synthesis of many Heterocycles derivatives. The cyclo condensation of chalcone with urea, thiourea and guanidine gives pyrimidine derivatives. Many of these newly synthesized compounds are evaluated as anticancer agent.



Kachroo et.al.,^[86] reported the synthesis of chalcones derivatives which were cyclised to pyrimidine analogs by using thiourea, urea and guanidine hydrochloride. The newly synthesized pyrimidine derivatives (61), (62) and (63) have been evaluated for their anti-inflammatory, antioxidant, antitubercular and antibacterial activities.

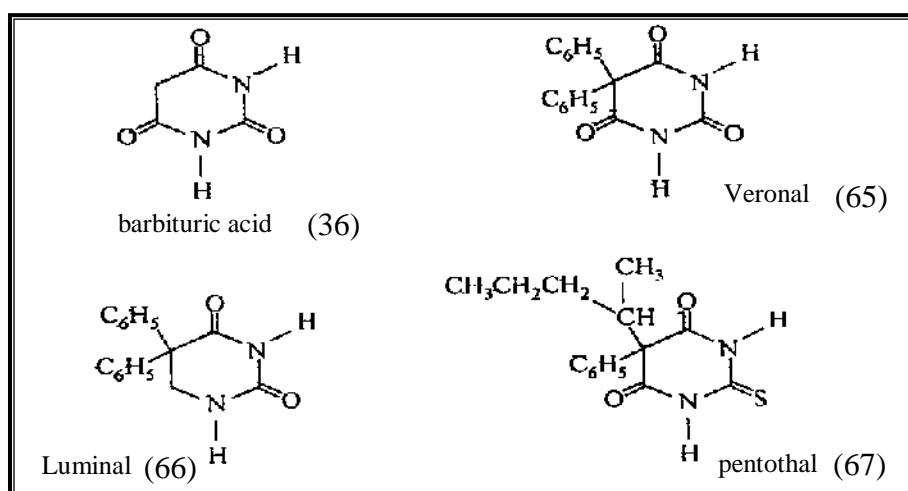


Tupare and Pawar^[87], reported the several substituted pyridazone derivative of acetophenone which are condensed with aromatic aldehydes, and resulting chalcones which are used for the synthesis of diaryl thiopyrimidines (64). Organic compounds containing pyrimidines, thiopyrimidines as a core unit are known to exhibit various biological activities and pharmaceutical activities.

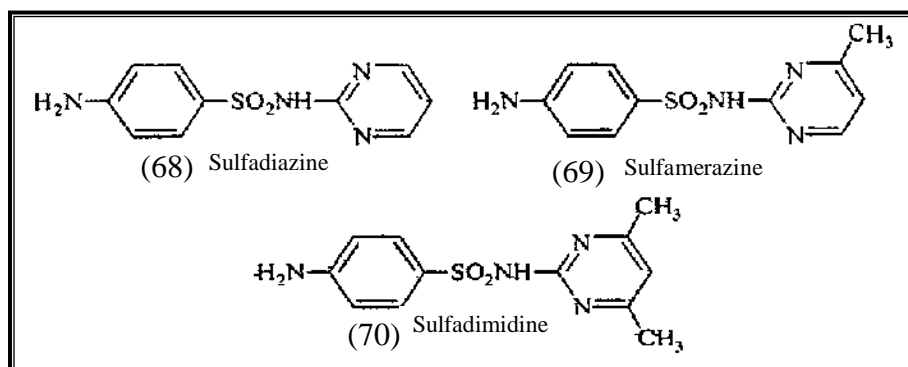


1.2.2 Naturally occurring and biologically active compounds^[88,89,62]

Pyrimidine itself is not found in nature but substituted pyrimidines and compounds containing the pyrimidine ring are widely distributed in nature. Derivatives of barbituric acid(36), i.e., oxygenated pyrimidines are perhaps the most widely used in medicines, for example, Veronal(65), Luminal(66) are used as hypnotics while Pentothal(67) is used as an anaesthetic.

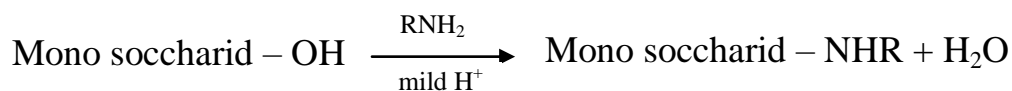


Several important sulfa drugs of pyrimidine derivatives are namely sulfadiazine(68), sulfamerazine(69) and sulfadimidine(70).

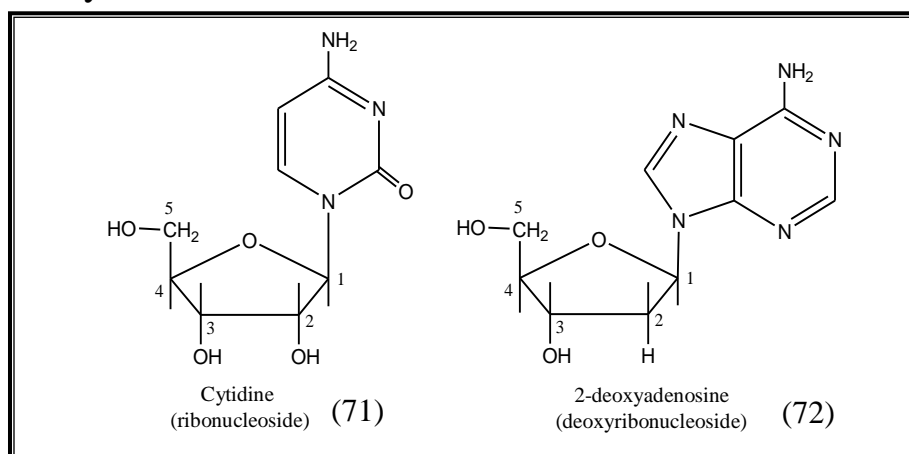


Sulfadiazine is still widely used but the last two are no longer used for chemotherapy of infections.

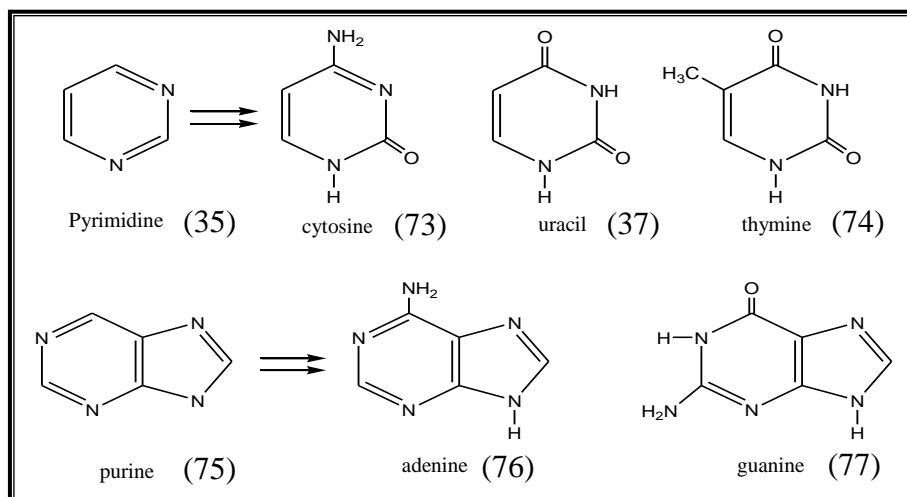
N-Glycosides: formed when a monosaccharide react with amine in presence of mild acid.



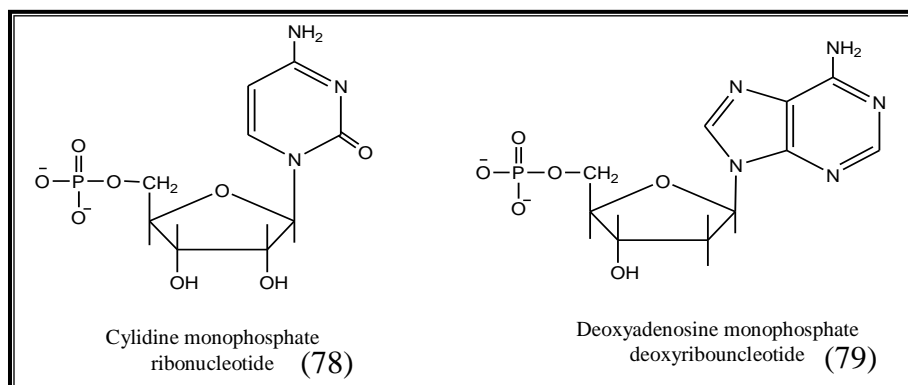
The N-glycosides of two sugars, D-ribose and 2-deoxy-D-ribose, formed from reaction of each sugar with contain heterocyclic amine are called ribonucleoside(71) and deoxyribonucleoside(72), because they form the building blocks of RNA and DNA respectively.



Only five common heterocyclic amines are used to form these nucleosides. These compounds have one ring, and are derived from pyrimidine (cytosine(73), uracil(37) and thymine(74)), and the two compounds are derived from purine(75) (purine is a fused pyrimidine and imidazole rings) these purine are called (adenine(76) and guanine(77)).

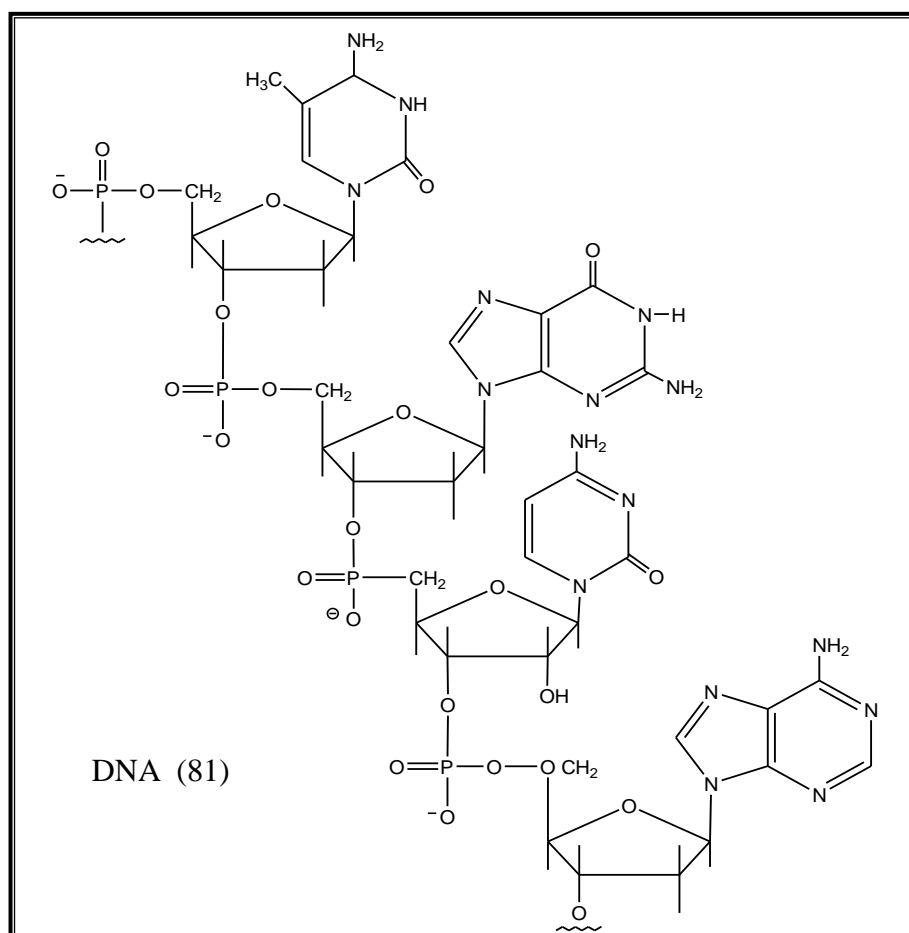
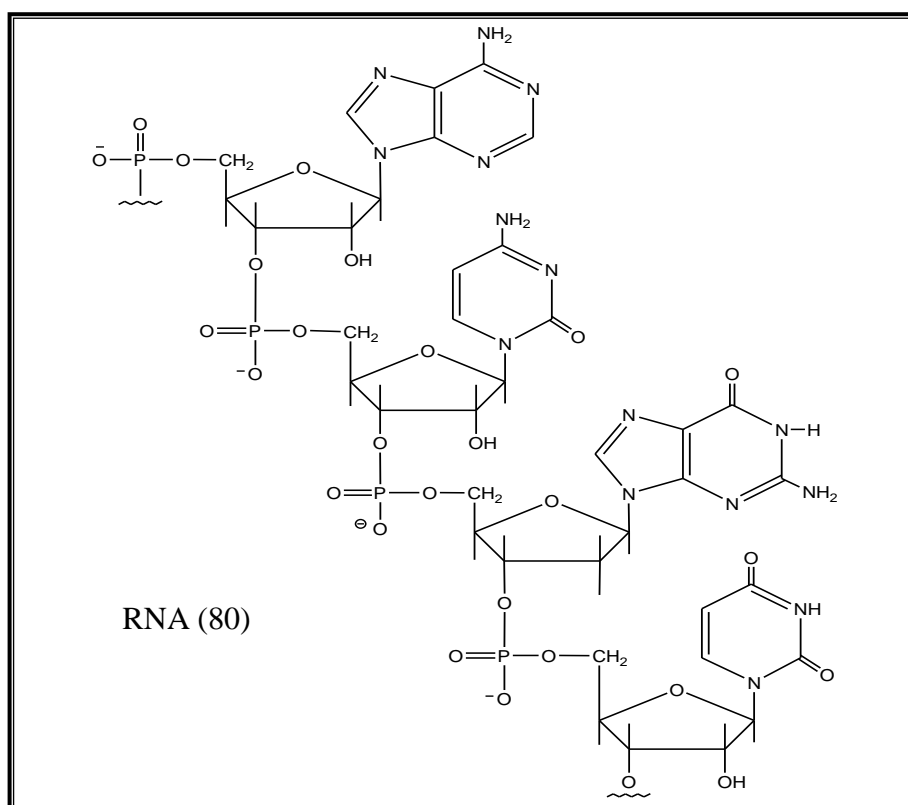


When hydroxyl group at C₅ of sugar nucleus is bonded to phosphate, the derivatives are called ribonucleotide(78) and deoxyribonucleotides(79) respectively.

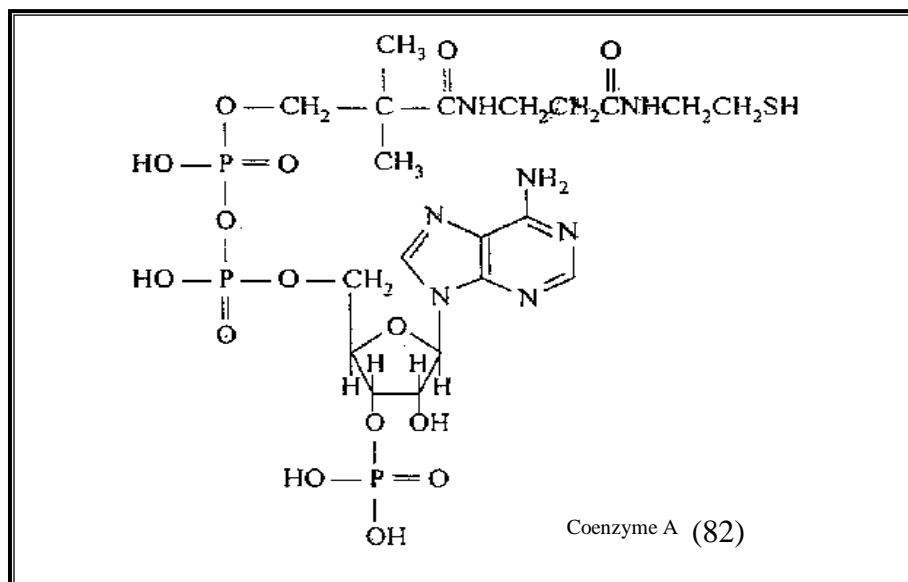


Ribonucleotides are the building blocks of the polymer ribonucleic acid (RNA)(80), the messenger molecules that convert genetic information into proteins, while deoxy ribonucleotide are building block of polymer deoxyribonucleic acid (DNA)(81), the molecules that are responsible for the storage of all genetic information.

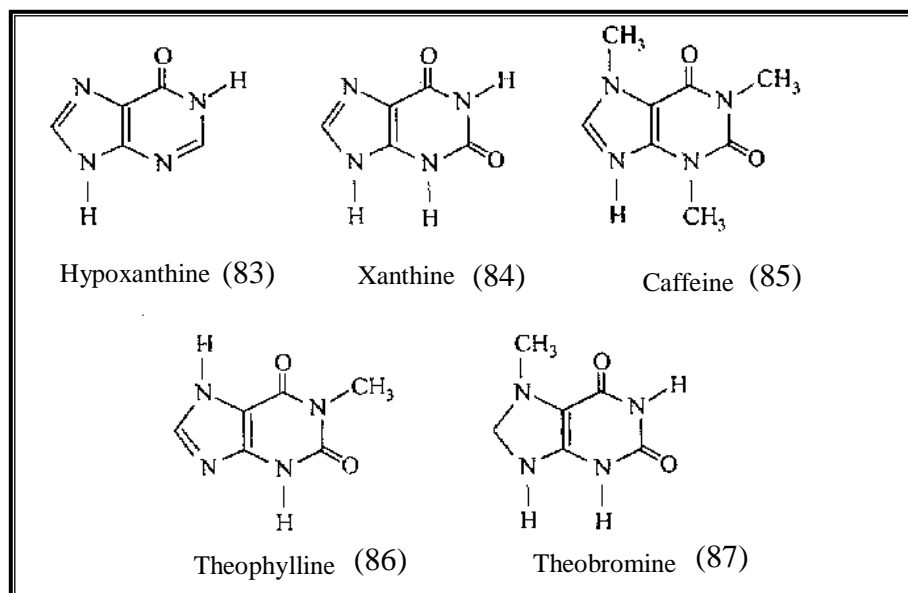
Short segments of RNA and DNA:



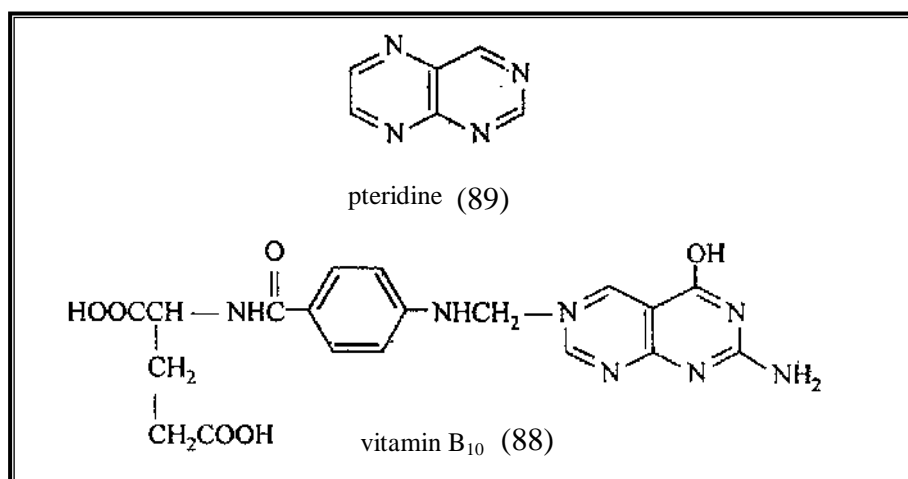
A widely distributed nucleotide that plays a decisive role in many metabolic processes is called coenzyme A(82). It is known to take place in processes like transacetylation reaction, fatty acids oxidation, etc.



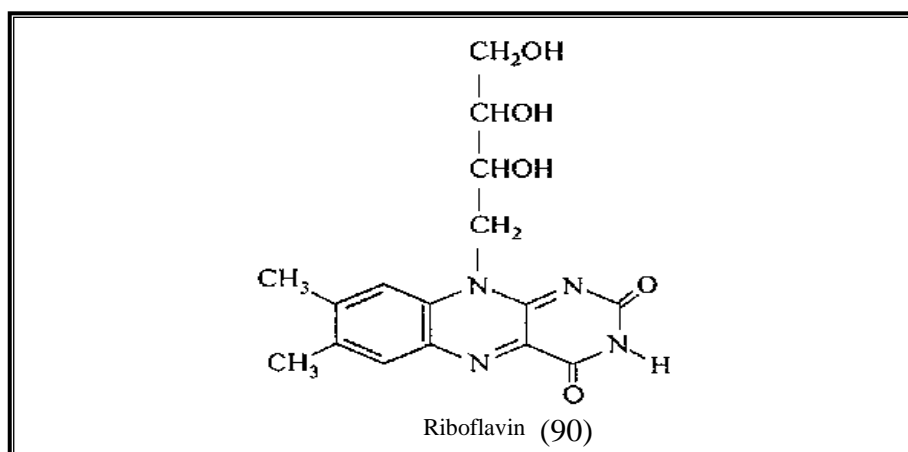
A variety of natural products such as alkaloids also contain the pyrimidine ring system, these include hypoxanthine(83), xanthine(84) which occur in tea and caffeine(85) and theophylline(86) are constituents of tea leaves. Theobromine(87) is found in cocoa beans.



Folic acid: The pteridine ring system is also widely distributed in nature. The important growth factor folic acid, vitamin B₁₀(88) is constructed of a pteridine(89) ring, *p*-amino benzoic acid and glutamic acid, i.e. pteroylglutamic acid. It is widely distributed and has been isolated from liver yeast.



Riboflavin(90): This substance has been called vit. B₂, lactaflavin or riboflavin and is a member of the water soluble vitamin B complex. It is widely distributed in nature both in animals and plants. It is unstable to light.



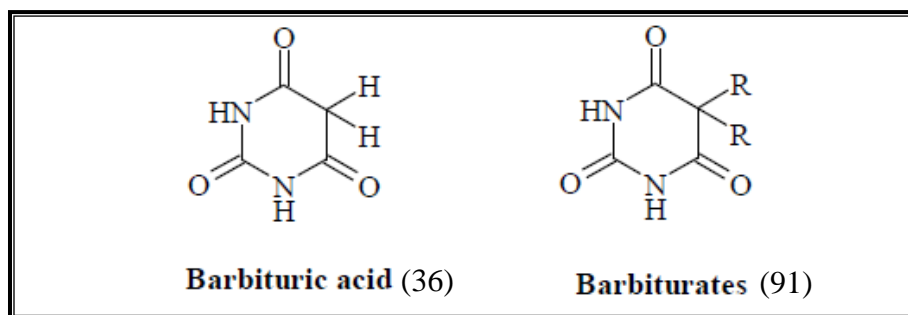
1.2.4 Pharmacologically active pyrimidines

Pyrimidines have a long and distinguished history extending from the days of their discovery as an important constituent of nucleic acids to their current use in the chemotherapy of AIDS. During the last two decades, several pyrimidines derivatives have been developed as chemotherapeutic agents and have found wide clinical applications. Many pyrimidines and related heterocyclic compounds are found to possess a wide important pharmacophore and privileged structure in medicinal chemistry^[87].

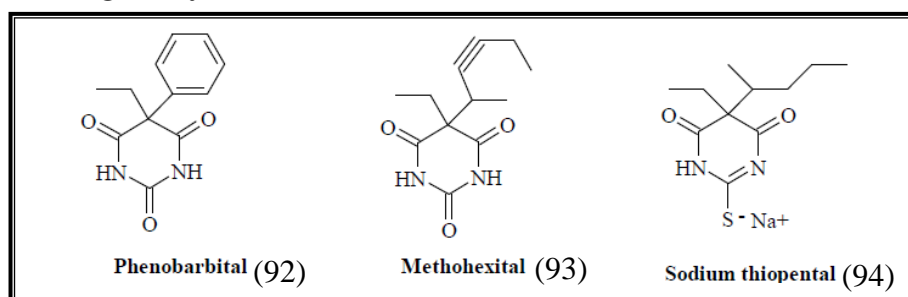
Pyrimidines and their derivatives are considered to be important for drugs and agricultural chemicals. The use of pyrimidines is critical to successful treatment of various diseases. Pyrimidine derivatives possess several interesting biological activities such as antimicrobial, antitumour, antifungal, anticancer, antiviral, antibacterial, antioxidant, antiallergic and antidepressant activities. Many pyrimidine derivatives are used for thyroid drugs and leukaemia^[90,91]. Although there are numerous classes of drugs that are routinely used to treat the diseases in humans, there are major four subcategories that contain pyrimidine base structure.

- Barbiturates
- Nitropyrimidines
- **Barbiturates**

The substituted barbiturates(91) represent a special class of compounds which have been used for sedative hypnotic action. They are depressants of the central nervous system (CNS) that impair or reduce the activity of the brain by acting as Gamma Amino Butyric Acid (GABA) potentiators.

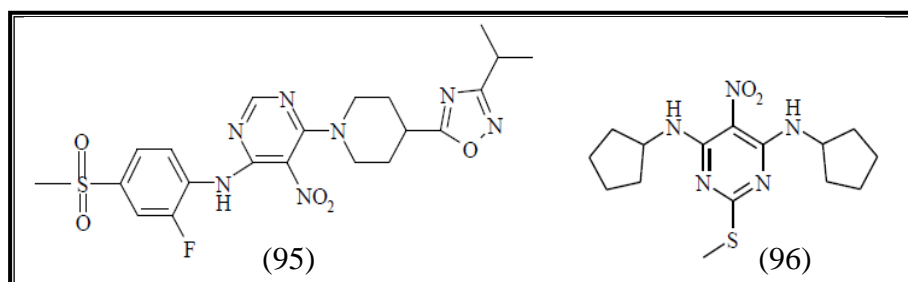


Phenobarbital(92) is most commonly used as anticonvulsant. It also have sedative and hypnotic action. Methohexital(93) is a short-acting, and has a rapid onset of action. Sodium thiopental(94) is a rapid-onset short-acting barbiturate general anaesthetic. Further substitution of side chains on the barbituric acid ring produce the pharmacologically active barbiturates^[92-94].



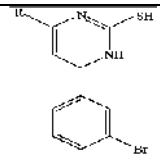
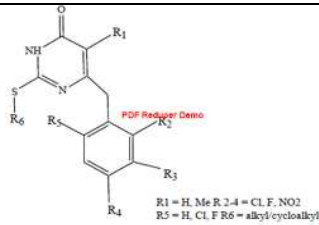
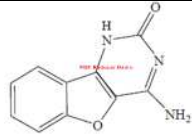
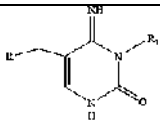
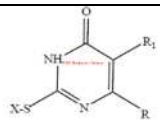
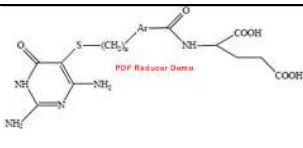
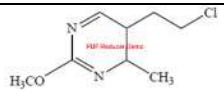
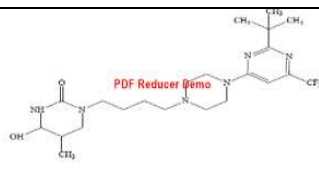
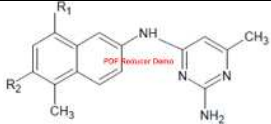
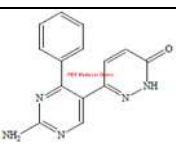
▪ Nitroimidine

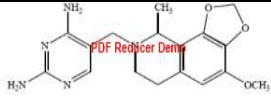
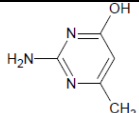
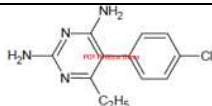
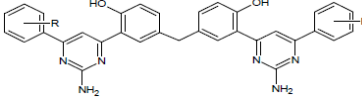
Nitroimidine category includes (95) and (96). (95) is agonist for the novel cannabinoid receptor. (96) acts as a positive allosteric modulator at GABAB receptor. It has been shown to produce anxiolytic effects and reduce self-administration of ethanol, cocaine and nicotine^[95,96].



1.2.4. Various pharmacological activities of pyrimidines:

Table (1-2): Various pharmacological activities of pyrimidines

Authors	Structure	Pharmacological Activity
Nimavat et.al. ^[97]		Antitubercular and Antimicrobial agents
Antonello et.al. ^[98]		Anti-HIV-1 agents in both cell-based and enzyme
Sangopure SS and Mulogi AM ^[99]		Antimicrobial activity
Somnath et.al. ^[100]		Antimicrobial activity
Viney Lather and A.K. Madan ^[101]		Anti-hiv activity
MichaelD. Varney et.al. ^[102]		Potent inhibitors of Glycyl-amideribonucleotide Trans-formylase with potent cell growth inhibition
Ghiya BJ.& Manoj Prabjavat ^[103]		Anticancer and antineoplastic activity
Geneste H.et.al. ^[104]		Dopamine D3-receptor antagonists activity.
Kaplina et.al. ^[105]		Herpes inhibiting activity
Tsutsumi et.al., ^[106]		Adenosine receptor antagonists

Pierre C. et.al. ^[107]		Dihydrofolate reductase inhibitors
Tayade DT. et.al. ^[108]		Antimicrobial activity
Rastelli G. et.al. ^[109]		Antimalarial activity
Nagaraj A. and Sanjeeva Reddy C. ^[110]		Antibacterial, Antifungal and Anti-Inflammatory Activities.

Aim of the work:

The aim of this work involves:

First: Building up a pyrimidine unit nucleus containing substituents at 2,4,6-positions, like oxo, imino and thioxo groups at position-2, benzenesulphonamido phenyl, ureidophenyl *p*[N-methylphenylazophenyl), *p*,N-phthalimidophenyl and *p*(N-phthalimido)benzamido-N'-phenyl groups at position-4 and *p*-chlorophenyl or *p*-nitrophenyl groups at position-6.

Second: Examination of antimicrobial activities of the 2,4,6-substituted pyrimidines compounds against Gram–Ve bacteria (*Serratia marcescens*, *pseudomonas aeruginosa*) and Gram+Ve bacteria (*staphylococcus aureus*, *streptococcus pyogenes*) and antifungal activities against *candida albicans*.

Chapter Two
Experimental Part

2.1. Chemicals

Table (2-1) Shows all the utilized chemicals in experimental course of this work.

Table (2-1): Chemicals and their manufactures

Chemicals	Supplied from	Purity %
4-amino benzoic acid	Merck	99.8
4-aminoacetophenon	Merck	99.8
Acetic acid (glacial)	Riedal-dehaën	98.9
Benzene	Scharlau	99.9
Benzene sulphonyl chloride	Merck	99
Chloroform	Scharlau	99.8
Dimethylsulphoxide	BDH	98.9
Ethanol	Scharlau	99.9
Ethylacetate	Merck	99.8
Hydrochloric acid	BDH	98.7
Methanol	Scharlau	99.9
N-methylaniline	Merck	97
<i>p</i> -chlorobenzaldehyde	BDH	98
Petroleum ether b.p.(60-80)	BDH	99.9
Phthalic anhydride	BDH	99.9
<i>p</i> -nitrobenzaldehyde	Aldrich	99
Potassium cyanate	Merck	99.9
Pyridine	BDH	98
Quanidine hydrochloride	Merck	98
Sodium hydroxide	BDH	98
Sodium nitrite	BDH	99.8
Thionyl chloride	Aldrich	99.7
Thiourea	Merck	99
Urea	Merck	98.9

2.2. Instruments

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

2.2.1. Thin layer chromatography (TLC)

The (TLC) was performed, using aluminum plates coated with (0.25mm) layer of silica gel F₂₅₄ (Fluka), spots were detected by iodine vapor.

2.2.2. Melting point measurements

Melting point were recorded by Digimelt MPA 161 (MSRS) electronic at Ibn- Al Haitham college.

2.2.3. Infrared spectra

Infrared spectra were recorded using (8300) (FT-IR) Shimadzu spectrophotometer in the range (4000–600)cm⁻¹, as (KBr discs) at Ibn- Sina advisory office.

2.2.4. Nuclear Magnetic Resonance (¹H NMR) and (¹³C NMR)

¹H NMR and ¹³CNMR spectra were carried out by: Ultra shield 300 MHZ, Bruker, Switzerland at University of Al- Albayt (in Jordan), and 500 MHZ, Bruker, Switzerland at University of Tahrán (in Iran), and are reported in ppm, DMSO -d₆ was used as solvent with TMS as an internal standard.

2.2.5. Mass spectroscopy

The Mass spectra recorded on Varian Saturn 2000 GC-MS-MS system, electron impact (EI) or chemical ionisation (CI) modes, Molecular mass, range 45- 650 Dalton, at Institute of Organic and Pharmaceutical Chemistry (IOPC), National Hellenic Research Foundation, Athens, Greece.

2.2.6. Antimicrobial activity

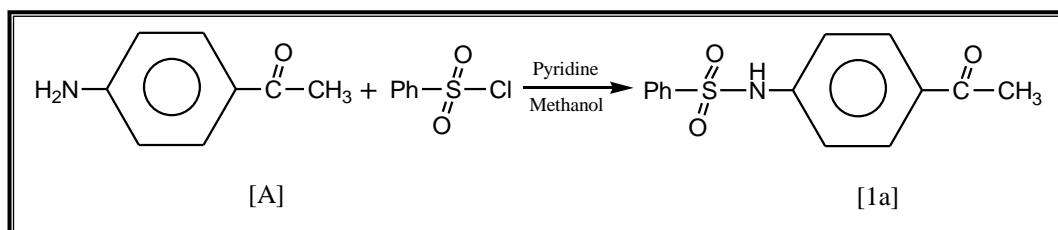
The antimicrobial activity was performed in Ibn Al- Haitham advisory office, the Central Service Laboratory and Central Environmental Laboratory, University of Baghdad.

▪ Series one:

2.3. Synthesis of chalcones (2-propene-1-one compounds)

A. Preparation of [N-(4-acetyl phenyl benzene sulphonamide)]^[111] [1a]

To (0.25g, 0.003mol) of p-aminoacetophenone and (0.23ml) pyridine in (10ml) absolute methanol, (0.4ml, 0.0031mol) benzenesulfonylchloride was added in small portion, reaction mixture was refluxed for 3hrs. Then reaction mixture was poured slowly into a stirred ice cold water, and kept it in refrigerator for 30 min. The formed precipitate was filtered, washed with water and dried. Recrystallized from (water-methanol) mixture. Physical properties are shown in Table (2-2).



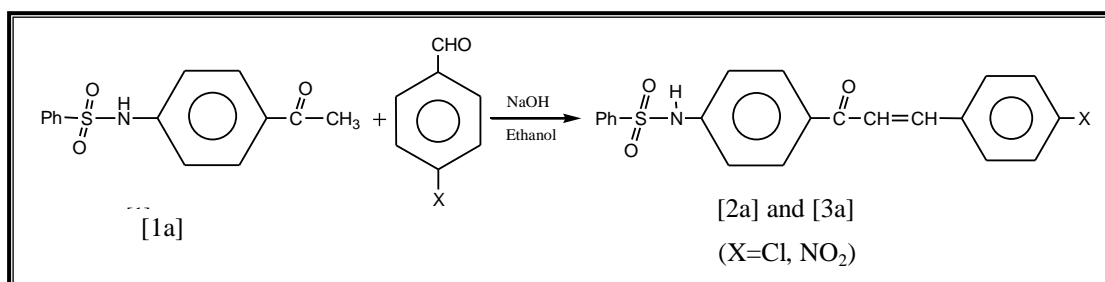
Equation (2-1): For synthesized compound [1a]

B. Synthesis of Chalcones:

[1(*p*-benzenesulphonamidophenyl)-3-*p*-chloro-2-propene-1-one]^[111]

[2a] and [1(*p*-benzenesulphonamidophenyl)-3-*p*-nitro-2-propene-1-one] [3a]

A mixture of equimolar amounts of (0.001mol) of *p*-substituted benzaldehyde and (0.26g, 0.001mol) of N(4-acetylphenyl)benzene-sulfonamide [1a] were dissolved in minimum amount of absolute ethanol (30ml). Sodium hydroxide (0.08g, 8%) was added and the mixture was refluxed for 8hrs. (in case of *p*-chloro benzaldehyde), while stirred for 12hrs (in case of *p*-nitro benzaldehyde). Reaction was monitored by TLC using (3:2) [petroleum ether-ethylacetate] eluent. Then reaction mixture was poured into ice cold water with constant stirring and kept in refrigerator for 30 min. The precipitate was obtained, filtered, washed with water and dried. Recrystallized from ethanol. Physical properties are shown in Table (2-2).

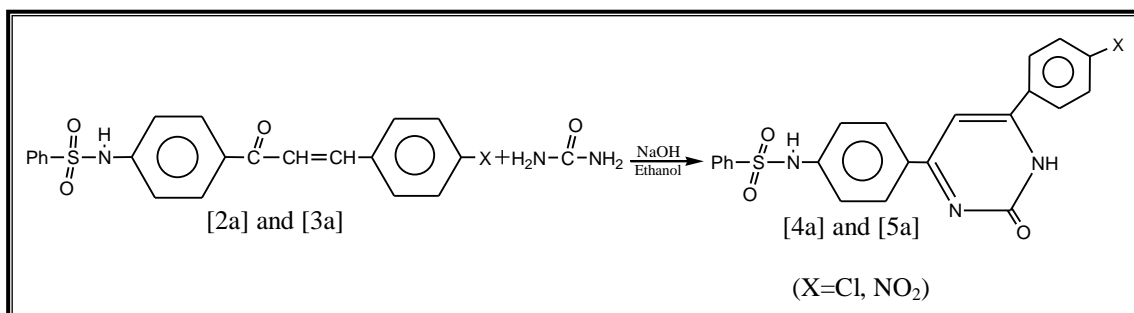


Equation (2-2): For synthesized compounds [2a] and [3a]

2.4. Synthesis of pyrimidines:

A. [4-(*p*-benzenesulphonamido)phenyl-6-*p*-chlorophenyl-2-oxo-(1H)pyrimidine] [4a] and [4-(*p*-benzenesulphonamido)phenyl-6-*p*-nitrophenyl-2-oxo-(1H)pyrimidine] [5a]

A mixture of chalcones [2a] or [3a] (0.0005mol), urea (0.06g, 0.001mol) and Sodium hydroxide (0.04g, 0.001mol) were dissolved in minimum amount of absolute ethanol (30ml) and refluxed for 24hrs. Reaction mixture was poured into stirred ice cold water, where pyrimidine precipitated out. The formed precipitate was filtered, washed with water and dried. Recrystallized from chloroform and petroleum ether. Physical properties are shown in Table (2-2).

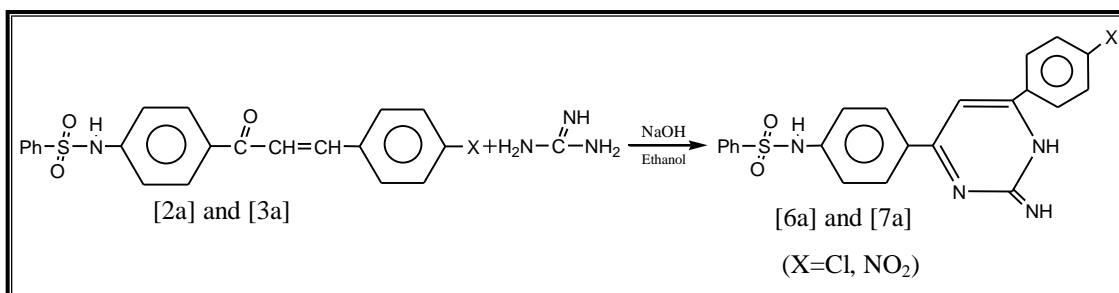


Equation (2-3): For synthesized compounds [4a] and [5a]

B. [4-(*p*-benzenesulphonamido)phenyl-6-*p*-chlorophenyl-2-imino-(1H)pyrimidine] [6a] and [4-(*p*-benzenesulphonamido)phenyl-6-*p*-nitrophenyl-2-imino-(1H)pyrimidine] [7a]

A mixture of chalcone [2a] or [3a] (0.0005mol), guanidine hydrochloride (0.095g, 0.001mol) and Sodium hydroxide (0.08g, 0.002mol) were dissolved in minimum amount of absolute ethanol (30ml) and refluxed for 24hrs. Reaction mixture was poured into stirred ice cold water, where pyrimidine precipitated out. The formed

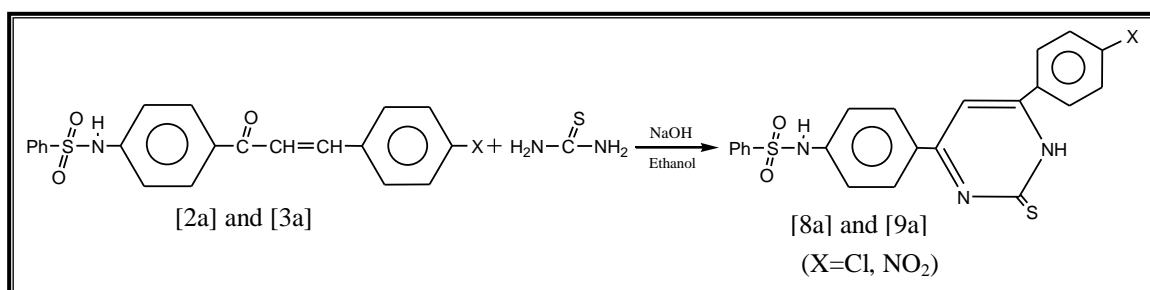
precipitate was filtered, washed with water and dried. Recrystallized from methanol and petroleum ether. Physical properties are shown in Table (2-2).



Equation (2-4): For synthesized compounds [6a] and [7a]

C.[4-(*p*-benzenesulphonamido)phenyl-6-*p*-chlorophenyl-2-thioxo-(1H)pyrimidine] [8a] and [4-(*p*-benzenesulphonamido)phenyl-6-*p*-nitrophenyl-2-thioxo-(1H)pyrimidine] [9a]

A mixture of chalcone [2a] and [3a] (0.0005mol), thiourea (0.076g, 0.001mol) and Sodium hydroxide (0.04g, 0.001mol) were dissolved in minimum amount of absolute ethanol (30ml) and refluxed for 24hrs. Reaction mixture was poured into stirred ice cold water, where pyrimidine precipitated out. The formed precipitate was filtered, washed with water and dried. Recrystallized from methanol and benzene. Physical properties are shown in Table (2-2).



Equation (2-5): For synthesized compounds [8a] and [9a]

Table (2-2): Physical properties for compounds series one

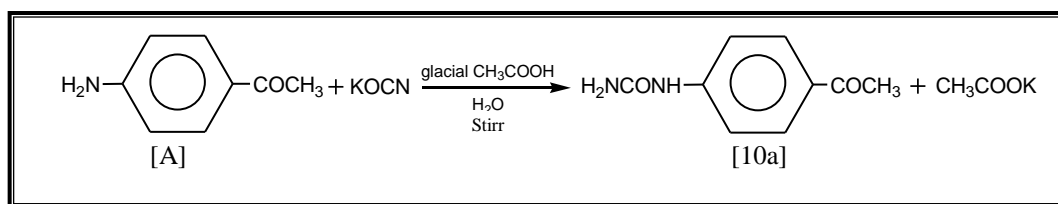
No.	Name of compound	M.wt	m.p C°	Wight of product	Yield %	Colour
[1a]	[N-(4-acetylphenylbenzene sulphonamide)]	275	129-132	0.4	48	Yellow
[2a]	[1(p-benzenesulphonamidophenyl)- 3-p-chloro-2-propene-1-one]	397.5	201-202	0.26	65	Yellow
[3a]	[1(p-benzenesulphonamidophenyl)- 3-p-nitro-2-propene-1-one]	408	212-214	0.25	61	Orange
[4a]	[4-(p-benzenesulphonamido)phenyl- 6-p-chlorophenyl-2-oxo-(1H) pyrimidine]	438.5	164-166	0.12	54	Pale- Yellow
[5a]	[4-(p-benzenesulphonamido)phenyl- 6-p-nitrophenyl-2-oxo-(1H) pyrimidine]	449	150-152	0.10	44	Brown
[6a]	[4-(p-benzenesulphonamido)phenyl- 6-p-chlorophenyl-2-imino-(1H) pyrimidine]	434.5	190-192	0.10	46	Yellow
[7a]	[4-(p-benzenesulphonamido)phenyl- 6-p-nitrophenyl-2-imino-(1H) pyrimidine]	448	146-148	0.14	62	orange
[8a]	[4-(p-benzenesulphonamido)phenyl- 6-p-chlorophenyl-2-thioxo-(1H) pyrimidine]	454.5	140-142	0.20	88	Yellow
[9a]	[4-(p-benzenesulphonamido)phenyl- 6-p-nitrophenyl-2-thioxo-(1H) pyrimidine]	465	130-132	0.15	64	Orange

▪ **Series two:**

2.5. Synthesis of chalcones (2-propene-1-one compounds)

A. Preparation of [4-acetylphenylurea]^[112] [10a]

To a stirred ice-bath cooling solution of (2.7g, 0.02mol) of *p*-aminoacetophenone in 5ml glacial acetic acid, a solution of (1.8g, 0.022mol) of potassium cyanate in 2-3ml H₂O was added slowly. Reaction mixture was stirred for 12hrs. Precipitate was formed, filtered and washed with H₂O, recrystallized from H₂O. Physical properties are shown in Table (2-3).



Equation (2-6): For synthesized compound [10a]

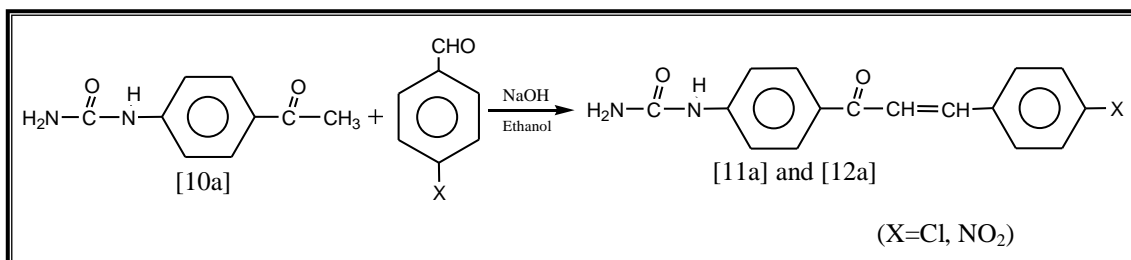
B. Synthesis of Chalcones:

[1(4-Ureido)phenyl-3-*p*-chlorophenyl-2-propene-1-one] [11a] and

[1(4-Ureido)phenyl-3-*p*-nitrophenyl-2-propene-1-one] [12a]

A mixture of equimolar amounts (0.002mol) of *p*-substituted benzaldehyde and (0.30g, 0.0021mol) of (*p*-acetophenonyl urea) [10a] were mixed and dissolved in minimum amount of absolute ethanol (30ml). Sodium hydroxide (0.09g, 0.0023mol) was added and the mixture was refluxed for 8hrs (in case of *p*-chloro benzaldehyde), while stirred for 12hrs (in case of *p*-nitro benzaldehyde). Reaction was monitored by TLC using (3:2) [petroleum ether-ethylacetate] eluent. Then reaction mixture was poured into ice cold water with constant stirring and kept in

refrigerator for 1/2h. The precipitate was obtained, filtered, washed with water and dried. Recrystallized from ethanol and drops of water. Physical properties are shown in Table (2-3).

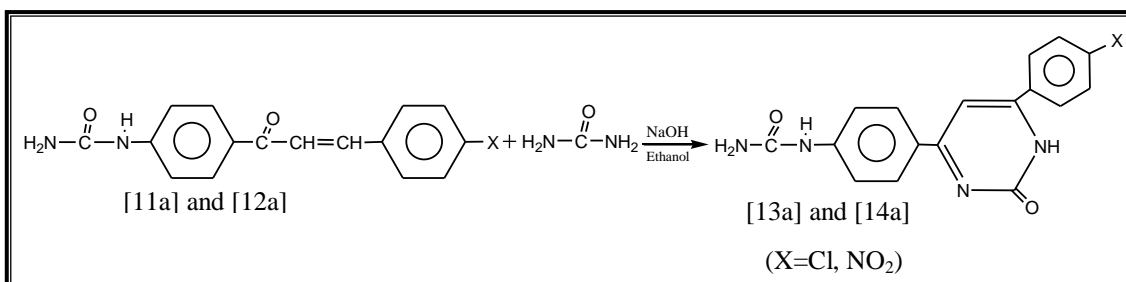


Equation (2-7): For synthesized compounds [11a] and [12a]

2.6. Synthesis of pyrimidines:

A. [4(*p*-Ureido-phenyl)-6-*p*-chlorophenyl-2-oxo-1H-pyrimidine] [13a] and [4(*p*-Ureido-phenyl)-6-*p*-nitrophenyl-2-oxo-1H-pyrimidine] [14a]

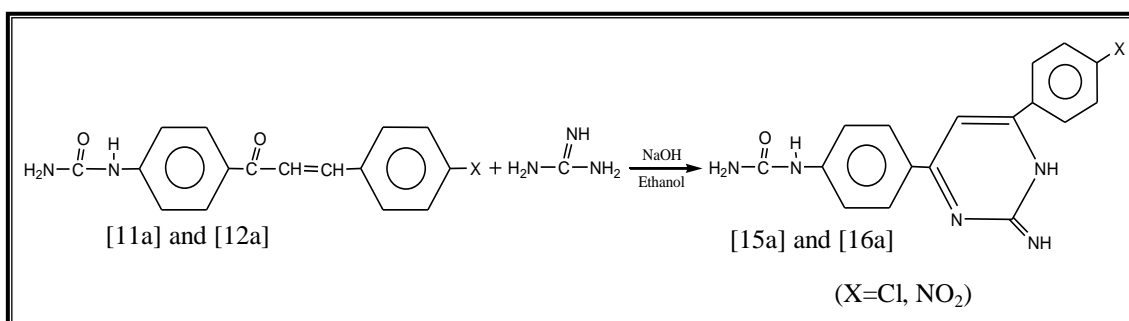
A mixture of chalcones [11a] or [12a] (0.0005mol), urea (0.06g, 0.001mol) and sodium hydroxide (0.04g, 0.001mol) were dissolved in minimum amount of absolute ethanol (30ml) and refluxed for 24hrs. Reaction mixture was poured into stirred ice cold water, where pyrimidine precipitated out. The formed precipitate was filtered, washed with water and dried. Recrystallized from chloroform and petroleum ether. Physical properties are shown in Table (2-3).



Equation (2-8): For synthesized compounds [13a] and [14a]

B. [4(*p*-Ureido-phenyl)-6-*p*-chlorophenyl-2-imino-1H-pyrimidine] [15a] and [4(*p*-Ureido-phenyl)-6-*p*-nitrophenyl-2-imino-1H-pyrimidine] [16a]

A mixture of chalcones [11a] or [12a] (0.0005mol), guanidine hydrochloride (0.095g, 0.001mol) and sodium hydroxide (0.08g, 0.002mol) were dissolved in minimum amount of absolute ethanol (30ml) and refluxed for 24hrs. Reaction mixture was poured into stirred ice cold water, where pyrimidine precipitated out. The formed precipitate was filtered, washed with water and dried. Recrystallized from methanol and petroleum ether. Physical properties are shown in Table (2-3).

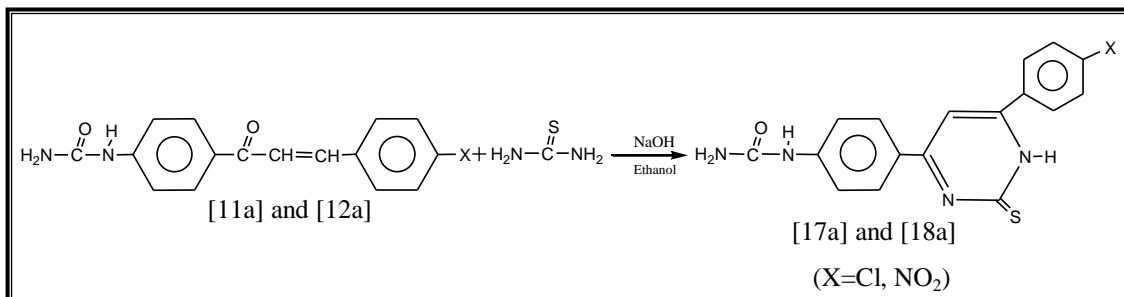


Equation (2-9): For synthesized compounds [15a] and [16a]

C. [4(*p*-Ureido-phenyl)-6-*p*-chlorophenyl-2-thioxo-1H-pyrimidine] [17a] and [4(*p*-Ureido-phenyl)-6-*p*-nitrophenyl-2-thioxo-1H-pyrimidine] [18a]

A mixture of chalcone [11a] and [12a] (0.0005mol), thiourea (0.076g, 0.001mol) and sodium hydroxide (0.04g, 0.001mol) were dissolved in minimum amount of absolute ethanol (30ml) and refluxed for 24hrs. Reaction mixture was poured into stirred ice cold water, where pyrimidine precipitated out. The formed precipitate was

filtered, washed with water and dried. Recrystallized from ethanol and petroleum ether. Physical properties are shown in Table (2-3).



Equation (2-10): For synthesized compounds [17a] and [18a]

Table (2-3): Physical properties for compounds series two

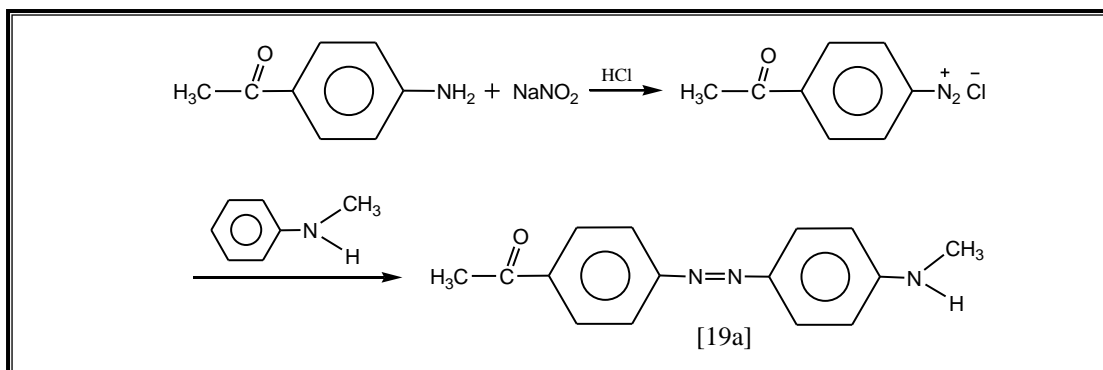
No.	Name of compound	M.wt	m.p. C°	Wight of product	Yield%	Colour
[10a]	[p-acetylphenylurea]	412	212-214	2.8	33	white
[11a]	[1(4-Ureido)phenyl-3-p-chloro-phenyl-2-propene-1-one]	300.5	170-172	0.4	66	Light brown
[12]	[1(4-Ureido)phenyl-3-p-nitrophenyl-2-propene-1-one]	311	232-234	0.36	57	yellow
[13a]	[4(p-Ureido-phenyl)-6-p-chloro-phenyl-2-oxo-1H-pyrimidine]	341.5	135-137	0.10	58	Light-orange
[14a]	[4(p-Ureido-phenyl)-6-p-nitro-phenyl-2-oxo-1H- pyrimidine]	352	150-152	0.096	54	brown
[15a]	[4(p-Ureido-phenyl)-6-p-chloro-phenyl-2-imino-1H-pyrimidine]	340.5	156-158	0.13	76	yellow
[16a]	[4(p-Ureido-phenyl)-6-p-nitro-phenyl-2-imino-1H-pyrimidine]	351	162-162	0.09	51	brown
[17a]	[4(p-Ureido-phenyl)-6-p-chloro-phenyl-2-thioxo-1H-pyrimidine]	357.5	145-147	0.10	55	yellow
[18a]	[4(p-Ureido-phenyl)-6-p-nitro-phenyl-2-thioxo-1H- pyrimidine]	368	165-167	0.07	38	orange

▪ **Series three:**

2.7. Synthesis of chalcones (2-propene-1-one compounds)

A. Synthesis of [*p*-acetyl-*p*'-(*N*-methylamino)azobenzene] [19a]

To a stirred solution of (1.12g, 0.008mol) of *p*-aminoacetophenone in 2ml conc. hydrochloric acid, cooled to 5°C in ice-bath. A chilled solution (0.65g, 0.009mol) of sodium nitrite in 3ml water was added in small portion within 30 minute^[113]. A solution of 1ml of *N*-methyl aniline in 0.5ml of acetic acid, was added to diazotized reaction mixture, then allowed to stand for 20 minute. The precipitate was formed, filtered, washed with water. Recrystallized from ethanol-water mixture. Physical properties are shown in Table (2-4).



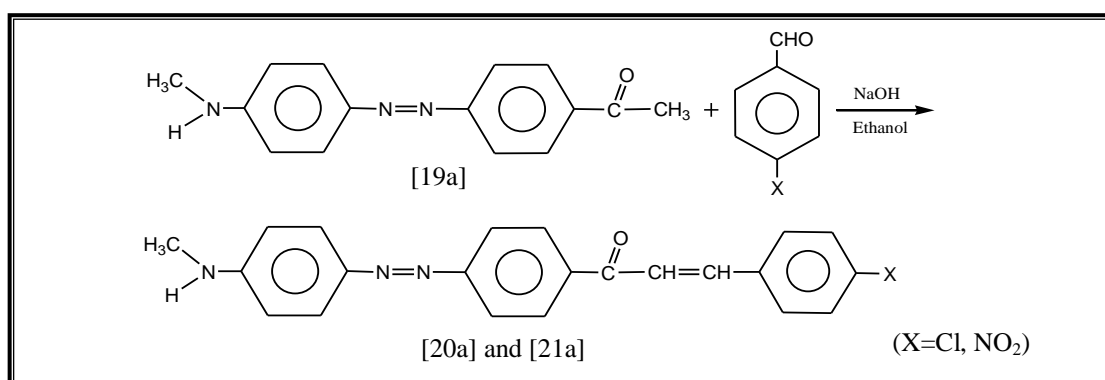
Equation (2-11): For synthesized compound [19a]

B. Synthesis of chalcones:

[1(4(*p*-*N*-methylaminophenyl)azophenyl-3-*p*-chlorophenyl-2-propene-1-one] [20a] and [1(4(*p*-*N*-methylaminophenyl)azophenyl-3-*p*-nitrophenyl-2-propene-1-one] [21a]

A mixture of equimolar amount of (0.001 mol) of *p*-substituted benzaldehyde and (0.2g, 0.001 mol) of *p*-(*N*-methylaminophenyl) azoacetophenone[19a] were dissolved in minimum amount of absolute ethanol (30ml). Sodium hydroxide (0.07g, 8%) was added

and the mixture was refluxed for 8hrs (in case of *p*-chloro benzaldehyde), while stirred for 12hrs (in case of *p*-nitro benzaldehyde). Reaction was monitored by TLC using (3:2) [petroleum ether-ethylacetate] eluent. Then reaction mixture was poured into ice cold water with constant stirring and kept in refrigerator for 1/2h. The precipitate was obtained, filtered, washed with water and dried. Recrystallized from ethanol– water mixture. Physical properties are shown in Table (2-4).



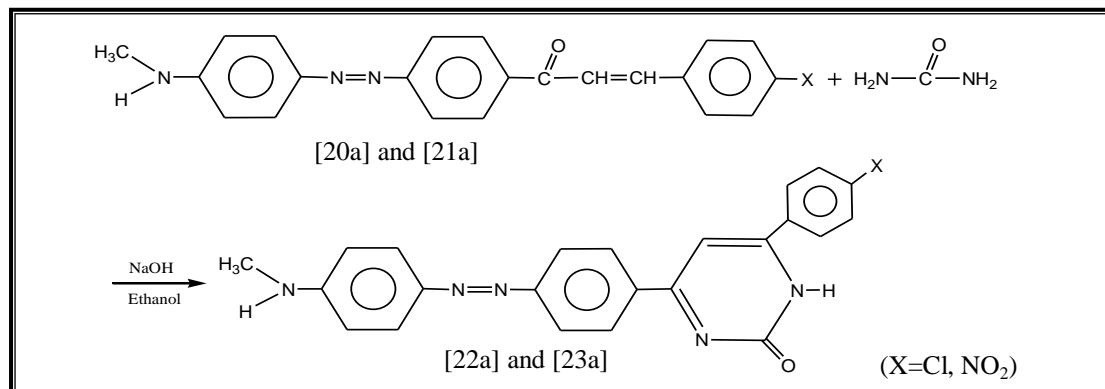
Equation (2-12): For synthesized compounds [20a] and [21a]

2.8. Synthesis of pyrimidines:

A. 4[4'(*p*,N-methylaminophenyl)azophenyl]-6-*p*-chlorophenyl-2-oxo(1H)pyrimidine [22a] and 4[4'(*p*-N-methylaminophenyl)azophenyl]-6-*p*-nitrophenyl-2-oxo(1H)pyrimidine [23a]

A mixture of chalcones [20a] or [21a] (0.0005mol), urea (0.06g, 0.001mol) and sodium hydroxide (0.04g, 0.001mol) were dissolved in minimum amount of absolute ethanol (30ml) and refluxed for 24hrs. Reaction mixture was poured into stirred ice cold water, where pyrimidine precipitated out. The formed precipitate was filtered, washed with water and dried. Recrystallized from

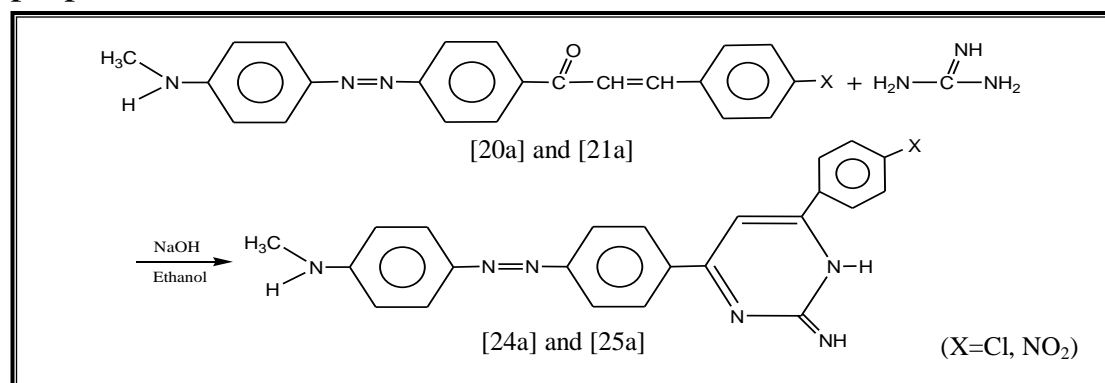
chloroform and petroleum ether. Physical properties are shown in Table (2-4).



Equation (2-13): For synthesized compounds [22a] and [23a]

B. 4[4'(p,N-methylaminophenyl)azophenyl]-6-p-chlorophenyl-2-imino(1H) pyrimidine [24a] and 4[4'(p,N-methylaminophenyl)azophenyl]-6-p-nitrophenyl-2-imino(1H)pyrimidine [25a]

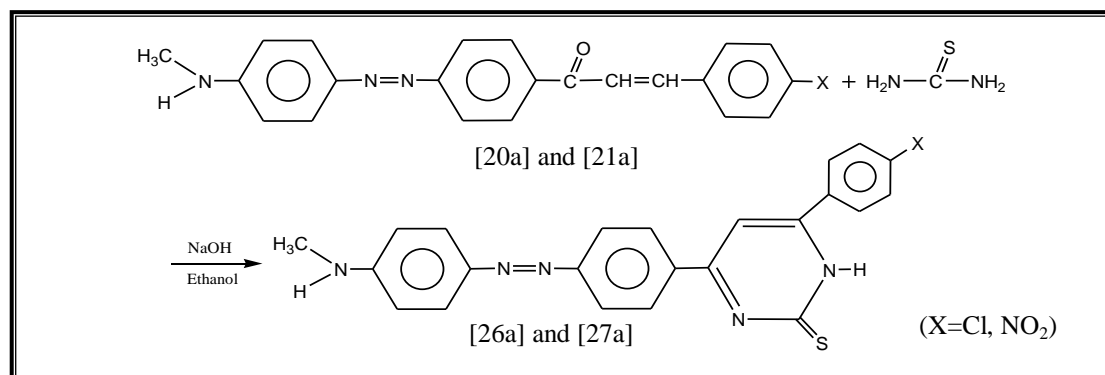
A mixture of chalcones [20a] and [21a] (0.0005mol), guanidine hydrochloride (0.095g, 0.001mol) and sodium hydroxide (0.08g, 0.002mol) were dissolved in minimum amount of absolute ethanol (30ml) and refluxed for 24hrs. Reaction mixture was poured into stirred ice cold water, where pyrimidine precipitated out. The formed precipitate was filtered, washed with water and dried. Recrystallized from methanol and petroleum ether. Physical properties are shown in Table (2-4).



Equation (2-14): For synthesized compounds [24a] and [25a]

C. 4[4'(p,N-methylaminophenyl)azophenyl]-6-p-chlorophenyl-2-thioxo(1H)pyrimidine [26a] and 4[4'(p,N-methylaminophenyl)azophenyl]-6-p-nitrophenyl-2-thioxo(1H)pyrimidine [27a]

A mixture of chalcone [20a] or [21a] (0.0005mol), thiourea (0.076g, 0.001mol) and sodium hydroxide (0.04g, 0.001mol) were dissolved in minimum amount of absolute ethanol (30ml) and refluxed for 24hrs. Reaction mixture was poured into stirred ice cold water, where pyrimidine precipitated out. The formed precipitate was filtered, washed with water and dried. Recrystallized from chloroform and petroleum ether. Physical properties are shown in Table (2-4).



Equation (2-15): For synthesized compounds [26a] and [27a]

Table (2-4): Physical properties for compounds series three

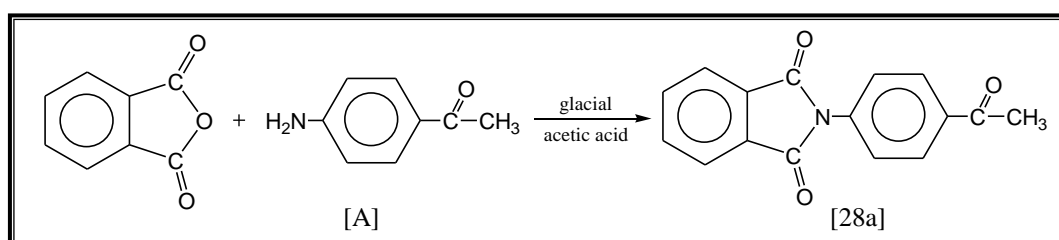
No.	Name of compound	M.wt	m.p. C°	Wight of product	Yield %	Colour
[19a]	[<i>p</i> -(<i>N</i> -methylaminophenyl)azoacetophenone]	253	87-89	1.5	74	Light-orange
[20a]	[1(4(<i>p</i> - <i>N</i> -methylaminophenyl)azophenyl-3- <i>p</i> -chlorophenyl-2-propene-1-one)]	375.5	115-117	0.3	79	orange
[21a]	[1(4(<i>p</i> - <i>N</i> -methylaminophenyl)azophenyl-3- <i>p</i> -nitrophenyl-2-propene-1-one)]	386	184-186	0.28	72	Red-orange
[22a]	[4(4'(<i>p</i> - <i>N</i> -methylaminophenyl-azo)phenyl)-6-chlorophenyl-2-oxo(1H)pyrimidine]	416.5	212-214	0.14	67	Pale-brown
[23a]	[4(4'(<i>p</i> - <i>N</i> -methylaminophenyl-azo)phenyl)-6-nitrophenyl-2-oxo(1H)pyrimidine]	427	206-208	0.12	56	Dark-brown
[24a]	[4(4'(<i>p</i> , <i>N</i> -methylaminophenyl-azo)phenyl)-6-chlorophenyl-2-imino(1H)pyrimidine]	415	204-206	0.16	77	Pale-brown
[25a]	[4(4'(<i>p</i> , <i>N</i> -methylaminophenyl-azo)phenyl)-6-nitrophenyl-2-imino(1H)pyrimidine]	426	160-162	0.091	42	orange
[26a]	[4(4'(<i>p</i> , <i>N</i> -methylaminophenyl-azo)phenyl)-6-chlorophenyl-2-thioxo(1H)pyrimidine]	432.5	193-195	0.15	69	brown
[27a]	[4(4'(<i>p</i> , <i>N</i> -methylaminophenyl-azo)phenyl)-6-nitrophenyl-2-thioxo(1H)pyrimidine]	443	155-157	0.08	36	Dark-brown

▪ Series four

2.9. Synthesis of chalcones (2-propene-1-one compounds)

A. Preparation of [N-(4-acetyl)phenylphthalimide]^[114] [28a]

A mixture of (0.13g, 0.001mol) p-aminoacetophenone [A] and phthalic anhydride (0.14g, 0.001mol) in 10 ml of glacial acetic acid was refluxed for (3–4)hr. Then reaction mixture was poured into a stirred ice cold water, and kept it in refrigerator for 30min. The formed precipitate was filtered, washed with water and dried. Recrystallized from ethanol. The physical properties are shown in Table (2–5).



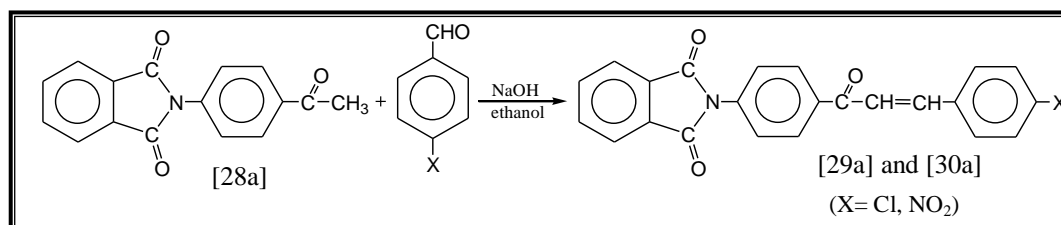
Equation (2–16): For synthesized compound [28a]

B. Synthesis of chalcones

[1(*p*,N-phthalimido)phenyl-3-*p*-chlorophenyl-2-propene-1-one] [29a]
and [1(*p*,N-phthalimido)phenyl-3-*p*-nitrophenyl-2-propene-1-one]
[30a]

A mixture of equimolar amount of (0.0011mol) of *p*-substituted benzaldehyde and (0.26g, 0.001mol) of N(2-acetyl-phenyl phthalimide) [28a] were dissolved in minimum amount of absolute ethanol (30ml). Sodium hydroxide (0.08g, 0.002mol) was added and the mixture was refluxed for 8hrs (in case of *p*-chloro benzaldehyde), while stirred for 12hrs (in case of *p*-nitro benzaldehyde). Reaction was monitored by TLC using (3:2) [petroleum ether-ethylacetate]

eluent. Then reaction mixture was poured into ice cold water with constant stirring and kept in refrigerator for 1/2h. The precipitate was obtained, filtered, washed with water and dried. Recrystallized from ethanol- water mixture. Physical properties are shown in Table (2-5).

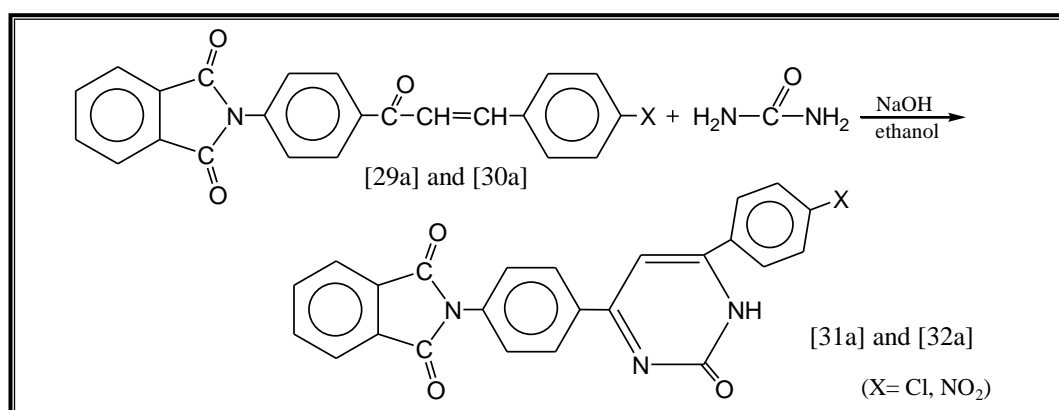


Equation (2–17): For synthesized compounds [29a] and [30a]

2.10. Synthesis of pyrimidines:

A. [4-(p,N-phthalimido)phenyl-6-p-chlorophenyl-2-oxo(1H)-pyrimidine] [31a] and [2(p,N-phthalimido)phenyl-6-p-nitrophenyl-2-oxo(1H)pyrimidine] [32a]

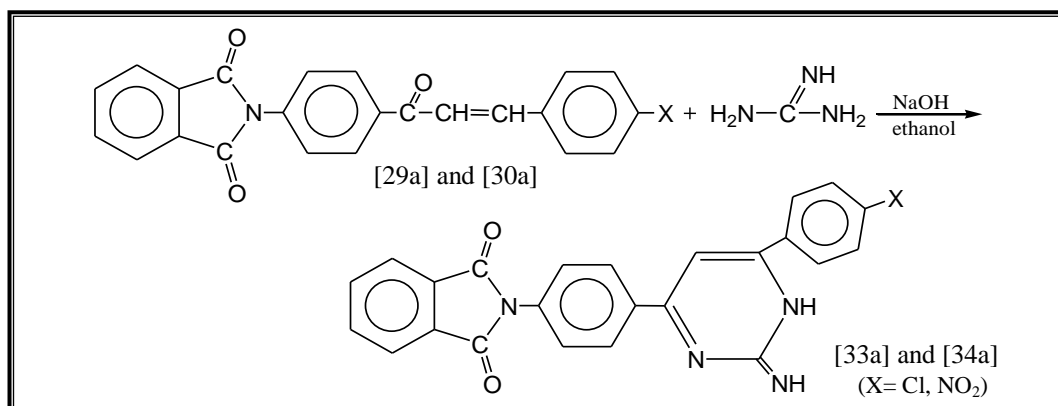
A mixture of chalcones [29a] or [30a] (0.0005mol), urea (0.06g, 0.001mol) and sodium hydroxide (0.04g, 0.001mol) were dissolved in minimum amount of absolute ethanol (30ml) and refluxed for 24hrs. Reaction mixture was poured into stirred ice cold water, where pyrimidine precipitated out. The formed precipitate was filtered, washed with water and dried. Recrystallized from chloroform and petroleum ether. Physical properties are shown in Table (2-5).



Equation (2–18): For synthesized compounds [31a] and [32a]

B. [4(*p*,*N*-phthalimido)phenyl-6-*p*-chlorophenyl-2-imino(1H)-pyrimidine] [33a] and [4-(*p*,*N*-phthalimido)phenyl-6-*p*-nitrophenyl-2-imino(1H)pyrimidine] [34a]

A mixture of chalcones [29a] or [30a] (0.0005mol), guanidine hydrochloride (0.095g, 0.001mol) and sodium hydroxide (0.08g, 0.002mol) were dissolved in minimum amount of absolute ethanol (30ml) and refluxed for 24hrs. Reaction mixture was poured into stirred ice cold water, where pyrimidine precipitated out. The formed precipitate was filtered, washed with water and dried. Recrystallized from methanol and petroleum ether. Physical properties are shown in Table (2-5).

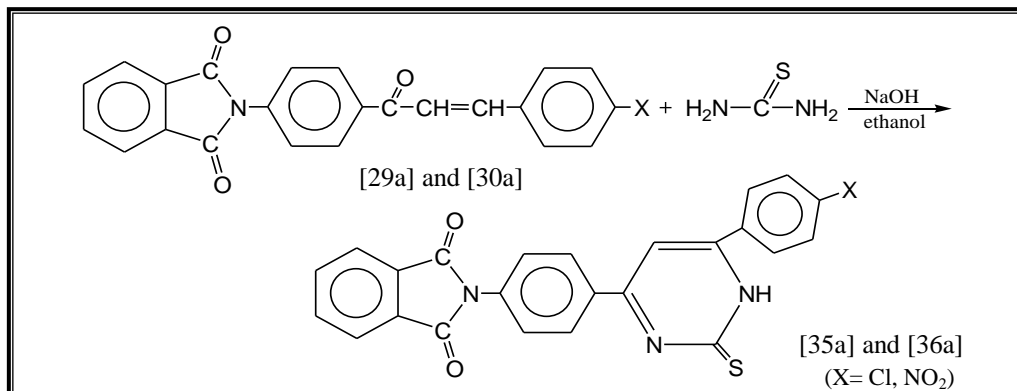


Equation (2–19): For synthesized compounds [33a] and [34a]

C. [4(*p*,*N*-phthalimido)phenyl-6-*p*-chlorophenyl-2-thioxo(1H)-pyrimidine] [35a] and [4-(*p*,*N*-phthalimido)phenyl-6-*p*-nitrophenyl-2-thioxo(1H)pyrimidine] [36a]

A mixture of chalcones [29a] or [30a] (0.0005mol), thiourea (0.076g, 0.001mol) and sodium hydroxide (0.04g, 0.001mol) were dissolved in minimum amount of absolute ethanol (30ml) and refluxed for 24hrs. Reaction mixture was poured into stirred ice cold water, where pyrimidine precipitated out. The formed precipitate was

filtered, washed with water and dried. Recrystallized from chloroform and petroleum ether. Physical properties are shown in Table (2-5).



Equation (2-20): For synthesized compounds [35a] and [36a]

Table (2-5): Physical properties for compounds series four

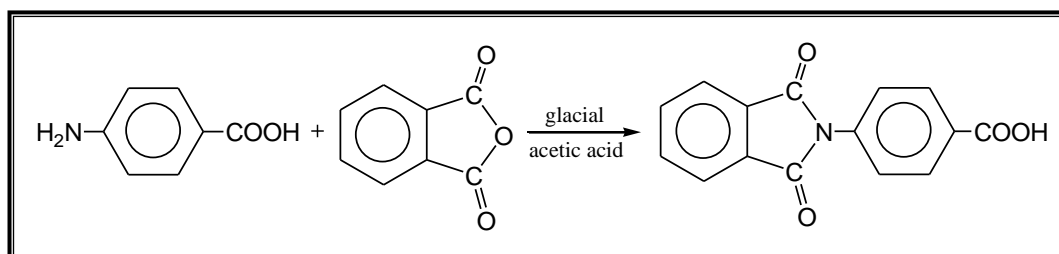
No.	Name of compound	M.wt	m.p. C°	Wight of product	Yield %	Colour
[28a]	[N-(4-acetyl)phenyl phthalimide]	265	247-248	0.2	75	White
[29a]	[1(<i>p</i> ,N-phthalimido)phenyl-3- <i>p</i> -chlorophenyl-2-propene-1-one]	387.5	258-260	0.27	69	Yellow
[30a]	[1(<i>p</i> ,N-phthalimido)phenyl-3- <i>p</i> -nitrophenyl-2-propene-1-one]	398	144-146	0.24	60	Orange
[31a]	[4-(<i>p</i> ,N-phthalimido)phenyl-6- <i>p</i> -chlorophenyl-2-oxo(1H) pyrimidine]	427.5	143-145	0.1	46	Orange
[32a]	[2(<i>p</i> ,N-phthalimido)phenyl-6- <i>p</i> -nitrophenyl-2-oxo(1H)-pyrimidine]	438	182-184	0.09	41	Pale brown
[33a]	[4(<i>p</i> ,N-phthalimido)phenyl-6- <i>p</i> -chlorophenyl-2-imino(1H)-pyrimidine]	426.5	158-160	0.12	56	Yellow
[34a]	[4-(<i>p</i> ,N-phthalimido)phenyl-6- <i>p</i> -nitro-phenyl-2-imino(1H)-pyrimidine]	437	170-172	0.17	77	Brown
[35a]	[4(<i>p</i> ,N-phthalimido)phenyl-6- <i>p</i> -chloro phenyl-2-thioxo(1H)- pyrimidine]	443.5	160-162	0.11	49	Orange
[36a]	[4-(<i>p</i> ,N-phthalimido)phenyl-6- <i>p</i> -nitro-phenyl-2-thioxo(1H)pyrimidine]	454	185-187	0.15	66	Brown

▪ Series Five**2.11. Synthesis of chalcones (2-propene-1-one compounds)****A. Synthesis of N'(4-acetylphenyl)p(N-phthalimido)benzamide [37a]**

This compound was prepared in three steps:

Step I. Preparation of 4-N-phthalimido benzoic acid^[115]

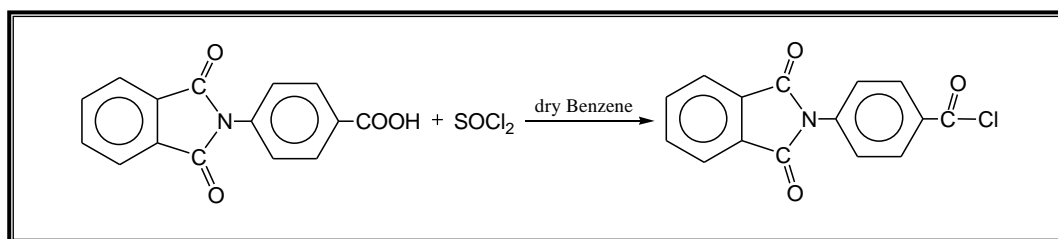
A mixture of phthalimic anhydride (0.72g, 0.004mol) and *p*-aminobenzoic acid (0.65g, 0.004mol) in (15ml) glacial acetic acid. The mixture was refluxed for (3-4) hr., then 25ml of ice cold distilled water was added to the reaction medium. The solid mass which was separated out was filtered and washed with water. It is dried and recrystallized from ethanol. Yield (85%), colour (white), m.p.= 292-293.



Equation (2-21): For synthesis (4-N-phthalimidobenzoic acid)

Step II. Preparation 4-N-phthalimido benzoyl chloride^[116]

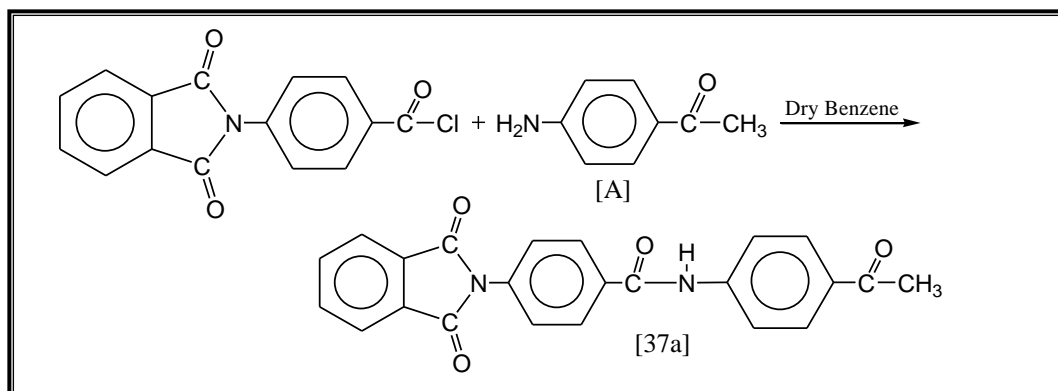
A mixture of compound 4-N-phthalimido benzoic acid (0.51g, 0.0019mol) and thionyl chloride (2 ml) in (20 ml) dry benzene was refluxed for 8hr, the excess of thionyl chloride and benzene were removed under vacuum. The product was crystal, Yield (62%), colour (White), m.p.=(260-262).



Equation (2-22): For synthesis (4-N-phthalimidobenzoylchloride)

Step III. Synthesis of N'(4-acetylphenyl)p(N-phthalimido)-benzamide [37a]

A mixture of 4-N-phthalimido benzoyl chloride (0.28g, 0.001mol) and p-amino acetophenone (0.13g, 0.001mol) in dry benzene (15ml) was refluxed for 10hr., then the reaction mixture was left to cool, the solvent were removed under reduce pressure. The solid product that formed was washed with ether and purified by recrystallized from ethanol.

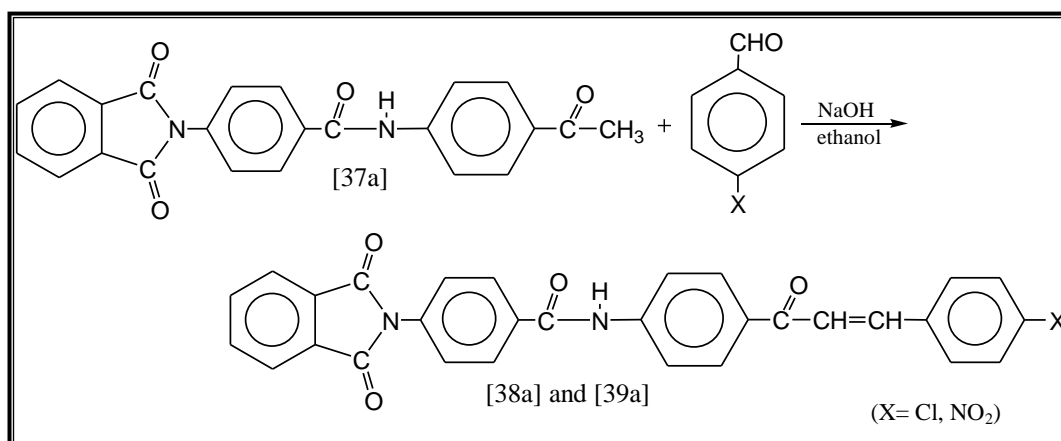


Equation (2-23): For synthesis compound [37a]

B. Synthesis of chalcones:

[1[*p*(N-phthalimido)benzamido-N'-phenyl]-3-*p*-chlorophenyl-2-propene-1-one] [38a] and [1[*p*(N-phthalimido)benzamido-N'-phenyl]-3-*p*-nitrophenyl-2-propene-1-one [39a]

A mixture of equimolar amount of (0.0011mol) of *p*-substituted benzaldehyde and (0.3g, 0.001mol) of N'(4-acetylphenyl)*p*(N-phthalimido)-benzamide [37a] were dissolved in minimum amount of absolute ethanol (30ml). Sodium hydroxide (0.08g, 0.002mol) was added and the mixture was refluxed for 8hrs (in case of *p*-chloro benzaldehyde), while stirred for 12hrs (in case of *p*-nitro benzaldehyde). Reaction was monitored by TLC using (3:2) [petroleum ether-ethylacetate] eluent. Then reaction mixture was poured into ice cold water with constant stirring and kept in refrigerator for 1/2h. The precipitate was obtained, filtered, washed with water and dried. Recrystallized from ethanol- water mixture. Physical properties are shown in Table (2-6).

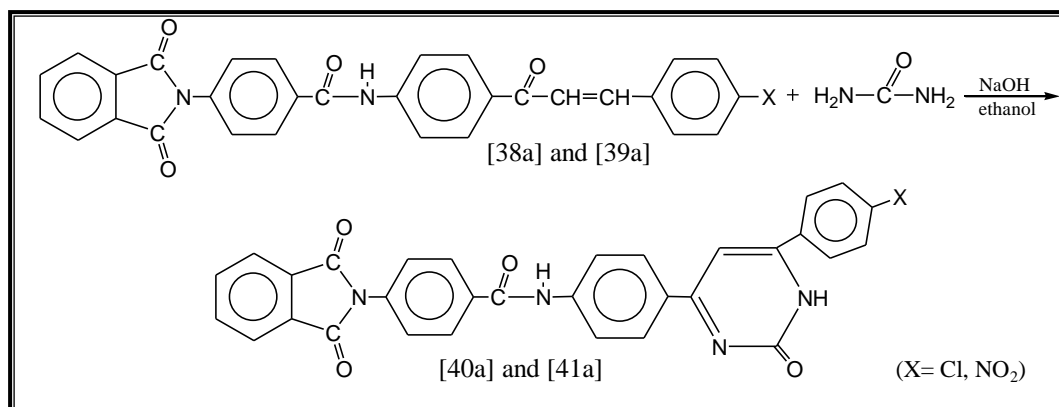


Equation (2-24): For synthesis compound [38a] and [39a]

2.12. Synthesis of pyrimidines

A. 4[*p*(N-phthalimido)benzamido)-N'-phenyl]-6-*p*-chlorophenyl-2-oxo(1H)pyrimidine] [40a] and 4[*p*(N-phthalimido)benzamido)-N'-phenyl]-6-*p*-nitrophenyl-2-oxo(1H)pyrimidine] [41a]

A mixture of chalcones [38a] or [39a] (0.0005mol), urea (0.06g, 0.001mol) and sodium hydroxide (0.04g, 0.001mol) were dissolved in minimum amount of absolute ethanol (30ml) and refluxed for 24hrs. Reaction mixture was poured into stirred ice cold water, where pyrimidine precipitated out. The formed precipitate was filtered, washed with water and dried. Recrystallized from chloroform and petroleum ether. Physical properties are shown in Table (2-6).

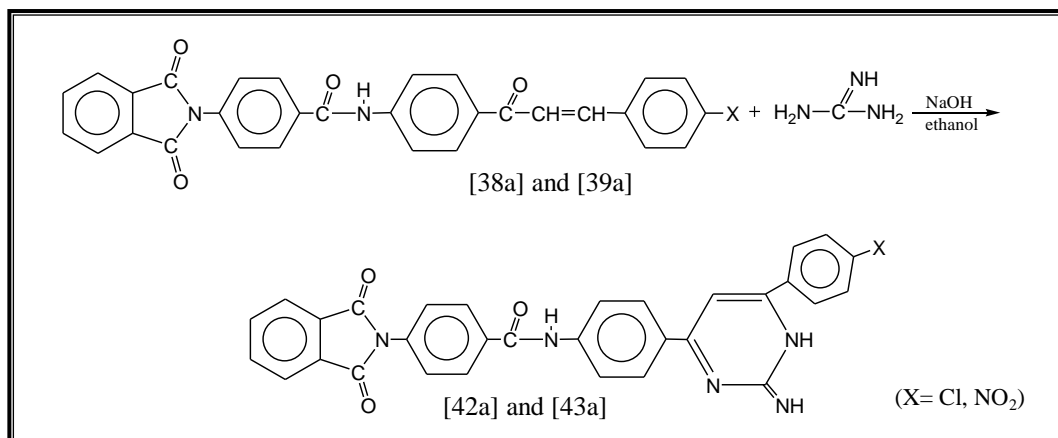


Equation (2-25): For synthesis compound [40a] and [41a]

B. 4[*p*(N-phthalimido)benzamido)-N'-phenyl]-6-*p*-chlorophenyl-2-imino(1H)pyrimidine] [42a] and 4[*p*(N-phthalimido)benzamido)-N'-phenyl]-6-*p*-nitrophenyl-2-imino (1H)pyrimidine] [43a]

A mixture of chalcones [38a] or [39a] (0.0005mol), guanidine hydrochloride (0.095g, 0.001mol) and sodium hydroxide (0.08g, 0.002mol) were dissolved in minimum amount of absolute ethanol (30ml) and refluxed for 24hrs. Reaction mixture was poured into

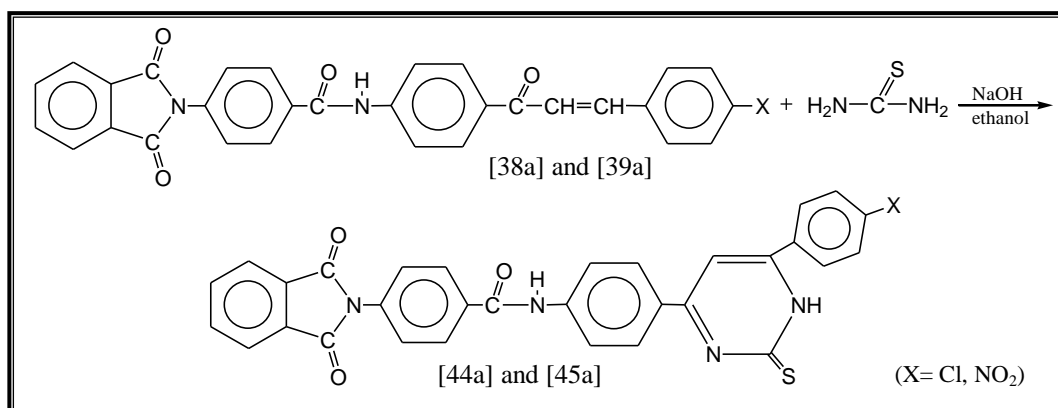
stirred ice cold water, where pyrimidine precipitated out. The formed precipitate was filtered, washed with water and dried. Recrystallized from methanol and petroleum ether. Physical properties are shown in Table (2-6).



Equation (2-26): For synthesis compound [42a] and [43a]

C. 4[*p*(N-phthalimido)benzamido)-N'-phenyl]-6-*p*-chlorophenyl-2-thioxo(1H)pyrimidine] [44a] and 4[*p*(N-phthalimido)benzamido)-N'-phenyl]-6-*p*-nitrophenyl-2-thioxo(1H)pyrimidine] [45a]

A mixture of chalcones [38a] or [39a] (0.0005mol), thiourea (0.076g, 0.001mol) and sodium hydroxide (0.04g, 0.001mol) were dissolved in minimum amount of absolute ethanol (30ml) and refluxed for 24hrs. Reaction mixture was poured into stirred ice cold water, where pyrimidine precipitated out. The formed precipitate was filtered, washed with water and dried. Recrystallized from chloroform and petroleum ether. Physical properties are shown in Table (2-6).



Equation (2-27): For synthesis compound [44a] and [45a]

Table (2-6): Physical properties for compounds series five

No.	Name of compound	M.wt	m.p. C°	Wight of product	Yield %	Colour
[37a]	N'(4-acetylphenyl) <i>p</i> (N-phthalimido)-benzamide	384	>300	0.3	78	Yellow
[38a]	[1[<i>p</i> (N-phthalimido)benzamido-N'-phenyl]-3- <i>p</i> -chlorophenyl-2-propene-1-one]	506.5	130-132	0.39	77	Light-yellow
[39a]	[1[<i>p</i> (N-phthalimido)benzamido-N'-phenyl]-3- <i>p</i> -nitrophenyl-2-propene-1-one]	517	293-295	0.3	53	Pale-brown
[40a]	4[<i>p</i> (N-phthalimido)benzamido)-N'-phenyl]-6- <i>p</i> -chlorophenyl-2-oxo(1H)pyrimidine]	546.5	130-132	0.12	43	Orange
[41a]	4[<i>p</i> (N-phthalimido)benzamido)-N'-phenyl]-6- <i>p</i> -nitrophenyl-2-oxo(1H)pyrimidine]	545	> 300	0.18	66	Brown
[42a]	4[<i>p</i> (N-phthalimido)benzamido)-N'-phenyl]-6- <i>p</i> -chlorophenyl-2-imino(1H)pyrimidine]	561.5	190-192	0.16	56	Orange
[43a]	4[<i>p</i> (N-phthalimido)benzamido)-N'-phenyl]-6- <i>p</i> -nitrophenyl-2-imino(1H)pyrimidine]	544	262-264	0.14	51	Red-brown
[44a]	4[<i>p</i> (N-phthalimido)benzamido)-N'-phenyl]-6- <i>p</i> -chlorophenyl-2-thioxo(1H)pyrimidine]	562.5	168-170	0.12	42	Pale orange
[45a]	4[<i>p</i> (N-phthalimido)benzamido)-N'-phenyl]-6- <i>p</i> -nitrophenyl-2-thioxo(1H)pyrimidine]	561	150-152	0.14	49	Red-brown

Chapter Three
Results & Discussio

3. Synthesis and characterization

Our research work involves two parts:

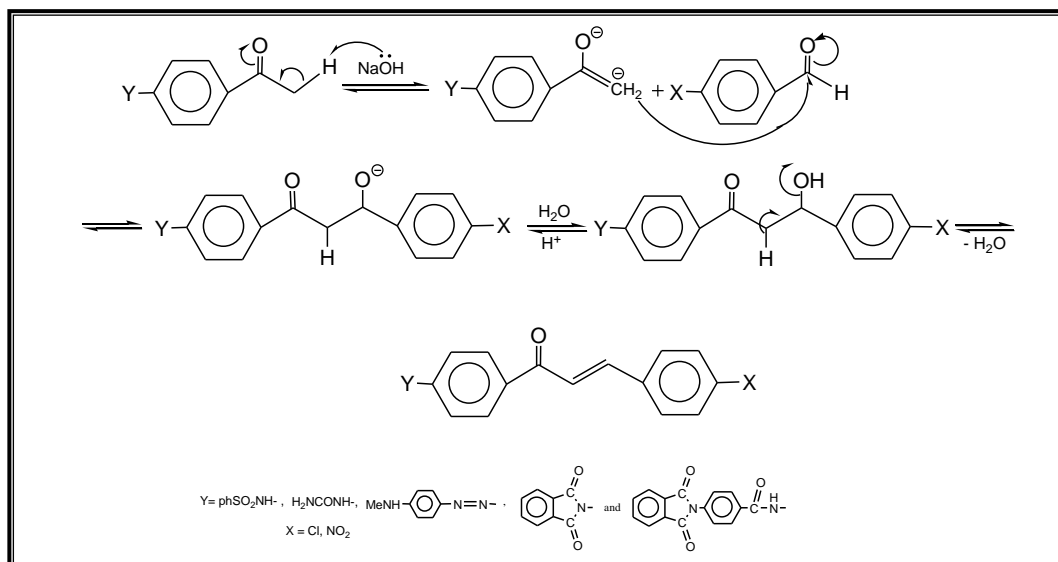
First: Building up a pyrimidine moiety containing different substituents in 2,4 and 6 positions, like oxo, thioxo and imino groups at position-2, and *p*-benzenesulphonamidophenyl, *p*-ureidophenyl, *p*(*N*-methylamino)phenylazophenyl, *P,N*-phthalimidophenyl and *p*(*N*-phthalimido)benzamido-*N'*-phenyl groups in position-4. While position-6 contains either *p*-chlorophenyl or *p*-nitrophenyl group. We believed that, presence of such substituents in pyrimidine unit would increase the extended of antimicrobial activities of pyrimidine unit nucleous effect.

In order to build up a pyrimidine unit nucleous containing such substituent at 2,4,6-positions. The following synthetic processes were followed:

I. Synthesis of 4-substituted acetophenone, like:

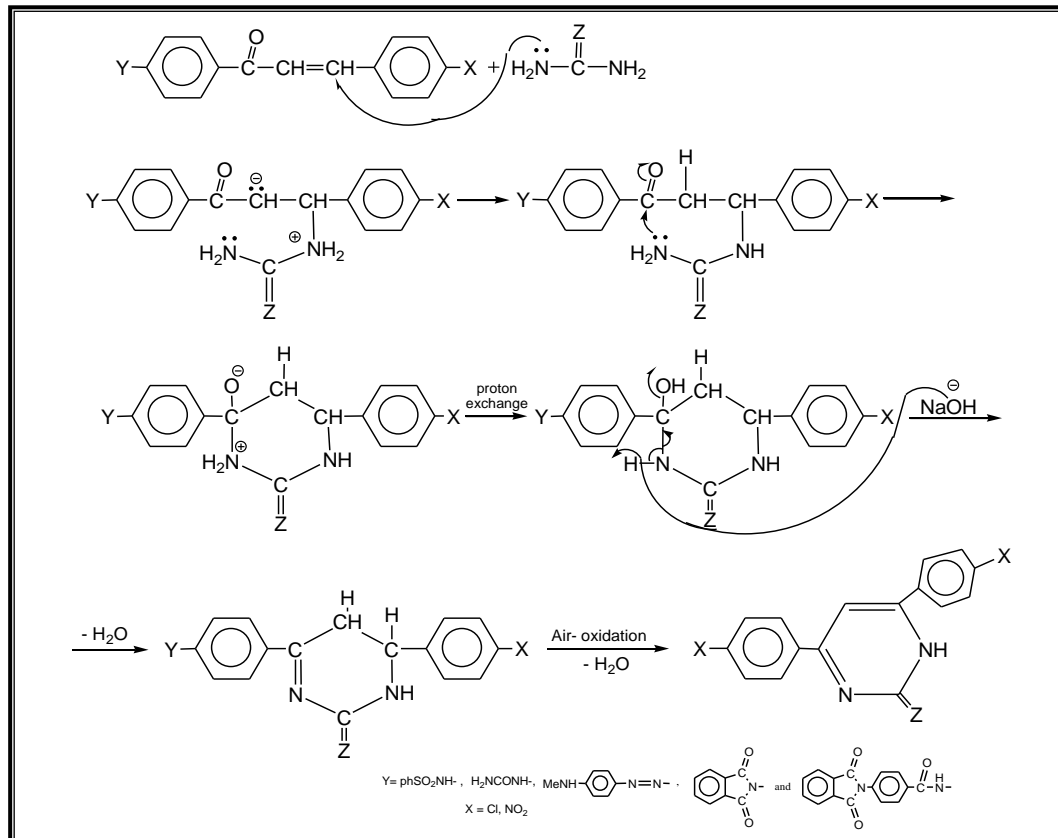
1. 4-acetylbenzenesulphonamide.
2. 4-acetylphenylurea. (4-ureidoacetophenone).
3. 4-acetyl-(*p*-*N*-methylphenylazobenzene).
4. *N*-(4-acetyl)phenyl phthalimide.
5. *N'*(4-acetylphenyl)-*p*(*N*-phthalimido)benzamide.

II. Chalconization- synthesis of above compounds (4-substituted acetophenone), with *p*-chlorobenzaldehyde and *p*-nitrobenzaldehyde as the following mechanism:



Scheme (3-1): Mechanism of chalcone

III. Building up- synthesis of pyrimidine units by condensation of above chalconized- compounds (as in II), with urea, thiourea and guanidine in order to obtain such substituent at 2,4,6-positions of pyrimidine unit nucleous. As the following mechanism:



Scheme (3-2): Mechanism of pyrimidine

Second: Examination of antimicrobial activities behaviors of the above synthesized chalcones and pyrimidines compounds, that containing biological and pharmaceutical active groups at 2,4,6-positions of pyrimidine unit against bacteria, Gram-Ve (*Serratia marcescens*, *Pseudomonas aeruginosa*) and Gram+Ve (*Staphylococcus aureus*, *Streptococcus pyogenes*), and against fungi (*Candida albicans*).

Series one:

3.1. Synthesis of chalcones (2-propene-1-one compounds)

- **Synthesis of 1(4-benzenesulphonamido)phenyl-3-*p*-chloro or *p*-nitro-phenyl-2-propene-1-one [2a] and [3a]**

These two chalcones were synthesized in two steps:

First: by condensation of *p*-aminoacetophenone with benzenesulphonylchloride in presence of pyridine to give 4-acetyl-benzenesulphonamide [1a], which was characterized by FTIR, ^1H NMR, ^{13}C NMR and Mass spectral analysis.

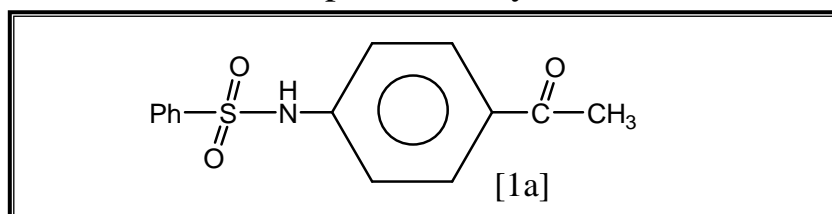


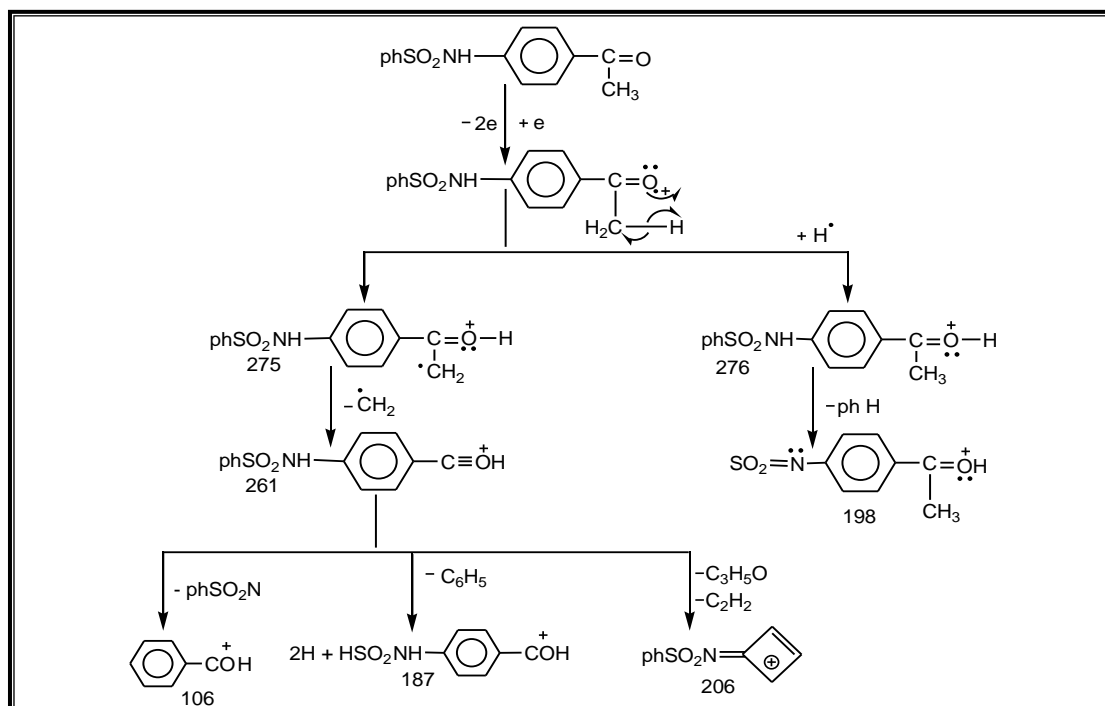
Figure (3-1): The structure of compound [1a]

FTIR spectrum of this compound [1a] Fig. (3-2), showed disappearance of asymmetric and symmetric ($-\text{NH}_2$) stretching bands at $(3394, 3332)\text{cm}^{-1}$ in starting material *p*-aminoacetophenone [A], Fig. (3-1) and appearance of band at $(3267)\text{cm}^{-1}$ of ($-\text{N}-\text{H}$) amide, and appearance of amide-II and amide-I of sulphonamido group bands at $(1330, 1157)\text{cm}^{-1}$ respectively, beside to the

stretching band of ketonic carbonyl group at $(1681)\text{cm}^{-1}$. All these bands are summarized in Table (3-1).

^1H NMR spectrum of this compound [1a] Fig. (3-3), showed methyl protons (s, 3H), two phenyl protons (m, 9H) and sulphonamido ($-\text{SO}_2\text{NH}-$) proton (s, 1H) at $\delta(\text{ppm})$: 3.5, 7.2- 7.8 and (10.9)ppm respectively. All these signals are summarized in Table (3-2). While ^{13}C NMR spectrum Fig. (3-4) showed following signals at $\delta(\text{ppm})$: (26, 117-141) and (195)ppm, would be attributed to methyl, two phenyl and carbonyl carbons groups respectively. All these signals are summarized in Table (3-3).

Mass spectral analysis of compound [1a] Fig (3-5), showed M^+ and $(\text{M}+\text{H})^+$ ions at m/z (275) and (276), as well as to the following fragments $m/z=$ 261, 206, 198, 187 and 106, which would be attributed to following suggested mechanism shown in the Scheme (3-3). All these fragments are summarized in Table (3-4).



Scheme (3-3): Suggested fragmentation mechanism of 4-Acetylphenylbenzenesulphonamide [1a]

Second: Condensation of 4-acetylbenzenesulphonamide with *p*-chlorobenzaldehyde and *p*-Nitrobenzaldehyde in alcoholic sodium hydroxide solution to give chalcones [2a] and [3a]. These compounds [2a] and [3a] were characterized by FTIR, ^1H NMR, ^{13}C NMR and Mass spectral analysis of compounds [2a].

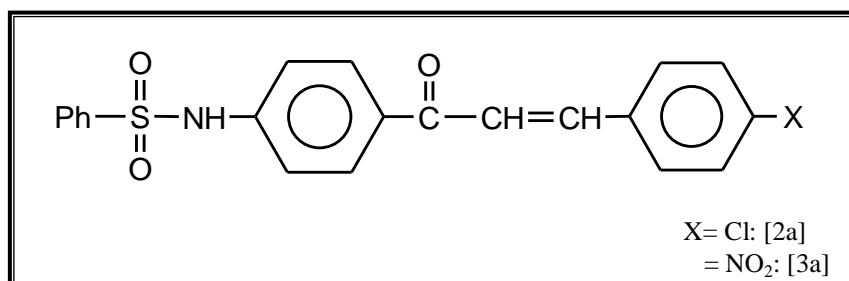


Figure (3–2): The structure of compounds [2a] and [3a]

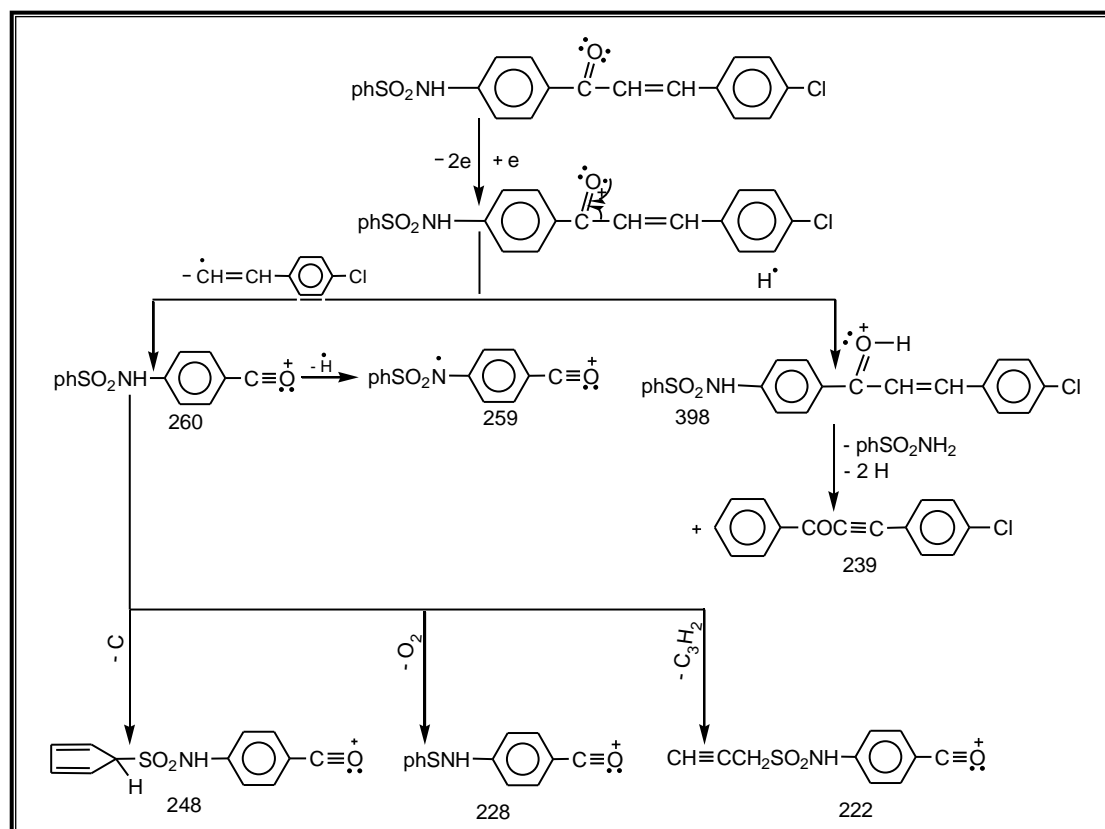
FTIR spectral analysis of compound [2a] and [3a], Figs. (3–6) and (3–10) respectively, showed sulphonamido group (N–H) stretching bands at (3267) and (3309) cm^{-1} , amide II and I bands of sulphonamido group at (1342, 1157) and (1342, 1161) cm^{-1} respectively, ketonic carbonyl stretching bands at (1654) and (1658) cm^{-1} , ethylenic stretching band conjugated with carbonyl ($-\overset{\text{O}}{\text{C}}-\text{CH}=\text{CH}-$) at (1604) cm^{-1} , as well as asymmetric and symmetric stretching bands of nitro group ($-\text{NO}_2$) in case of compound [3a] at (1516, 1340) cm^{-1} respectively. All these bands are summarized in Table (3–1).

^1H NMR, spectral analysis of compounds [2a] and [3a], Figs. (3–7) and (3–11) respectively showed ethylenic protons ($-\text{CH}=\text{CH}-$) as (2H) doublet signals $\delta(7.25)$ and (7.25)ppm respectively, and three phenyl protons as (13H) multiplet signals at $\delta(7.4-8.0)$ and (7.5–8.2)ppm respectively, beside a singlet signal (1H) of

sulphonamido ($-\text{SO}_2\text{-NH}-$) protons at $\delta(10.95)$ and (10.98) ppm respectively. All these signals are summarized in Table (3-2).

^{13}C NMR, spectral analysis for compounds [2a] and [3a], Figs. (3-8) and (3-12) respectively, showed Ketonic carbonyl carbons ($\text{C}=\text{O}$) at $\delta(187)$ and (184) ppm, ethylenic carbons ($-\text{CH}=\text{CH}-$) and aromatic carbons at $\delta(117-142)$ and $(117-148)$ ppm respectively. All these signals are summarized in Table (3-3)

While Mass spectrum of compounds [2a] Fig (3-9), showed, M^+ and $(\text{M}+\text{H})^+$ ions at (m/z) (397) and (398) respectively, as well as to the following fragments $m/z= 260, 259, 248, 239, 228$ and 222 , which would be attributed to the following fragments suggested mechanism shown in the Scheme (3-4). All these fragments are summarized in Table (3-5).



Scheme (3-4): Suggested fragmentation mechanism of 1-(p-benzenesulphonamido)phenyl-3-p-chloro-2-propene-1-one

3.2. Synthesis of pyrimidines

3.2.1. Synthesis of [4-(*p*-benzenesulphonamido)phenyl-6-*p*-chloro or *p*-nitrophenyl-2-oxo-(1H)-pyrimidine] [4a] and [5a]

Reaction of chalcones [2a] and [3a] with urea in alcoholic alkaline solutions of sodium hydroxide gave pyrimidines [4a] and [5a], which were characterized by FTIR for compounds [4a] and [5a], ^1H NMR, ^{13}C NMR, and Mass for compound [4a] spectral analysis.

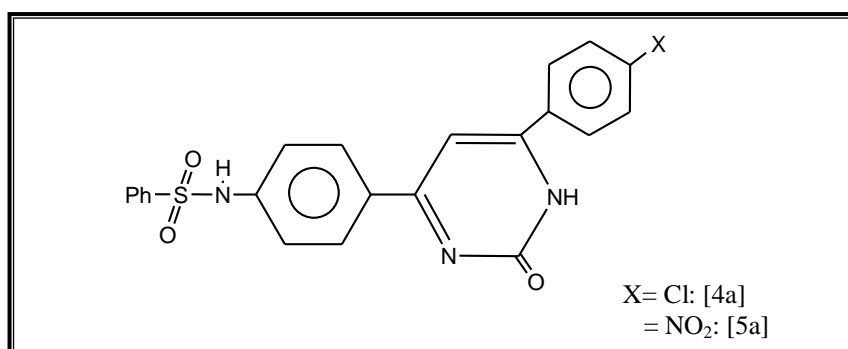


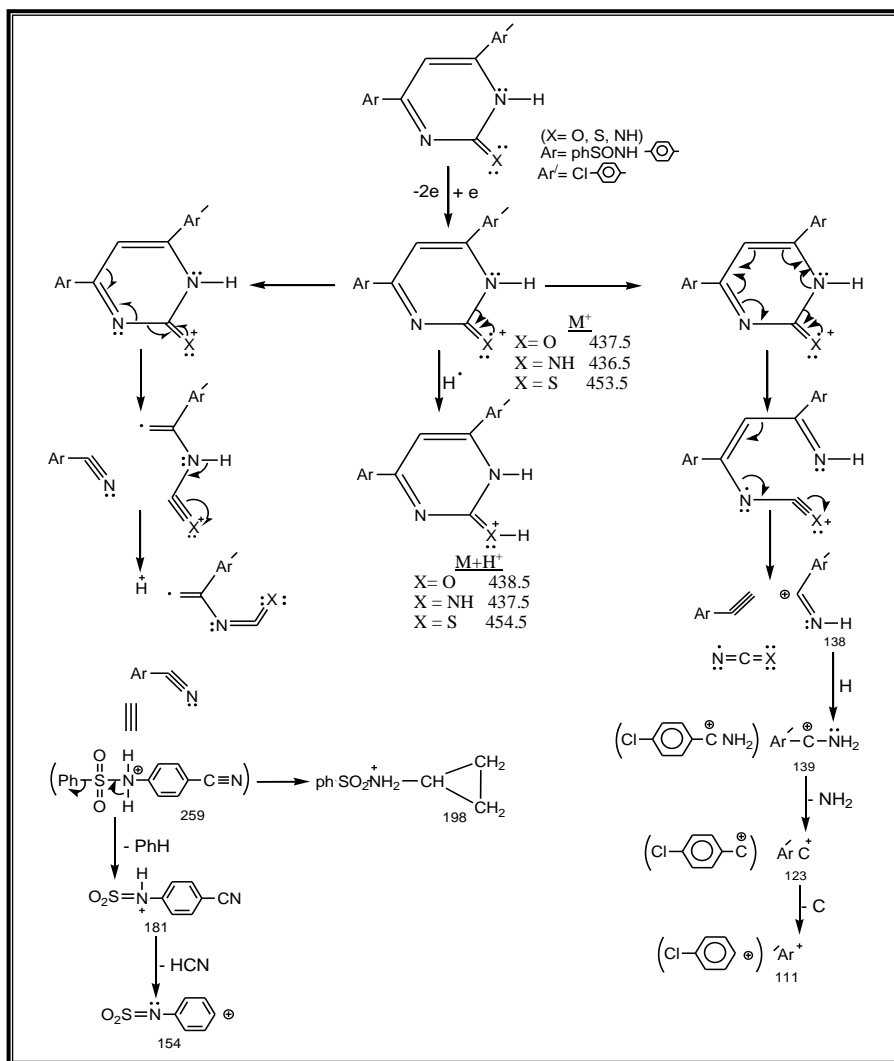
Figure (3–3): The structure of compounds [4a] and [5a]

FTIR spectral analysis of compounds [4a] and [5a], Fig. (3–13) and (3–17), showed ($-\text{NH}$) stretching bands of carbamido ($\text{O}=\text{C}-\text{NH}$) of pyrimidine ring and sulphonamido ($-\text{SO}_2-\text{NH}-$) bands at $(3410, 3255)\text{cm}^{-1}$ and $(3154, 3116)\text{cm}^{-1}$, as well as to carbamido ($\text{C}=\text{O}$) stretching bands of pyrimidine ring at $(1654, 1658)\text{cm}^{-1}$, and ($-\text{CH}=\text{C}-$) ethylenic and ($-\text{C}=\text{N}-$) stretching bands of pyrimidine ring at $(1604, 1600)\text{cm}^{-1}$ respectively. Also sulphonamide ($-\text{SO}_2-\text{NH}-$) group, showed ($\text{S}=\text{O}$) stretching band (Amide I) at $(1161, 1161)\text{cm}^{-1}$ and ($-\text{NH}$) bending band (Amide II) at $(1330, 1342)\text{cm}^{-1}$ and asymmetrical, symmetrical stretching bands of ($-\text{NO}_2$) group in case of compound [5a] at $(1516, 1342)\text{cm}^{-1}$ respectively. All these bands were summarized in Table (3–1).

^1H NMR, spectral analysis of compound [4a], Fig. (3-14) showed singlet signal of ethylenic proton ($-\text{CH}=\text{C}-$) at $\delta(7.2)\text{ppm}$, and three phenyl protons as (13H) multiplet signals at $\delta(7.3-7.7)\text{ppm}$, beside a singlet signal (1H) of ($-\text{NH}$) amide pyrimidine ring proton at $\delta(8.1)\text{ppm}$, and a singlet signal (1H) of sulphonamido ($-\text{SO}_2-\text{NH}-$) proton at $\delta(10.9)\text{ppm}$. All these signals are summarized in Table (3-2).

^{13}C NMR spectral analysis for compound [4a] Fig. (3-15), showed carbamido carbonyl carbons ($\text{C}=\text{O}$) of pyrimidine ring at $\delta(185)\text{ppm}$, ethylenic ($\text{CH}=\text{C}-$) carbons, ($-\text{C}=\text{N}-$) pyrimidine ring and aromatic carbons at $\delta(117-141)\text{ppm}$. All these signals are summarized in Table (3-3).

While Mass spectrum of compound [4a] Fig. (3-16), showed ($\text{M}+\text{H}$) $^+$ ion at (m/z) (438), as well as to following fragments $m/z=304, 280, 259, 198, 181, 167, 139, 123$ and 111, which would be attributed to the following fragments suggested mechanism in Scheme (3-5). All these fragments were summarized in Table (3-6).



Scheme (3–5): Suggested fragmentation mechanism of [4-(*p*-benzenesulphonamido)phenyl-6-*p*-chloro phenyl-2-oxo, imino or thioxo-(1H)-pyrimidine] [4a], [5a] and [6a]

3.2.2. Synthesis of [4-(*p*-benzenesulphonamido)phenyl-6-*p*-chloro or *p*-nitro phenyl-2-imino-(1H) pyrimidine] [6a] and [7a]

Reaction of chalcones [2a] and [3a] with guanidine hydrochloride in alcoholic alkaline solutions of sodium hydroxide gave pyrimidines [6a] and [7a], which were characterized by FTIR for compounds [6a] and [7a], ^1H NMR, ^{13}C NMR, and Mass spectral analysis for compound [6a].

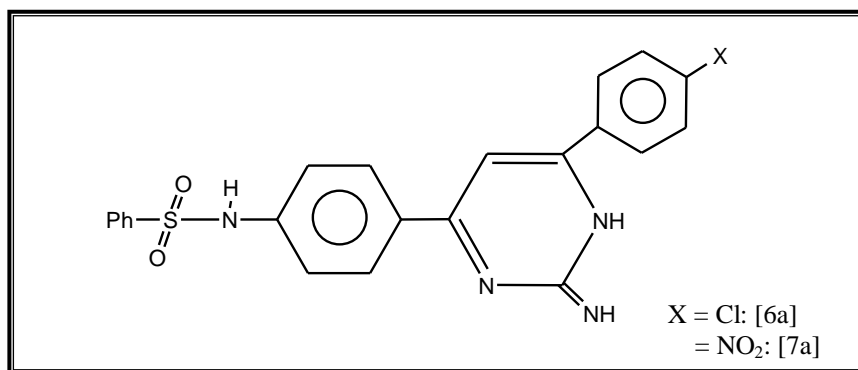


Figure (3-4): The structure of compounds [6a] and [7a]

FTIR spectral analysis of compounds [6a] and [7a], Figs. (3-18) and (3-22), showed (–NH) stretching bands of imidino ($\text{HN}=\overset{\text{I}}{\text{C}}-\text{NH}$) pyrimidine ring, and sulphonamido (–SO₂–NH–) bands at (3340, 3278, 3201) cm^{-1} and (3491, 3390, 3290) cm^{-1} , as well as ethylenic (–CH=C–) and (–C=N–) stretching bands of pyrimidine ring at (1604) and (1604) cm^{-1} respectively. Also sulphonamide (–SO₂–NH–) group, showed (S=O) stretching bands (Amide I) at (1161, 1161) cm^{-1} and (N–H) bending band (Amide II) at (1334, 1346) cm^{-1} and asymmetrical, symmetrical stretching bands of (–NO₂) group in case of compound [7a] at (1516, 1346) cm^{-1} respectively. All these bands were summarized in Table (3-1).

¹H NMR, spectrum of compound [6a], Fig. (3-19) showed singlet signal of ethylenic proton (–CH=C–) of pyrimidine ring at $\delta(7.2)$ ppm, and three phenyl protons as (13H) multiplet signals at $\delta(7.4-7.9)$ ppm, beside a singlet signal (1H) of (–NH) pyrimidine ring proton at $\delta(7.7)$ ppm, singlet signal of imidino (–C=NH) in pyrimidine ring as (1H) at $\delta(8.1)$ ppm, and a singlet signal (1H) of sulphonamido (–SO₂–NH–) proton at $\delta(11.0)$ ppm. All these signals are summarized in Table (3-2).

^{13}C NMR spectral analysis for compound [6a] Fig. (3–20), showed imidino carbon ($-\text{C}=\text{NH}$) of pyrimidine ring at $\delta(152)\text{ppm}$, ethylenic carbon ($-\text{CH}=\text{C}-$), ($-\text{C}=\text{N}-$) and aromatic carbons at $\delta(118-141)\text{ppm}$. All these signals are summarized in Table (3–3).

While Mass spectrum of compound [6a] Fig. (3–21) showed, $(\text{M}+\text{H})^+$ ion at (m/z) at (437), as well as to following fragments $m/z=298$, 278, 259, 198, 181, 139, 123 and 111, which would be attributed to the following fragments suggested mechanism in Scheme (3–5). All these fragments are summarized in Table (3–7).

3.2.3. Synthesis of [4-(*p*-benzenesulphonamido)phenyl-6-*p*-chloro or *p*-nitro phenyl-2-thioxo-(1H)-pyrimidine] [8a] and [9a]

Reaction of chalcones [2a] and [3a] with thiourea in alcoholic alkaline solutions of sodium hydroxide gave pyrimidines [8a] and [9a], which were characterized by FTIR for compounds [8a] and [9a], ^1H NMR, ^{13}C NMR, and Mass spectral analysis for compound [8a].

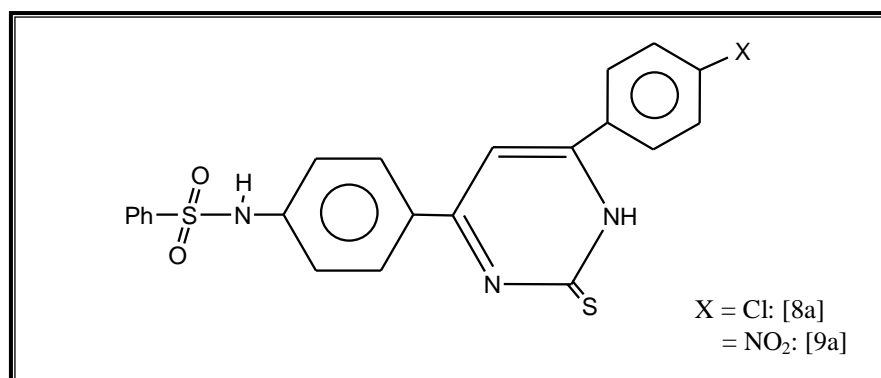


Figure (3–5): The structure of compounds [8a] and [9a]

FTIR spectral analysis of compounds [8a] and [9a], Figs. (3–23) and (3–27) showed ($-\text{NH}$) stretching bands of thiocarbamido ($\text{S}=\text{C}-\text{NH}$) of pyrimidine ring and sulphonamido ($-\text{SO}_2-\text{NH}-$) bands

at (3360, 3248) cm^{-1} and (3476, 3384) cm^{-1} , as well as to thiocarbamido (C=S) stretching bands of pyrimidine ring at (1230) and (1222) cm^{-1} , ethylenic ($-\text{CH}=\text{C}-$) and ($-\text{C}=\text{N}-$) stretching bands of pyrimidine ring at (1604, 1604) cm^{-1} respectively. Also sulphonamide ($-\text{SO}_2-\text{NH}-$) group, showed (S=O) stretching band (Amide I) at (1161, 1161) cm^{-1} and (N-H) bending band (Amide II) at (1330, 1338) cm^{-1} , and asymmetrical, symmetrical stretching bands of ($-\text{NO}_2$) group in case of compound [9a] at (1516, 1336) cm^{-1} respectively. All these bands are summarized in Table (3-1).

^1H NMR, spectrum of compound [8a], Fig. (3-24) showed singlet signal of ethylenic proton ($-\text{CH}=\text{C}-$) ring at $\delta(7.1)\text{ppm}$, and three phenyl protons as (13H) multiplet signals at $\delta(7.3-7.8)\text{ppm}$, beside a singlet signal (1H) of ($-\text{NH}$) pyrimidine ring proton at $\delta(8.1)\text{ppm}$, and a singlet signal (1H) of sulphonamido ($-\text{SO}_2-\text{NH}-$) proton at $\delta(10.4)\text{ppm}$. All these signals are summarized in Table (3-2).

^{13}C NMR spectral analysis for compound [8a] Fig. (3-25), showed thiocarbamido (C=S) in pyrimidine ring carbon at $\delta(175)\text{ppm}$, ethylenic carbon ($\text{CH}=\text{C}-$), ($-\text{C}=\text{N}-$) pyrimidine ring and aromatic carbons at $\delta(118-145)\text{ppm}$. All these signals are summarized in Table (3-3).

While Mass spectrum of compound [8a] Fig. (3-26) showed, ($\text{M}+\text{H}$) $^+$ ion at (m/z) at (454), as well as to following fragments m/z=199, 181, 154, 139, 123 and 111, which would be attributed to the following fragments suggested mechanism in the Scheme (3-5). All these fragments are summarized in Table (3-8)^[117-120].

Series two:**3.3. Synthesis of chalcones (2-propene-1-one compounds)****Synthesis of [1(4-ureido)phenyl-3-*p*-chloro or *p*-nitro phenyl-2-propene-1-one] [11a] and [12a]**

All these two chalcones were synthesized in two steps:

First: Reaction of *p*-aminoacetophenone with potassium cyanate in water- acetic acid solution gave 4-acetylphenylurea [10a], which was characterized by its FTIR, ^1H NMR, ^{13}C NMR and Mass spectral analysis.

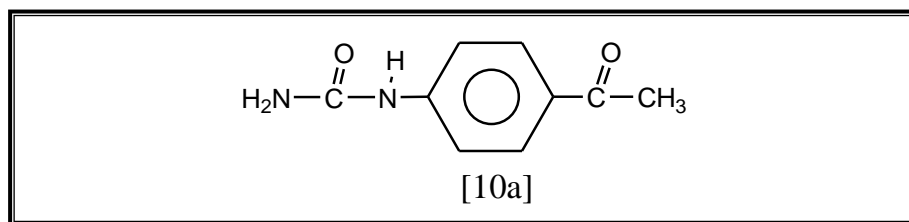


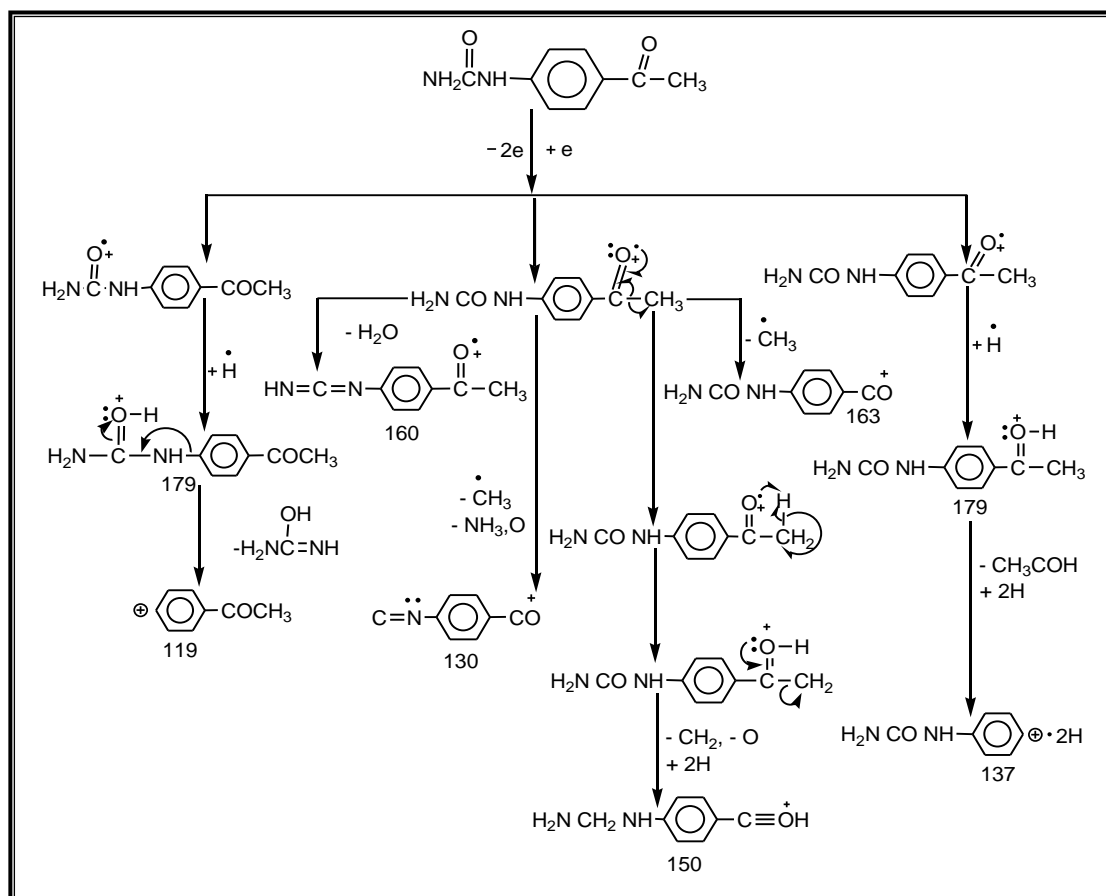
Figure (3–6): The structure of compound [10a]

FTIR spectrum of compound [10a], Fig. (3–28), showed asymmetric and symmetric (NH_2 -) stretching bands and (NH -) stretching band at $(3406, 3305, 3213)\text{cm}^{-1}$ respectively, as well as to two carbonyl stretching bands of ketonic carbonyl (CH_3CO -) at $(1708)\text{cm}^{-1}$ and amide carbonyl ureido (H_2NCONH -) at $(1670)\text{cm}^{-1}$. All these bands are summarized in Table (3–9).

^1H NMR spectrum of compound [10a] Fig. (3–29), showed a singlet signal of ($-\text{NH}_2$) protons at $\delta(6.1)\text{ppm}$, and singlet signal of ($-\text{NH}$ -) ureido proton as (1H) at $\delta(9.0)\text{ppm}$, as well as a singlet signal of methyl protons as (3H) at $(2.5)\text{ppm}$, and multiplet signals (4H) of phenyl protons at $\delta(7.5- 7.9)\text{ppm}$. All these signals are summarized in Table (3–10).

^{13}C NMR spectrum of compound [10a] Fig. (3–30), showed methyl carbon at $\delta(26)\text{ppm}$, and two carbonyl carbons at $\delta(155$ and $195)\text{ppm}$, which belongs to ureido carbonyl and ketonic carbonyl carbons respectively, as well as to phenyl carbons at $\delta(117$ – $145)\text{ppm}$. All these signals are summarized in Table (3–11)

Mass spectral analysis of compound [10a] Fig. (3–31), showed M^+ and $(\text{M}+\text{H})^+$ ions m/z at (178) and (179) respectively, as well as to following fragments m/z at 163, 160, 150, 137 130 and 119 which would be attributed to the following fragmentation suggested mechanism Scheme (3–6). All these fragments are summarized in Table (3–12).



Scheme (3–6): Suggested fragmentation mechanism of 4-acetylphenylurea [10a]

Second: Condensation of 4-acetylphenylurea [10a] with *p*-chlorobenzaldehyde or *p*-nitrobenzaldehyde in alcoholic alkaline solution of sodium hydroxide gave chalcones [11a] and [12a], which were characterized by FTIR for compounds [11a] and [12a], ^1H NMR, ^{13}C NMR and Mass spectral analysis for compound [11a].

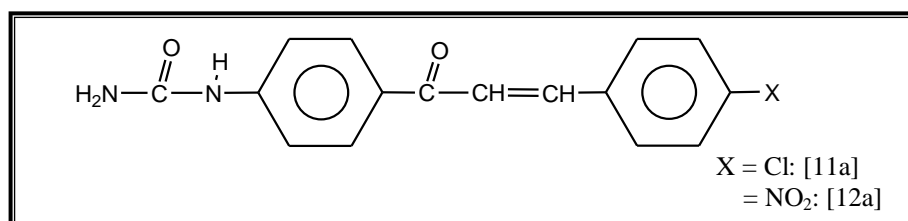


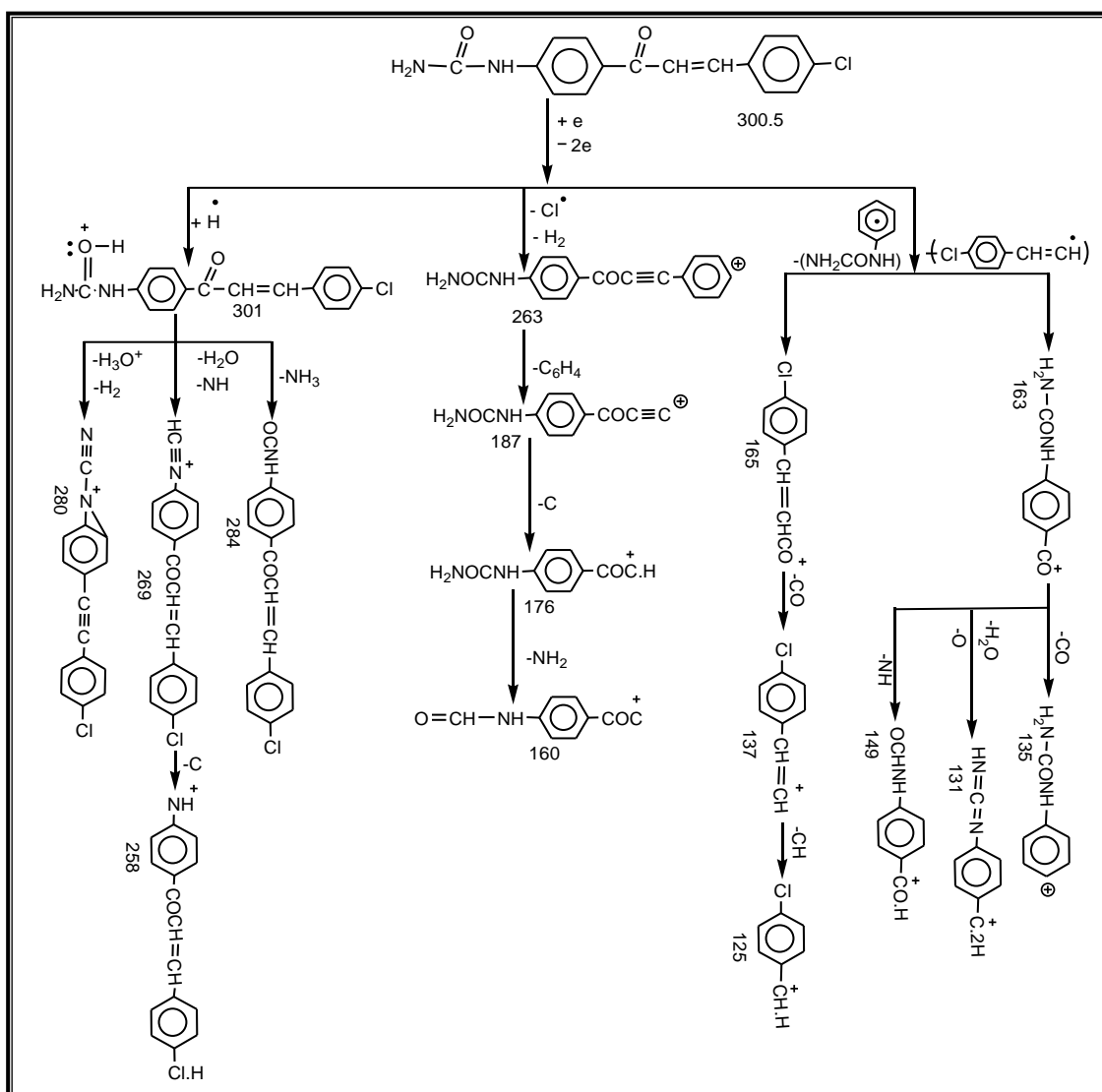
Figure (3-7): The structure of compounds [11a] and [12a]

FTIR spectral analysis of compounds [11a] and [12a], Figs. (3-32) and (3-36) showed ($-\text{NH}$) and ($-\text{NH}_2$) asymmetrical and symmetrical stretching bands at (3394, 3360, 3217) and (3370, 3363, 3190) cm^{-1} , beside ketonic carbonyl ($\text{O}=\text{C}-\text{C}$) and amide carbonyl ($\text{O}=\text{C}-\text{N}-$) of ureido group stretching bands at (1685, 1654) and (1732, 1654) cm^{-1} , ethylenic ($-\text{CH}=\text{CH}-$) stretching bands of chalcones at (1589) and (1589) cm^{-1} respectively. Also asymmetrical and symmetrical stretching bands of ($-\text{NO}_2$) group in case of compound [12a] at (1527, 1338) cm^{-1} respectively. All these bands are summarized in Table (3-9).

^1H NMR spectrum of compounds [11a] and [12a], Figs. (3-33) and (3-37), showed a singlet signal of ($-\text{NH}_2$) protons at $\delta(6.1)$ and (6.0)ppm, singlet signal of ($-\text{N}-\text{H}$) ureido proton at $\delta(9.0, 9.1)$ ppm, as well as multiplet signals of (10H) protons for aromatic and ethylenic ($-\text{CH}=\text{CH}-$) protons at $\delta(7.1-8.1)$ and (8.1-8.3)ppm respectively. All these signals are summarized in Table (3-10).

^{13}C NMR, spectrum of compounds [11a] and [12a], Figs. (3–34) and (3–38), showed two carbonyl carbons of unsaturated ketone at $\delta(185)$ and $(184)\text{ppm}$ and ureido carbonyl carbons $\delta(156)$ and $(152)\text{ppm}$ respectively, beside to the aromatic and ethylenic carbons at $\delta(118–142)$ and $(116–130)\text{ppm}$ respectively. All these signals are summarized in Table (3–11).

Mass spectrum analysis of compound [11a], Fig. (3–35), showed $(\text{M}+\text{H})^+$ ions (m/z) (301), as well as to following fragments $m/z=(301, 284, 280, 269, 263, 258, 187, 176, 165, 163, 160, 149, 137, 135, 131$ and $125)$ which would be attributed to the following suggested mechanism shown in Scheme (3–7). All these fragments are summarized in Table (3–13).



Scheme (3-7): Suggested fragmentation mechanism of [1(4-uriedo)phenyl-3-p-chloro phenyl-2-prepene-1-one] [11a]

3.4. Synthesis of pyrimidines:

3.4.1. Synthesis of 4(*p*-ureido-phenyl)-6-*p*-chloro or *p*-nitro-phenyl-2-oxo(1H)pyrimidine [13a] and [14a]

Reaction of chalcones [11a] and [12a] with urea in alcoholic alkaline solutions of sodium hydroxide gave pyrimidines [13a] and [14a], which were characterized by FTIR for compounds [13a] and [14a] ^1H NMR, ^{13}C NMR spectral analysis for compound [13a].

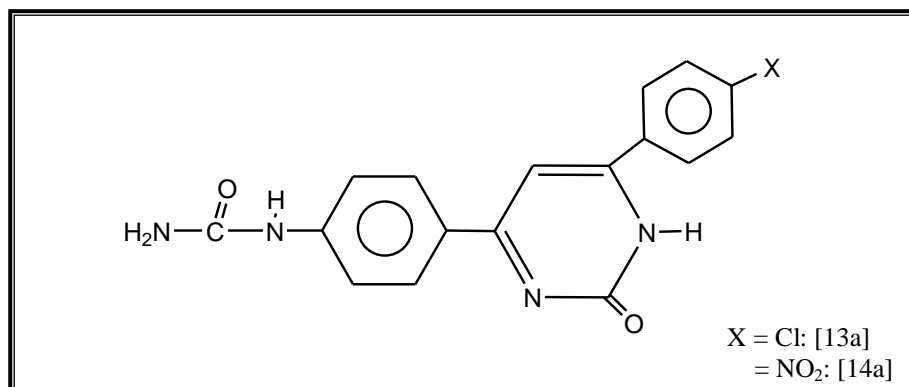


Figure (3–8): The structure of compounds [13a] and [14a]

FTIR spectral analysis of compounds [13a] and [14a], Figs. (3–39) and (3–42) showed asymmetrical and symmetrical ($-\text{NH}_2$) stretching bands with ($-\text{NH}$) stretching bands of ureido group ($\text{H}_2\text{N}-\text{CO}-\text{NH}-$) and carbamido group ($\text{O}=\text{C}-\text{NH}$) of pyrimidine ring at (3471, 3433, 3367, 3217) and (3480, 3410, 3250, 3150) cm^{-1} . As well as to amide carbonyl ($\text{O}=\text{C}-\text{N}$) stretching bands of ureido group at (1678), (1681) cm^{-1} , ethylenic ($-\text{CH}=\text{C}-$) and ($-\text{C}=\text{N}-$) stretching bands of pyrimidine ring at (1593) and (1593) cm^{-1} respectively. Also asymmetrical and symmetrical stretching bands of ($-\text{NO}_2$) group in case of compound [14a] at (1519, 1346) cm^{-1} . All these bands are summarized in Table (3–9).

^1H NMR, spectrum of compound [13a] Fig. (3–40), showed singlet signal of ethylenic ($-\text{CH}=\text{C}-$) proton at $\delta(6.1)\text{ppm}$, ($-\text{NH}$) singlet signal of pyrimidine ring proton at $\delta(6.5)\text{ppm}$, beside (NH_2) singlet signal of protons at $\delta(7.9)\text{ppm}$, ($\text{N}-\text{H}$) singlet signal at $\delta(9.0)\text{ppm}$ of ureido group, as well as a multiplet signals of (8H) protons for aromatic protons at $\delta(7.1-7.8)\text{ppm}$. All these signals are summarized in Table (3–10).

^{13}C NMR spectrum of compound [13a] Fig. (3–41), showed two carbonyl carbons of ($\text{C}=\text{O}$), ureido carbonyl carbon ($\text{H}_2\text{N}-\text{CO}-\text{NH}$) at $\delta(163)\text{ppm}$ and carbamido of pyrimidine ring ($\text{C}=\text{O}$) at $\delta(187)\text{ppm}$, beside to the aromatic, ($-\text{C}=\text{N}-$) ring and ethylenic carbons at $\delta(117-147)\text{ppm}$. All these signals are summarized in Table (3–11).

3.4.2. Synthesis of 4(*p*-Ureido-phenyl)-6-*p*-chloro or *p*-nitro-phenyl-2-imino(1H)pyrimidine [15a] and [16a]

Reaction of chalcones [11a] and [12a] with guanidine hydrochloride in alcoholic alkaline solutions of sodium hydroxide gave pyrimidines [15a] and [16a], which were characterized by FTIR for compounds [15a] and [16a], ^1H NMR, ^{13}C NMR spectral analysis for compound [15a].

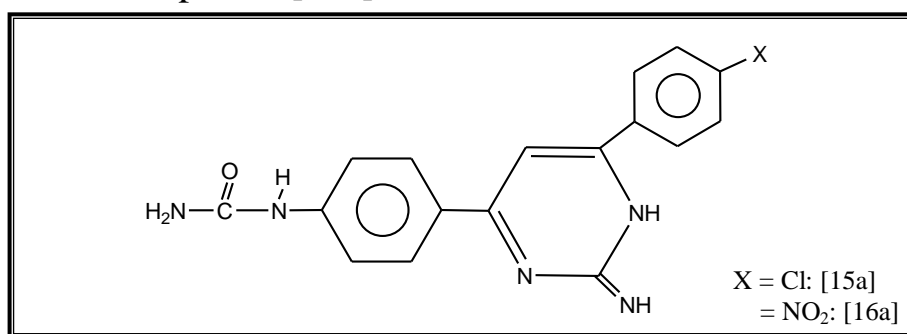


Figure (3–9): The structure of compounds [15a] and [16a]

FTIR spectral analysis of compounds [15a] and [16a], Figs. (3–43) and (3–46) showed asymmetrical and symmetrical ($-\text{NH}_2$) stretching bands, with ($-\text{NH}$) stretching bands of ureido group ($\text{H}_2\text{NCONH}-$) and imidino group ($\text{HN}=\text{C}-\text{NH}$) of pyrimidine ring at (3468, 3340, 3336, 3197) and (3425, 3367, 3313, 3201) cm^{-1} , beside to carbonyl ($\text{H}_2\text{NCONH}-$) of ureido group at (1662) and (1670) cm^{-1} , ethylenic ($-\text{CH}=\text{C}-$) and ($-\text{C}=\text{N}-$) stretching bands of pyrimidine ring at (1589) and (1635) cm^{-1} respectively. Also asymmetrical and symmetrical stretching bands of ($-\text{NO}_2$) group in case of compound [16a] at (1531, 1350) cm^{-1} . All these bands are summarized in Table (3–9).

^1H NMR, spectrum of compounds [15a], Fig. (3–44) showed ethylenic proton (1H) signal at $\delta(5.9)\text{ppm}$, singlet signal of ($-\text{NH}$) of pyrimidine ring proton at $\delta(6.6)\text{ppm}$, beside a singlet signal of imidino group proton ($-\text{C}=\text{NH}$) of pyrimidine ring at $\delta(7.3)\text{ppm}$, a singlet signal of ($-\text{NH}$) ureido group at $\delta(8.8)\text{ppm}$ and singlet signal of (NH_2) ureido group at $\delta(7.5)\text{ppm}$, as well as a multiplet signals of (8H) protons for aromatic protons at $\delta(7.6-8.2)\text{ppm}$. All these signals are summarized in Table (3–10).

^{13}C NMR spectrum of compound [15a] Fig. (3–45), showed carbonyl carbon of ($\text{C}=\text{O}$) ureido group at $\delta(163)\text{ppm}$, imidino group ($-\text{C}=\text{NH}$) of pyrimidine ring carbon at $\delta(148)\text{ppm}$, as well as the aromatic, ethylenic and ($-\text{C}=\text{N}-$) carbons at $\delta(119-144)\text{ppm}$. All these signals are summarized in Table (3–11).

3.4.3. Synthesis of 4(*p*-Ureido-phenyl)-6-*p*-chloro or *p*-nitro-phenyl-2-thioxo(1H)pyrimidine [17a] and [18a]

Reaction of chalcones [11a] and [12a] with thiourea in alcoholic alkaline solutions of sodium hydroxide gave pyrimidines [17a] and [18a], which were characterized by FTIR for compounds [17a] and [18a], ^1H NMR and ^{13}C NMR spectral analysis for compound [17a].

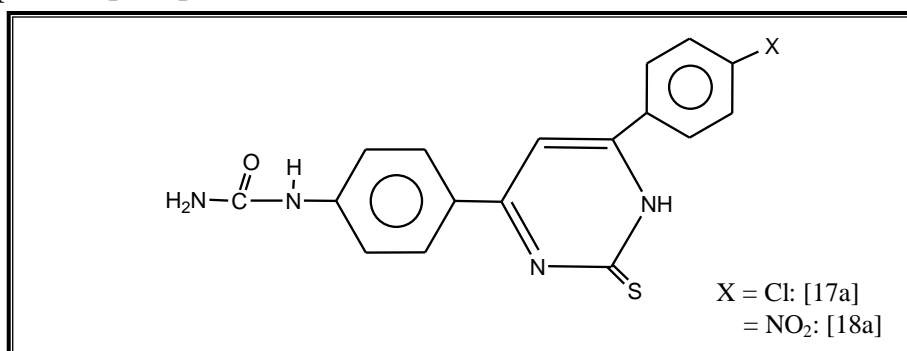


Figure (3–10): The structure of compounds [17a] and [18a]

FTIR spectral analysis of compounds [17a] and [18a], Figs. (3–47) and (3–50), showed asymmetrical and symmetrical ($-\text{NH}_2$) stretching bands, with ($-\text{NH}$) stretching bands of ureido ($\text{H}_2\text{NCONH}-$) group and thiocarbamido ($\text{S}=\text{C}-\text{NH}-$) group of pyrimidine ring at $(3450, 3340, 3197)\text{cm}^{-1}$ and $(3464, 3371, 3201)\text{cm}^{-1}$, as well as to carbonyl ($\text{H}_2\text{NCONH}-$) stretching bands of ureido group at (1678) and $(1678)\text{cm}^{-1}$, and thiocarbamido ($\text{NH}-\text{C}=\text{S}$) group stretching bands of pyrimidine ring at (1234) and $(1238)\text{cm}^{-1}$, ethylenic ($-\text{CH}=\text{C}-$) and ($-\text{C}=\text{N}-$) stretching bands of pyrimidine ring at (1585) and $(1577)\text{cm}^{-1}$ respectively. Also asymmetrical and symmetrical stretching bands of ($-\text{NO}_2$) group in case of compound [18a] at $(1527, 1334)\text{cm}^{-1}$. All these bands are summarized in Table (3–9).

^1H NMR, spectrum of compound [17a], Fig. (3–48), showed singlet signal of ethylenic ($-\text{CH}=\text{C}-$) proton at $\delta(6.0)\text{ppm}$, a singlet signal of ($-\text{NH}$) ring at $\delta(7.0)\text{ppm}$, beside singlet signal of ($-\text{NH}_2$) ureido at $\delta(7.2)\text{ppm}$, and a singlet signal of ($-\text{NH}$) ureido at $(8.8)\text{ppm}$, as well as a multiplet signals of (8H) protons for aromatic at $(7.3-8.4)$. All these signals are summarized in Table (3–10).

^{13}C NMR spectrum of compound [17a] Fig. (3–49), showed carbonyl carbon of ($\text{C}=\text{O}$) ureido group at $\delta(156)\text{ppm}$, thiocarbamido in pyrimidine ring carbon ($\text{C}=\text{S}$) at $\delta(187)\text{ppm}$, as well as the aromatic and ethylenic ($-\text{CH}=\text{C}-$) and ($-\text{C}=\text{N}-$) carbons at $\delta(114-147)\text{ppm}$. All these signals are summarized in Table (3–11)^[117-120].

Series three:

3.5. Synthesis of chalcones (2-propene-1-one compounds)

Synthesis of 1(4(*p*,N-methylaminophenyl)azophenyl-3-*p*-chloro or-*p*-nitrophenyl-2-propene-1-one) [20a] and [21a].

These two chalcones were synthesized in two steps:

First: Reaction of *p*-aminoacetophenone with a sodium nitrite in hydrochloric acid solution to give, the diazonium salt which was coupled with N-methyl aniline to give *p*-acetyl-*p'*-(N-methyl amino)azobenzene [19a] which was characterized by its FTIR, ^1H NMR, ^{13}C NMR spectral analysis.

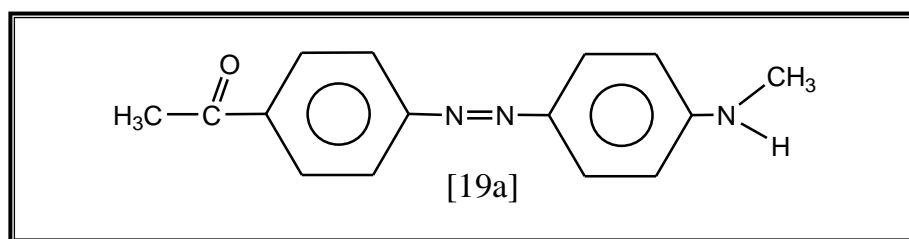


Figure (3–11): The structure of compound [19a]

FTIR spectrum of compound [19a], Fig. (3–51) showed (–NH) of amino group stretching band at $(3383)\text{cm}^{-1}$, (–N=N–) of azo stretching band at $(1500)\text{cm}^{-1}$, beside ketonic carbonyl (CH_3CO –) stretching band at $(1674)\text{cm}^{-1}$. All these bands are summarized in Table (3–14).

^1H NMR spectrum Fig. (3–52), showed a singlet signal of ($\text{CH}_3\text{–C=O}$) methyl protons at $\delta(2.6)\text{ppm}$, a singlet signal of amino (–NH) proton at $\delta(3.4)\text{ppm}$, beside a singlet signal of (–N– CH_3) methyl protons as (3H) at $\delta(3.7)\text{ppm}$, as well as a multiplet signals of two phenyl protons as (8H) at $\delta(7.1\text{–}8.1)\text{ppm}$. All these signals are summarized in Table (3–15).

^{13}C NMR, spectrum of compound [19a] Fig. (3–53), showed methyl carbon signal of ($\text{CH}_3\text{–C=O}$) at $\delta(27)\text{ppm}$, (–N– CH_3) methyl carbon signal at $\delta(33)\text{ppm}$, and aromatic carbons signals at $\delta(111\text{–}153)\text{ppm}$, beside (C=O) carbonyl carbon signal at $\delta(197)\text{ppm}$. All these signals are summarized in Table (3–16).

Second: Condensation of *p*-acetyl-*p'*-(N-methylamino)-azobenzene [19a] with *p*-chlorobenzaldehyde or *p*-nitrobenzaldehyde in alcoholic alkaline solution of sodium hydroxide gave chalcones [20a] and [21a], which were characterized by FTIR. ^1H NMR and ^{13}C NMR spectral analysis for compound [20a].

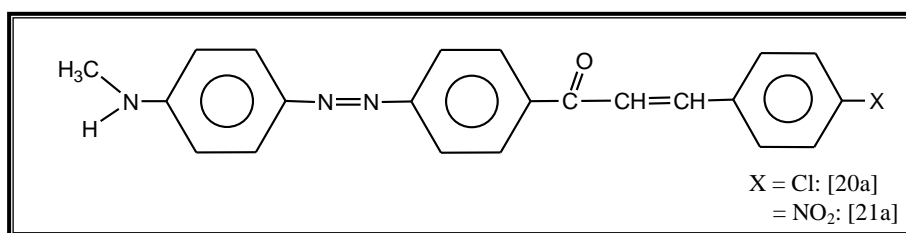


Figure (3–12): The structure of compounds [20a] and [21a]

FTIR spectral analysis of compounds [20a] and [21a], Figs (3–54) and (3–57) respectively, showed amino ($-\text{NH}$) stretching bands at (3425) and $(3406)\text{cm}^{-1}$, ketonic carbonyl stretching bands ($\text{C}=\text{O}$) at (1658) and $(1658)\text{cm}^{-1}$, ethylenic ($-\text{CH}=\text{CH}-$) stretching bands at (1597) and $(1593)\text{cm}^{-1}$, beside ($-\text{N}=\text{N}-$) azo group stretching bands at (1496) and $(1500)\text{cm}^{-1}$, as well as asymmetric and symmetric stretching bands of ($-\text{NO}_2$) group in case of compound [21a] at $(1519, 1338)\text{cm}^{-1}$ respectively. All these band are summarized in Table (3–14).

^1H NMR, spectrum of compounds [20a] and [21a], Figs. (3–55) and (3–58) respectively, showed a singlet signal of amino ($-\text{NH}$) proton at $\delta(3.4)$ and $(3.4)\text{ppm}$, singlet signal of methyl group ($-\text{N}-\text{CH}_3$) protons at $\delta(3.7)$ and $(3.7)\text{ppm}$, as well as ethylenic ($-\text{CH}=\text{CH}-$) protons signals as a doublet (2H) at $\delta(7.2)$ and $(7.2)\text{ppm}$ respectively, beside a multiplet signals of aromatic protons as (12H) at $\delta(7.4-8.3)\text{ppm}$ and $\delta(7.6-8.4)\text{ppm}$ respectively. All these signals are summarized in Table (3–15).

^{13}C NMR spectrum of compounds [20a] and [21a], Figs. (3–56) and (3–59) respectively, showed methyl carbon of ($-\text{N}-\text{CH}_3$) at $\delta(33)$ and $(33)\text{ppm}$, aromatic and ethylenic ($-\text{CH}=\text{CH}-$) carbons at $(117-153)\text{ppm}$ and $(117-153)\text{ppm}$ respectively, as well as a ketonic carbonyl carbons ($\text{C}=\text{O}$) at $\delta(187)$ and $(187)\text{ppm}$ respectively. All these signals are summarized in Table (3–16).

3.6 Synthesis of pyrimidines:

3.6.1. Synthesis of 4[4'(p,N-methylaminophenyl)azo phenyl]-6-p-chloro or p-nitrophenyl-2-oxo(1H)pyrimidine [22a] and [23a]

Reaction of chalcones [20a] and [21a] with urea in alcoholic alkaline solutions of sodium hydroxide gave pyrimidines [22a] and [23a], which were characterized by FTIR for compounds [22a] and [23a], ^1H NMR, ^{13}C NMR spectral analysis for compound [22a].

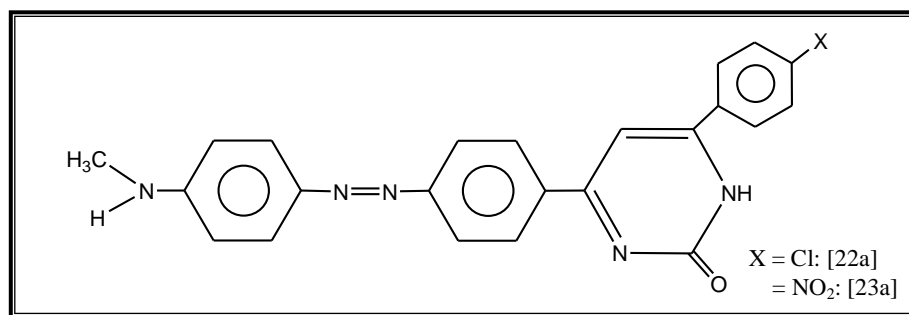


Figure (3–13): The structure of compounds [22a] and [23a]

FTIR spectral analysis of compounds [22a] and [23a], Figs. (3–60) and (3–63), showed (–NH) stretching bands of amino group (CH_3NH), and carbamido ($\text{O}=\text{C}-\text{NH}$) group in pyrimidine ring at (3479, 3429, 3380) and (3471, 3410, 3340) cm^{-1} , carbamido carbonyl ($\text{O}=\text{C}-\text{NH}$) group in pyrimidine ring stretching bands at (1651) and (1651) cm^{-1} , beside ethylenic ($-\text{CH}=\text{C}-$) and ($-\text{C}=\text{N}-$) stretching bands of pyrimidine ring at (1597) and (1597) cm^{-1} , and azo group ($-\text{N}=\text{N}-$) stretching bands at (1492) and (1500) cm^{-1} respectively. Also asymmetrical and symmetrical stretching bands of ($-\text{NO}_2$) group in case of compound [23a] at (1519, 1342) cm^{-1} . All these bands are summarized in Table (3–14).

^1H NMR, spectrum of compound [22a] Fig. (3–61), showed singlet signal of amino (–NH) proton at $\delta(3.4)\text{ppm}$, singlet signal of

(–N–CH₃–) methyl protons at $\delta(3.7)$ ppm, as well as to singlet signal (–NH) of carbamido group in pyrimidine ring proton at $\delta(6.6)$ ppm, beside a multiplet signal of aromatic and ethylenic (–CH=C–) proton as (13H) at (7.2–8.0)ppm. All these signals are summarized in Table (3–15).

¹³C NMR spectrum of compound [22a] Fig. (3–62), showed methyl carbons (–N–CH₃) at $\delta(33)$ ppm, carbonyl carbon of (C=O) carbamido group in pyrimidine ring at $\delta(185)$ ppm, as well as ethylenic (–CH=C–), aromatic and (–C=N–) pyrimidine ring carbons at $\delta(117–155)$ ppm. All these signals are summarized in Table (3–16).

3.6.2. Synthesis of 4[4'(p,N-methylaminophenyl)azophenyl]-6-p-chloro or p-nitrophenyl-2-imino(1H)pyrimidine [24a] and [25a]

Reaction of chalcones [20a] and [21a] with guanidine hydrochloride in alcoholic alkaline solutions of sodium hydroxide gave pyrimidines [24a] and [25a], which were characterized by FTIR for compounds [24a] and [25a], ¹H NMR, ¹³C NMR spectral analysis for compound [24a].

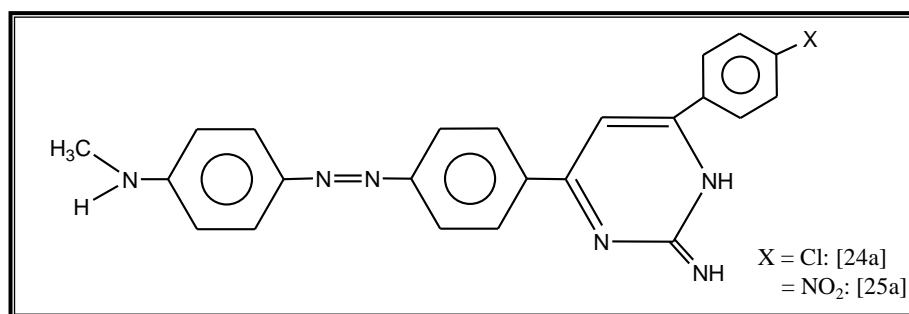


Figure (3–14): The structure of compounds [24a] and [25a]

FTIR spectral analysis of compounds [24a] and [25a], Figs. (3–64) and (3–67) showed (-NH) stretching bands of amino group ($\text{CH}_3\text{-NH}$) and imidino group (HN=C-NH) in pyrimidine ring at (3487, 3402, 3244) and (3591, 3402, 3209) cm^{-1} , beside ethylenic (-CH=C-) and (-C=N-) stretching bands of pyrimidine ring at (1597) and (1600) cm^{-1} , and azo group (-N=N-) stretching bands at (1492) and (1500) cm^{-1} respectively. Also asymmetrical and symmetrical stretching bands of (-NO_2) group in case of compound [25a] at (1535, 1346) cm^{-1} . All these bands are summarized in Table (3–14).

^1H NMR, spectrum of compound [24a], Fig. (3–65) showed singlet signal (-N-CH_3) methyl protons as (3H) at $\delta(3.8)\text{ppm}$, as well as (-NH) pyrimidine ring proton as (1H) at $\delta(6.7)\text{ppm}$, beside a multiplet signals of aromatic, ethylenic (-CH=C-) and imidino group (-C=NH) in pyrimidine ring protons as (14H) at $\delta(6.6\text{--}7.8)\text{ppm}$. All these signals are summarized in Table (3–15).

^{13}C NMR spectrum of compound [24a] Fig. (3–66), showed methyl carbon of (-N-CH_3) at $\delta(33)\text{ppm}$, imidino group (-C=NH) carbon of pyrimidine ring at $\delta(162)\text{ppm}$, as well as ethylenic (-CH=C-), (-C=N-) carbon of pyrimidine ring and aromatic carbons at $\delta(117\text{--}152)\text{ppm}$. All these signals are summarized in Table (3–16).

3.6.3. Synthesis of 4[4'(p,N-methylaminophenyl)azophenyl]-6-p-chloro or nitrophenyl-2-thioxo(1H)pyrimidine [26a] and [27a]

Reaction of chalcones [20a] and [21a] with thiourea in alcoholic alkaline solutions of sodium hydroxide gave pyrimidines [26a] and [27a], which were characterized by FTIR for compounds [26a] and [27a], ^1H NMR, ^{13}C NMR spectral analysis for compound [26a].

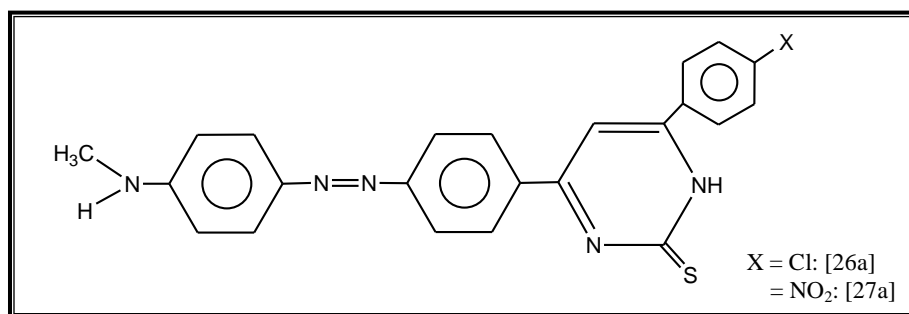


Figure (3–15): The structure of compounds [26a] and [27a]

FTIR spectral analysis of compounds [26a] and [27a], Figs. (3–68) and (3–71) showed (–NH) stretching bands of amino group (CH₃–NH), and thiocarbamido (S=C–NH) group in pyrimidine ring at (3440, 3433, 3155) and (3367, 3217, 3136)cm⁻¹, beside ethylenic (–CH=C–) and (–C=N–) stretching band at (1597) and (1573)cm⁻¹, azo group (–N=N–) stretching bands at (1492) and (1500)cm⁻¹, thiocarbamido thion group (C=S) at (1157) and (1238)cm⁻¹ respectively. Also asymmetrical and symmetrical stretching bands of (–NO₂) group in case of compound [27a] at (1527, 1334)cm⁻¹. All these bands are summarized in Table (3–14).

^1H NMR, spectrum of compound [26a], Fig. (3–69) showed singlet signal of (–NH) amino proton at $\delta(3.5)$ ppm, singlet signal of (–N–CH₃) methyl protons at $\delta(3.7)$ ppm, as well as singlet signal of

(–NH) thiocarbamido group in pyrimidine ring at $\delta(6.7)$ ppm, beside a multiplet signals of aromatic and ethylenic (–CH=C–) protons as (13H) at $\delta(7.2–8.6)$ ppm. All these signals are summarized in Table (3–15).

^{13}C NMR spectrum of compound [26a] Fig. (3–70), showed methyl carbon of (–N–CH₃) at $\delta(33)$ ppm, thiocarbamido carbon (–C=S) in pyrimidine ring at $\delta(177)$ ppm, as well as ethylenic (–CH=C–), aromatic and (–C=N–) of pyrimidine ring carbons at $\delta(117–144)$ ppm. All these signals are summarized in Table (3–16)^[117-120].

Series four:

3.7. Synthesis of chalcones (2-propene-1-one compounds)

Synthesis of [1(*p*,N-phthalimido)phenyl-3-*p*-chloro or *p*-nitrophenyl-2-propene-1-one[29a] and [30a]

These two chalcones were synthesized in two steps:

First: By reaction of *p*-aminoacetophenone with phthalic anhydride in the presence of glacial acetic acid to give [4-(N-acetyl)phenyl phthalimide] [28a] which was characterized by FTIR spectral analysis.

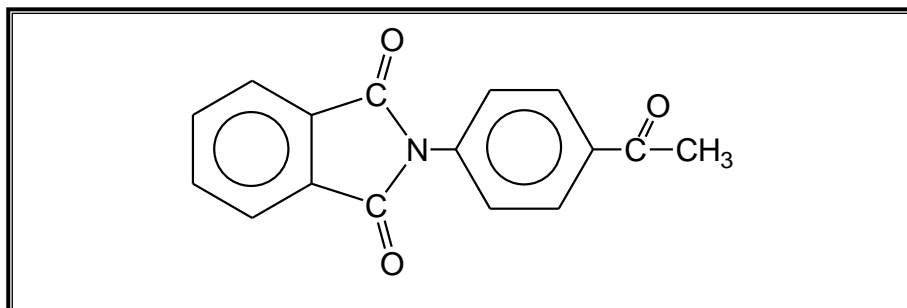


Figure (3–16): The structure of compound [28a]

FTIR spectrum of this compound [28a] Fig. (3–72), showed ketonic carbonyl group at $(1714)\text{cm}^{-1}$, beside to the stretching band of phthalimide carbonyl group at (1745) and $(1788)\text{cm}^{-1}$. All these bands are summarized in Table (3–17).

Second: condensation of 4-N-acetylphenyl phthalimide with *p*-chlorobenzaldehyde and *p*-nitrobenzaldehyde in alcoholic sodium hydroxide solution to give chalcones [29a] and [30a]. These compounds [29a] and [30a] were characterized by FTIR spectral analysis. ^1H NMR, ^{13}C NMR spectral analysis for compound [29a].

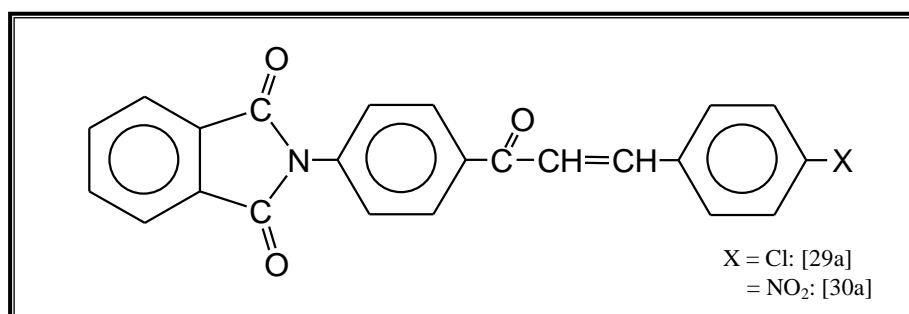


Fig. (3–17): The structure of compounds [29a] and [30a]

FTIR spectral analysis of compounds [29a] and [30a], Figs. (3–73) and (3–76) respectively, showed phthalimido carbonyl group at $(1740)\text{cm}^{-1}$ and $(1745)\text{cm}^{-1}$, beside ketonic carbonyl stretching band at (1658) and $(1666)\text{cm}^{-1}$, ethylenic stretching bands at (1593) and $(1593)\text{cm}^{-1}$ respectively, as well as asymmetrical and symmetrical stretching bands of ($-\text{NO}_2$) group in case of compound [30a] at $(1519, 1342)\text{cm}^{-1}$. All these bands are summarized in Table (3–17).

^1H NMR, spectrum of compound [29a], Fig. (3–74) showed signals of ethylenic ($-\text{CH}=\text{CH}-$) protons as (2H) at $\delta(6.6)\text{ppm}$, as

well as a multiplet signals of aromatic protons as (12H) at $\delta(7.5-8.1)$ ppm. All these signals are summarized in Table (3-18).

^{13}C NMR spectrum of compound [29a] Fig. (3-75), showed signals of ketonic carbonyl carbon at $\delta(187)$ ppm, phthalimido carbonyl carbon at $\delta(167)$ ppm, as well as aromatic and ethylenic carbons at $\delta(112-144)$ ppm. All these signals are summarized in Table (3-19).

3.8. Synthesis of pyrimidines:

3.8.1. Synthesis of 4(*p*,*N*-phthalimido)phenyl-6-*p*-chloro or *p*-nitrophenyl-2-oxo, (1H) pyrimidine [31a] and [32a]

Reaction of chalcones [29a] and [30a] with urea in alcoholic alkaline solutions of sodium hydroxide gave pyrimidines [31a] and [32a], which were characterized by FTIR spectral analysis. ^1H NMR and ^{13}C NMR spectral analysis for compound [31a].

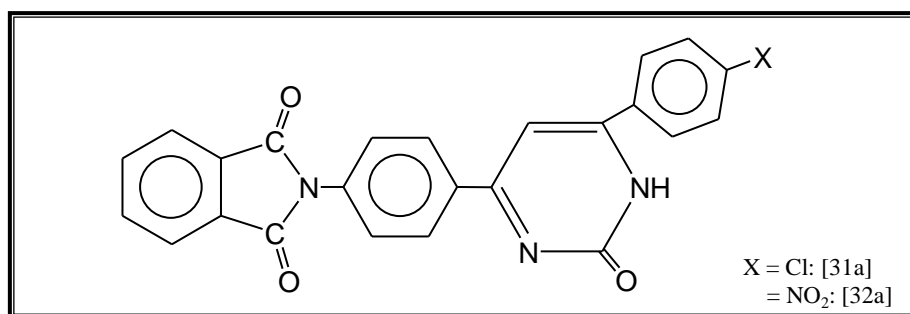


Fig. (3-18): The structure of compounds [31a] and [32a]

FTIR spectral analysis of compounds [31a] and [32a], Figs. (3-77) and (3-80) showed ($-\text{NH}$) stretching bands of carbamido ($\text{O}=\text{C}-\text{NH}$) of pyrimidine ring at (3450, 3302, 3197) and (3464, 3375, 3294), and well as to carbamido ($\text{C}=\text{O}$) stretching bands of

pyrimidine ring at (1678, 1662) cm^{-1} , and ($-\text{CH}=\text{C}$) ethylenic and ($-\text{C}=\text{N}-$) stretching bands of pyrimidine ring at (1593, 1593) cm^{-1} , as well as asymmetrical and symmetrical stretching bands of ($-\text{NO}_2$) group in case of compound [32a] at (1519, 1342) cm^{-1} respectively. All these bands are summarized in Table (3-17).

^1H NMR, spectrum of compound [31a], Fig. (3-78) showed singlet signals of ($-\text{NH}$) pyrimidine ring as (1H) at $\delta(6.8)\text{ppm}$. As well as a multiplet signals of aromatic and ethylenic protons as (13H) at $\delta(7.2- 8.9)\text{ppm}$. All these signals are summarized in Table (3-18).

^{13}C NMR spectrum of compound [31a] Fig. (3-79), showed signals of phthalimido ($\text{C}=\text{O}$) carbonyl carbon at $\delta(185)\text{ppm}$, carbamido ($\text{C}=\text{O}$) carbonyl carbon at $\delta(153)\text{ppm}$. As well as aromatic, ethylenic ($-\text{CH}=\text{C}-$) and ($-\text{C}=\text{N}-$) carbons at $\delta(112-139)\text{ppm}$. All these signals are summarized in Table (3-19).

3.8.2. Synthesis of 4(*p*,*N*-phthalimido)phenyl-6-*p*-chloro or *p*-nitrophenyl-2-imino(1H)pyrimidine [33a] and [34a]

Reaction of chalcones [29a] and [30a] with guanidine hydrochloride in alcoholic alkaline solutions of sodium hydroxide gave pyrimidines [33a] and [34a], which were characterized by FTIR spectral analysis. ^1H NMR and ^{13}C NMR spectral analysis for compound [33a].

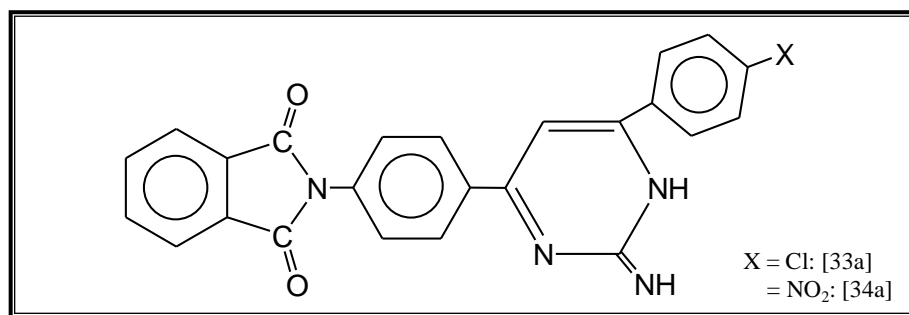


Fig. (3–19): The structure of compounds [33a] and [34a]

FTIR spectral analysis of compounds [33a] and [34a], Figs. (3–81) and (3–84) showed (–NH) stretching bands of imidino ($\text{HN}=\overset{\text{I}}{\text{C}}-\text{NH}$) of pyrimidine ring at (3394, 3321, 3250) and (3475, 3363, 3213) cm^{-1} , also imidino (–C=NH) stretching bands at (1681, 1654) cm^{-1} , ethylenic(–CH=C–), (–C=N–) stretching bands of pyrimidine ring at (1593, 1593) cm^{-1} respectively. As well as asymmetrical and symmetrical stretching bands of (–NO₂) group in case of compound [34a] at (1519, 1342) cm^{-1} respectively. All these bands were summarized in Table (3–17).

¹H NMR, spectrum of compound [33a], Fig. (3–82) showed a singlet signal of imidino proton (–C=NH) as (1H) at $\delta(9.4)$ ppm, a singlet signal of (–NH) pyrimidine ring as (1H) at $\delta(6.7)$ ppm, as well as a multiplet signals of aromatic and ethylenic (–CH=C–) protons as (13H) at $\delta(6.7-8.2)$ ppm. All these signals are summarized in Table (3–18).

¹³C NMR spectrum of compound [33a], Fig. (3–83), showed signals of phthalimido (C=O) carbonyl carbon at $\delta(170)$ ppm, imidino (–C=NH) carbon signal at $\delta(153)$ ppm, as well as aromatic, ethylenic (–CH=C–) and (–C=N–) carbons signals at $\delta(119-141)$ ppm. All these signals are summarized in Table (3–19).

3.8.3. Synthesis of 4(*p*,*N*-phthalimido)phenyl-6-*p*-chloro or *p*-nitrophenyl-2-thioxopyrimidine [35a] and [36a]

Reaction of chalcones [29a] and [30a] with thiourea in alcoholic alkaline solutions of sodium hydroxide gave pyrimidines [35a] and [36a], which were characterized by FTIR spectral analysis. ^1H NMR and ^{13}C NMR spectral analysis for compound [35a].

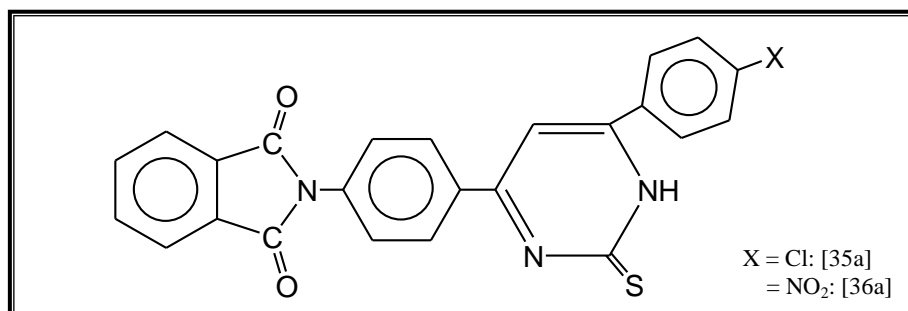


Fig. (3–20): The structure of compounds [35a] and [36a]

FTIR spectral analysis of compounds [35a] and [36a], Figs. (3–85) and (3–88) showed (–NH) stretching bands of thiocarbamido (S=C–NH) of pyrimidine ring at (3398, 3271, 3190) and (3433, 3367, 3236) cm^{-1} , as well as to thiocarbamido (C=S) stretching bands of pyrimidine ring at (1261) and (1257) cm^{-1} , ethylenic(–CH=C–) and (–C=N–) stretching bands of pyrimidine ring at (1597, 1593) cm^{-1} respectively, and asymmetrical, symmetrical stretching bands of (–NO₂) group in case of compound [36a] at (1516, 1342) cm^{-1} respectively. All these bands are summarized in Table (3–17).

^1H NMR, spectrum of compound [35a], Fig. (3–86) showed a singlet signal of (–NH) pyrimidine ring as (1H) at $\delta(7.2)$ ppm, as well as a multiplet signals of aromatic and ethylenic (–CH=C–) as (13H) at $\delta(7.2– 7.9)$ ppm. All these signals are summarized in Table (3–18).

^{13}C NMR spectrum of compound [35a] Fig. (3–87), showed signals of phthalimido (C=O) carbonyl carbon at $\delta(167)\text{ppm}$, thiocarbamido (C=S) carbon at $\delta(175)\text{ppm}$, as well as aromatic, ethylenic ($-\text{CH}=\text{C}$) and ($-\text{C}=\text{N}-$) carbons at $\delta(119-143)\text{ppm}$. All these signals are summarized in Table (3–19) ^[117-120].

Series Five:

3.9. Synthesis of chalcones (2-propene-1-one compounds)

A. Synthesis of N(4-acetylphenyl)p(N-phthalimido)benzamide [37a]

This compound was synthesized in three steps:

Step I. Synthesis of 4-N-phthalimidobenzoic acid

Reaction of phthalic anhydride with p-amino benzoic acid in presence of glacial acetic acid gave the compound (4-N-phthalimido benzoic acid), which was characterized by FTIR spectral analysis.

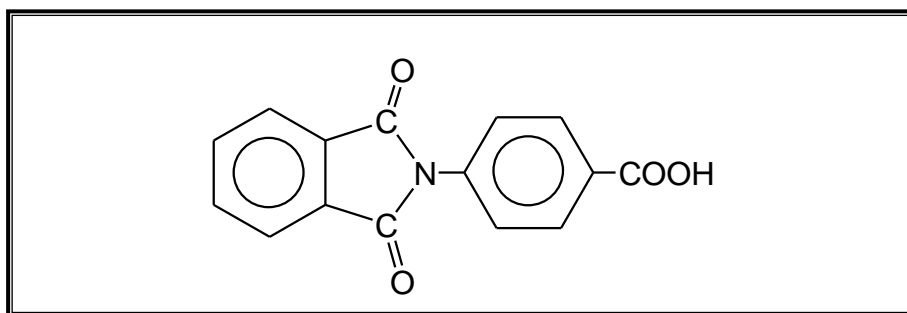


Fig. (3–21): The structure of compound 4-N-phthalimidobenzoic acid

FTIR spectrum of this compound Fig. (3–89), showed $(3084-2549)\text{cm}^{-1}$ stretching bands for carboxylic acid, as well as to carbonyl (C=O) of carboxylic acid stretching band at $(1708)\text{cm}^{-1}$, phthalimido carbonyl stretching bands at $(1784, 1724)\text{cm}^{-1}$.

Step II. Synthesis of 4-N-phthalimidobenzoyl chloride

Reaction of 4-N-phthalimidobenzoic acid with thionyl chloride in the presence of dry benzene gave the compound (4-N-phthalimidobenzoyl chloride, which was characterized by FTIR spectral analysis.

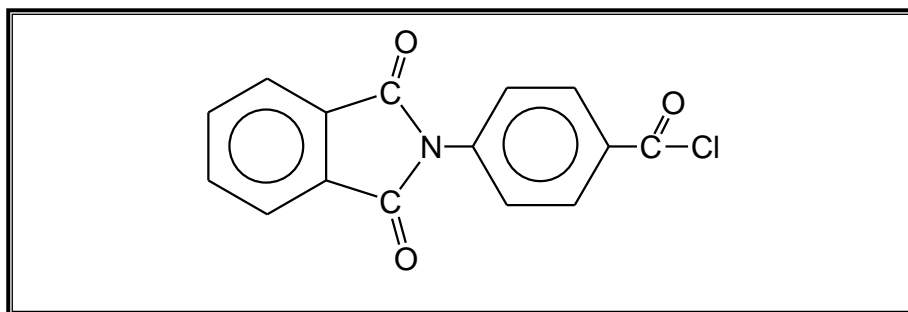


Fig. (3–22): The structure of compound 4-N-phthalimidobenzoyl chloride

FTIR spectrum of this compound Fig. (3–90), showed bands of carbonyl stretching band of the acid chloride at $(1730)\text{cm}^{-1}$, as well as phthalimido carbonyl stretching band at $(1776, 1751)\text{cm}^{-1}$.

Step III. Synthesis of N(4-acetylphenyl)p(N-phthalimido)benzamide [37a]

Reaction of 4-N-phthalimidobenzoyl chloride with p-aminoacetophenone in dry benzene gave the titled compound [37a], which was characterized by FTIR spectral analysis.

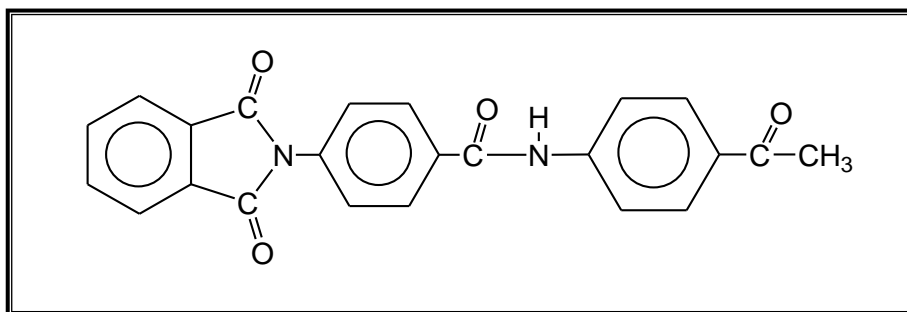


Fig. (3–23) The structure of compound [37a]

FTIR spectrum of compound [37a], Fig. (3–91), showed (--NH) stretching bands of amido group at $(3348)\text{cm}^{-1}$, as well as to carbonyl of amido stretching bands at $(1670)\text{cm}^{-1}$, ketonic carbonyl stretching band at $(1710)\text{cm}^{-1}$, and phthalimido carbonyl stretching band at $(1776, 1724)\text{cm}^{-1}$. All these bands are summarized in Table (3–20).

3.9.1 Synthesis of 1[*p*(N-phthalimido)benzamido-N-phenyl]-3-*p*-chloro or *p*-nitrophenyl-2-propene-1-one [38a] and [39a]

Condensation of N(4-acetylphenyl)*p*(N-phthalimido)benzamide [37a] with *p*-chlorobenzaldehyde or *p*-nitrobenzaldehyde in alcoholic alkaline solution of sodium hydroxide gave chalcones [38a] and [39a], which were characterized by FTIR spectral analysis. ^1H NMR and ^{13}C NMR spectral analysis for compound [38a].

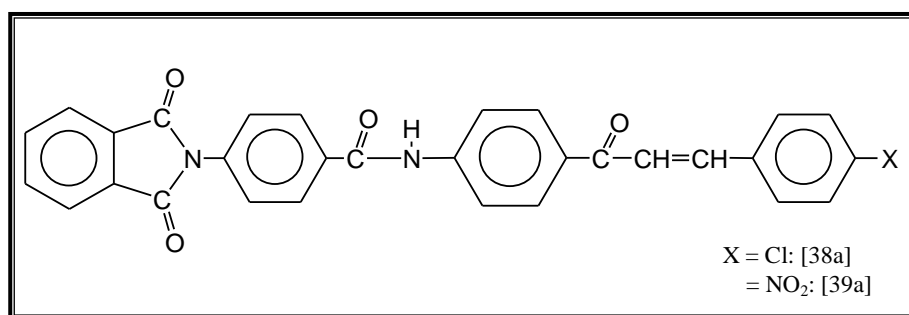


Fig. (3–24): The structure of compounds [38a] and [39a]

FTIR spectra of compounds [38a] and [39a], Figs. (3–92) and (3–95) showed (--NH) stretching bands of amide group at (3298) and $(3387)\text{cm}^{-1}$, as well as to carbonyl of amide stretching band at (1653) and $(1654)\text{cm}^{-1}$, ketonic carbonyl stretching bands at (1653) and $(1654)\text{cm}^{-1}$, ethylenic stretching bands at (1595) and $(1593)\text{cm}^{-1}$

respectively, and asymmetrical and symmetrical stretching bands of ($-\text{NO}_2$) group in case of compound [39a] at $(1516, 1323)\text{cm}^{-1}$ respectively. All these bands are summarized in Table (3–20).

^1H NMR, spectrum of compound [38a], Fig. (3–93) showed signals of ethylenic ($-\text{CH}=\text{CH}-$) protons as (2H) at $\delta(6.6)\text{ppm}$, a singlet signal of ($-\text{NH}$) amide as (1H) at $\delta(10.4)\text{ppm}$, as well as a multiplet signals of aromatic protons as (16H) at $\delta(7.4- 8.6)\text{ppm}$. All these signals are summarized in Table (3–21).

^{13}C NMR spectrum of compound [38a] Fig. (3–94), showed signals of ketonic ($\text{C}=\text{O}$) carbon at $\delta(187)\text{ppm}$, carbonyl of amide ($\text{C}=\text{O}$) carbon at $\delta(155)\text{ppm}$, phthalimido carbonyl ($\text{C}=\text{O}$) carbon at $\delta(168)\text{ppm}$, as well as aromatic and ethylenic ($-\text{CH}=\text{CH}-$) carbons at $\delta(114-143)\text{ppm}$. All these signals are summarized in Table (3–22).

3.10. Synthesis of pyrimidines:

3.10.1. Synthesis of 4[*p*(N-phthalimido)benzamido-N-phenyl]-6-*p*-chloro or *p*-nitrophenyl-2-oxo(1H) pyrimidine [40a] and [41a]

Reaction of chalcones [38a] and [39a] with urea in alcoholic alkaline solutions of sodium hydroxide gave pyrimidines [40a] and [41a], which were characterized by FTIR spectral analysis. ^1H NMR and ^{13}C NMR spectral analysis for compound [40a].

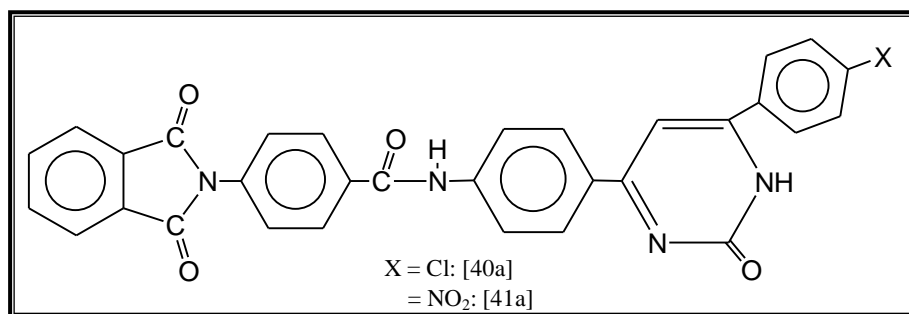


Fig. (3–25): The structure of compounds [40a] and [41a]

FTIR spectral analysis of compounds [40a] and [41a], Figs. (3–96) and (3–99) showed (–NH) stretching bands of amide and carbamido (–NH–C=O) of pyrimidine ring at (3456, 3433, 3344) and (3433, 3363, 3240) cm^{-1} , as well as to carbonyl of carbamido stretching bands at (1627) and (1658) cm^{-1} , also carbonyl of amide stretching bands at (1600) and (1658) cm^{-1} , ethylenic(CH=C–) and (C=N) of pyrimidine ring at (1546) and (1597) cm^{-1} respectively, and asymmetrical and symmetrical stretching bands of (–NO₂) group in case of compound [41a] at (1516, 1319) cm^{-1} respectively. All these bands were summarized in Table (3–20).

^1H NMR, spectrum of compound [40a], Fig. (3–97) showed a singlet signal of (–NH) amide as (1H) at $\delta(10.7)$ ppm, a singlet signal of (–NH) pyrimidine ring as (1H) at $\delta(6.6)$ ppm, beside ethylenic

(CH=C-) proton as (1H) at $\delta(6.1)$ ppm, as well as a multiplet signals of aromatic protons as (16H) at $\delta(7.4-7.9)$ ppm. All these signals are summarized in Table (3-21).

^{13}C NMR spectrum of compound [40a] Fig. (3-98), showed signals of amide (C=O) carbonyl carbon at $\delta(167)$ ppm, phthalimido (C=O) carbonyl carbon at $\delta(187)$ ppm, carbamido (C=O) carbonyl carbon at $\delta(185)$ ppm, as well as aromatic, ethylenic (-CH=C-) and (-C=N-) carbons at $\delta(112-153)$ ppm. All these signals are summarized in Table (3-22).

3.10.2. Synthesis of 4[*p*(N-phthalimido)benzamido-N-phenyl]-6-*p*-chloro or *p*-nitrophenyl-2-imino(1H) pyrimidine [42a] and [43a]

Reaction of chalcones [38a] and [39a] with guanidine hydrochloride in alcoholic alkaline solutions of sodium hydroxide gave pyrimidines [42a] and [43a], which were characterized by FTIR spectral analysis. ^1H NMR and ^{13}C NMR spectral analysis for compound [42a].

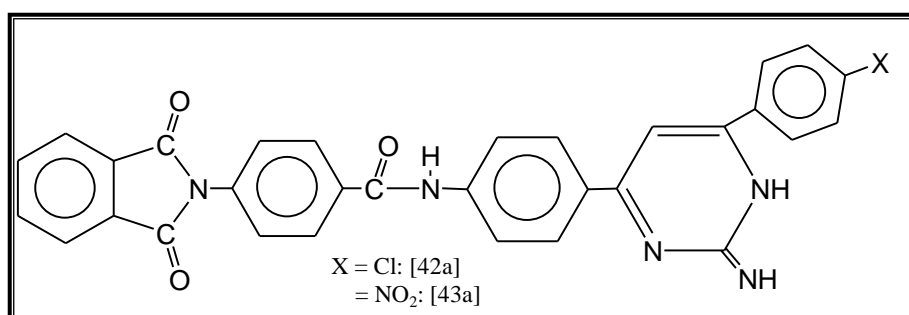


Fig. (3-26): The structure of compounds [42a] and [43a]

FTIR spectral analysis of compounds [42a] and [43a], Figs. (3-100) and (3-103) showed (-NH) stretching bands of amide and

imidino ($\text{HN}=\overset{\text{I}}{\text{C}}-\text{NH}$) pyrimidine ring at (3394, 3313, 3159) and (3412, 3329, 3305) cm^{-1} , as well as ethylenic ($-\text{CH}=\text{C}-$), ($-\text{C}=\text{N}$) and ($-\text{C}=\text{NH}$) imidino stretching bands at (1593, 1597) cm^{-1} , ($\text{C}=\text{O}$) carbonyl of amide stretching bands at (1670, 1658) cm^{-1} , and asymmetrical and symmetrical stretching bands of ($-\text{NO}_2$) group in case of compound [43a] at (1516, 1319) cm^{-1} respectively. All these bands were summarized in Table (3–20).

^1H NMR, spectrum of compound [42a], Fig. (3–101) showed a singlet signal of amide ($-\text{NH}$) as (1H) at $\delta(11.0)$ ppm, beside a singlet signal of imidino ($-\text{C}=\text{NH}$) proton as (1H) at $\delta(10.8)$ ppm, a singlet signal of ($-\text{NH}$) pyrimidine ring proton as (1H) at $\delta(6.7)$ ppm, as well as a multiplet signals of aromatic and ethylenic ($-\text{CH}=\text{C}-$) as (17H) at $\delta(7.3-9.9)$ ppm. All these signals are summarized in Table (3–21).

^{13}C NMR spectrum of compound [42a] Fig. (3–102), showed signals of amide ($\text{C}=\text{O}$) carbonyl carbon at $\delta(168)$ ppm, phthalimido ($\text{C}=\text{O}$) carbonyl carbon at $\delta(195)$ ppm, imidino ($-\text{C}=\text{NH}$) carbon in pyrimidine ring at $\delta(153)$ ppm, as well as aromatic, ethylenic ($-\text{CH}=\text{C}-$) and ($-\text{C}=\text{N}$) carbons at $\delta(118-143)$ ppm. All these signals are summarized in Table (3–22).

3.10.3. Synthesis of 4[*p*-(*N*-phthalimido)benzamido-*N*-phenyl]-6-*p*-chloro or *p*-nitrophenyl-2-thioxo(1H) pyrimidine [44a] and [45a]

Reaction of chalcones [38a] and [39a] with thiourea in alcoholic alkaline solutions of sodium hydroxide gave pyrimidines [44a] and [45a], which were characterized by FTIR spectral analysis. ^1H NMR and ^{13}C NMR spectral analysis for compound [44a].

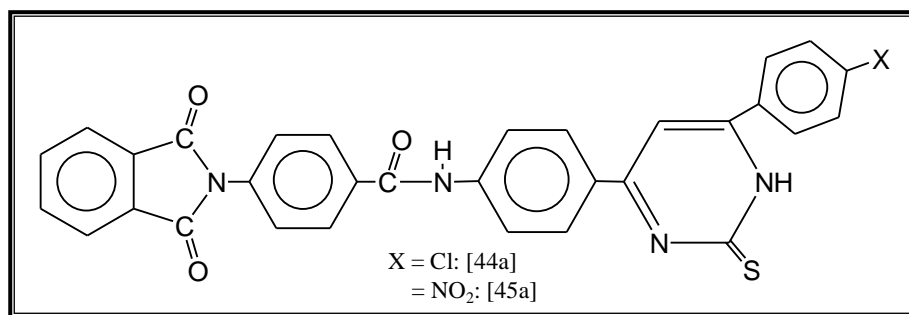


Fig. (3–27): The structure of compounds [44a] and [45a]

FTIR spectral of compounds [44a] and [45a], Figs. (3–104) and (3–107) showed (–NH) stretching bands of amide and thiocarbamido (S=C–NH) of pyrimidine ring at (3430, 3356, 3271) and (3433, 3305, 3251) cm^{-1} , as well as to thiocarbamido (C=S) stretching bands of pyrimidine ring at (1269) and (1269) cm^{-1} , carbonyl of amide (C=O) stretching bands at (1666) and (1658) cm^{-1} , ethylenic (–C=NH–) and (–C=N–) stretching bands at (1597, 1593) cm^{-1} , respectively. And asymmetrical, symmetrical stretching bands of (–NO₂) group in case of compound [45a] at (1516, 1323) cm^{-1} respectively. All these bands are summarized in Table (3–20).

^1H NMR, spectrum of compound [44a], Fig. (3–105) showed a singlet signal of (–NH) amide proton as (1H) at $\delta(10.6)\text{ppm}$, a

singlet signal of (–NH) pyrimidine ring proton as (1H) at $\delta(6.6)$ ppm, beside a singlet signal of ethylenic (–CH=C–) proton as (1H) at $\delta(5.5)$ ppm, as well as a multiplet signals of aromatic protons as (16H) at $\delta(7.3–7.9)$ ppm. All these signals are summarized in Table (3–21).

^{13}C NMR spectrum of compound [44a] Fig. (3–106), showed signals of amide (C=O) carbonyl carbon at $\delta(165)$ ppm, phthalimido (C=O) carbonyl carbon at $\delta(167)$ ppm, beside thiocarbamido (C=S) carbon at $\delta(175)$ ppm, as well as aromatic, ethylenic(–CH=C–) and (–C=N–) carbons at $\delta(112–143)$ ppm. All these signals are summarized in Table (3–22)^[117-120].

Table (3–1): FT-IR spectral data (Wave number ν^-) of the compounds series one

Comp. No.	ν (-NH)	ν (C=O) Ketone	ν (-CH=CH-) ethylene	ν (-CH=C-) ethylene (-C=N-) ring	ν (SO ₂ -NH) Amide II & I	ν (-NO ₂)	ν (-C=O) Carbamido	ν (-C=NH) Imidino	ν (-C=S) Thio-carbamido	others
[1a]	3267	1681	–	–	1330 1157	–	–	–	–	ν CH aliph. 2998 ν CH aroma. 3074
[2a]	3267	1654	1604	–	1342 1157	–	–	–	–	ν CH aliph. 2987 ν CH aroma. 3078
[3a]	3309	1658	1604	–	1342 1161	1516 1340	–	–	–	ν CH aliph. 2931 ν CH aroma. 3074
[4a]	3410 3255	–	–	1604	1330 1161	–	1654	–	–	ν CH aliph. 2935 ν CH aroma. 3097
[5a]	3154 3116	–	–	1600	1342 1161	1516 1342	1658	–	–	ν CH aliph. 2943 ν CH aroma. 3043
[6a]	3340 3278 3201	–	–	1604	1334 1161	–	–	1604	–	ν CH aliph. 2927 ν CH aroma. 3097
[7a]	3491 3390 3290	–	–	1604	1346 1161	1516 1396	–	1604	–	ν CH aliph. 2889 ν CH aroma. 3116
[8a]	3360 3248	–	–	1604	1330 1161	–	–	–	1230	ν CH aliph. 2924 ν CH aroma. 3066
[9a]	3476 3384	–	–	1604	1338 1161	1516 1336	–	–	1222	ν CH aliph. 2866 ν CH aroma. 3074

aliph. = aliphatic; aroma. = aromatic.

Table (3-2): ¹H-NMR spectral data of the compounds series one

Comp. No.	-CH₃	Aromatic -H	SO₂-NH	Ethylene -CH=CH-	Pyrimidine -NH ring	-C=NH imidino	-C=CH- ring
[1a]	3.5	7.2–7.8	10.9	–	–	–	–
[2a]	–	7.4–8.0	10.95	7.25	–	–	–
[3a]	–	7.5–8.02	10.98	7.25	–	–	–
[4a]	–	7.3–7.7	10.9	–	8.1	–	7.2
[6a]	–	7.4–7.9	11.0	–	7.7	8.1	7.2
[8a]	–	7.3–7.8	10.4	–	8.1	–	7.1

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

Comp. No.	–CH₃	Aromatic–C	C=O Ketone	ethylene– CH=CH–	C=O carbamido	–C=N- ring + –CH=C– ring	–C=NH imidino	C=S Thio carbamido
[1a]	26	117–141	195	–	–	–	–	–
[2a]	–	117–142	187	117–142	–	–	–	–
[3a]	–	117–148	184	117–148	–	–	–	–
[4a]	–	117–141	–	–	185	117–141	–	–
[6a]	–	118–141	–	–	–	118–141	152	–
[8a]	–	118–145	–	–	–	118–145	–	175

Table (3–4): Fragmentation of 4-Acetylphenylbenzenesulphonamide [1a]

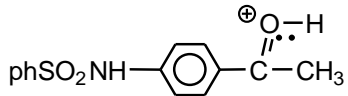
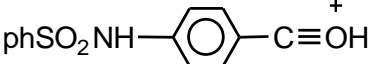
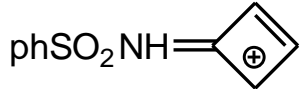
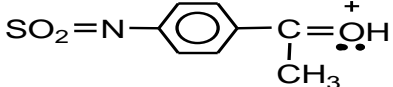
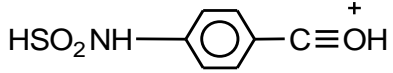
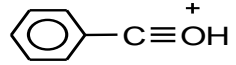
% Abundance	Fragments	Possible positive ion
100% (276)	$(M+H)^+$	
4% (261)	$(M-CH_2)^+$	
4% (206)	$(M-C_4H_5O)^+$	
21% (198)	$(M-C_6H_6)^+$	
5% (187)	$(M-C_7H_5)^+$	
1% (106)	$(M-C_6H_6SO_2)^+$	

Table (3–5): Fragmentation of 1(*p*-benzenesulphonamido)phenyl-3-*p*-chloro-2-propene-1-one [2a]

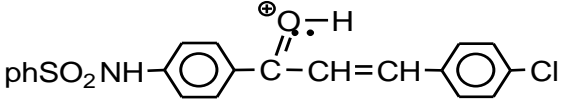
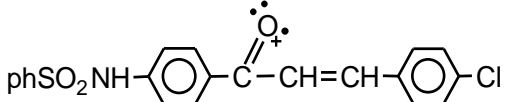
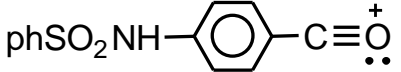
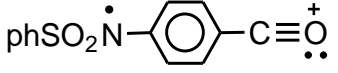
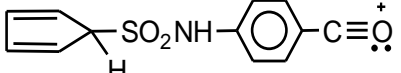
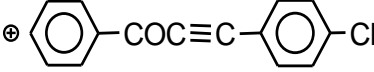
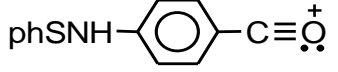
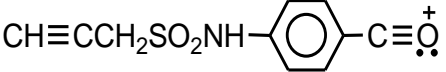
% Abundance	Fragments	Possible positive ion
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1% (397)	(M^+)	
36% (260)	$(M-C_8H_6Cl)^+$	
100% (259)	$(M-C_8H_7Cl)^+$	
20% (248)	$(M-C_9H_6Cl)^+$	
11% (239)	$(M-C_6H_8NO_2S)^+$	
23% (228)	$(M-C_8H_6O_2Cl)^+$	
7% (222)	$(M-C_{11}H_8Cl)^+$	

Table (3–6): Fragmentation of [4-(p-benzenesulphonamido)phenyl-6-p-chlorophenyl-2-oxo-(1H)-pyrimidine] [4a]

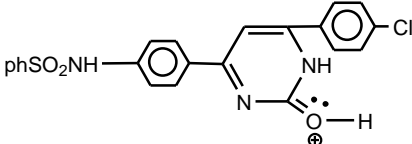
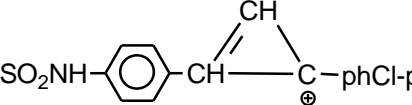
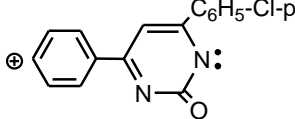
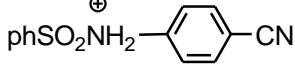
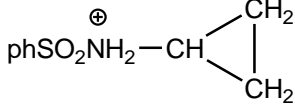
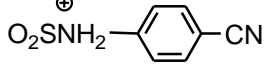
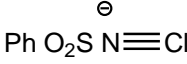
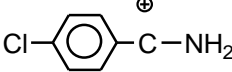

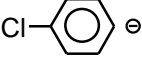
% Abundance	Fragments	Possible positive ion
100% (438)	$(M+H)^+$	
27% (304)	$(M-C_6H_5N_2O)^+$	
5% (280)	$(M-C_6H_7NO_2S)^+$	
4% (259)	$(M-C_9H_7NOCl)^+$	
12% (198)	$(M-C_{13}H_7N_2OCl)^+$	
6% (181)	$(M-C_{15}H_{12}NOCl)^+$	
6% (167)	$(M-C_{15}H_{12}N_2OCl)^+$	
15% (139)	$(M-C_{15}H_{10}N_2O_3S)^+$	
3% (123)	$(M-C_{15}H_{12}N_3O_3S)^+$	
1% (111)	$(M-C_{16}H_{12}N_3O_3S)^+$	

Table (3–7): Fragmentation of [4-(p-benzenesulphonamido)phenyl-6-p-chlorophenyl-2-imino-(1H)-pyrimidine] [6a]

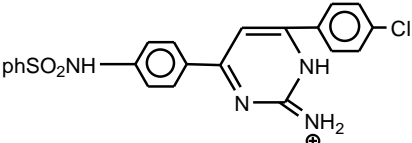
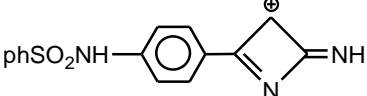
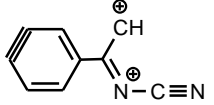
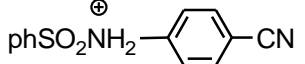
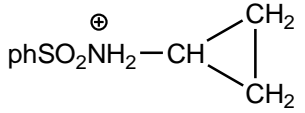
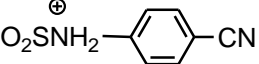
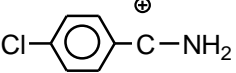
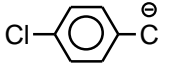
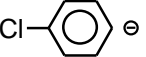
% Abundance	Fragments	Possible positive ion
46% (437)	$(M+H)^+$	
3% (298)	$(M-C_{15}H_{12}N_3O_2S)^+$	
4% (278)	$(M-C_{13}H_{13}N_2O_2SCl)^+$	
2% (259)	$(M-C_9H_6N_2Cl)^+$	
4% (198)	$(M-C_{13}H_5N_3Cl)^+$	
12% (181)	$(M-C_{15}H_{11}N_2Cl)^+$	
33% (139)	$(M-C_{15}H_{11}N_3O_2S)^+$	
17% (123)	$(M-C_{15}H_9N_2O_2S)^+$	
4% (111)	$(M-C_{14}H_9N_2O_2S)^+$	

Table (3–8): Fragmentation of [4-(p-benzenesulphonamido)phenyl-6-p-chlorophenyl-2-thioxo-(1H)-pyrimidine] [8a]

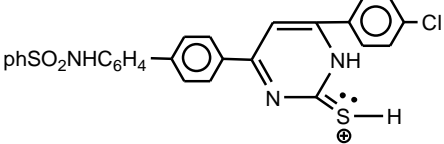
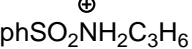
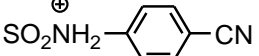
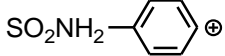
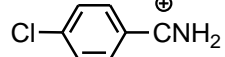
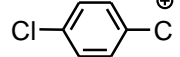

% Abundance	Fragments	Possible positive ion
1% (454)	$(M+H)^+$	
7% (199)	$(M-C_{13}H_3N_2S_2Cl)^+$	
32% (181)	$(M-C_{15}H_{10}NO_2Cl)^+$	
39% (154)	$(M-C_{14}H_9NS_2Cl)^+$	
100% (139)	$(M-C_{15}H_{10}N_2O_2S_2)^+$	
23% (123)	$(M-C_{15}H_8NO_2S_2)^+$	
18% (111)	$(M-C_{14}H_8NO_2S_2)^+$	

Table (3–9): FT-IR spectral data (Wave number ν) of the compounds series two

Comp. No.	$\nu(-NH_2)$ & $\nu(-NH)$	$\nu(C=O)$ Ketone	$\nu(N-C=O)$ ureido	$\nu(-CH=CH-)$ ethylene	$\nu(-CH=C-)$ ethylene & $(-C=N-)$	ν ($-NO_2$)	ν ($-C=O$) Carbamido	ν ($-C=NH$) Imidino	ν ($-C=S$) Thiocarbamido	others
[10a]	3406 3305 3213	1708	1670	–	–	–	–	–	–	ν CH aliph. 2877 ν CH aroma. 3039
[11a]	3394 3360 3217	1685	1654	1589	–	–	–	–	–	ν CH aliph. 2927 ν CH aroma. 3082
[12a]	3370 3363 3190	1732	1654	1589	–	1527 1338	–	–	–	ν CH aliph. 2870 ν CH aroma. 3113
[13a]	3471 3433 3367 3217	–	1678	–	1593	–	1678	–	–	ν CH aliph. 2978 ν CH aroma. 3062
[14a]	3480 3410 3250 3150	–	1681	–	1593	1519 1346	1681	–	–	ν CH aliph. 2974 ν CH aroma. 3092
[15a]	3468 3340 3336 3197	–	1662	–	1589	–	–	1598	–	ν CH aliph. 2954 ν CH aroma. 3091
[16a]	3425 3367 3313 3201	–	1670	–	1635	1531 1350	–	1635	–	ν CH aliph. 2927 ν CH aroma. 3075
[17a]	3450 3340 3197	–	1678	–	1585	–	–	–	1234	ν CH aliph. 2978 ν CH aroma. 3056
[18a]	3464 3371 3201	–	1678	–	1577	1527 1334	–	–	1238	ν CH aliph. 2978 ν CH aroma. 3109

aliph. = aliphatic; aroma. = aromatic.

Table (3–10): ¹H-NMR spectral data of the compounds series two

Comp. No.	–CH₃	Aromatic–H	–NH₂ ureido	–NH ureido	Ethylene –C=C–	–NH ring	–C=N–H imidino
[10a]	2.5	7.5–7.9	6.1	9.0	–	–	–
[11a]	–	7.1–8.1	6.1	9.0	7.1–8.1	–	–
[12a]	–	8.1–8.3	6.0	9.1	8.1–8.3	–	–
[13a]	–	7.1–7.8	7.9	9.0	6.1	6.5	–
[15a]	–	7.6–8.2	7.5	8.8	5.9	6.6	7.3
[17a]	–	7.3–8.4	7.2	8.8	6.0	7.0	–

Table (3–11): ^{13}C -NMR spectral data of the compounds series two

Comp. No.	$-\text{CH}_3$	Ethylene $-\text{C}=\text{C}-$ & Aromatic-C	C=O uriedo	C=O Ketone	$-\text{C}=\text{N}-$ ring	C=O carbamido	$-\text{C}=\text{N}-\text{H}$ imidino	C=S Thio- carbamido
[10a]	26	117–145	155	195	–	–	–	–
[11a]	–	118–142	156	185	–	–	–	–
[12a]	–	116–130	152	184	–	–	–	–
[13a]	–	117–147	163	–	117–147	187	–	–
[15a]	–	119–144	163	–	119–144	–	148	–
[17a]	–	114–147	156	–	114–147	–	–	187

Table (3–12): Fragmentation of 4-actylphenylurea [10a]

% Abundance	Fragments	Possible positive ion
1% (178)	M^+	$\text{H}_2\text{N CO NH}-\text{C}_6\text{H}_4-\overset{\ominus}{\text{C}}\text{O}-\text{CH}_3$ <p style="text-align: center;">or</p> $\text{H}_2\text{N CO NH}-\text{C}_6\text{H}_4-\overset{\oplus}{\text{C}}\text{O}-\text{CH}_3$
100% (179)	$(M+H)^+$	$\overset{\oplus}{\text{O}}-\text{H}$ $\text{H}_2\text{N}-\overset{\parallel}{\text{C}}-\text{NH}-\text{C}_6\text{H}_4-\text{COCH}_3$
6% (163)	$(M-\text{CH}_3)^+$	$\text{H}_2\text{N CO NH}-\text{C}_6\text{H}_4-\overset{\oplus}{\text{C}}\text{O}$
6% (160)	$(M-\text{H}_2\text{O})^+$	$\text{HN}=\text{C}=\text{N}-\text{C}_6\text{H}_4-\overset{\oplus}{\text{C}}\text{O}-\text{CH}_3$
20% (150)	$[M-(\text{CH}_2+\text{O})+2\text{H}]$	$\text{H}_2\text{N CO NH}-\text{C}_6\text{H}_4-\text{C}\equiv\overset{\oplus}{\text{O}}\text{H}$
18% (137)	$[M-\text{CH}_3\text{COH}+2\text{H}]$	$\text{H}_2\text{N CH}_2 \text{NH}-\text{C}_6\text{H}_4-\text{C}\equiv\overset{\oplus}{\text{O}}\text{H}$
17% (130)	$[M-(\text{CH}_3+\text{NH}_3+\text{O})]$	$\text{C}=\overset{\ominus}{\text{N}}-\text{C}_6\text{H}_4-\overset{\oplus}{\text{C}}\text{O}$
2% (119)	$\text{M}-\text{H}_2\text{N}-\overset{\text{NH}}{\parallel}{\text{C}}-\text{OH}$	$\oplus \text{C}_6\text{H}_4-\text{COCH}_3$

Table (3-13): Fragmentation of [1(4-ureido)phenyl-3-*p*-chlorophenyl-2-propene-1-one] [11a]

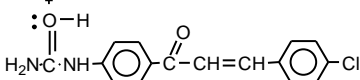
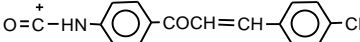
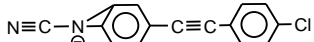
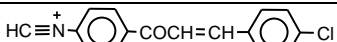
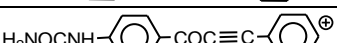
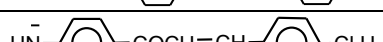


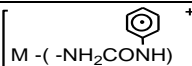
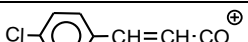
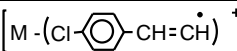
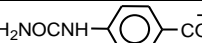
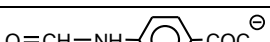
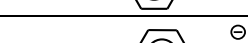
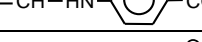
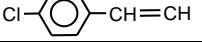
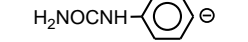
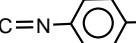
% Abundance	Fragments	Possible positive ion
45% (301)	[M+H] ⁺	
8% (284)	[M-NH ₂] ⁺	
55% (280)	[M-(H ₂ +H ₃ O)] ⁺	
86% (269)	[M-(-NH+OH)] ⁺	
57% (263)	[M-(-Cl+H ₂)] ⁺	
47% (258)	[M-C] ⁺	
32% (187)	[M-C ₆ H ₄] ⁺	
14% (176)	[M-C] ⁺	
47% (165)		
11% (163)		
34% (160)	[M-NH] ⁺	
27% (149)	[M-NH] ⁺	
7% (137)	[M-CO] ⁺	
10% (135)	[M-CO] ⁺	
15% (131)	[M-(H ₂ O+O)] ⁺	
12% (125)	[M-CH] ⁺	

Table (3–14): FT-IR spectral data (Wave number ν^-) of the compounds series three

Comp. No.	ν (-NH)	ν (C=O) Ketone	ν (-N=N-) Azo	ν (-CH=CH-) ethylene	ν (-CH=C-) ethylene (-C=N-) ring	ν (-NO ₂)	ν (-C=O) Carbamido	ν (-C=NH) Imidino	ν (-C=S) Thio- carbamido	others
[19a]	3383	1674	1500	–	–	–	–	–	–	ν CH aliph. 2893 ν CH aroma. 3059
[20a]	3425	1658	1496	1597	–	–	–	–	–	ν CH aliph. 2924 ν CH aroma. 3059
[21a]	3406	1658	1500	1593	–	1519 1338	–	–	–	ν CH aliph. 2877 ν CH aroma. 3078
[22a]	3479 3429 3380	–	1492	–	1597	-	1651	–	–	ν CH aliph. 2924 ν CH aroma. 3075
[23a]	3471 3410 3340	–	1500	–	1597	1519 1342	1651	–	–	ν CH aliph. 2970 ν CH aroma. 3078
[24a]	3487 3402 3244	–	1492	–	1597	–	–	1597	–	ν CH aliph. 2947 ν CH aroma. 3055
[25a]	3591 3402 3209	–	1500	–	1600	1535 1346	–	1600	–	ν CH aliph. 2990 ν CH aroma. 3074
[26a]	3440 3433 3155	–	1492	–	1597	–	–	–	1157	ν CH aliph. 2931 ν CH aroma. 3047
[27a]	3367 3217 3136	–	1500	–	1573	1527 1334	–	–	1238	ν CH aliph. 2924 ν CH aroma. 3050

aliph. = aliphatic; aroma. = aromatic.

Table (3–15): ¹H-NMR spectral data of the compounds series three

Comp. No.	CH₃CO–	–NH amine	–N–CH₃ amine	Aromatic– H	ethylene– C=C–	–NH ring	–C=NH imidino
[19a]	2.6	3.4	3.7	7.1–8.1	–	–	–
[20a]	–	3.4	3.7	7.4–8.3	7.2	–	–
[21a]	–	3.4	3.7	7.6–8.4	7.2	–	–
[22a]	–	3.4	3.7	7.2–8.0	7.2–8.0	6.6	–
[24a]	–	3.6	3.8	6.6–7.8	6.6–7.8	6.7	6.6–7.8
[26a]	–	3.5	3.7	7.2–8.6	7.2–8.6	6.7	–

Table (3–16): ¹³C-NMR spectral data of the compounds series three

Comp. No.	CH₃CO–	–N–CH₃	Ethylene (–C=C–) & Aromatic–C	C=O Ketone	–C=N– ring	C=O carbamido	–C=NH imidino	C=S Thio- carbamido
[19a]	27	33	111–153	197	–	–	–	–
[20a]	–	33	117–153	187	–	–	–	–
[21a]	–	33	117–153	187	–	–	–	–
[22a]	–	33	117–155	–	117–155	185	–	–
[24a]	–	33	117–152	–	117–152	–	162	–
[26a]	–	33	117–144	–	117–144	–	–	177

Table (3–17): FT-IR spectral data (Wave number ν^-) of the compounds series four

Comp. No.	ν (-NH)	$\nu(\text{C=O})$ Ketone	ν (C=O) Pthalimide	ν (CH=CH-) ethylene	ν (-CH=C-) ethylene (-C=N-) ring	ν (-NO ₂)	$\nu(-\text{C=O})$ Carbamido	ν (-C=NH) Imidino	$\nu(-\text{C=S})$ Thio-carbamido	others
[28a]	–	1714	1745 1788	–	–	–	–	–	–	νCH aliph. 2918 νCH aroma. 3059
[29a]	–	1658	1720	1593	–	–	–	–	–	νCH aliph. 2870 νCH aroma. 3059
[30a]	–	1666	1720	1593	–	1519 1342	–	–	–	νCH aliph. 2974 νCH aroma. 3059
[31a]	3450 3302 3197	–	1710	–	1593	–	1678	–	–	νCH aliph. 2904 νCH aroma. 3032
[32a]	3464 3375 3294	–	1705	–	1593	1519 1342	1662	–	–	νCH aliph. 2978 νCH aroma. 3055
[33a]	3394 3321 3250	–	1705	–	1593	–	–	1681	–	νCH aliph. 2877 νCH aroma. 3059
[34a]	3475 3363 3213	–	1715	–	1593	1519 1342	–	1654	–	νCH aliph. 2978 νCH aroma. 3062
[35a]	3398 3271 3190	–	1700	–	1597	–	–	–	1261	νCH aliph. 2993 νCH aroma. 3059
[36a]	3433 3367 3236	–	1700	–	1593	1516 1342	–	–	1257	νCH aliph. 2978 νCH aroma. 3059

aliph. = aliphatic; aroma. = aromatic.

Table (3–18): ¹H NMR spectral data of the compounds series four

Comp. No.	Aromatic-H	Ethylene –C=C–	–NH ring	–C=NH imidino
[29a]	7.5–8.1	6.6	–	–
[31a]	7.2–8.9	7.2– 8.9	6.8	–
[33a]	6.7–8.2	6.7– 8.2	6.7	9.4
[35a]	7.2–7.9	7.2– 7.9	7.2	–

Table (3–19): ¹³C-NMR spectral data of the compounds series four

Comp. No.	C=O Ketone	C=O phthalimide	Aromatic-C	Ethylene -CH=CH-	Ethylene -CH=C- & C=N	C=O carbamido	-C=NH imidino	C=S Thio- carbamido
[29a]	187	167	112–144	112– 144	–	–	–	–
[31a]	–	185	112–139	–	112– 139	153	–	–
[33a]	–	170	119–141	–	119– 141	–	153	–
[35a]	–	167	119–143	–	119– 143	–	–	175

Table (3–20): FT-IR spectral data (Wave number ν^-) of the compounds series five

Comp. No.	ν (-NH)	ν (C=O) Pthalimide	ν (C=O) amid	ν (C=O) Ketone	ν (CH=CH-) ethylene	ν (-CH=C-) ethylene (-C=N-) ring	ν (-NO ₂)	ν (-C=O) Carbamido	ν (-C=NH) Imidino	ν (-C=S) Thio-carbamido	others
[37a]	3348	1776 1724	1670	1710	–	–	–	–	–	–	ν CH aliph. 2916 ν CH aroma. 3061
[38a]	3298	1712	1653	1653	1595	–	–	–	–	–	ν CH aliph. 2981 ν CH aroma. 3066
[39a]	3387	1716	1654	1654	1593	–	1516 1323	–	–	–	ν CH aliph. 2862 ν CH aroma. 3005
[40a]	3456 3433 3344	1700	1600	–	–	1546	–	1627	–	–	ν CH aliph. 2947 ν CH aroma. 3035
[41a]	3433 3363 3240	1730	1658	–	–	1597	1516 1319	1658	–	–	ν CH aliph. 2924 ν CH aroma. 3047
[42a]	3394 3313 3159	1715	1670	–	–	1593	–	–	1670	–	ν CH aliph. 2993 ν CH aroma. 3055
[43a]	3412 3329 3305	1725	1658	–	–	1597	1516 1319	–	1658	–	ν CH aliph. 2927 ν CH aroma. 3059
[44a]	3430 3356 3271	1710	1666	–	–	1597	–	–	–	1269	ν CH aliph. 2908 ν CH aroma. 3043
[45a]	3433 3305 3251	1720	1658	–	–	1593	1516 1323	–	–	1269	ν CH aliph. 2997 ν CH aroma. 3055

Table (3–21): ^1H NMR spectral data of the compounds series five

Comp. No.	–NH amide	Aromatic–H	Ethylene –C=C–	–NH ring	–C=NH imidino
[38a]	10.4	7.4–8.6	6.6	–	–
[40a]	10.7	7.4–7.9	6.1	6.6	–
[42a]	11.0	7.3–9.9	7.3– 9.9	6.7	10.8
[44a]	10.6	7.3–7.9	5.5	6.6	–

Table (3–22): ^{13}C -NMR spectral data of the compounds series five

Comp. No	C=O Ketone	C=O amide	C=O phthalimide	Aromatic-C	Ethylene –CH=CH–	Ethylene –CH=C– & C=N	C=O carbamido	–C=NH imidino	C=S Thio- carbamido
[38a]	187	155	168	114–143	114– 143	–	–	–	–
[40a]	–	167	187	112–153	–	112– 153	185	–	–
[42a]	–	168	195	118–143	–	118– 143	–	153	–
[44a]	–	165	167	112–143	–	112– 143	–	–	175

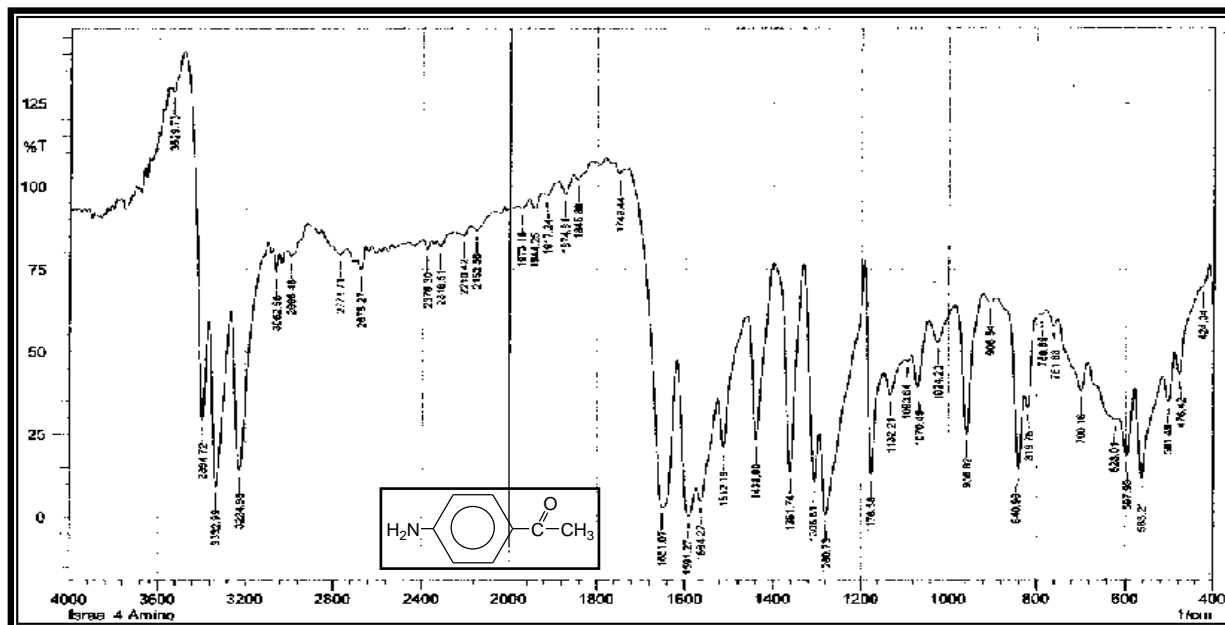


Figure (3–1): FTIR-Spectrum of compound [A]

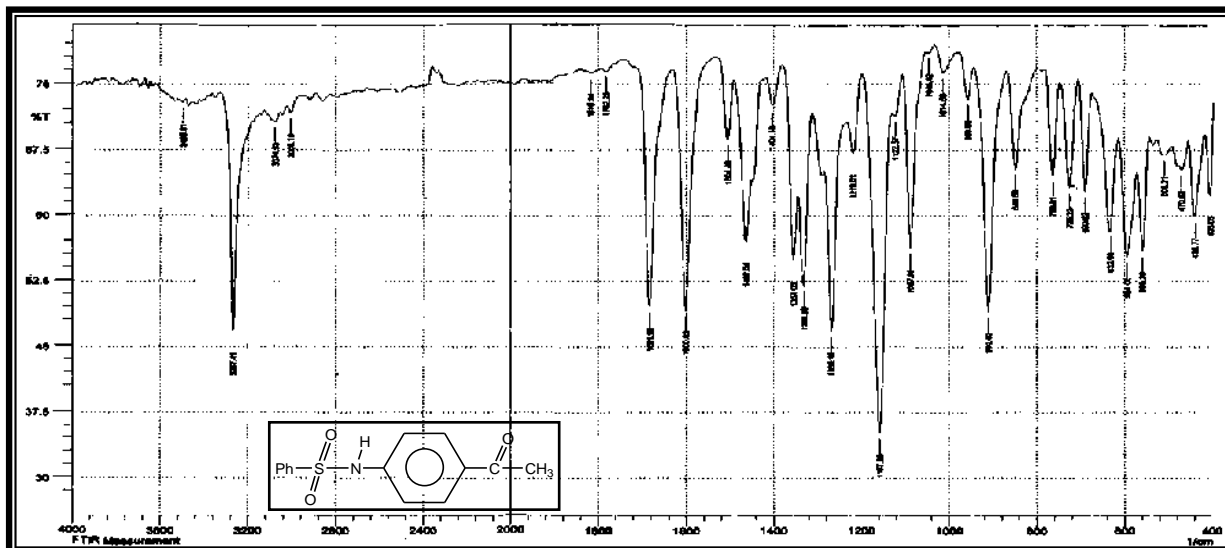
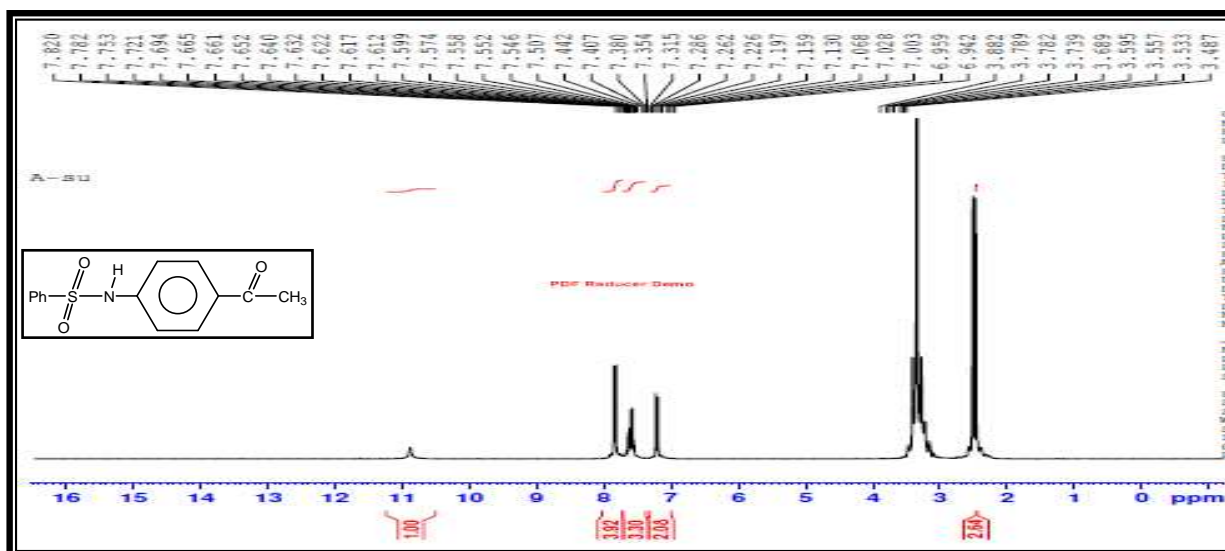


Figure (3-2): FTIR-Spectrum of compound [1a]

Figure (3-3): ^1H NMR- Spectrum of compound [1a]

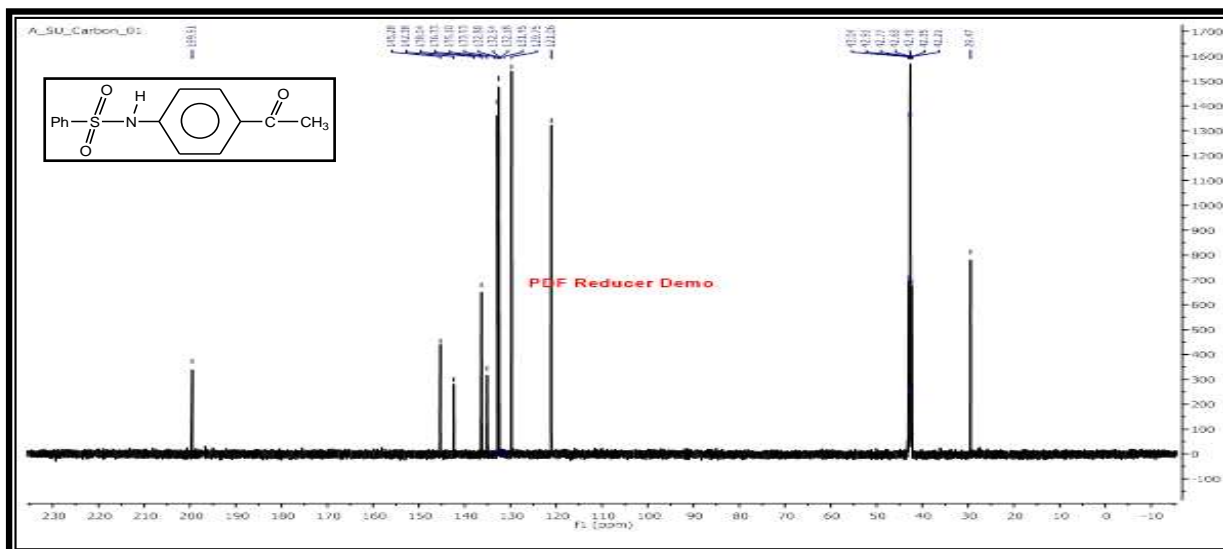


Figure (3–4): ^{13}C NMR- Spectrum of compound [1a]

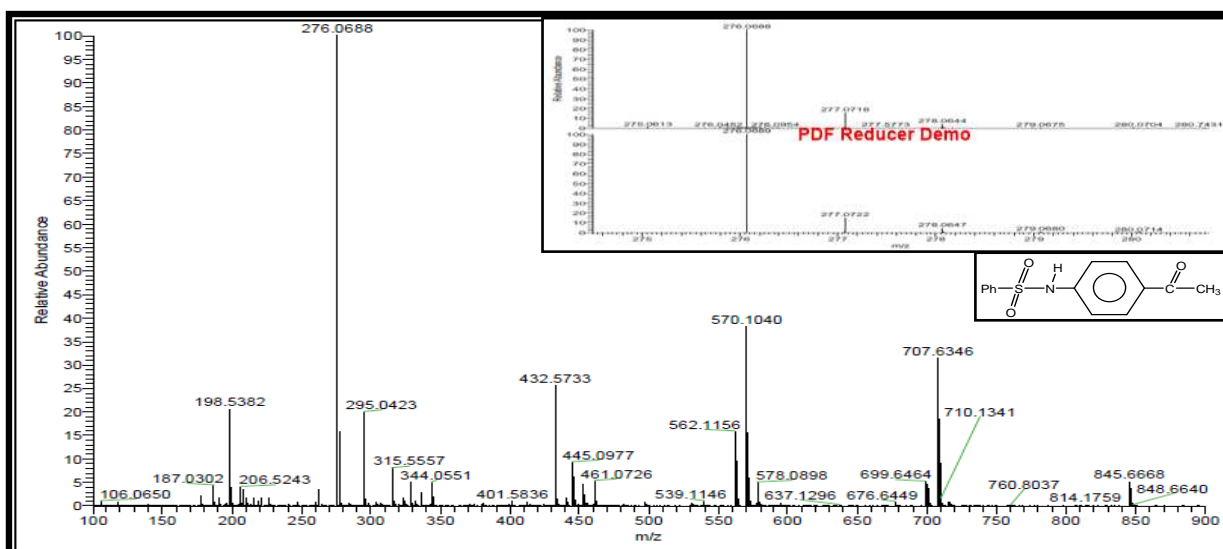


Figure (3–5): Mass- Spectrum of compound [1a]

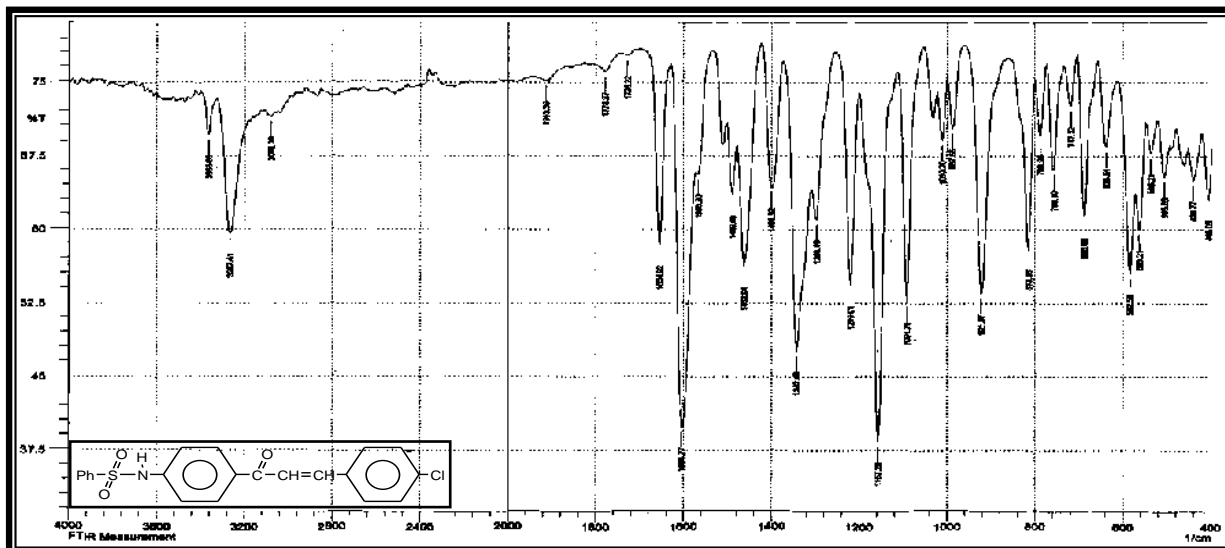


Figure (3-6): FTIR- Spectrum of compound [2a]

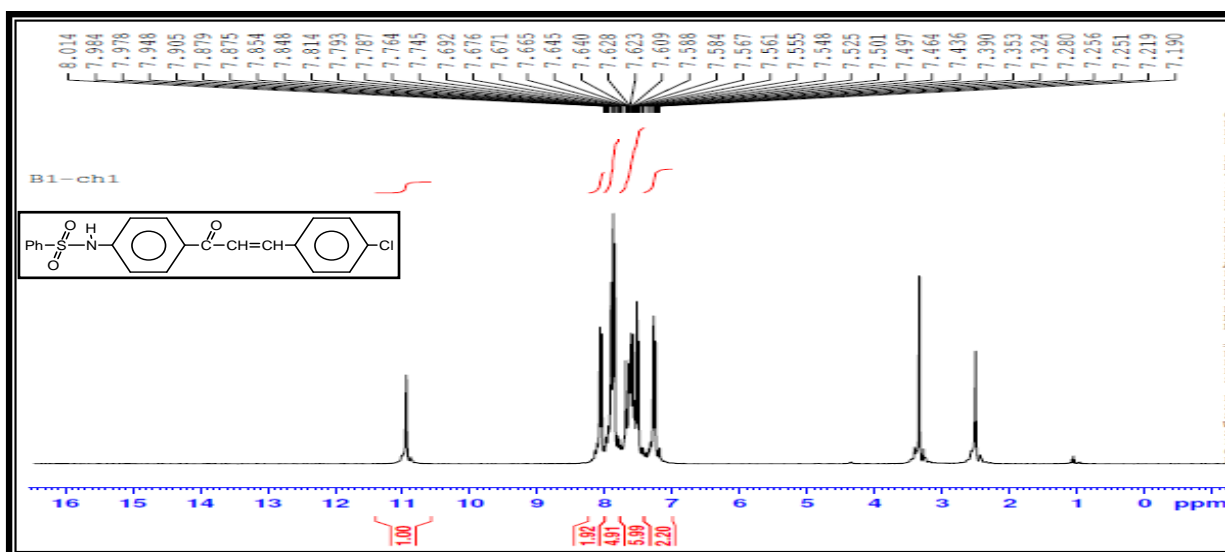


Figure (3-7): ¹H NMR- Spectrum of compound [2a]

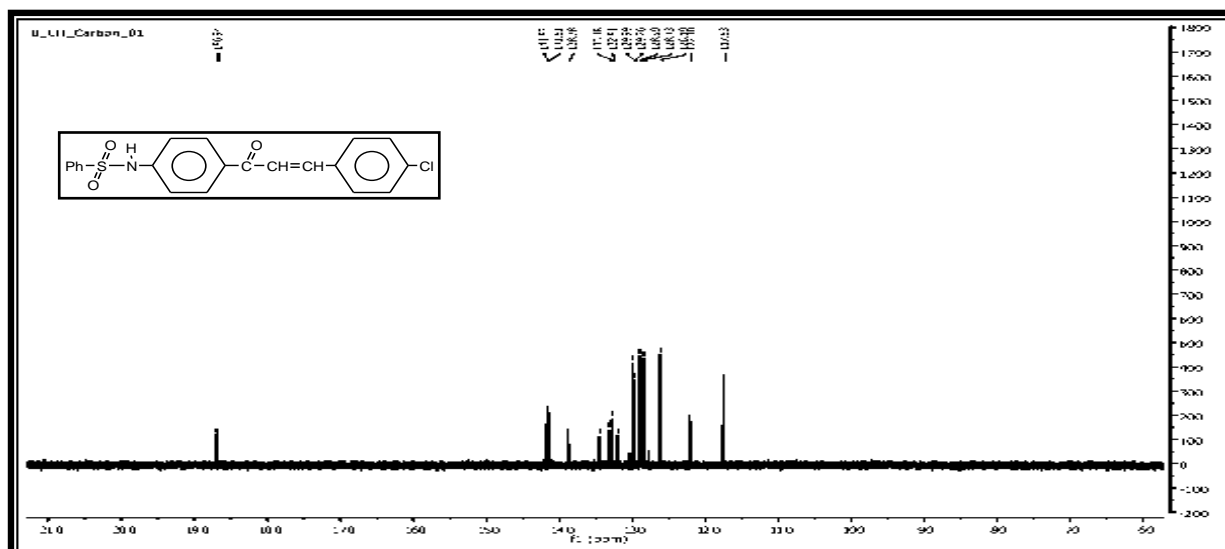


Figure (3–8): ^{13}C NMR- Spectrum of compound [2a]

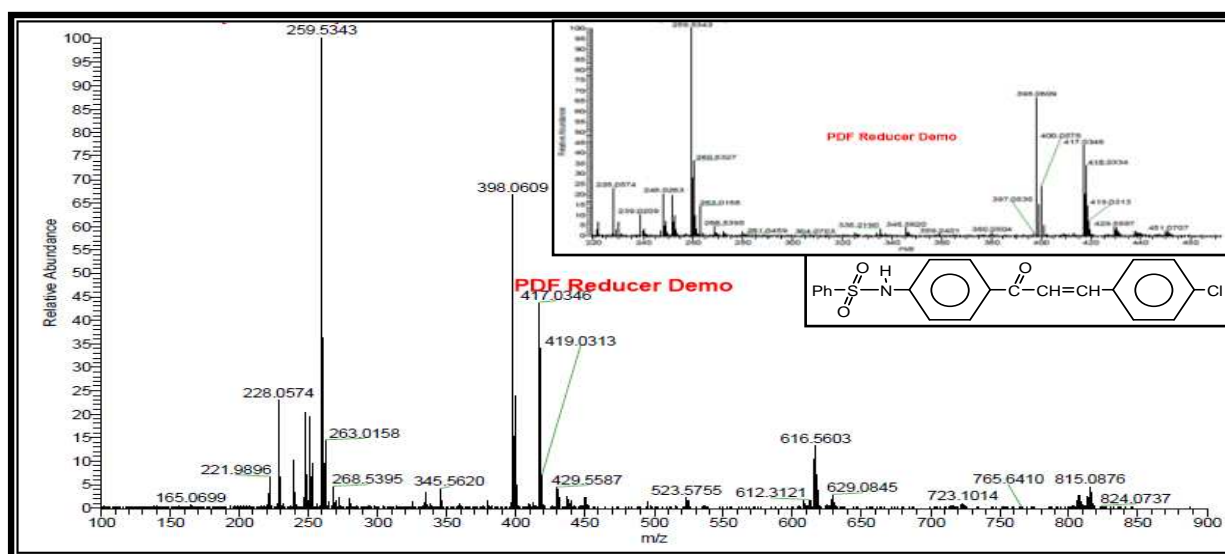


Figure (3–9): Mass- Spectrum of compound [2a]

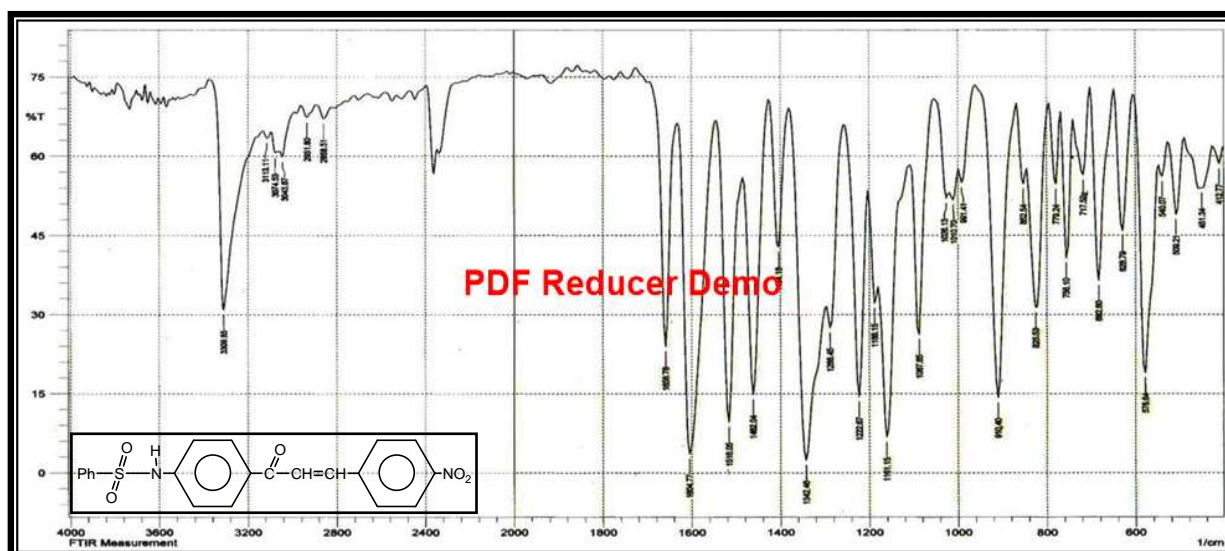
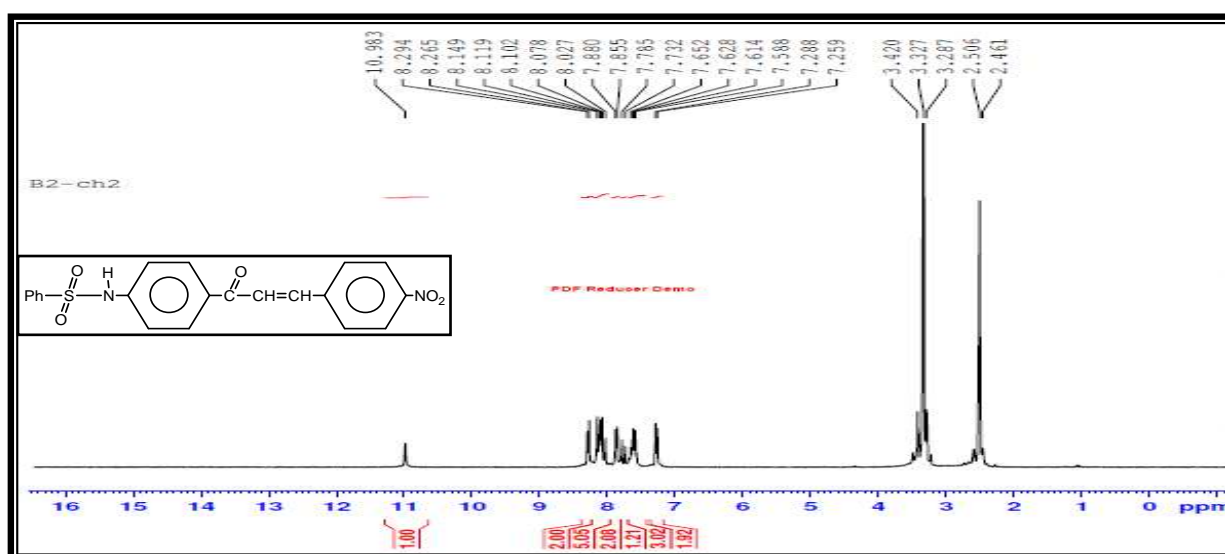
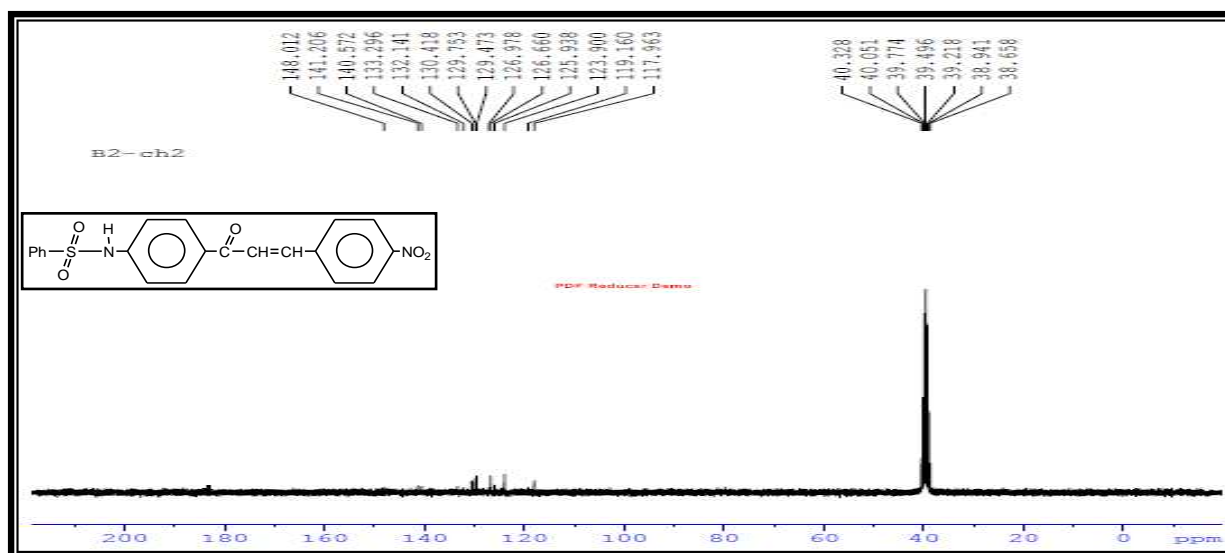


Figure (3–10): FTIR- Spectrum of compound [3a]

Figure (3–11): ¹H NMR- Spectrum of compound [3a]Figure (3–12): ¹³C NMR- Spectrum of compound [3a]

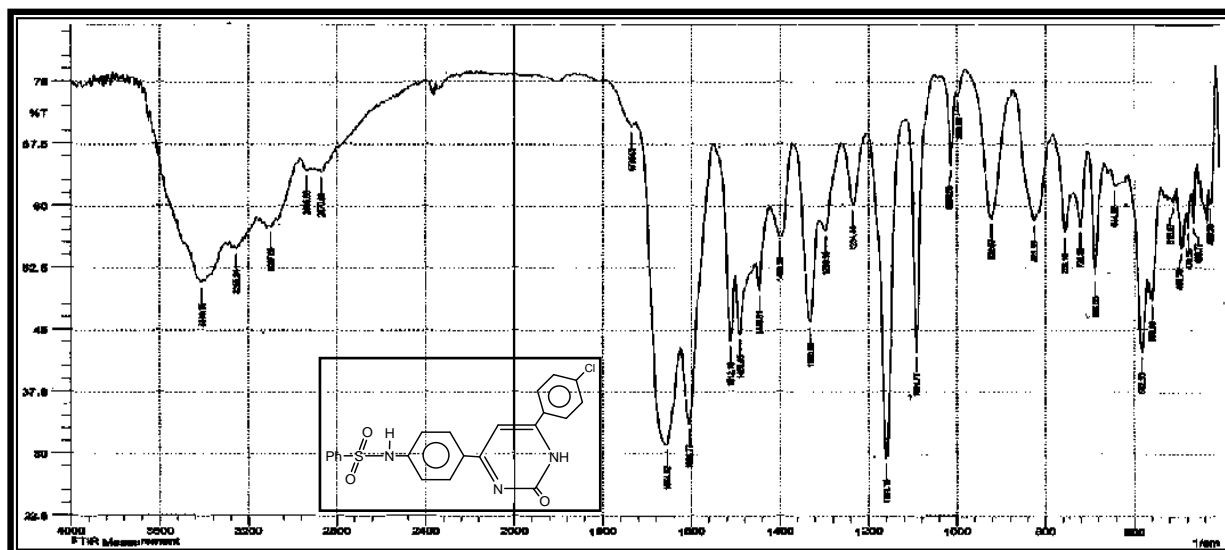


Figure (3–13): FTIR- Spectrum of compound [4a]

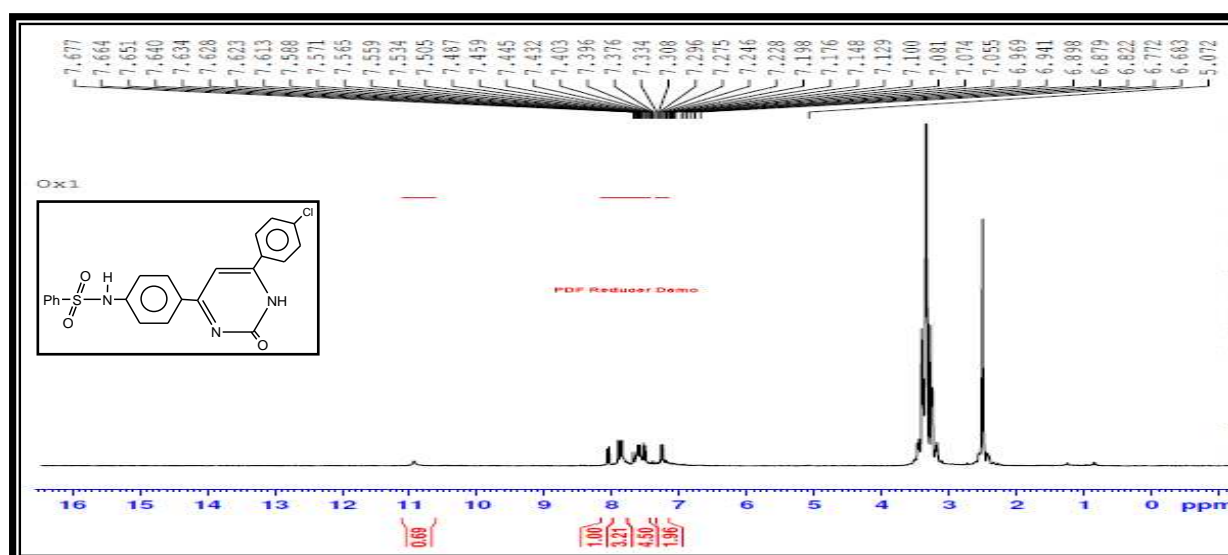


Figure (3–14): ¹H NMR- Spectrum of compound [4a]

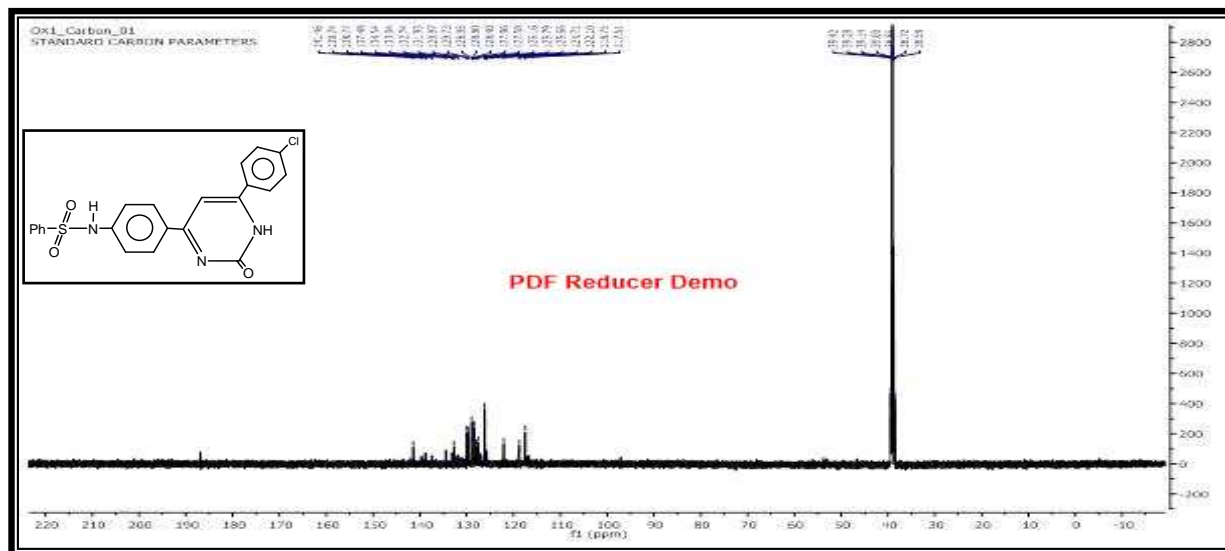


Figure (3–15): ^{13}C NMR- Spectrum of compound [4a]

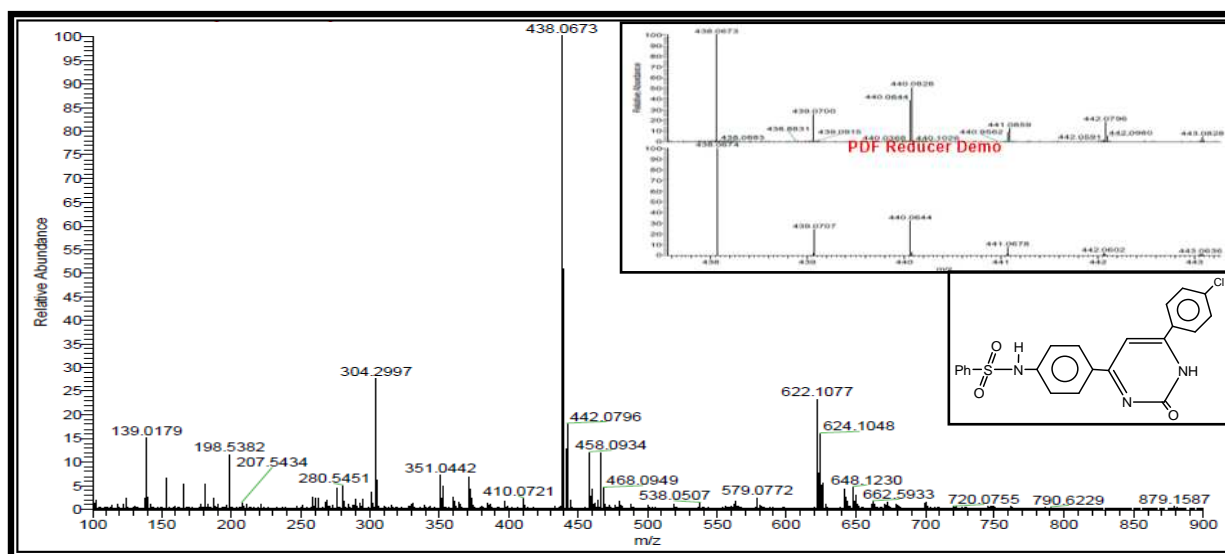


Figure (3–16): Mass- Spectrum of compound [4a]

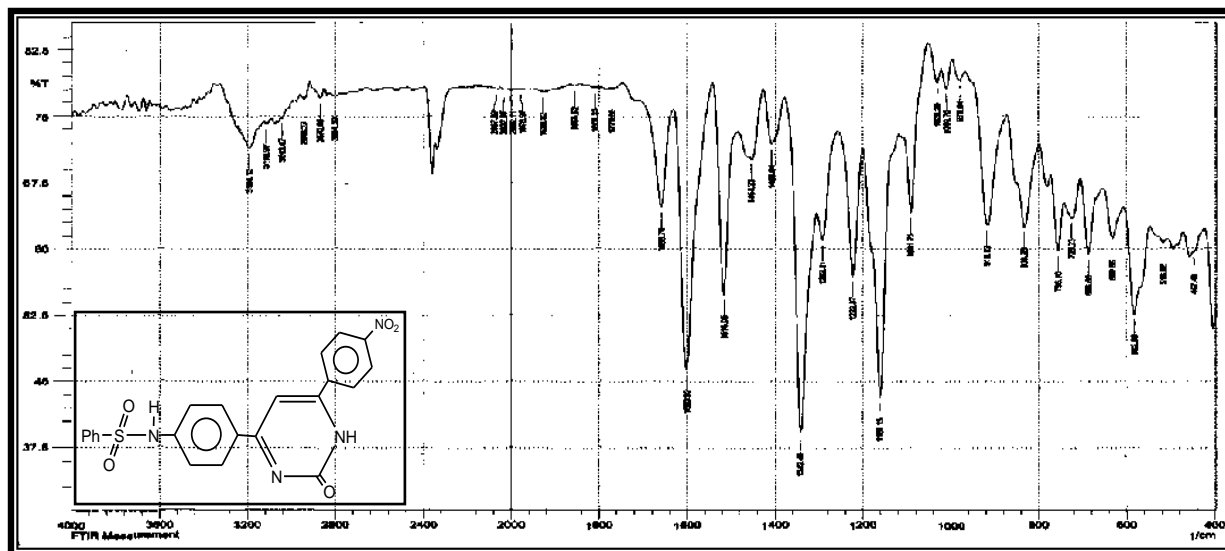


Figure (3-17): FTIR- Spectrum of compound [5a]

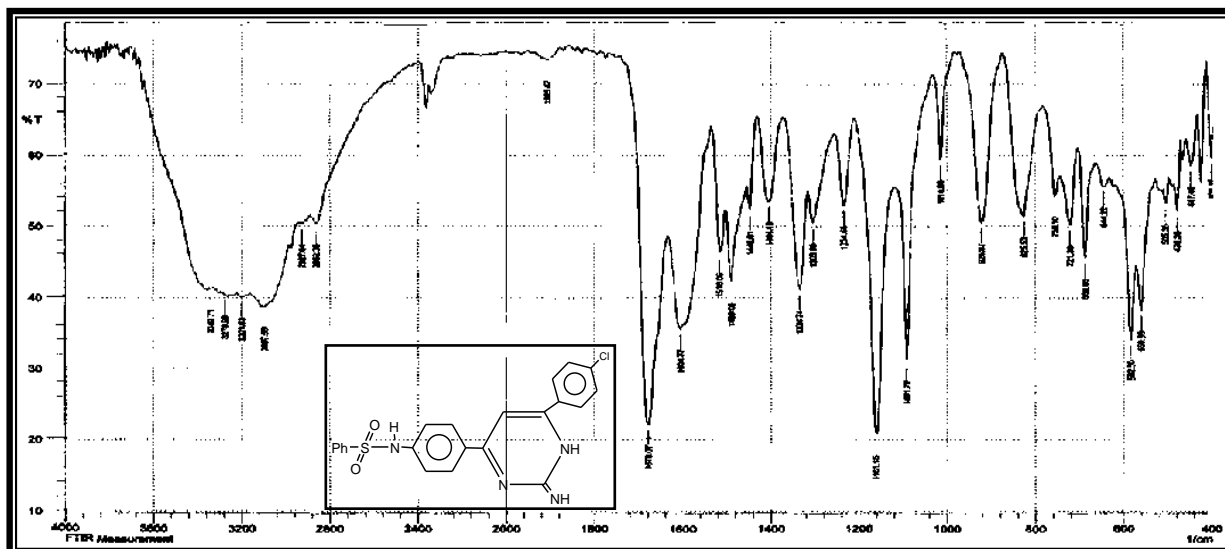


Figure (3-18): FTIR- Spectrum of compound [6a]

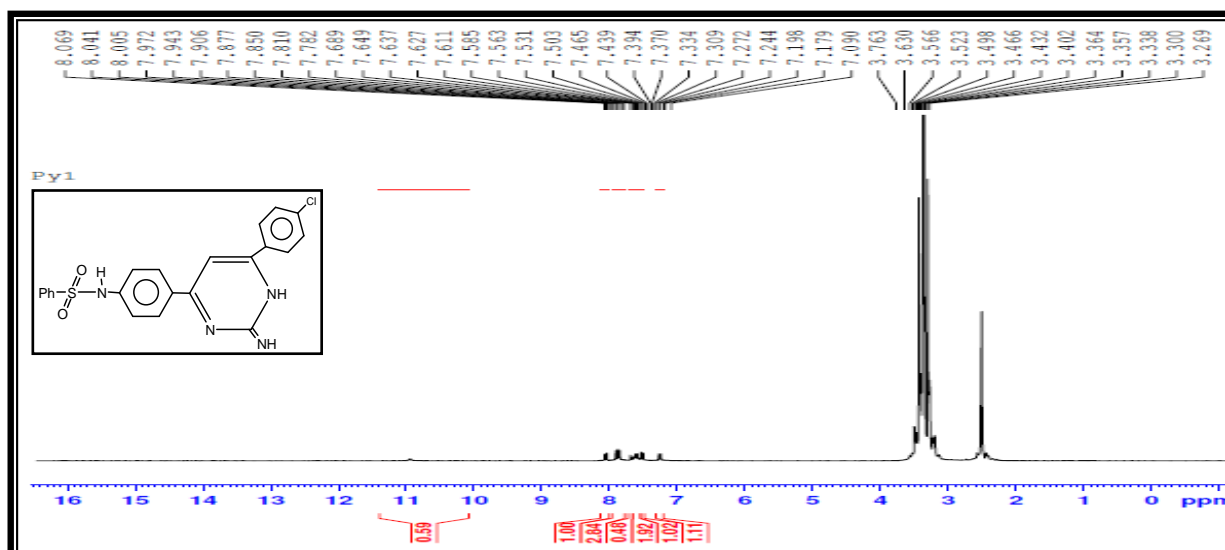


Figure (3-19): ¹H NMR- Spectrum of compound [6a]

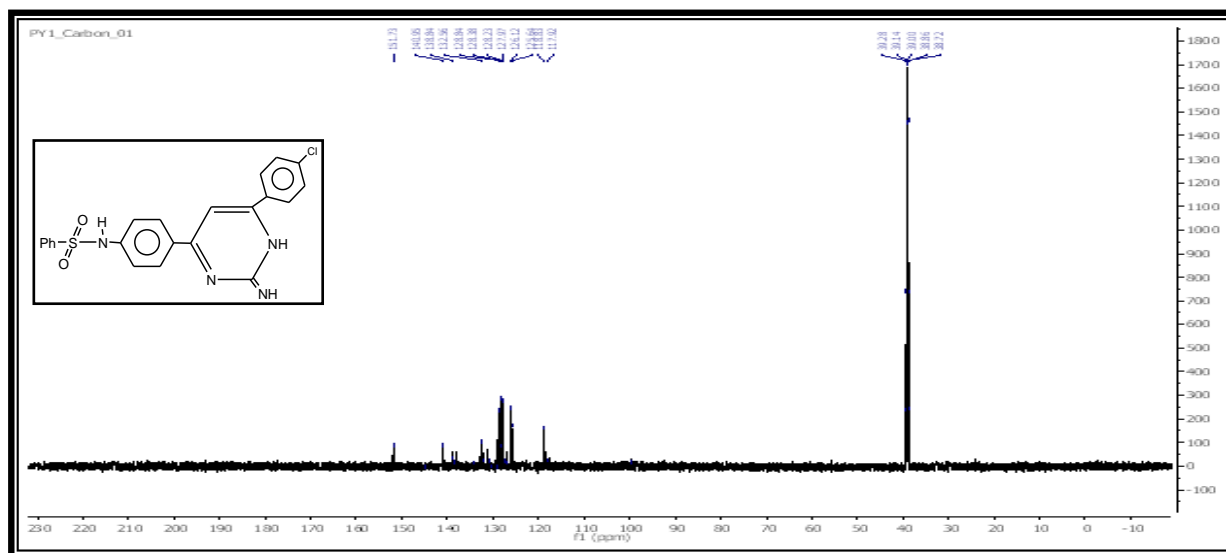


Figure (3–20): ^{13}C NMR- Spectrum of compound [6a]

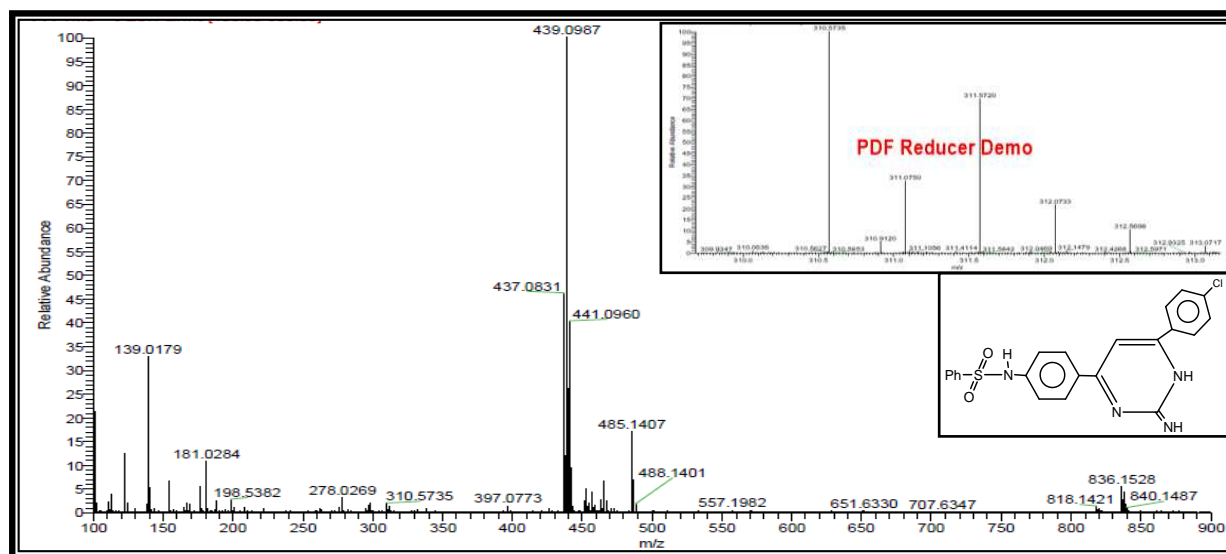


Figure (3–21): Mass- Spectrum of compound [6a]

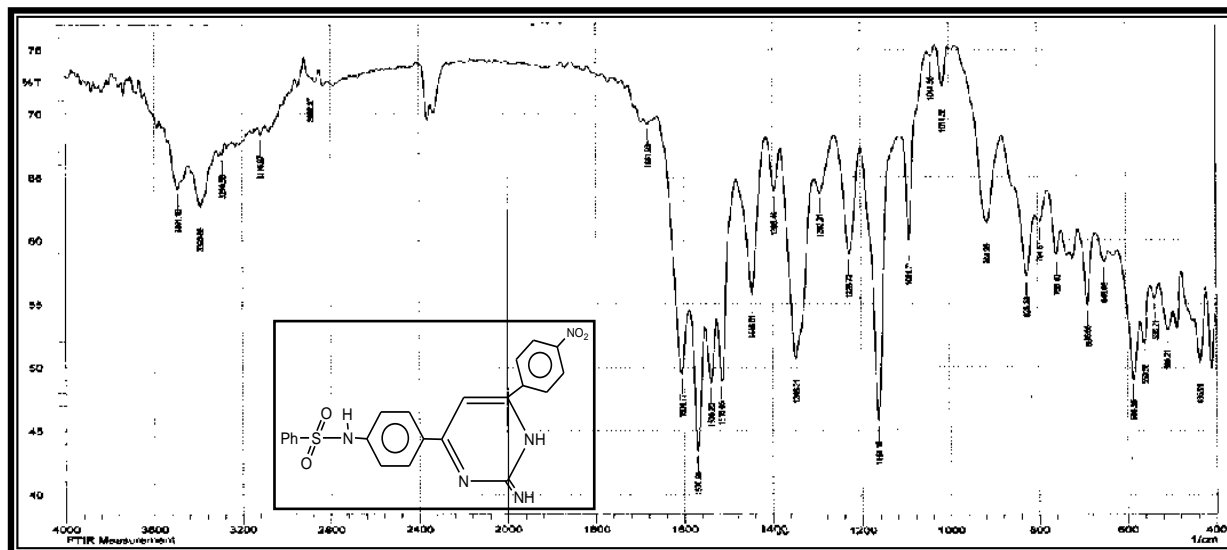


Figure (3–22): FTIR- Spectrum of compound [7a]

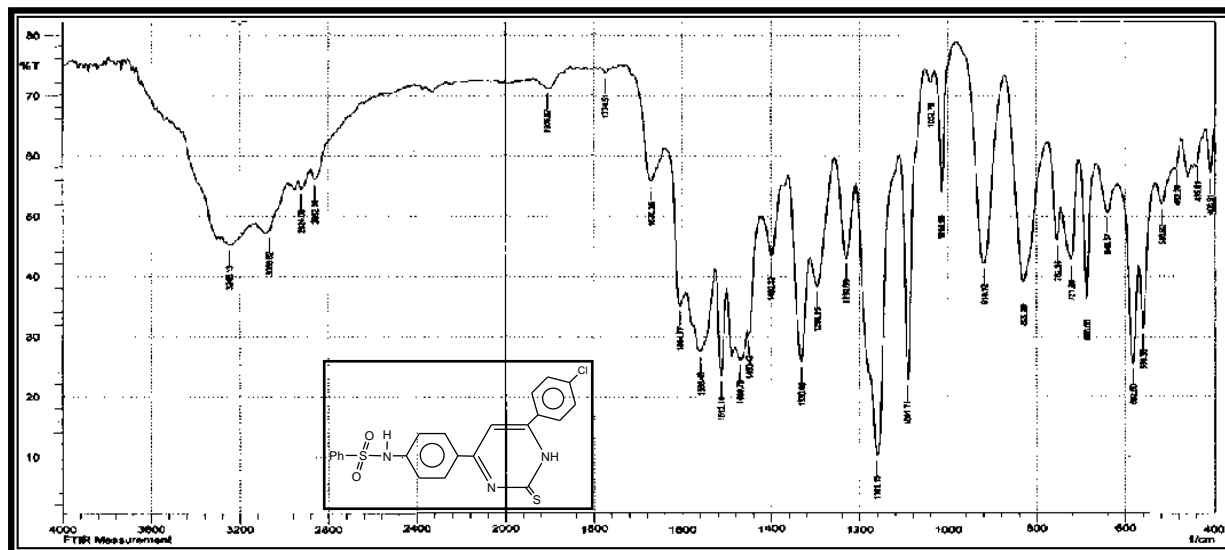


Figure (3–23): FTIR- Spectrum of compound [8a]

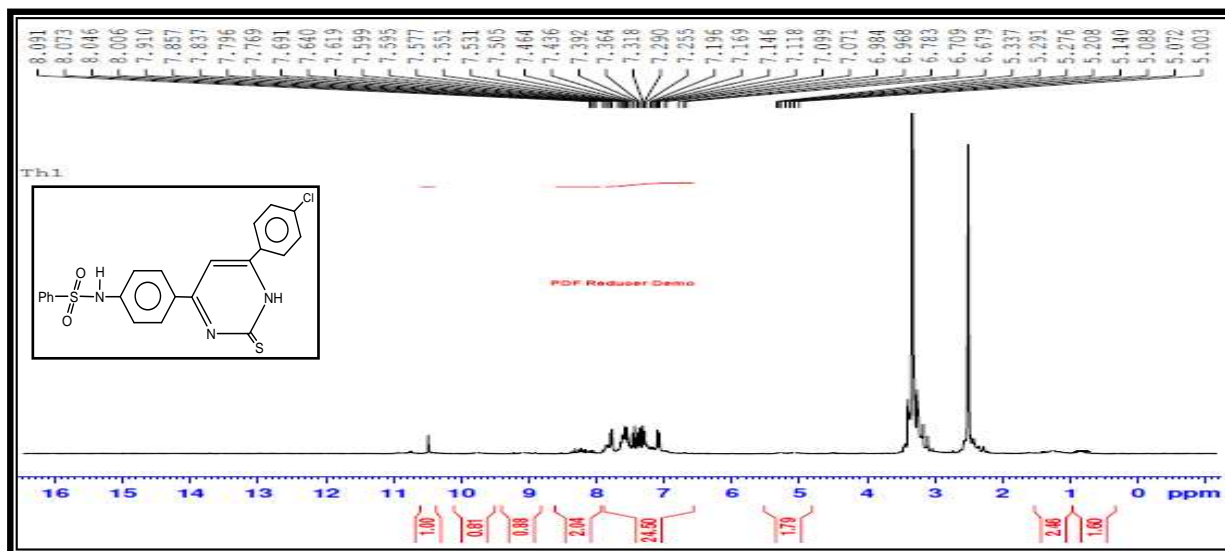


Figure (3–24): ¹H NMR- Spectrum of compound [8a]

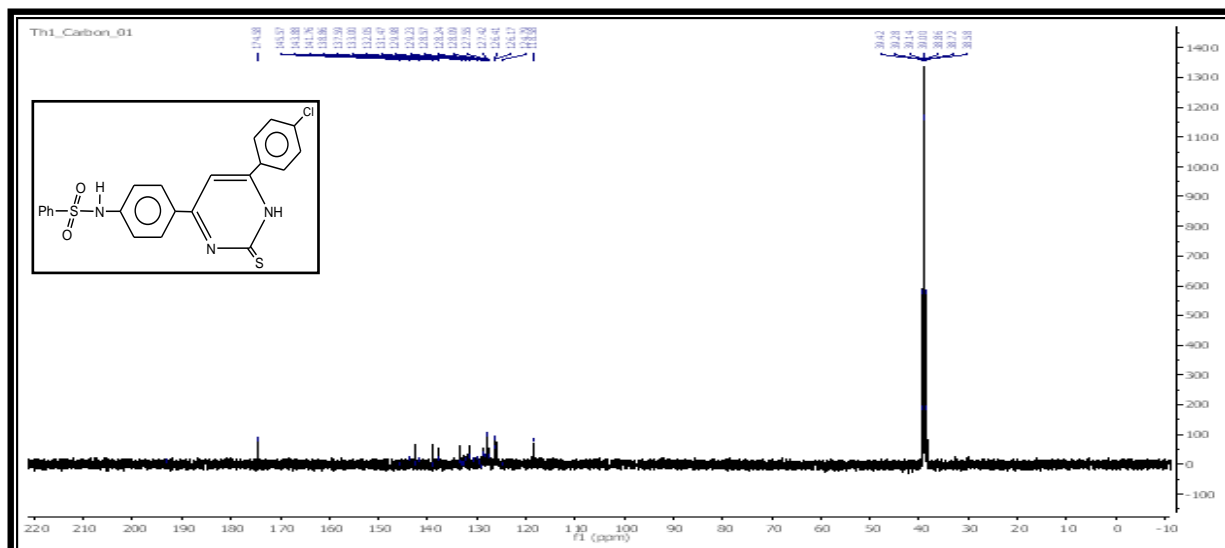


Figure (3–25): ^{13}C NMR- Spectrum of compound [8a]

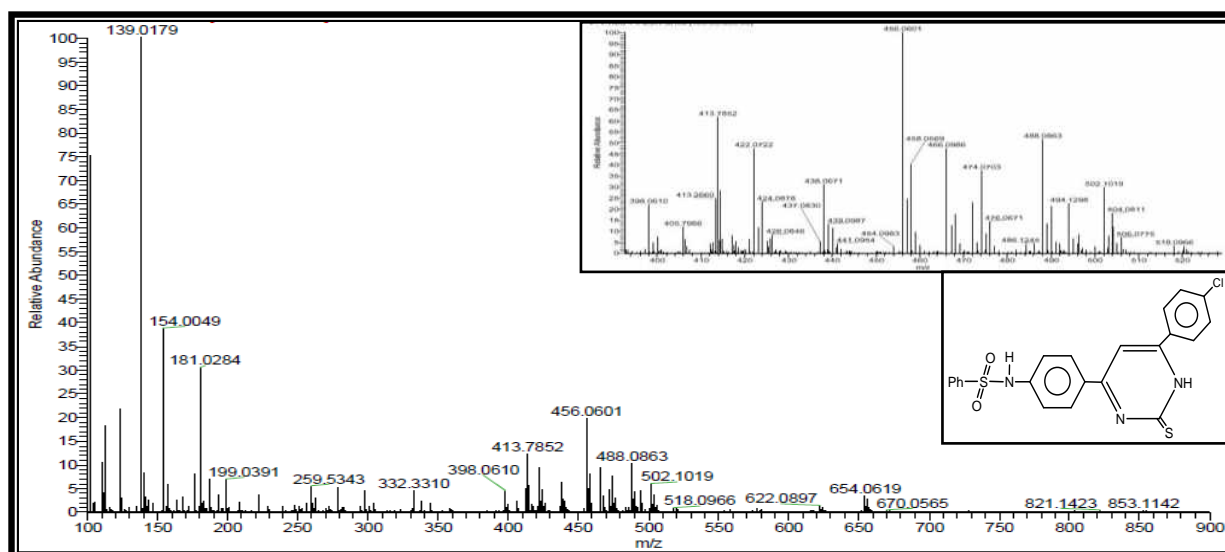


Figure (3–26): Mass- Spectrum of compound [8a]

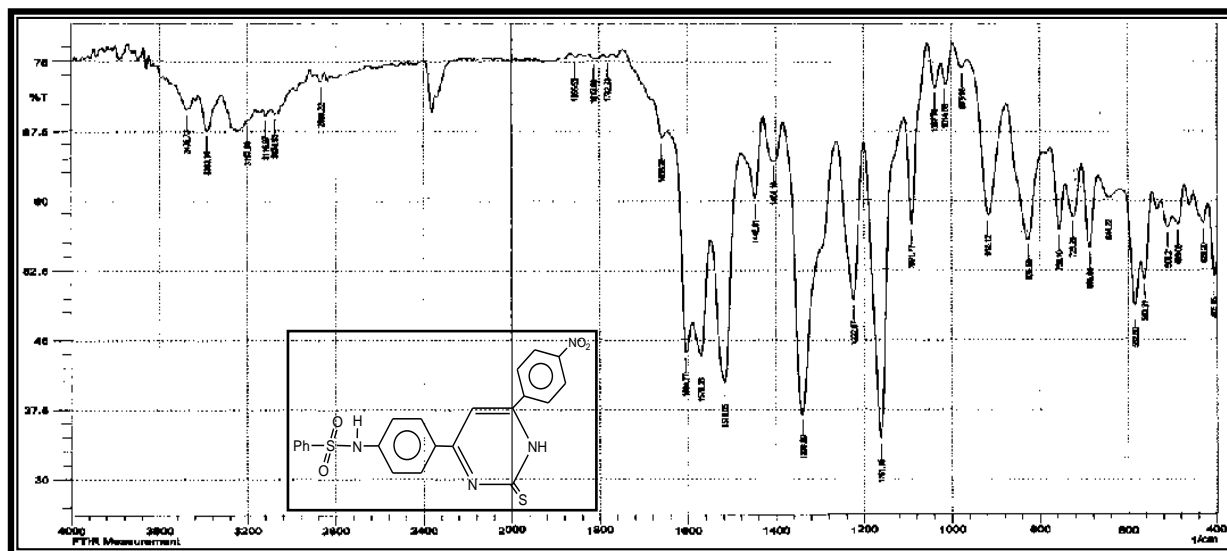


Figure (3–27): FTIR- Spectrum of compound [9a]

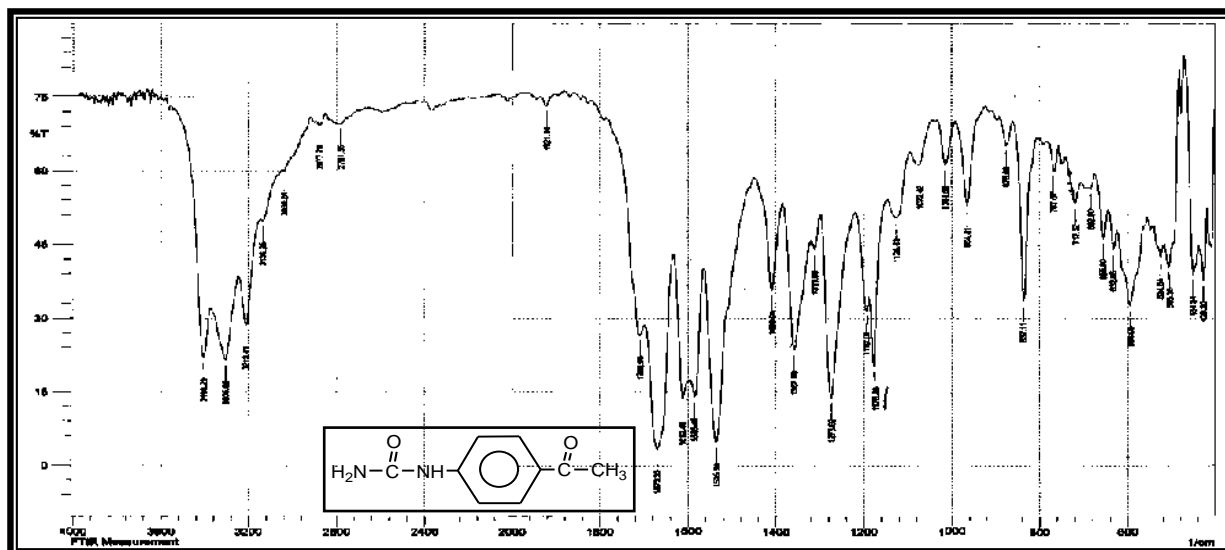


Figure (3–28): FTIR- Spectrum of compound [10a]

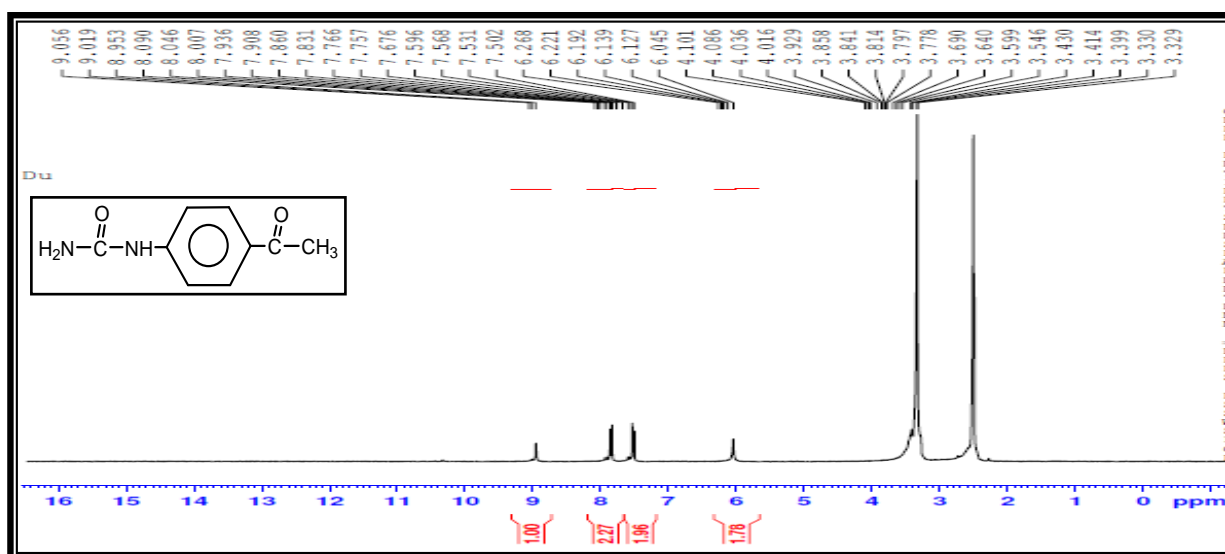


Figure (3–29): ¹H NMR- Spectrum of compound [10a]

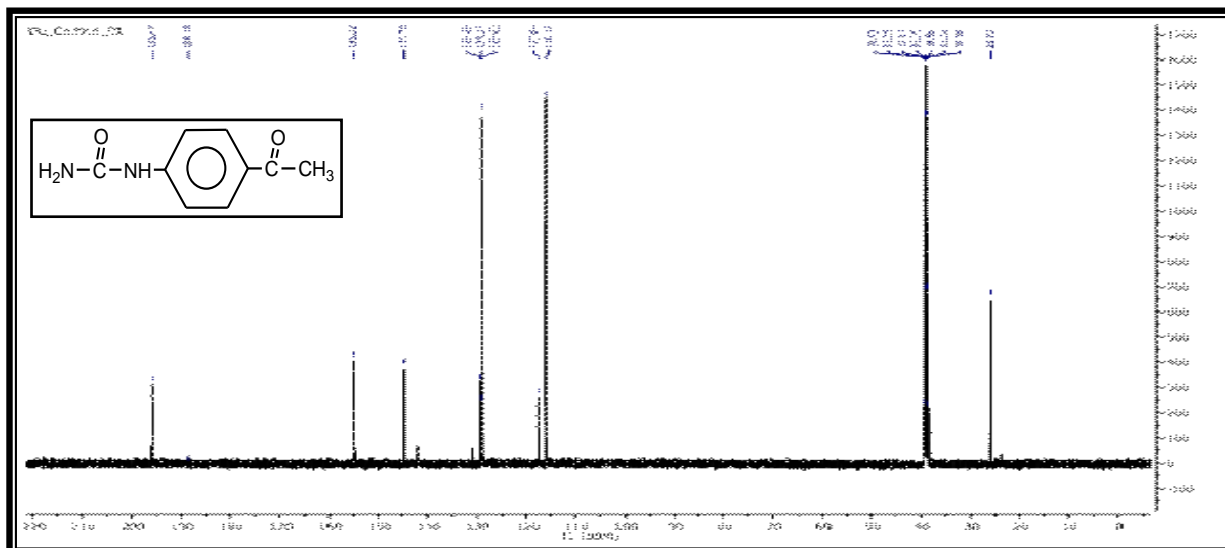


Figure (3–30): ^{13}C NMR- Spectrum of compound [10a]

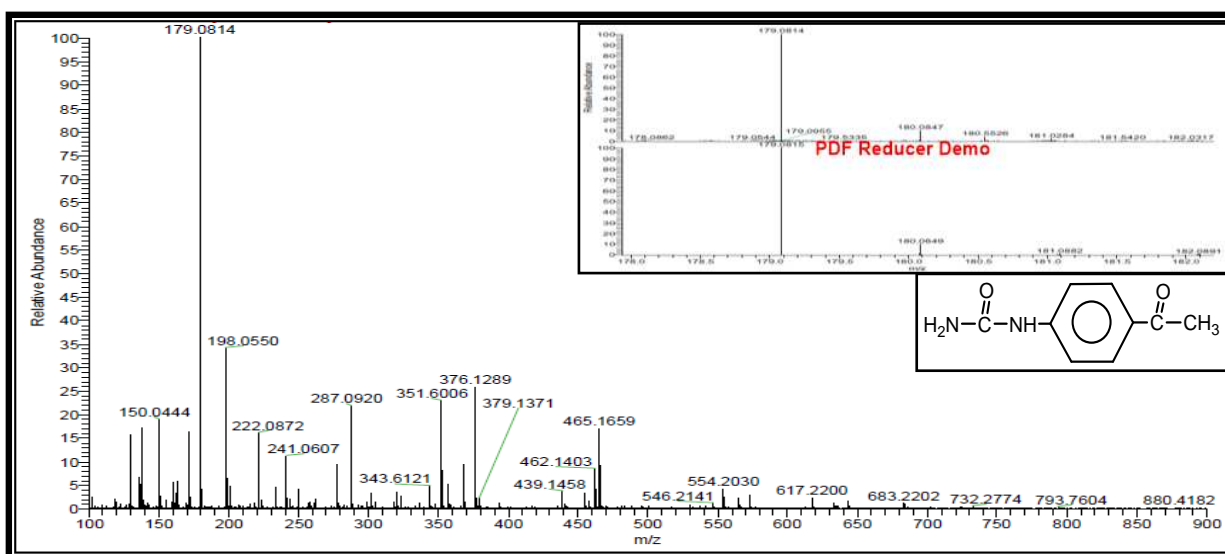


Figure (3–31): Mass- Spectrum of compound [10a]

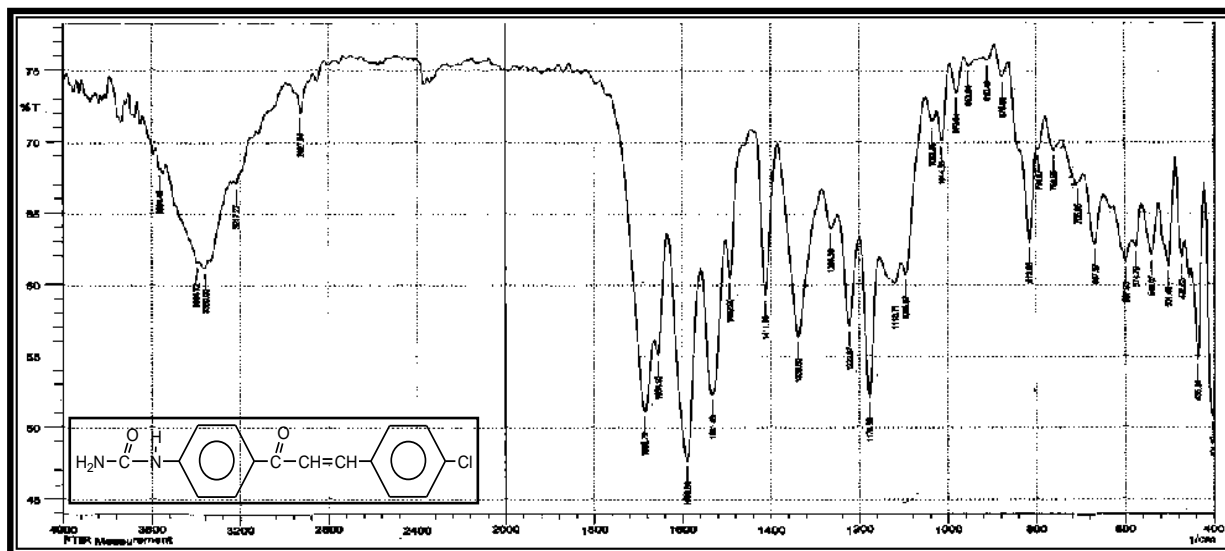


Figure (3–32): FTIR- Spectrum of compound [11a]

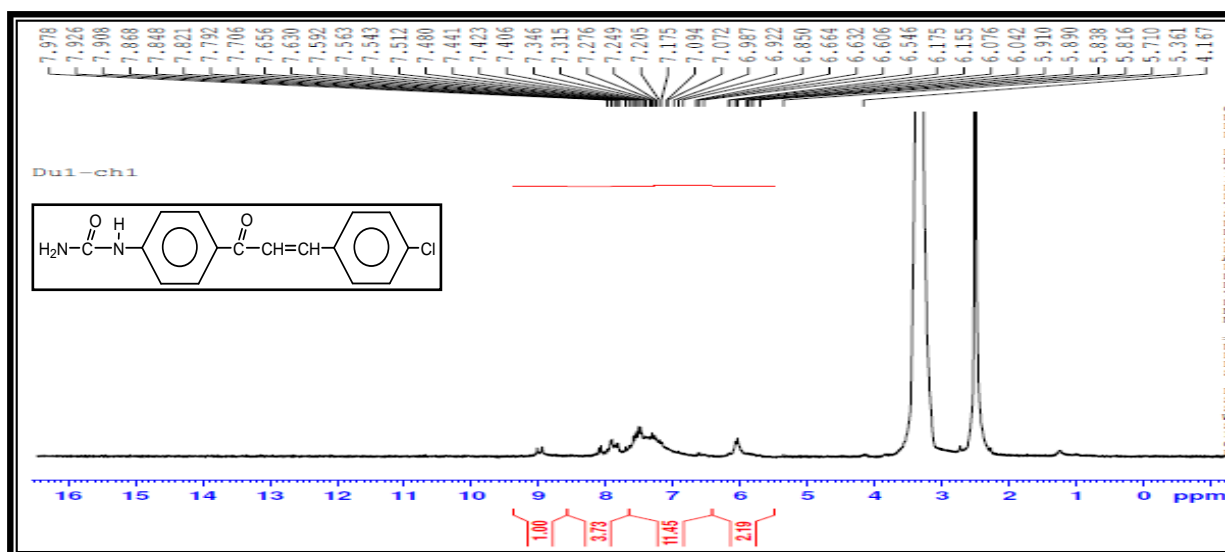


Figure (3–33): ¹H NMR- Spectrum of compound [11a]

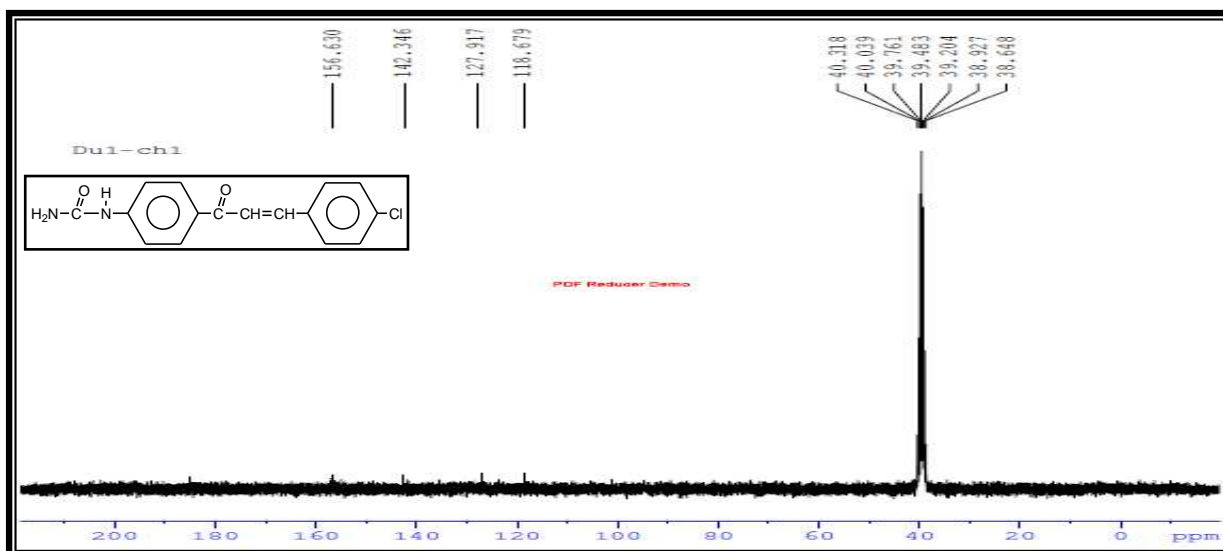


Figure (3–34): ^{13}C NMR- Spectrum of compound [11a]

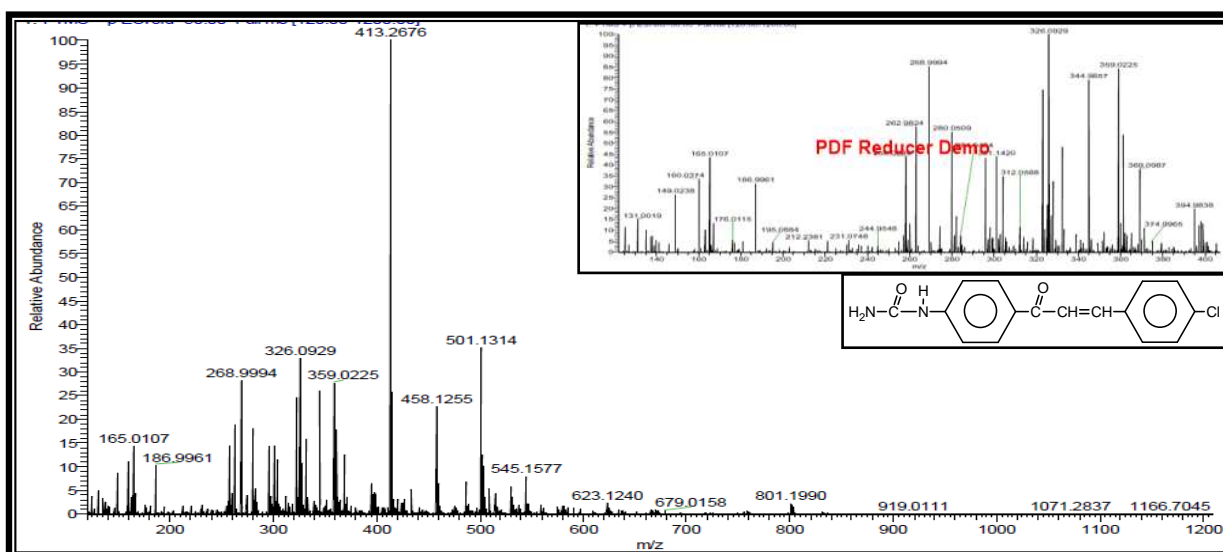


Figure (3–35): Mass- Spectrum of compound [11a]

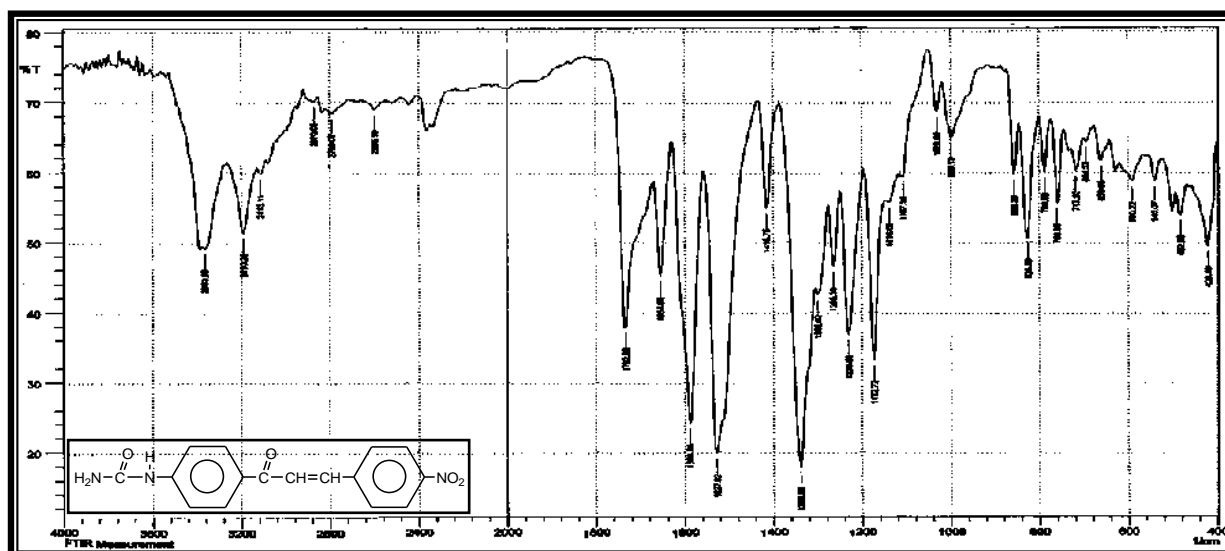
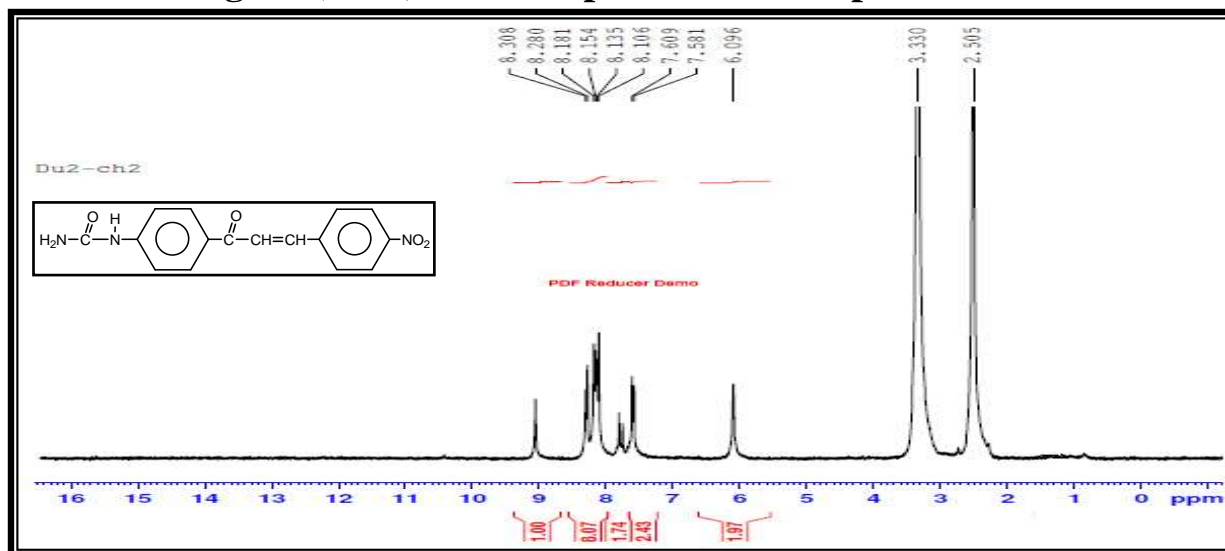
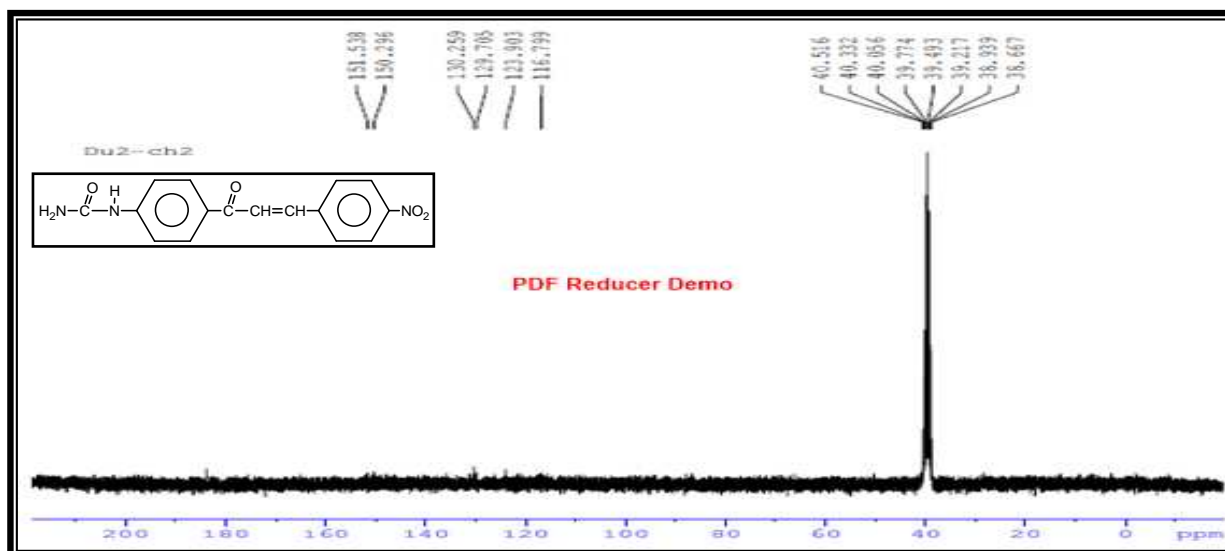


Figure (3-36): FTIR- Spectrum of compound [12a]

Figure (3-37): ¹H NMR- Spectrum of compound [12a]Figure (3-38): ¹³C NMR- Spectrum of compound [12a]

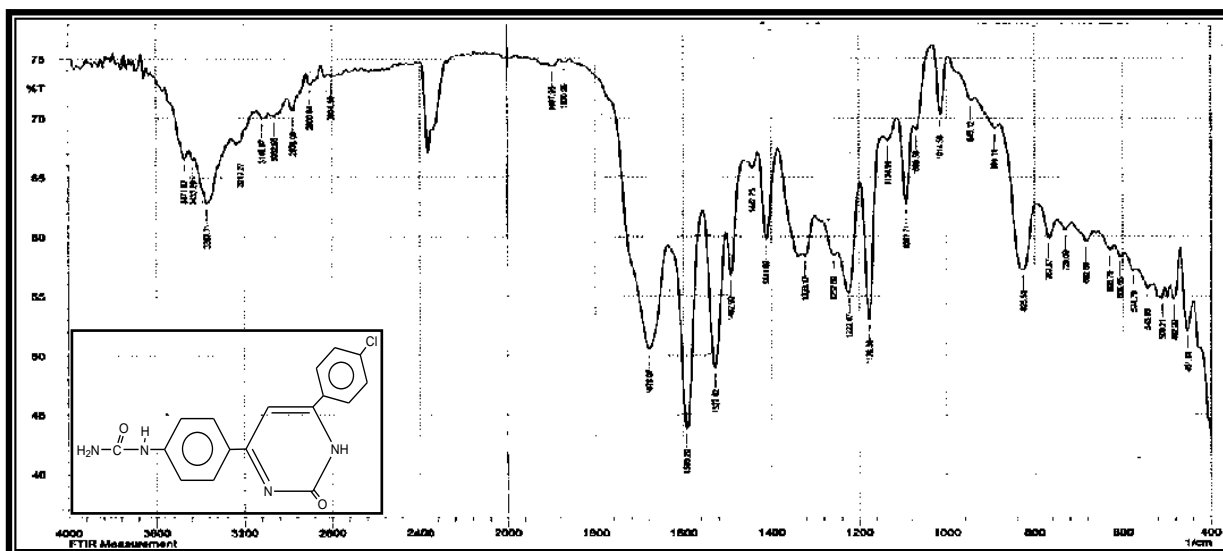
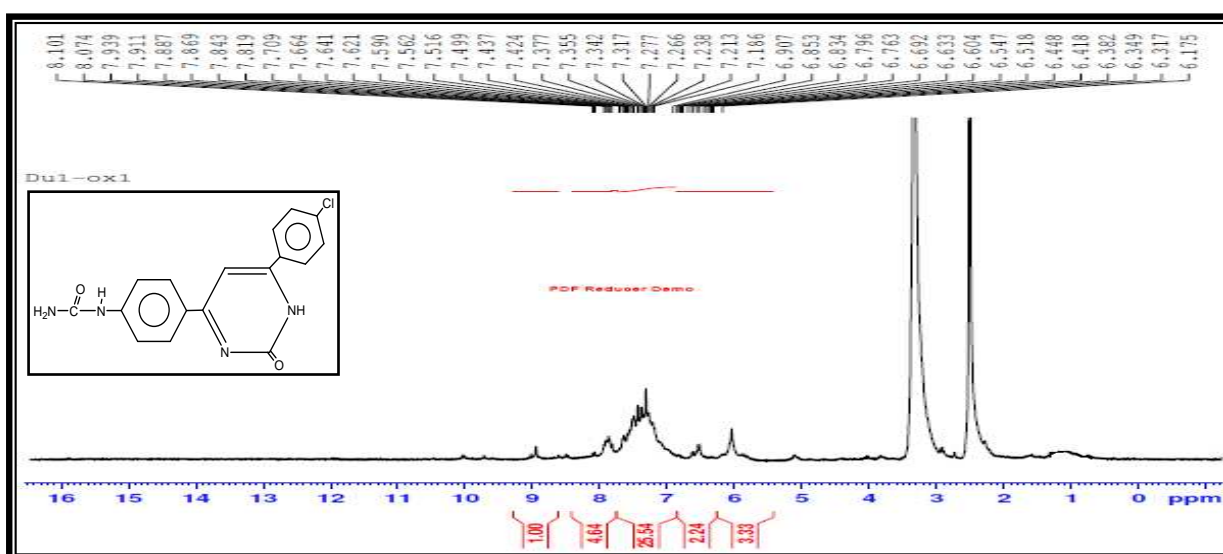
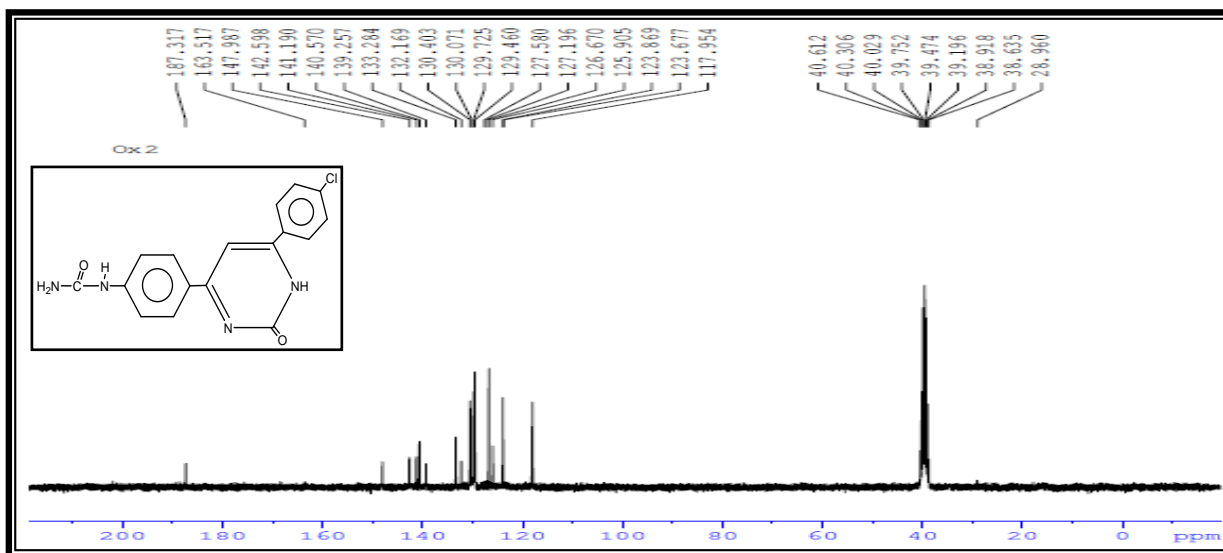


Figure (3-39): FTIR- Spectrum of compound [13a]

Figure (3-40): ^1H NMR- Spectrum of compound [13a]Figure (3-41): ^{13}C NMR- Spectrum of compound [13a]

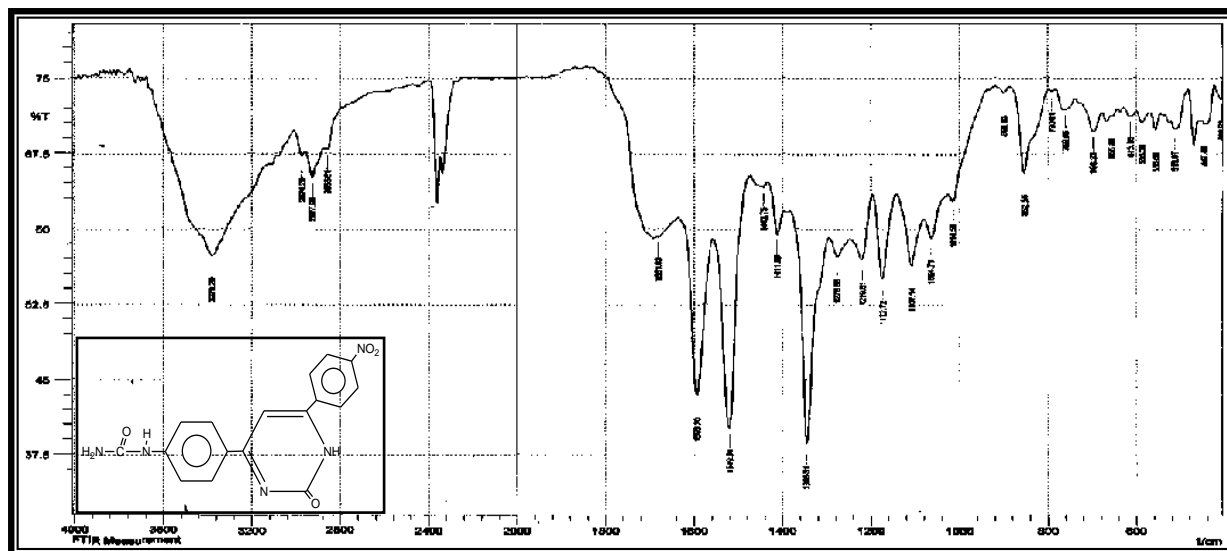


Figure (3-42): FTIR- Spectrum of compound [14a]

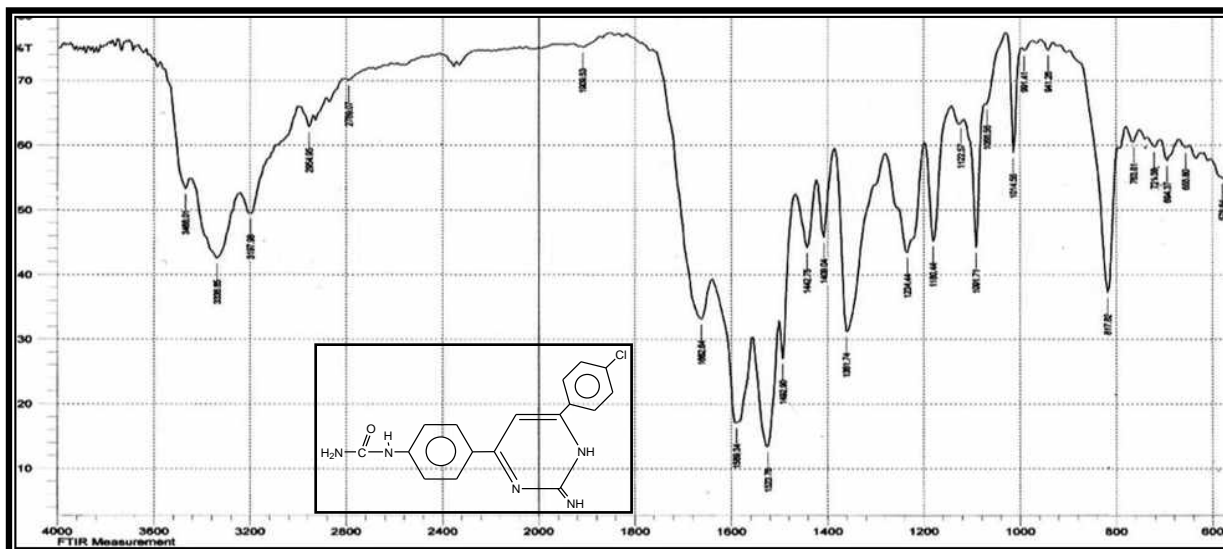
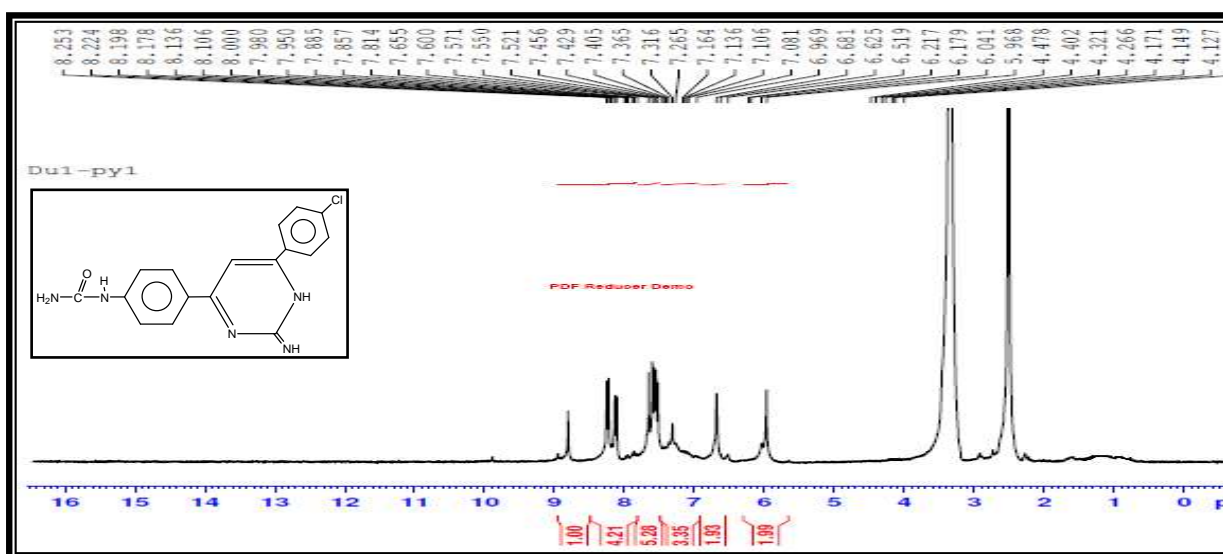
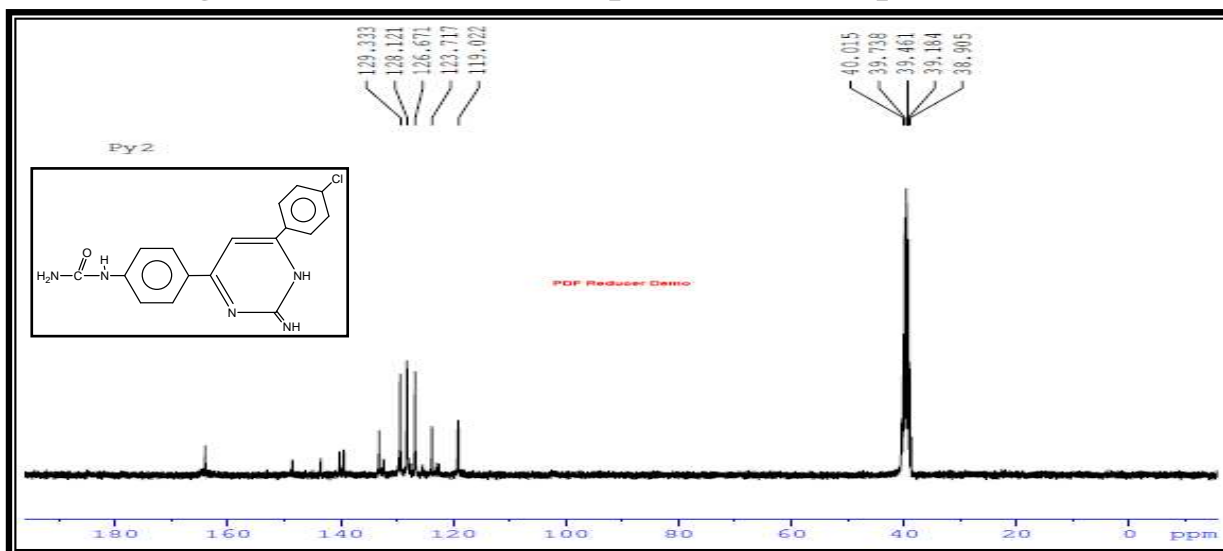


Figure (3-43): FTIR- Spectrum of compound [15a]

Figure (3-44): ¹H NMR- Spectrum of compound [15a]Figure (3-45): ¹³C NMR- Spectrum of compound [15a]

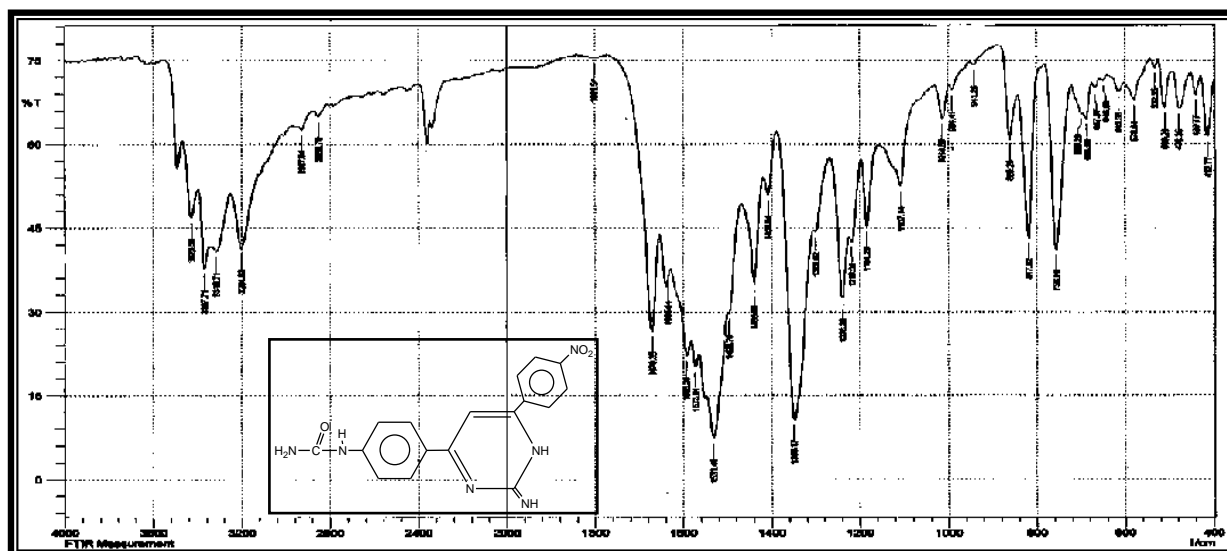


Figure (3-46): FTIR- Spectrum of compound [16a]

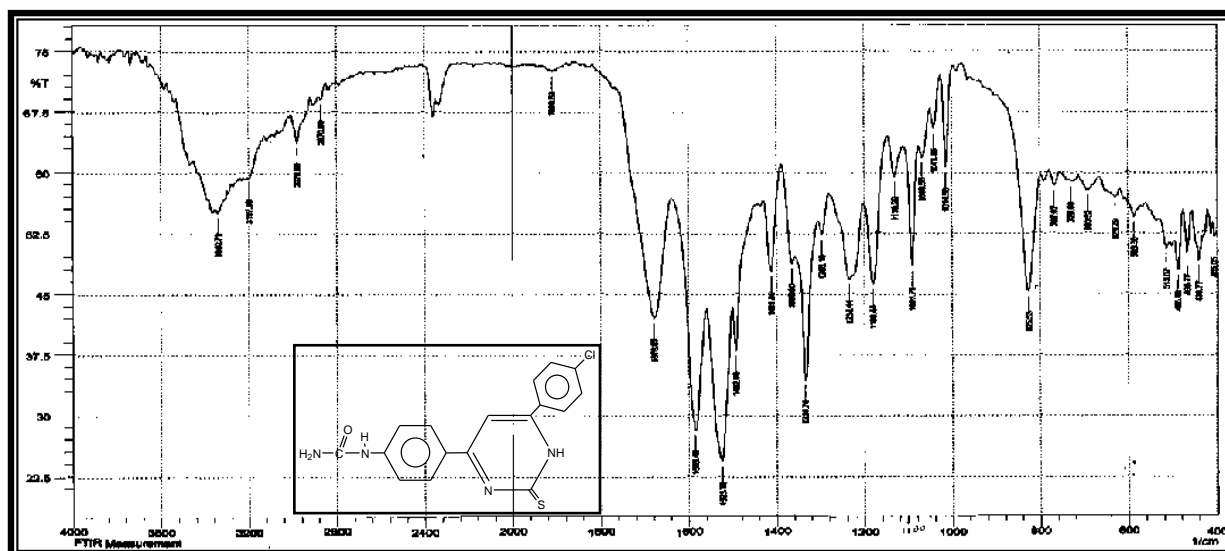
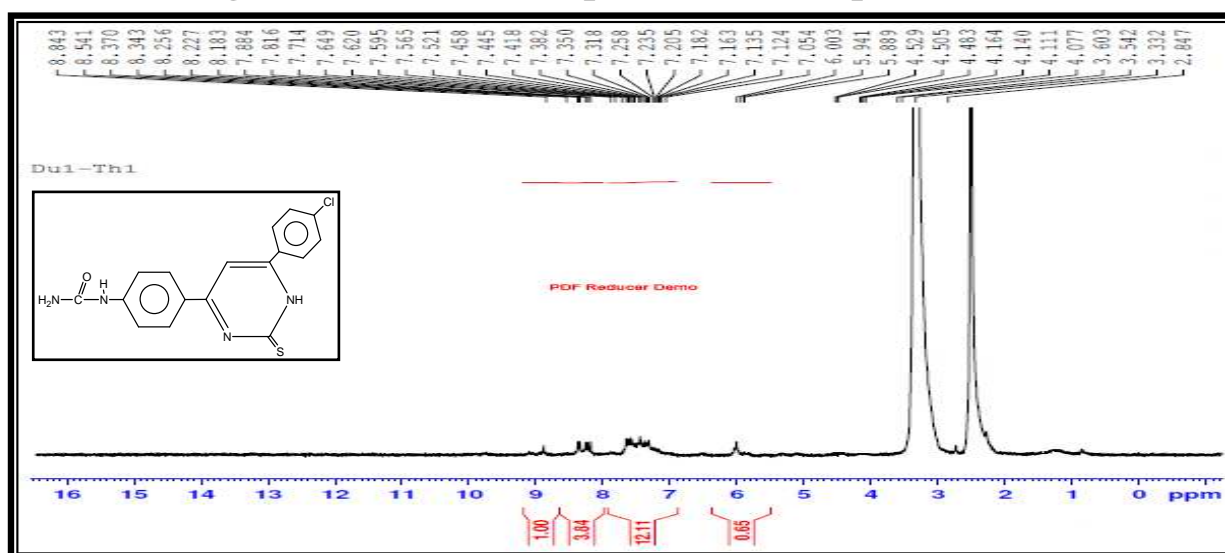
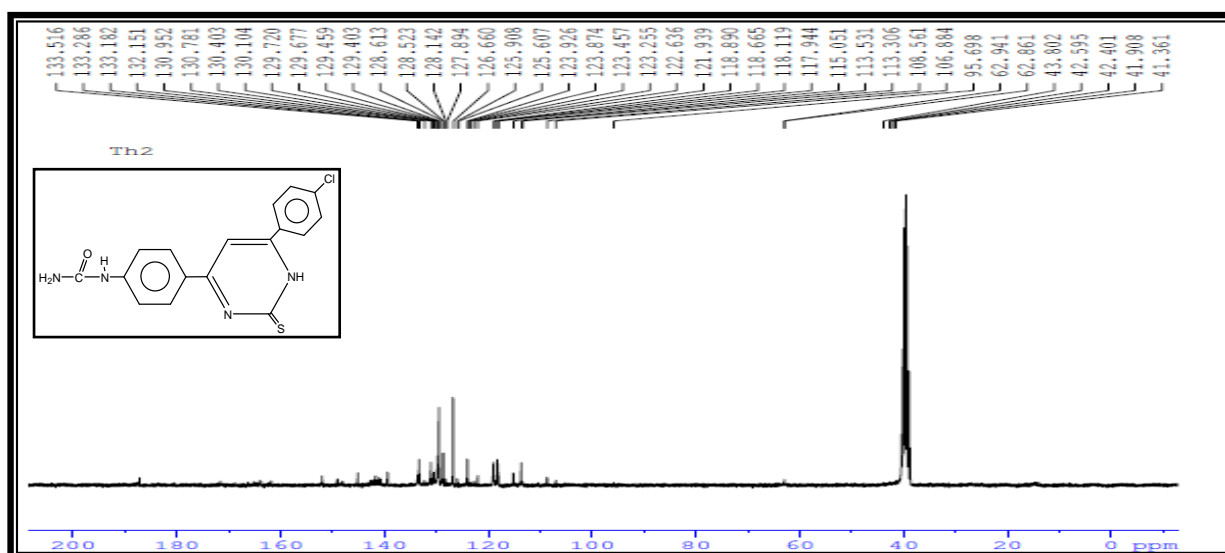


Figure (3-47): FTIR- Spectrum of compound [17a]

Figure (3-48): ^1H NMR- Spectrum of compound [17a]Figure (3-49): ^{13}C NMR- Spectrum of compound [17a]

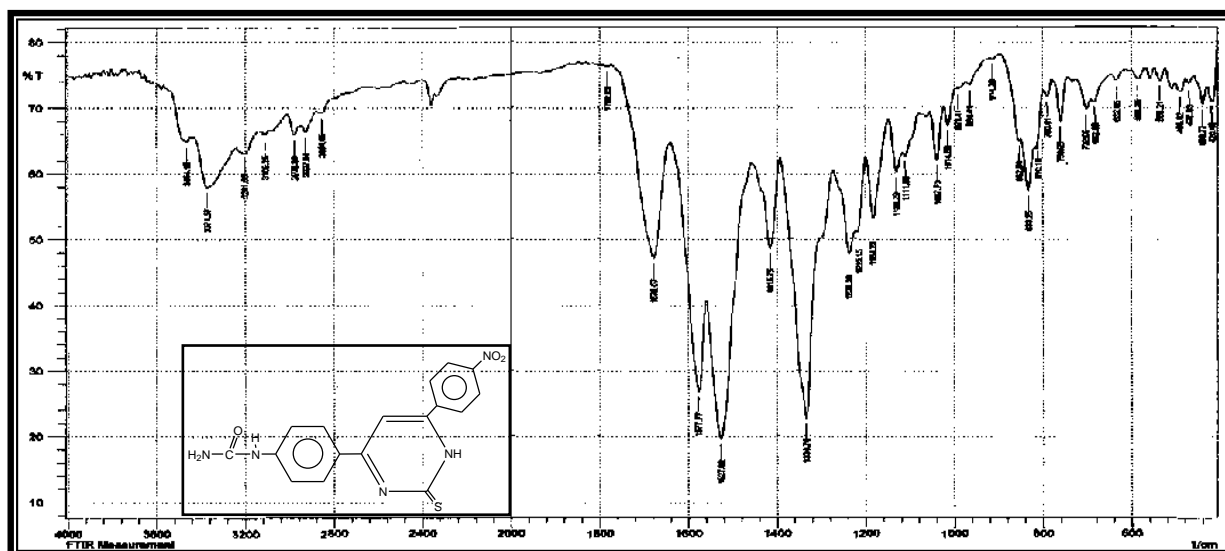


Figure (3-50): FTIR- Spectrum of compound [18a]

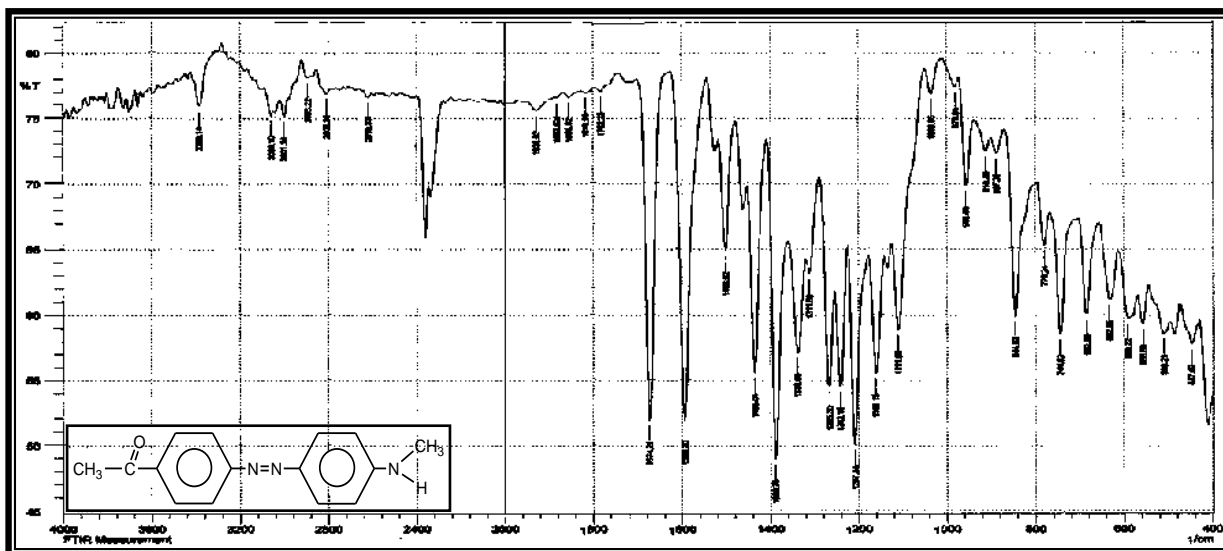
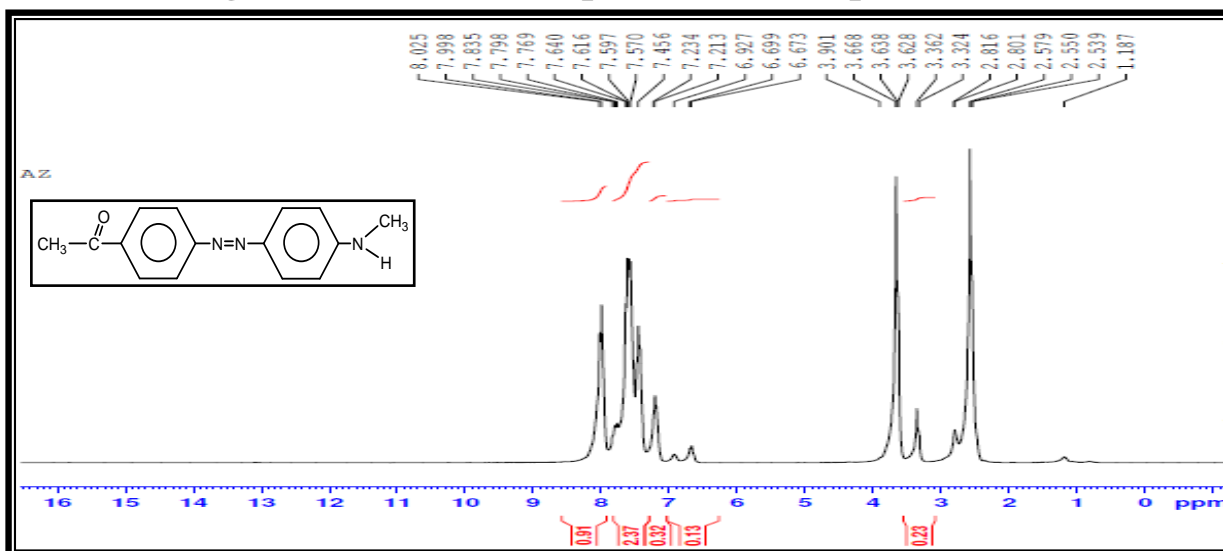
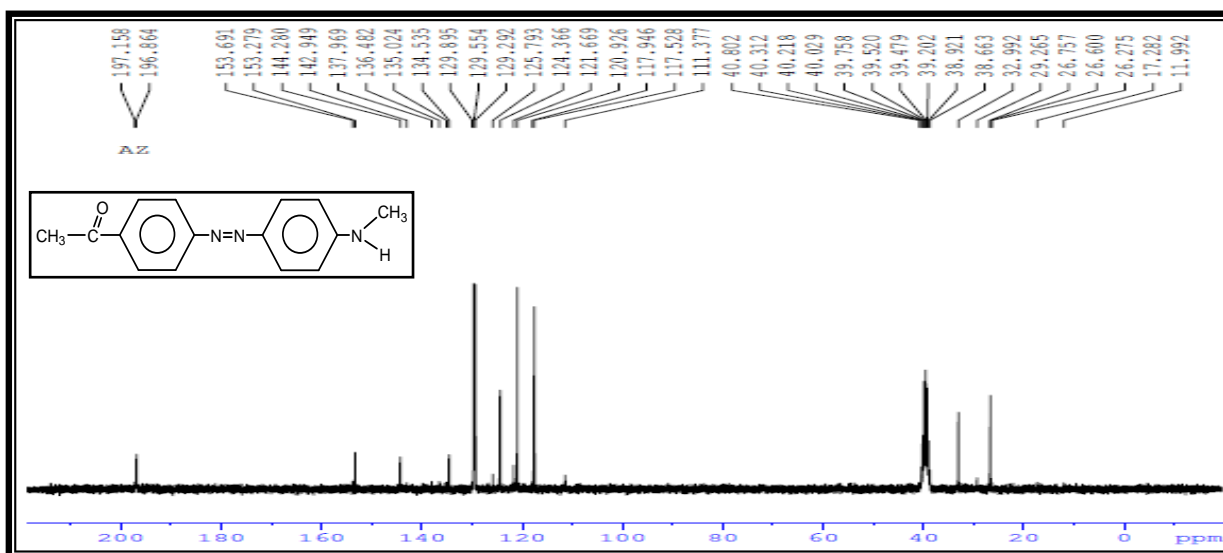


Figure (3-51): FTIR- Spectrum of compound [19a]

Figure (3-52): ¹H NMR- Spectrum of compound [19a]Figure (3-53): ¹³C NMR- Spectrum of compound [19a]

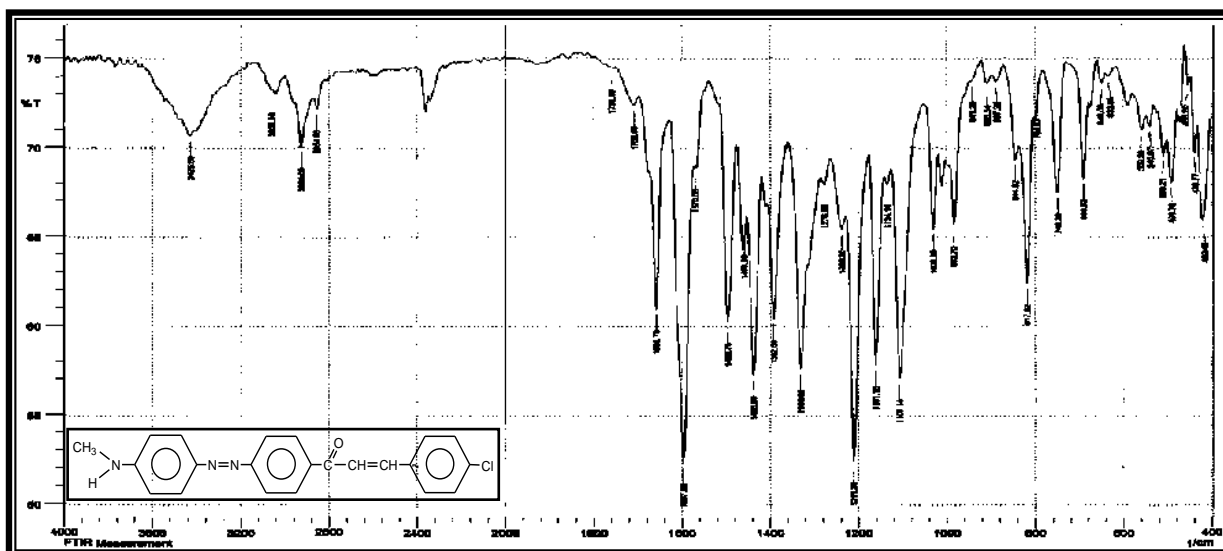
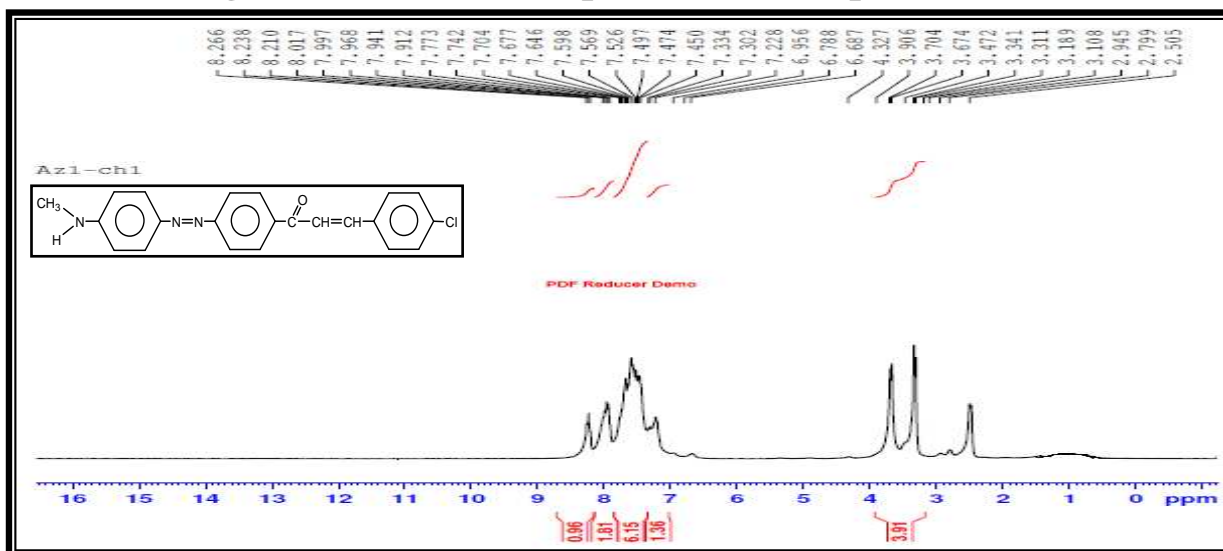
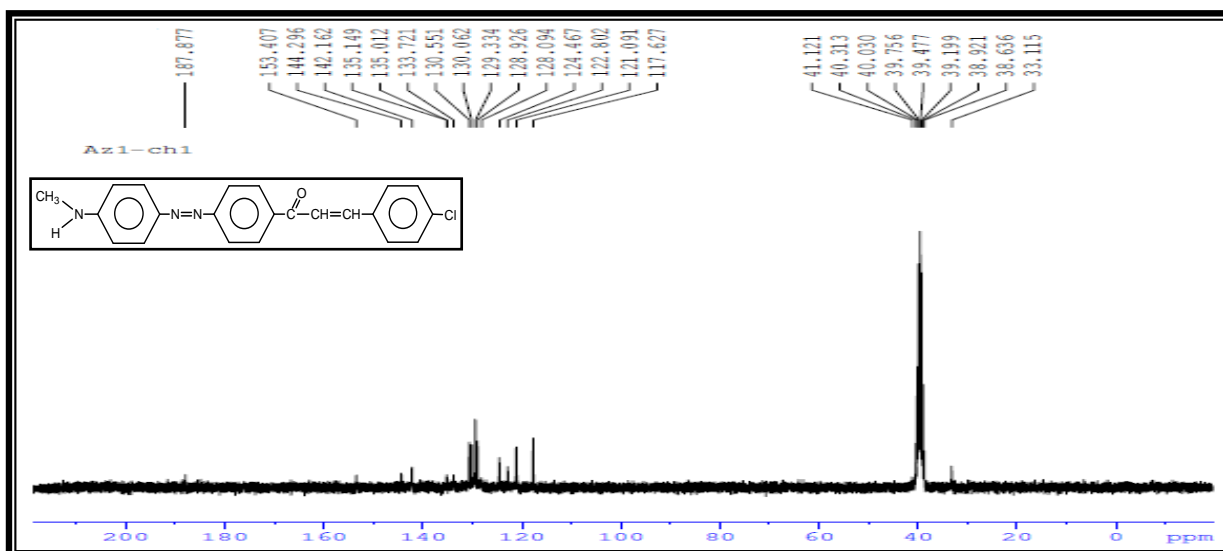


Figure (3-54): FTIR- Spectrum of compound [20a]

Figure (3-55): ¹H NMR- Spectrum of compound [20a]Figure (3-56): ¹³C NMR- Spectrum of compound [20a]

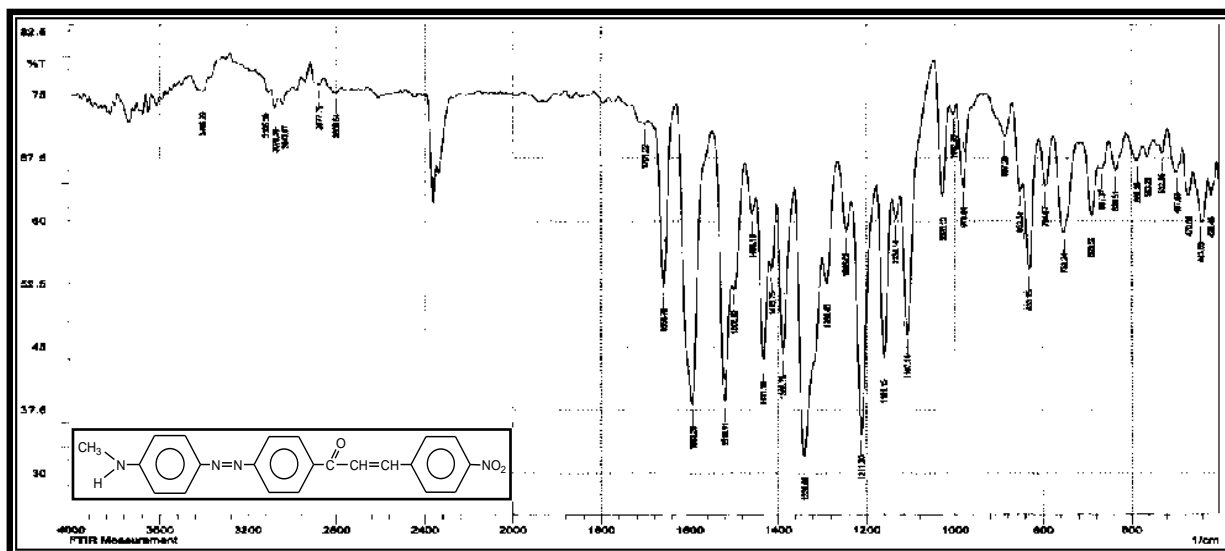
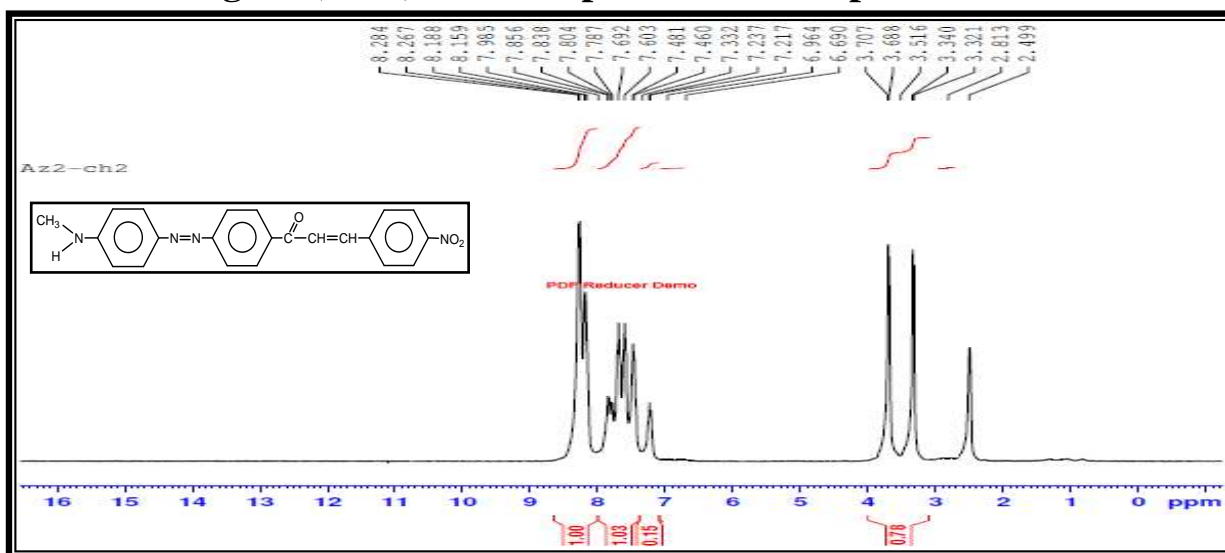
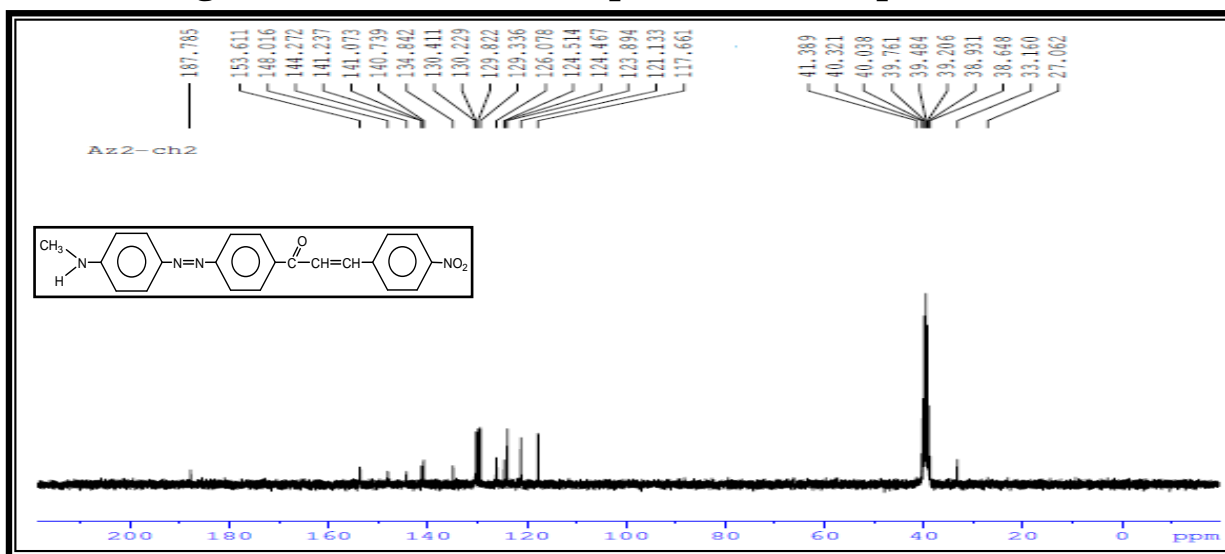


Figure (3-57): FTIR- Spectrum of compound [21a]

Figure (3-58): ¹H NMR- Spectrum of compound [21a]Figure (3-59): ¹³C NMR- Spectrum of compound [21a]

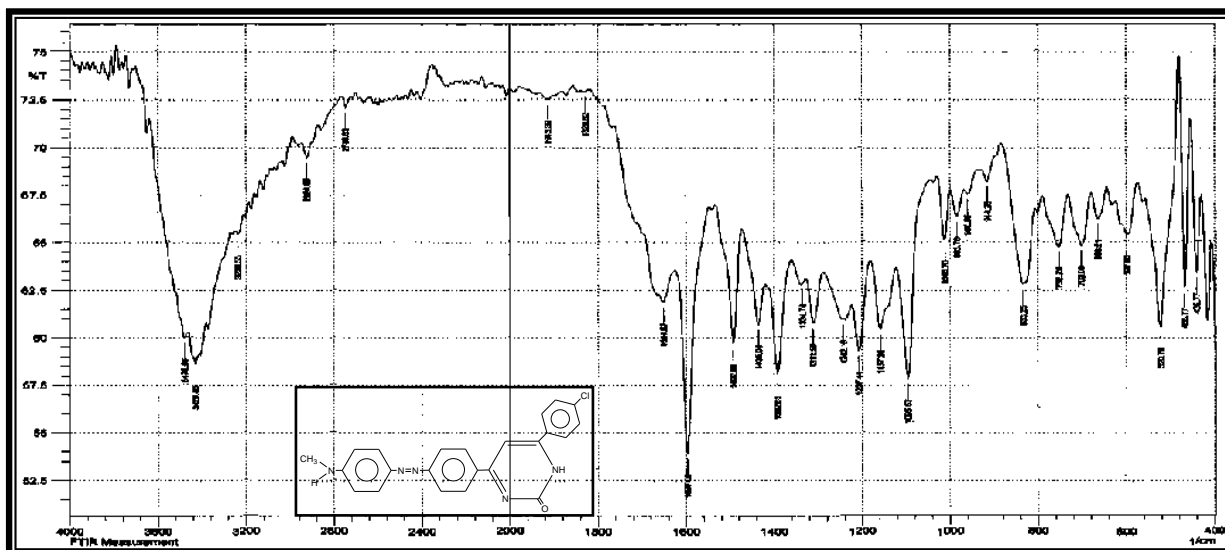
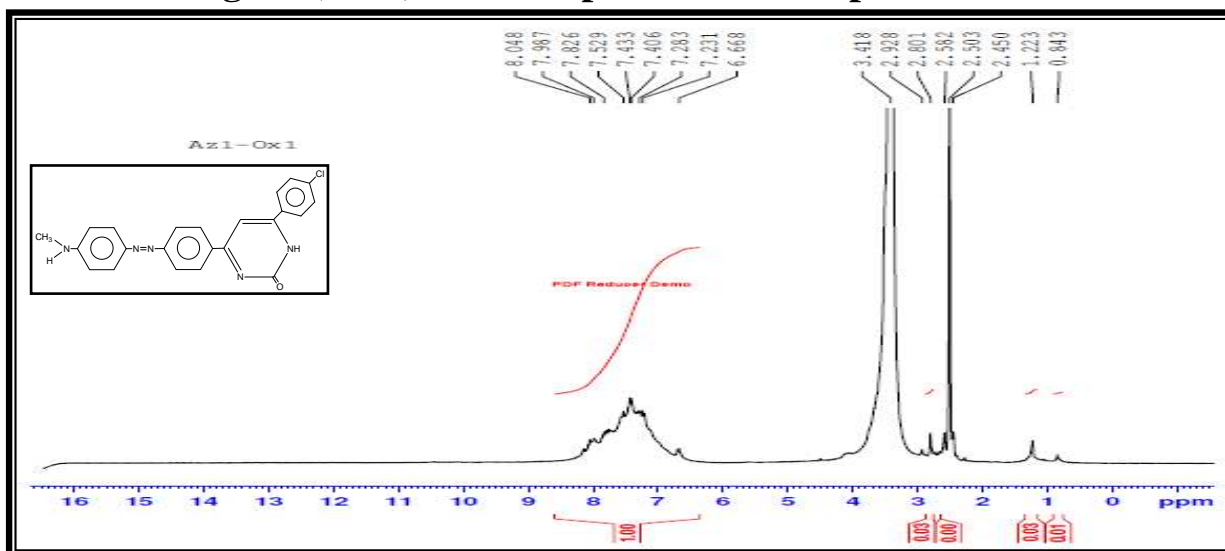
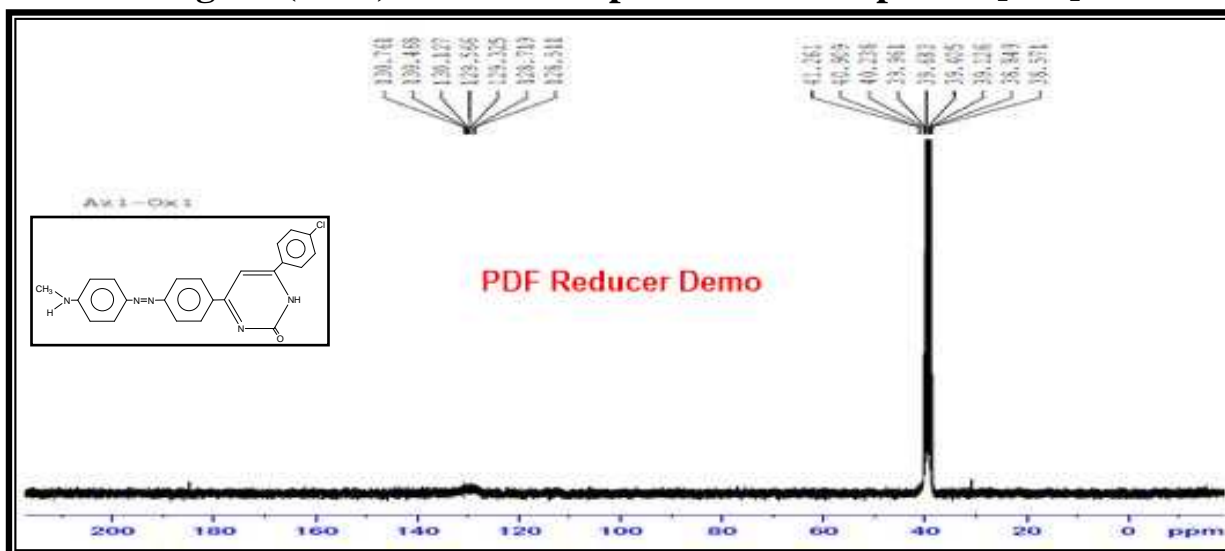


Figure (3-60): FTIR- Spectrum of compound [22a]

Figure (3-61): ¹H NMR- Spectrum of compound [22a]Figure (3-62): ¹³C NMR- Spectrum of compound [22a]

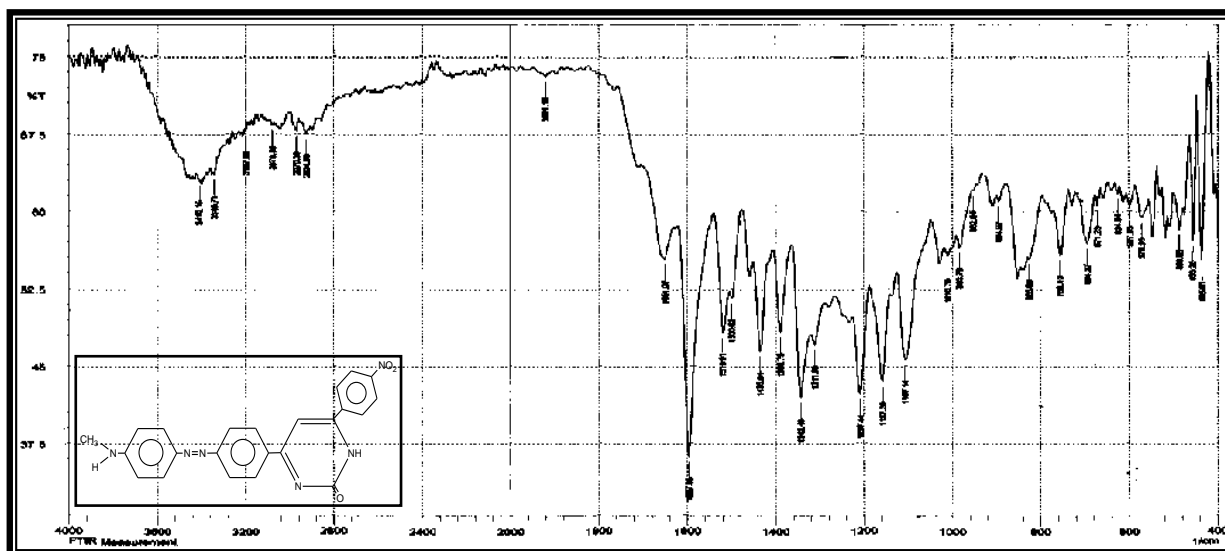


Figure (3–63): FTIR- Spectrum of compound [23a]

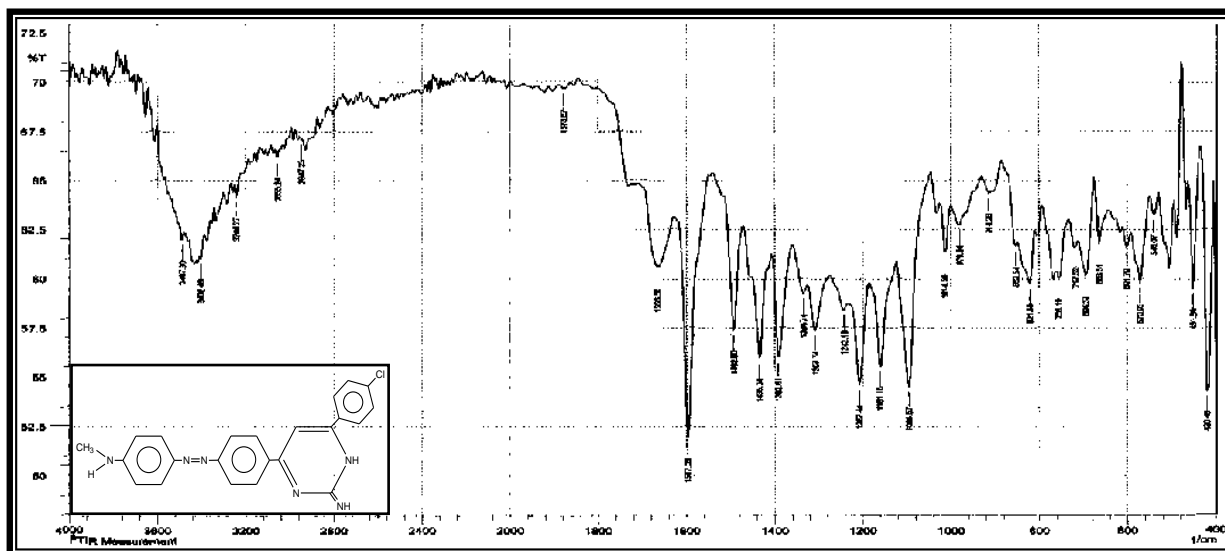
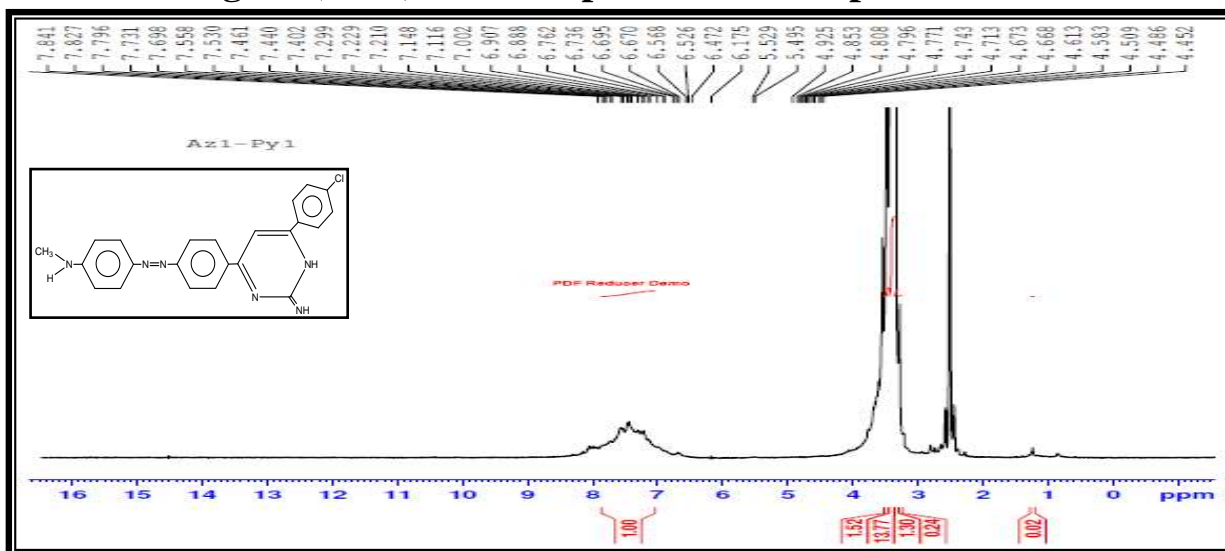
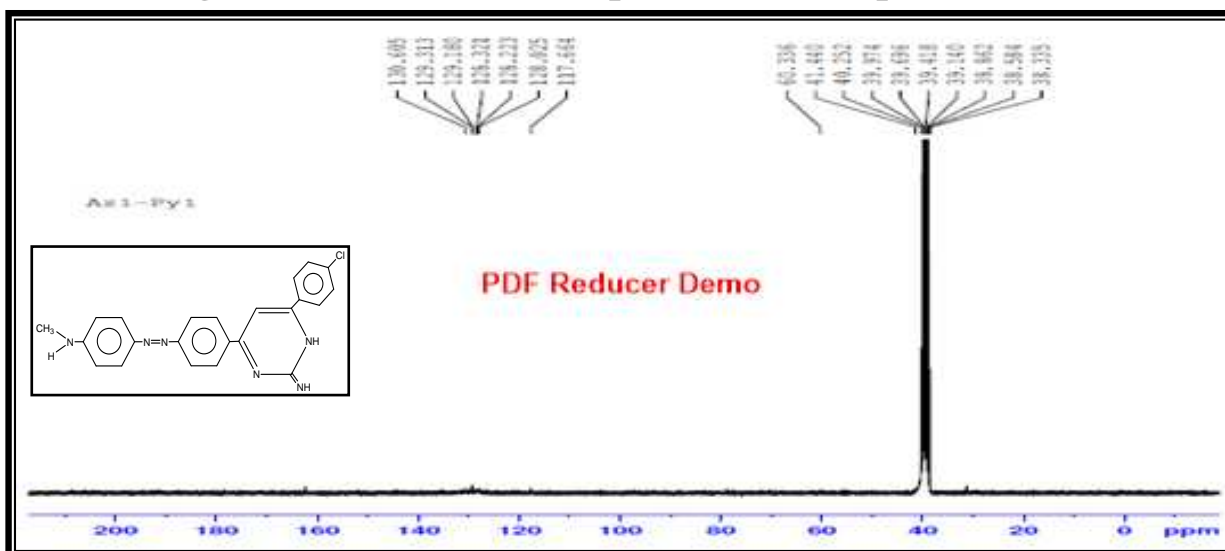


Figure (3-64): FTIR- Spectrum of compound [24a]

Figure (3-65): ¹H NMR- Spectrum of compound [24a]Figure (3-66): ¹³C NMR- Spectrum of compound [24a]

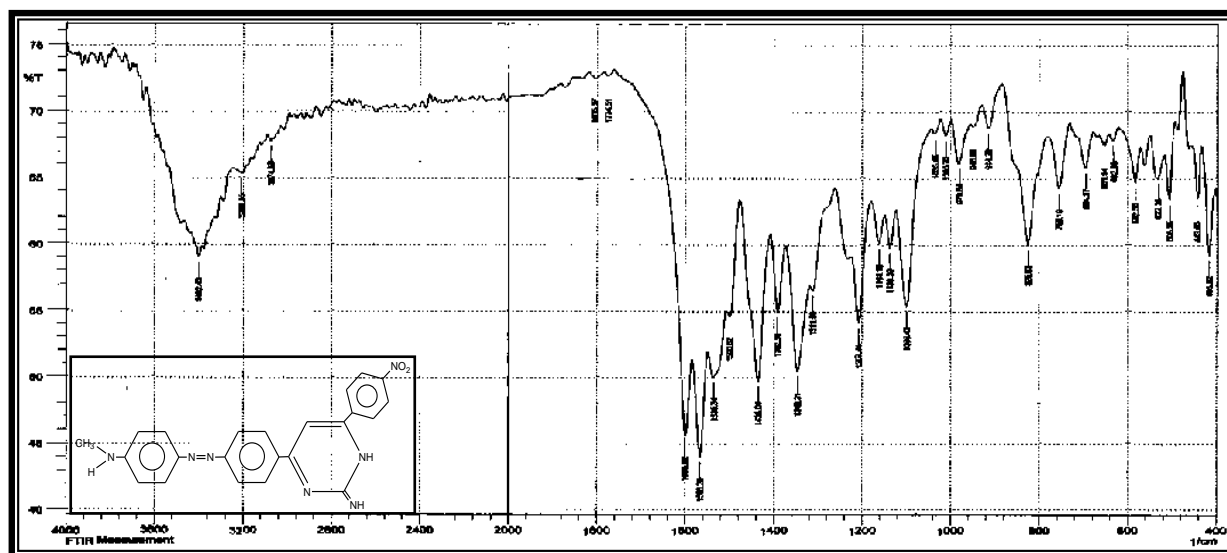


Figure (3-67): FTIR- Spectrum of compound [25a]

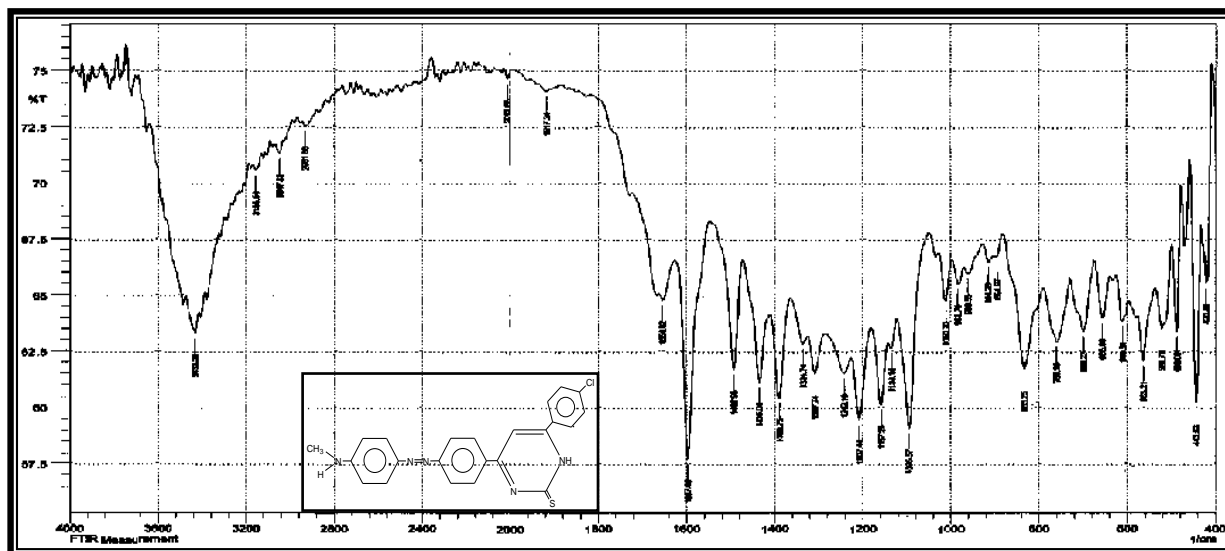
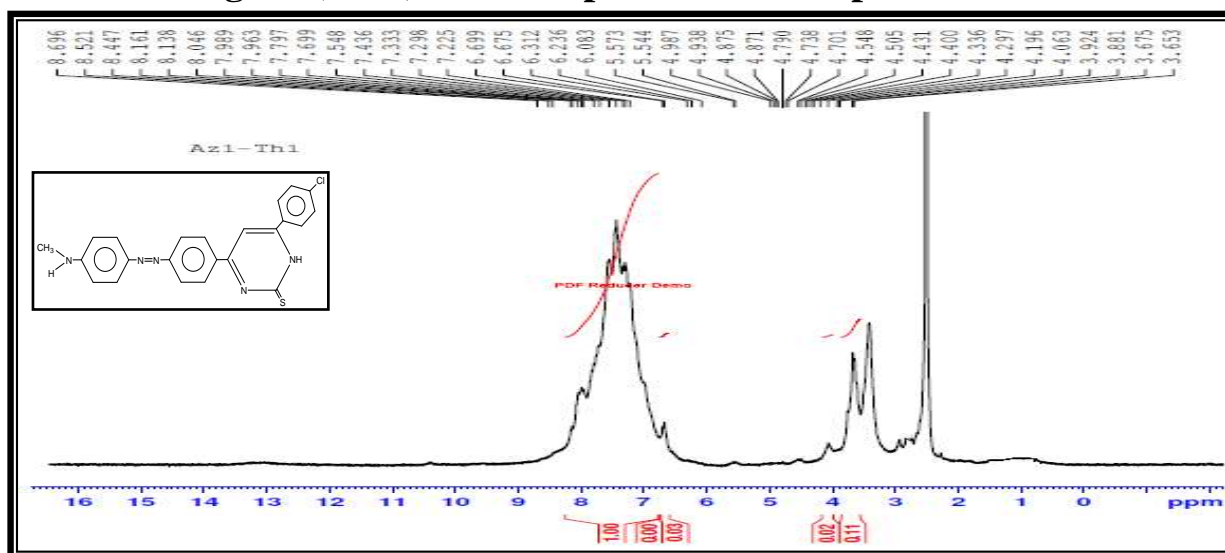
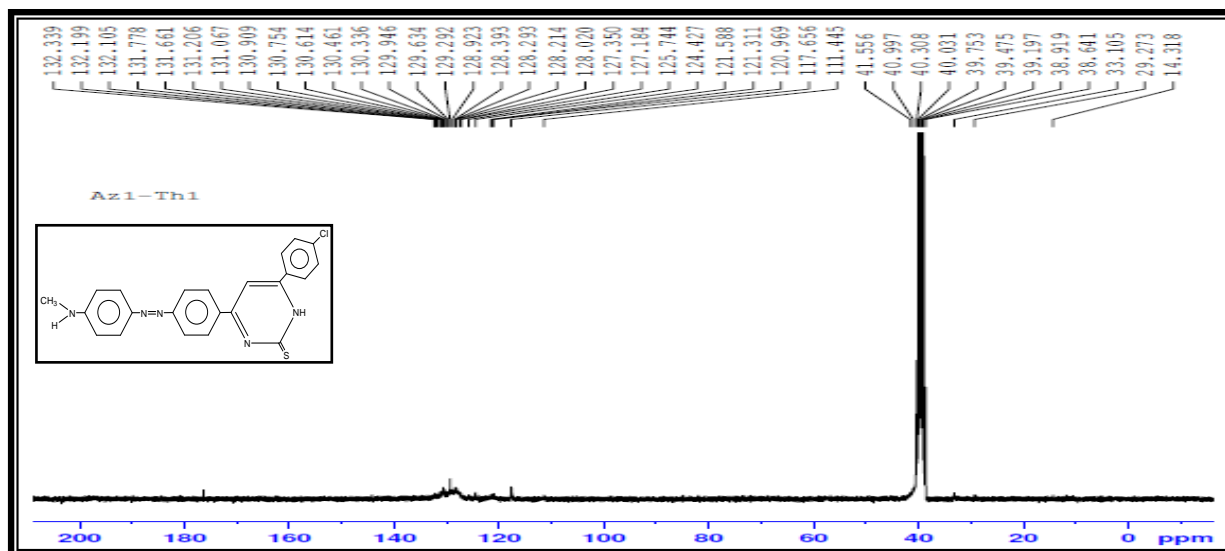


Figure (3-68): FTIR- Spectrum of compound [26a]

Figure (3-69): ¹H NMR- Spectrum of compound [26a]Figure (3-70): ¹³C NMR- Spectrum of compound [26a]

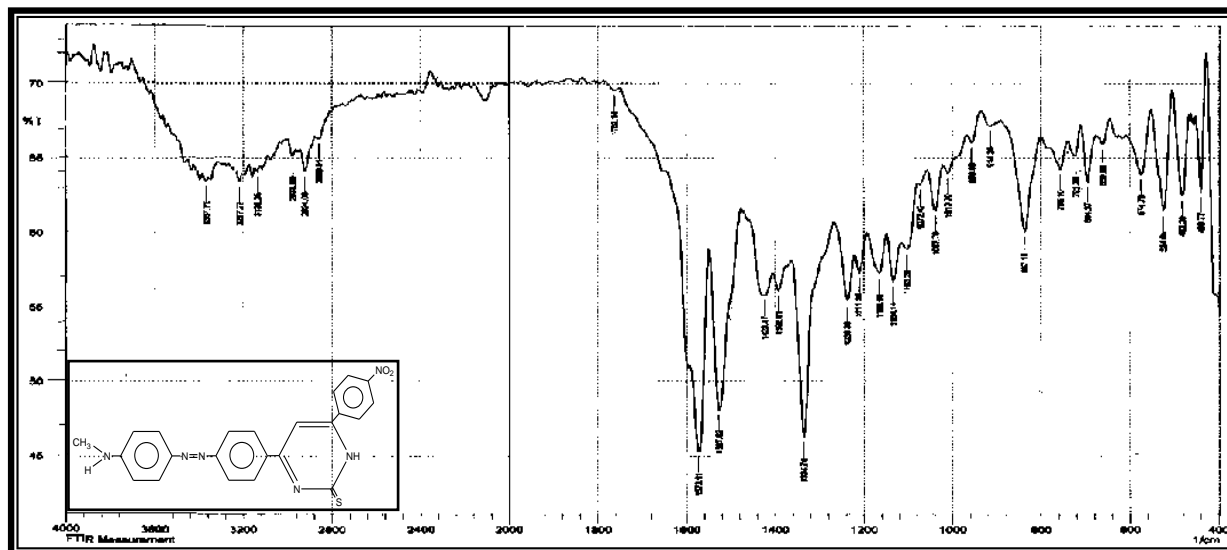


Figure (3-71): FTIR- Spectrum of compound [27a]

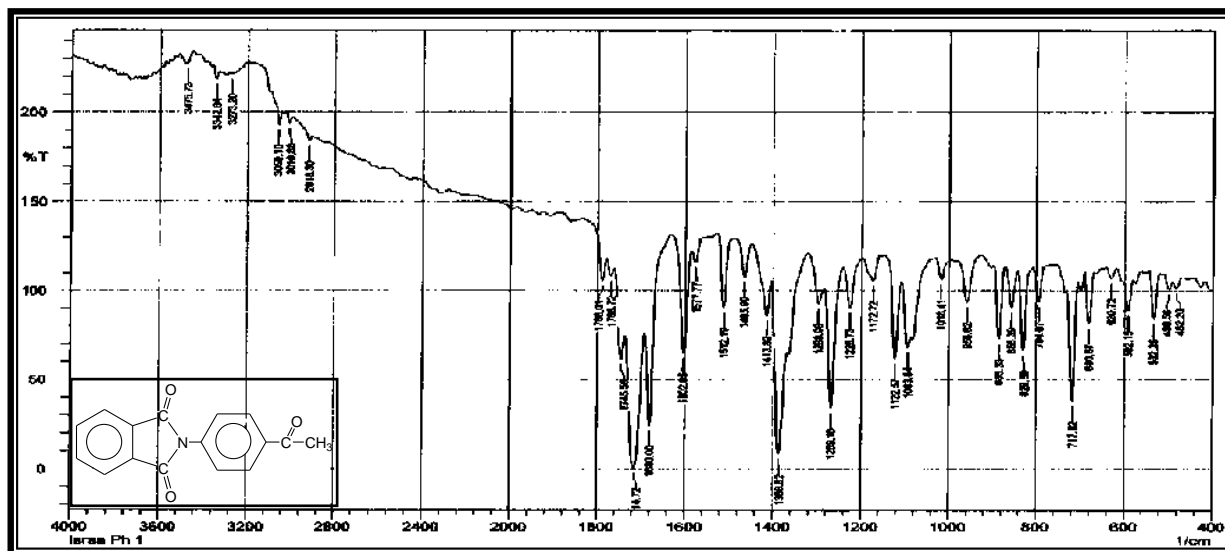


Figure (3-72): FTIR- Spectrum of compound [28a]

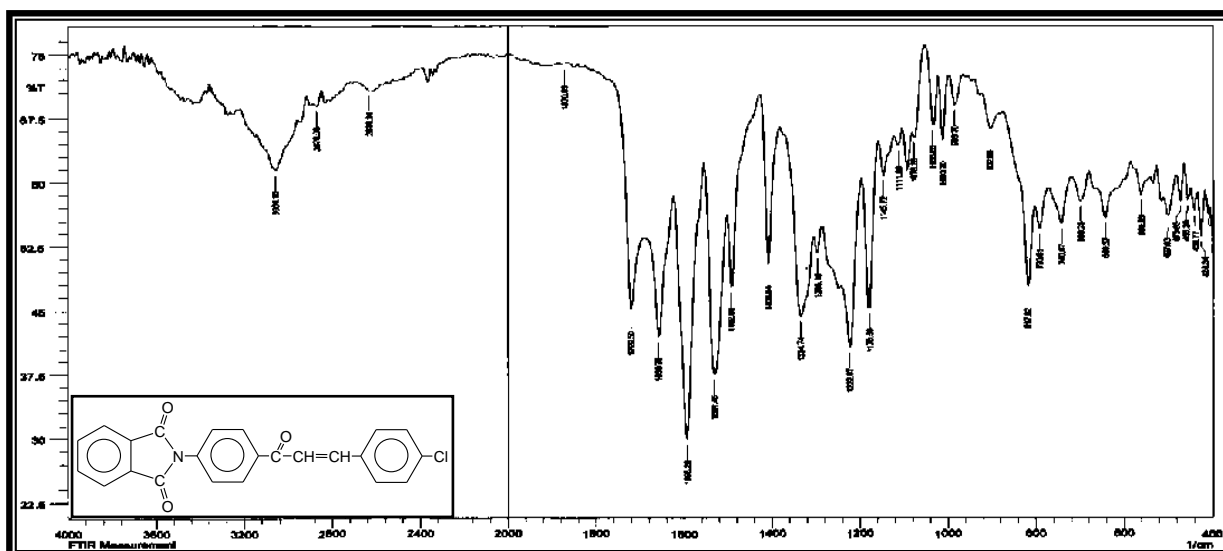
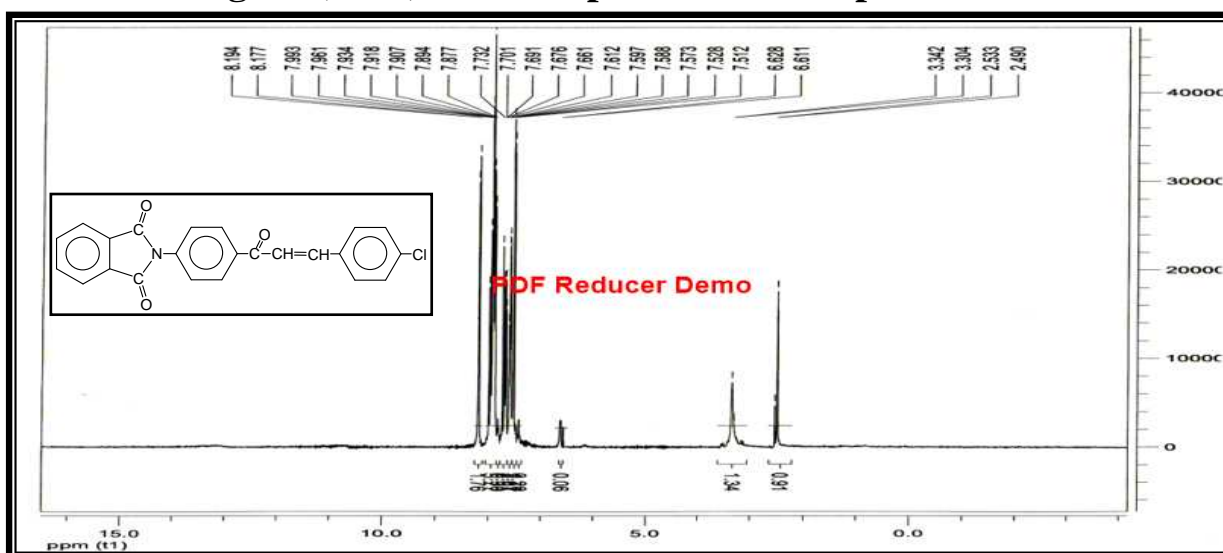
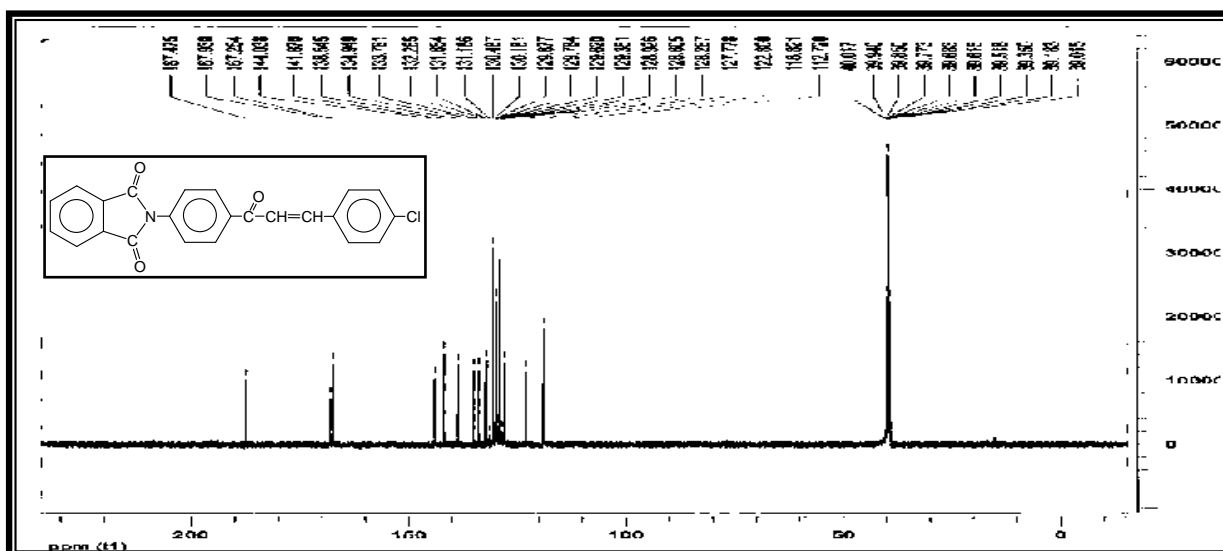


Figure (3-73): FTIR- Spectrum of compound [29a]

Figure (3-74): ¹H NMR- Spectrum of compound [29a]Figure (3-75): ¹³C NMR- Spectrum of compound [29a]

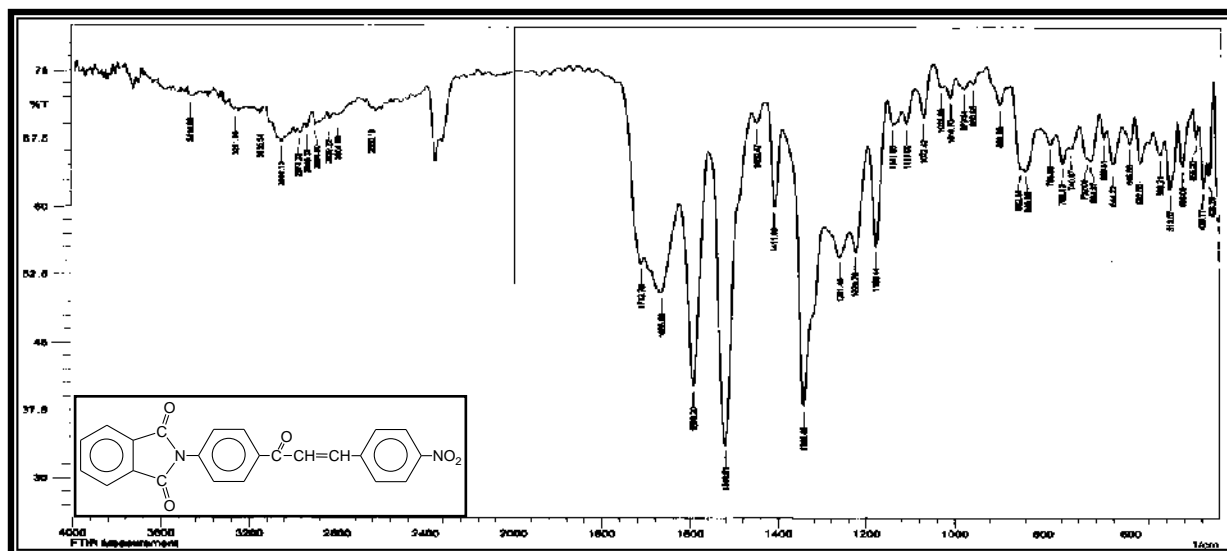


Figure (3-76): FTIR- Spectrum of compound [30a]

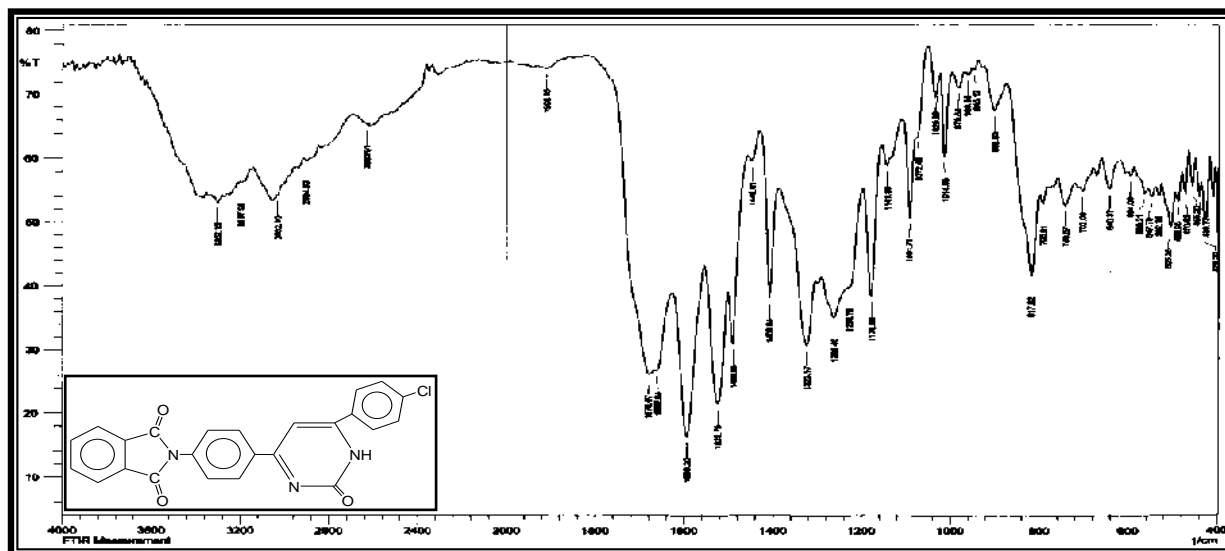
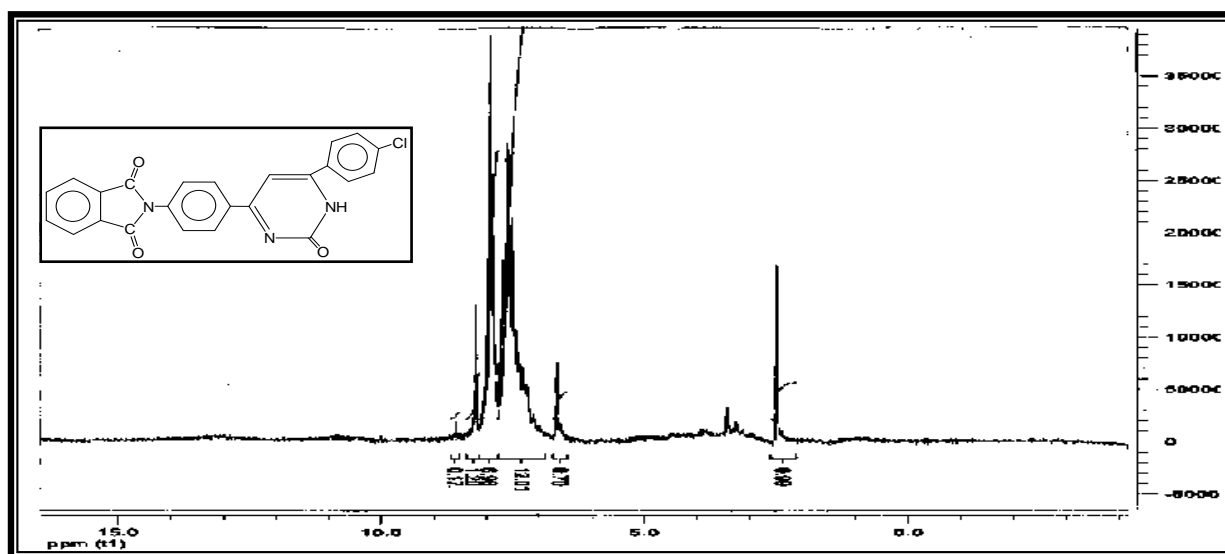
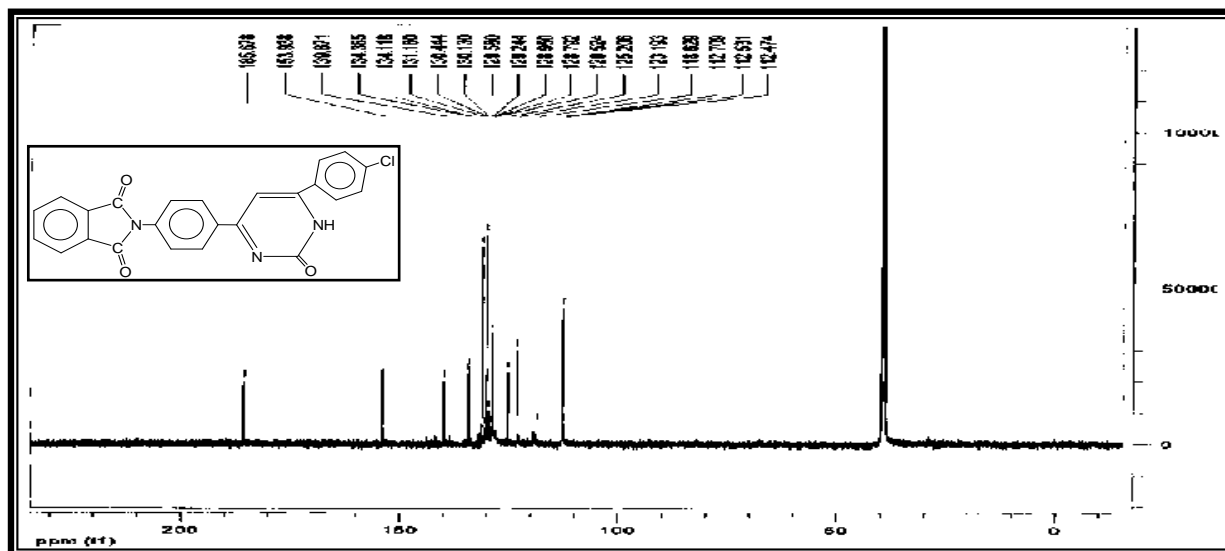


Figure (3-77): FTIR- Spectrum of compound [31a]

Figure (3-78): ^1H NMR- Spectrum of compound [31a]Figure (3-79): ^{13}C NMR- Spectrum of compound [31a]

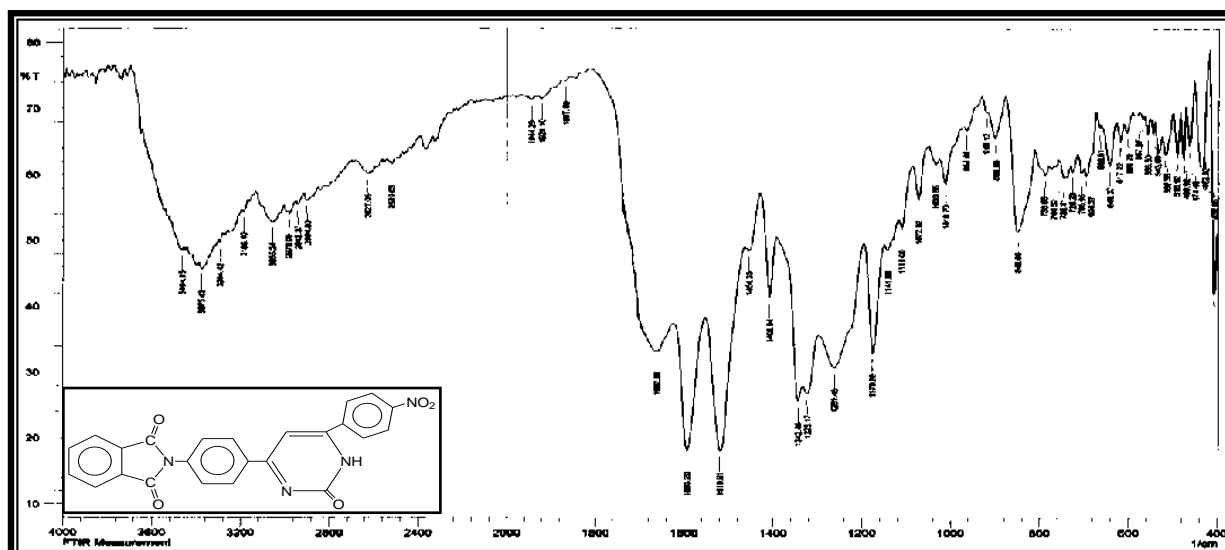


Figure (3–80): FTIR- Spectrum of compound [32a]

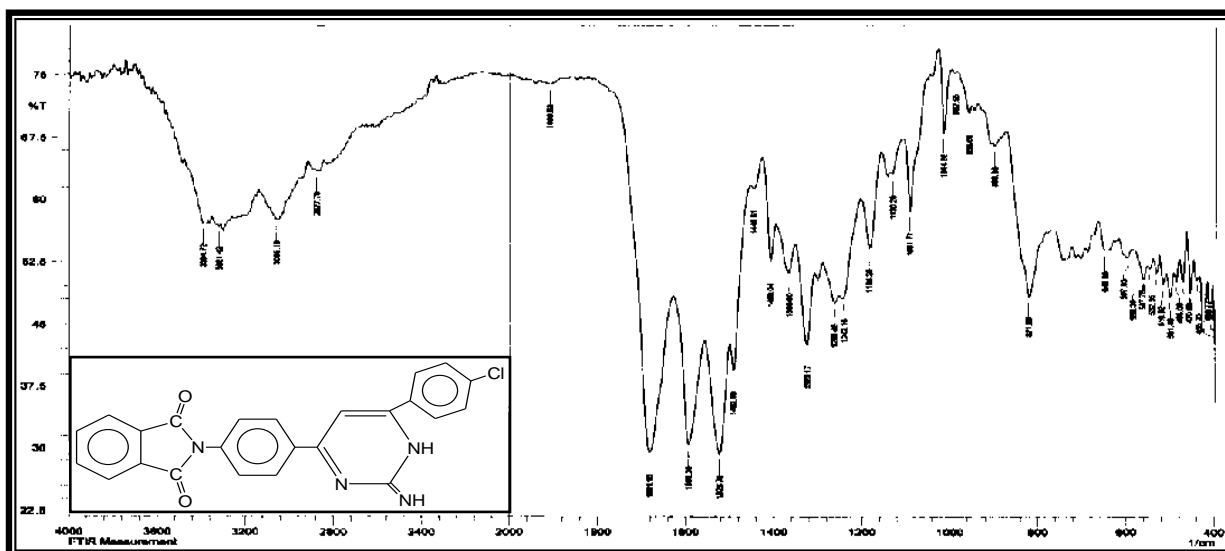
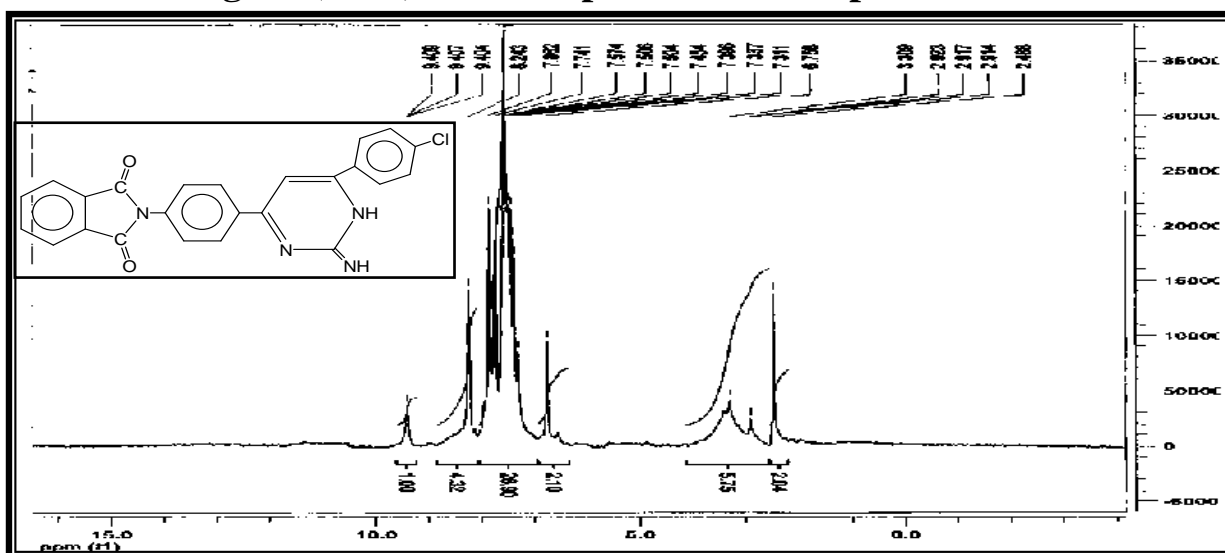
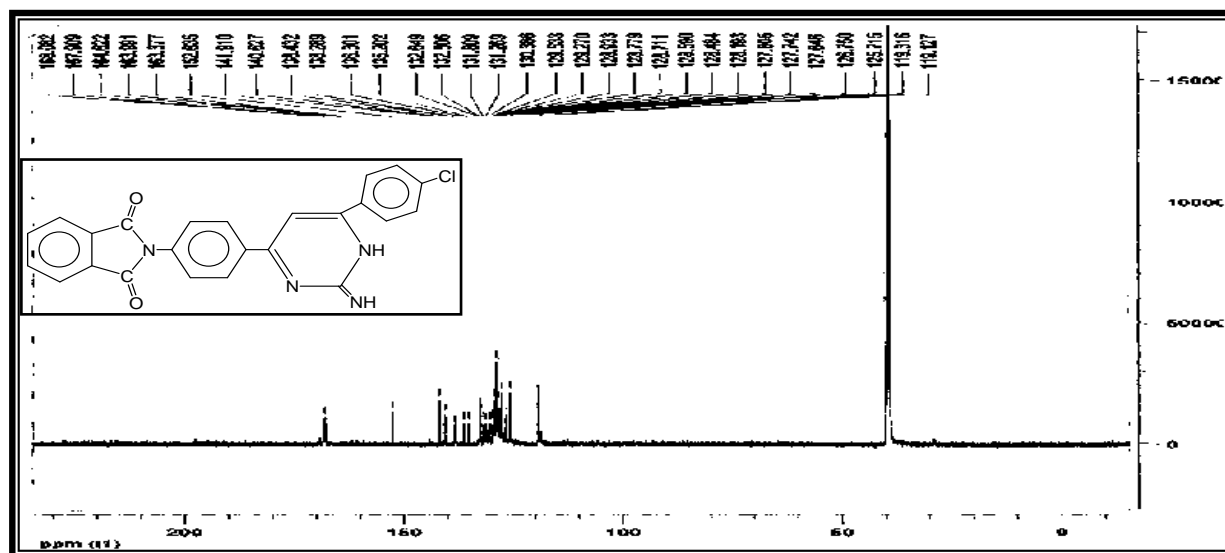


Figure (3-81): FTIR- Spectrum of compound [33a]

Figure (3-82): ¹H NMR- Spectrum of compound [33a]Figure (3-83): ¹³C NMR- Spectrum of compound [33a]

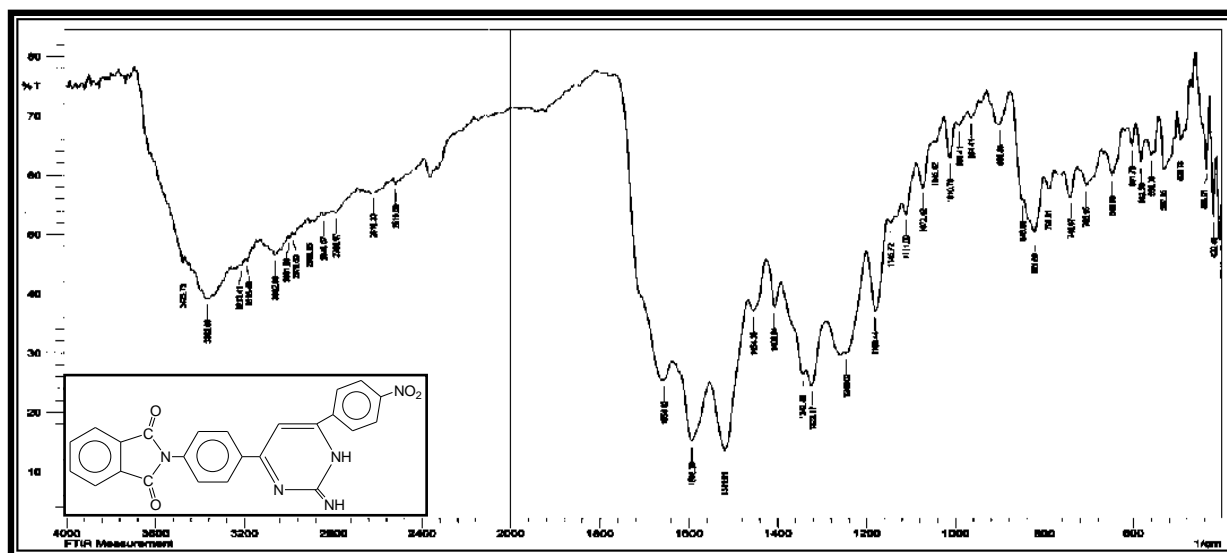


Figure (3-84): FTIR- Spectrum of compound [34a]

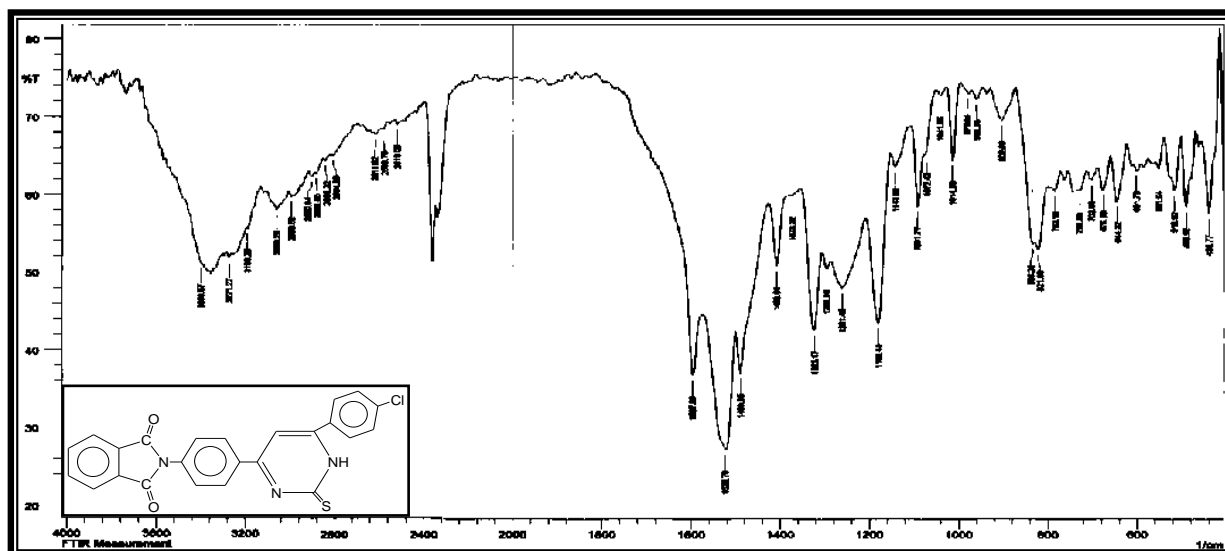
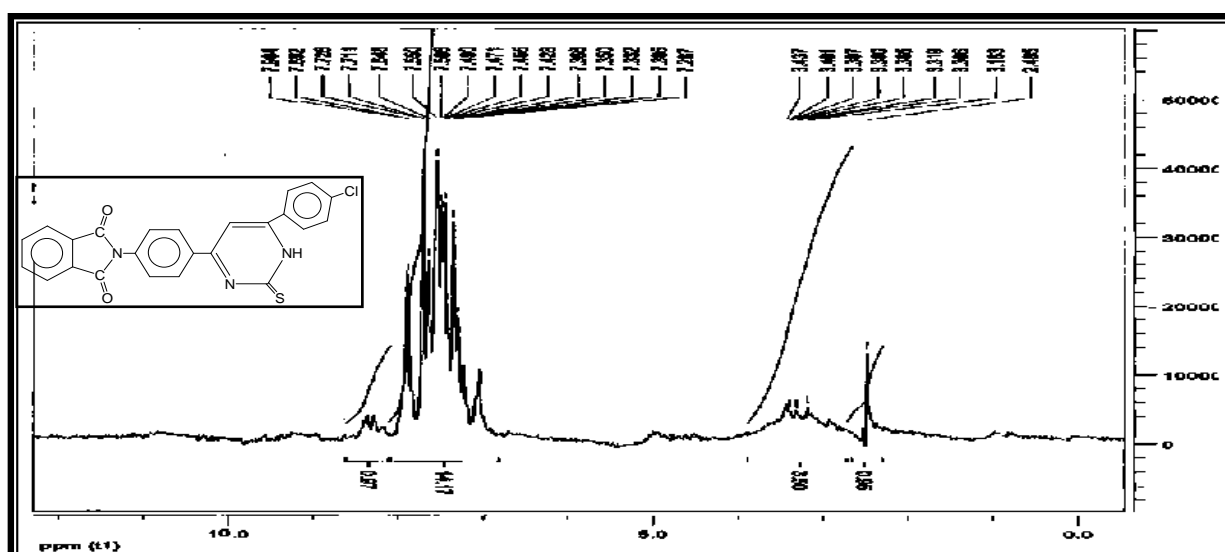
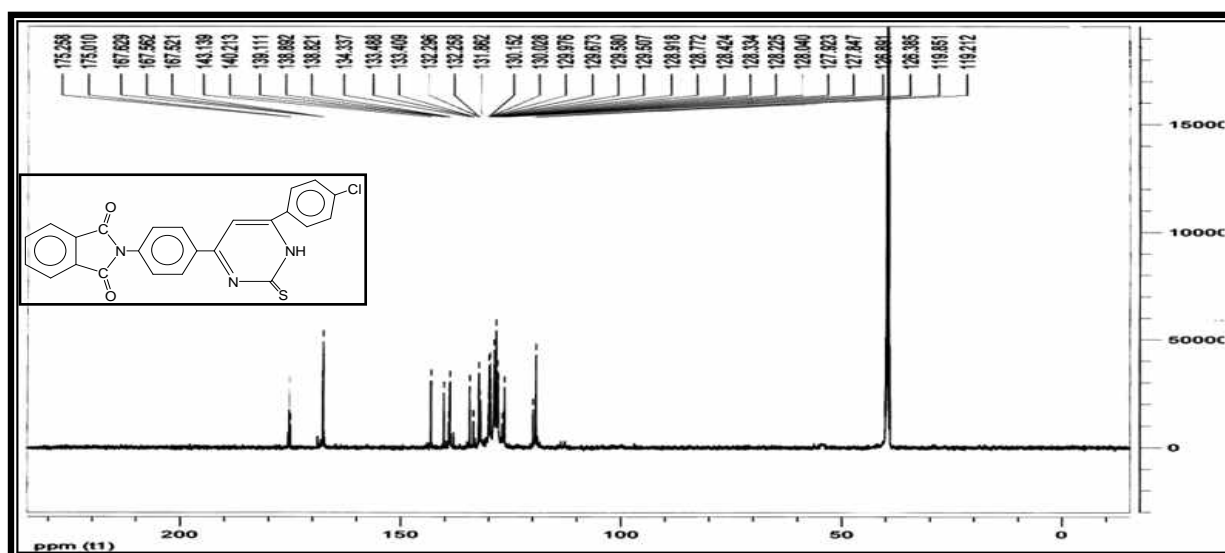


Figure (3-85): FTIR- Spectrum of compound [35a]

Figure (3-86): ¹H NMR- Spectrum of compound [35a]Figure (3-87): ¹³C NMR- Spectrum of compound [35a]

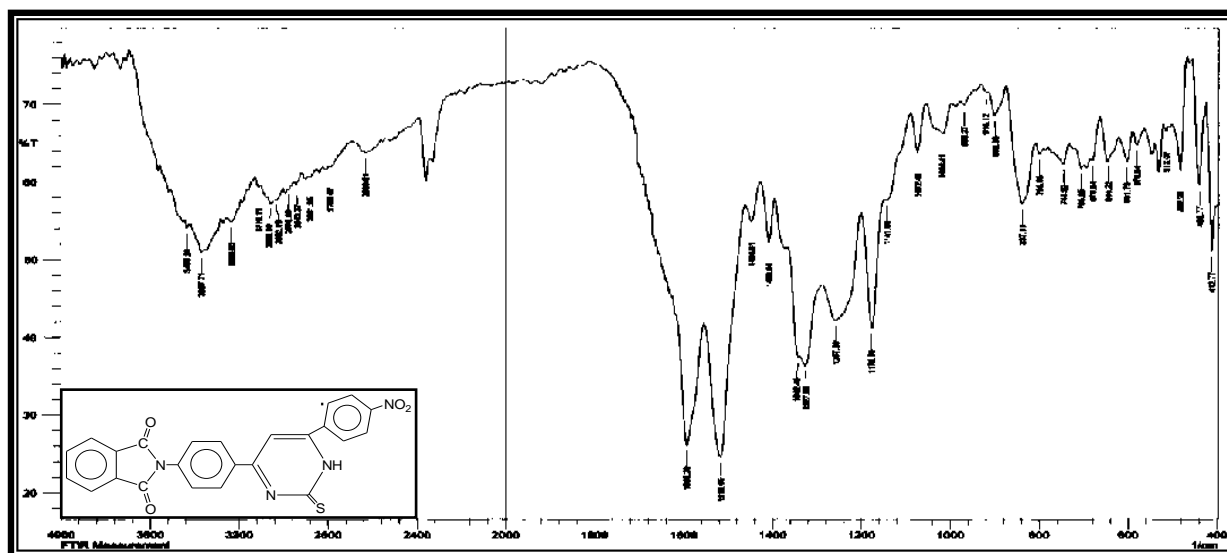


Figure (3-88): FTIR- Spectrum of compound [36a]

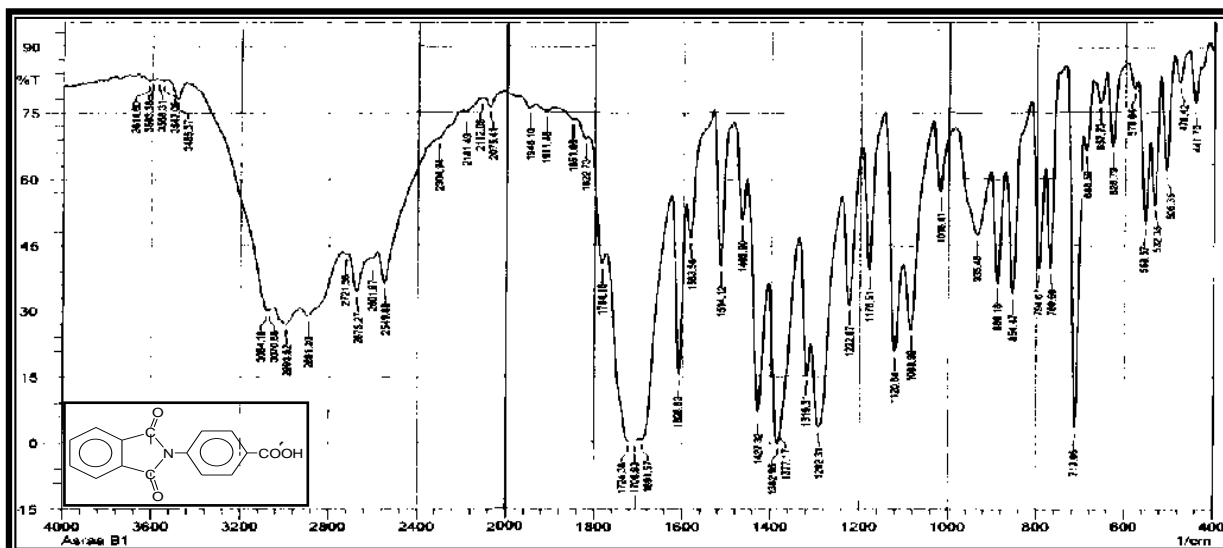


Figure (3–89): FTIR- Spectrum of compound 4-N-phthalimidobenzoic acid

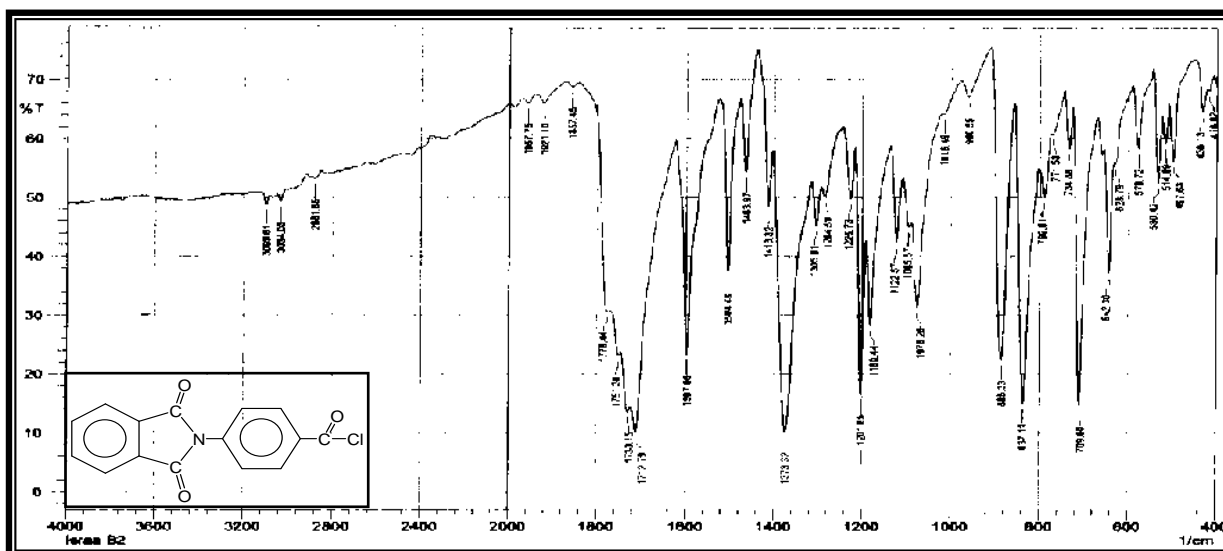


Figure (3–90): FTIR- Spectrum of compound 4-N-phthalimidobenzoyl chloride

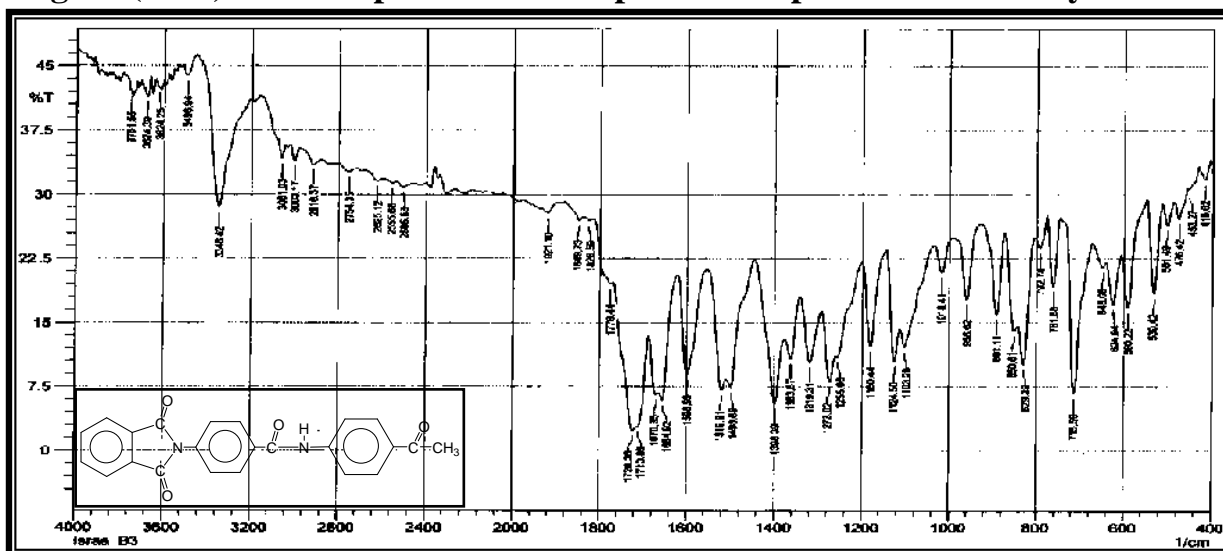


Figure (3–91): FTIR- Spectrum of compound [37a]

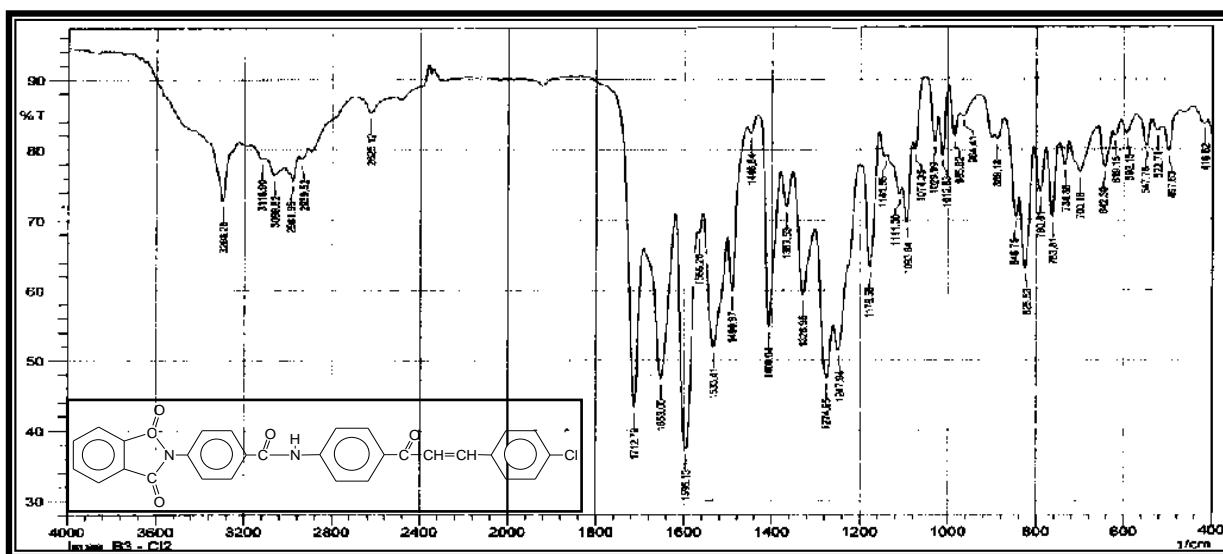
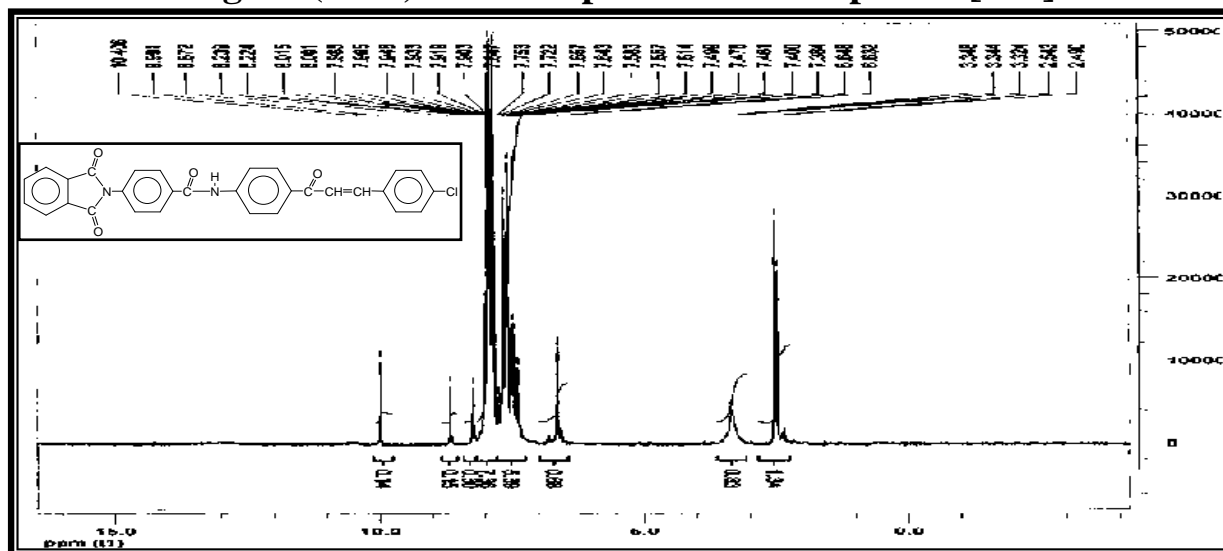
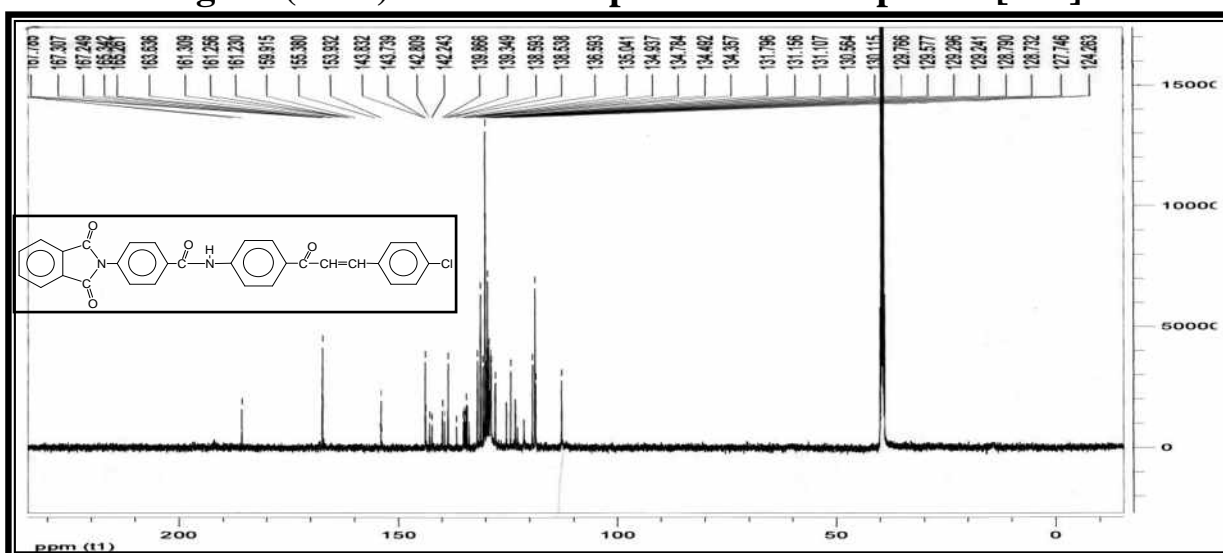


Figure (3-92): FTIR- Spectrum of compound [38a]

Figure (3-93): ^1H NMR- Spectrum of compound [38a]Figure (3-94): ^{13}C NMR- Spectrum of compound [38a]

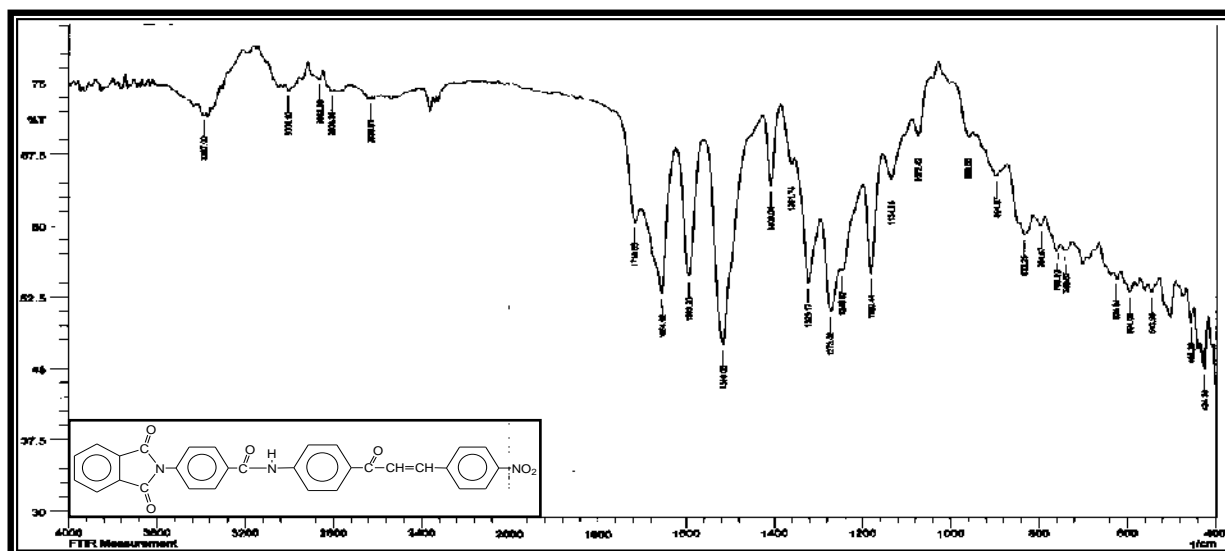


Figure (3-95): FTIR- Spectrum of compound [39a]

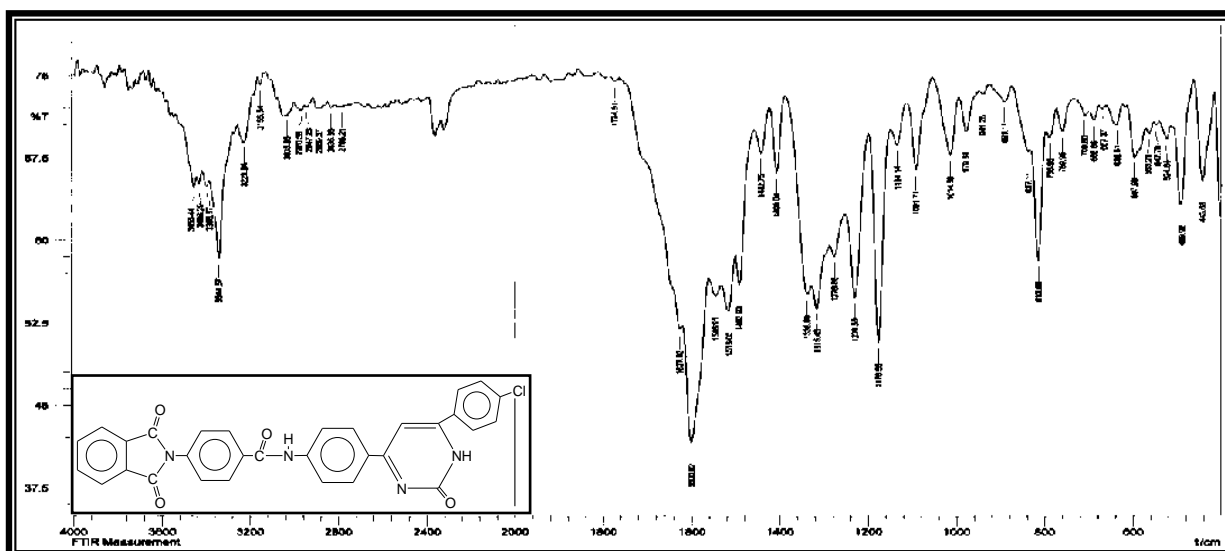


Figure (3-96): FTIR- Spectrum of compound [40a]

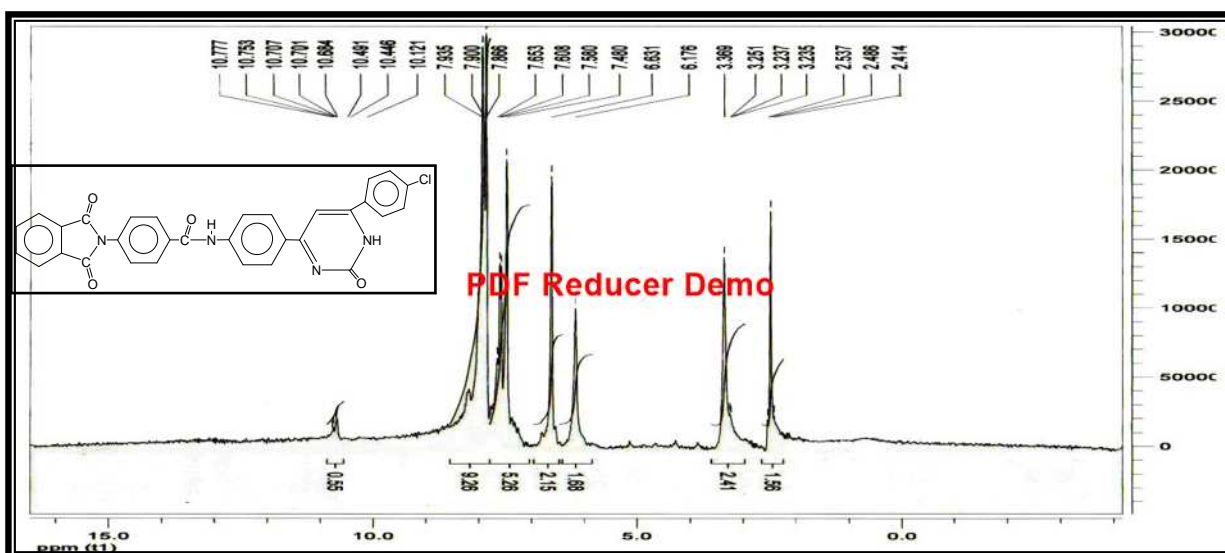


Figure (3-97): ¹H NMR- Spectrum of compound [40a]

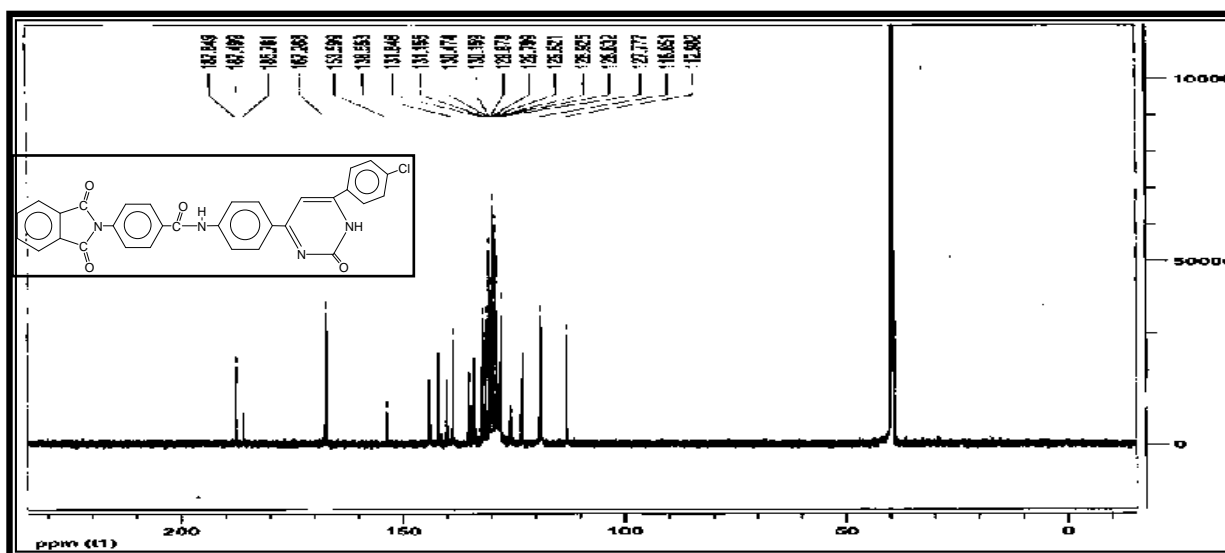


Figure (3-98): ¹³C NMR- Spectrum of compound [40a]

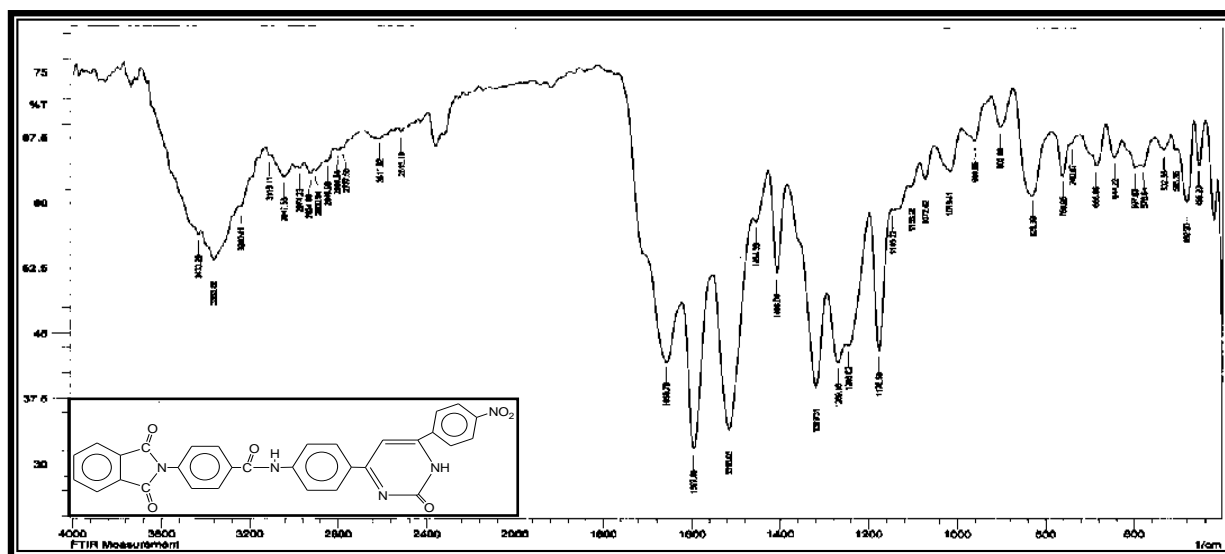


Figure (3-99): FTIR- Spectrum of compound [41a]

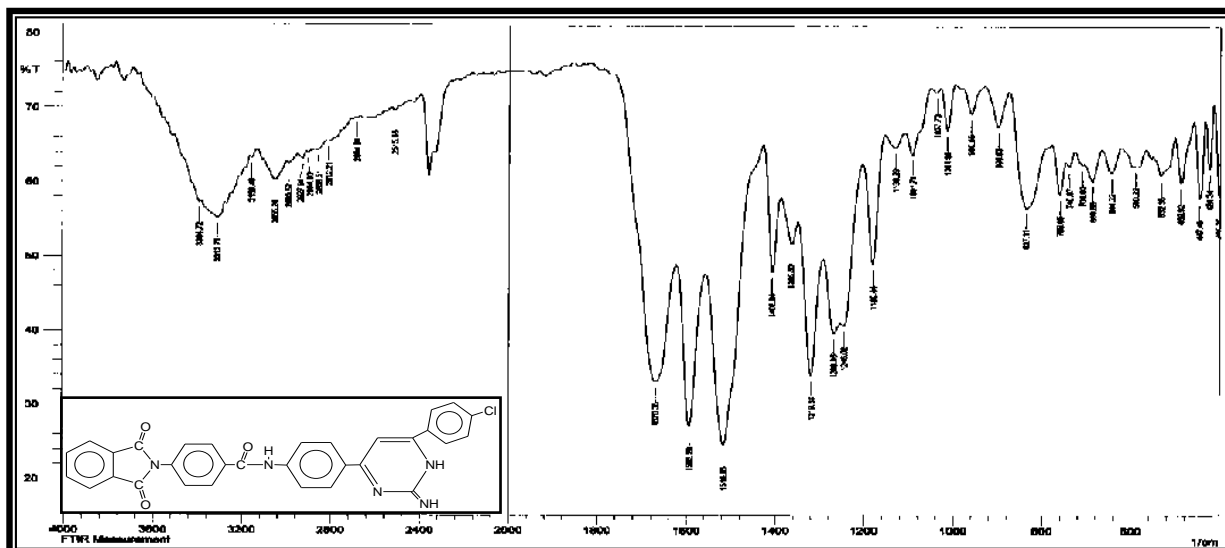
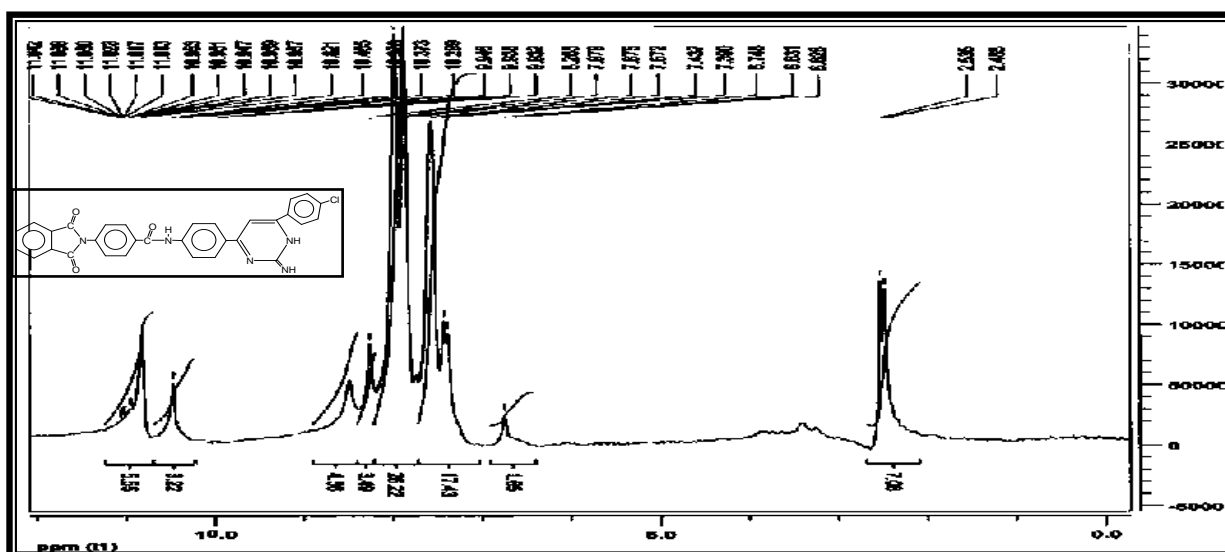


Figure (3-100): FTIR- Spectrum of compound [42a]



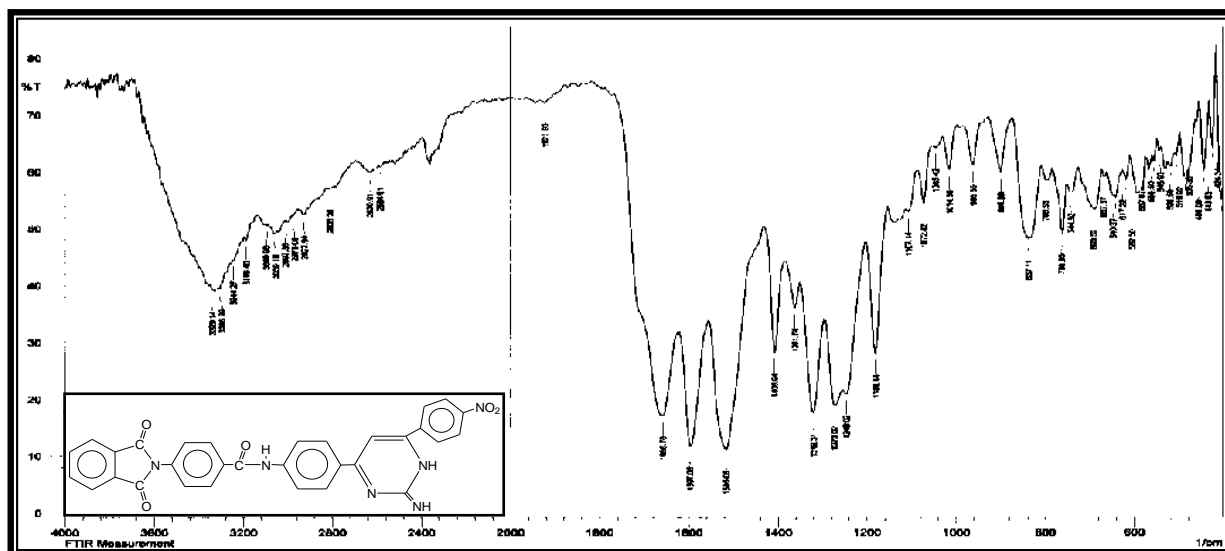


Figure (3-103): FTIR- Spectrum of compound [43a]

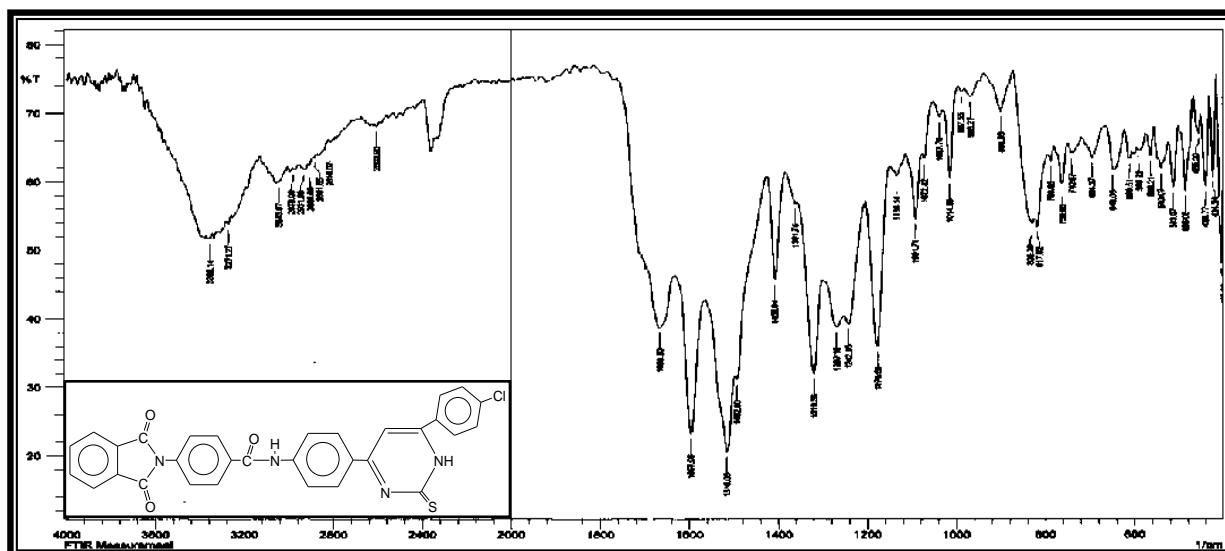
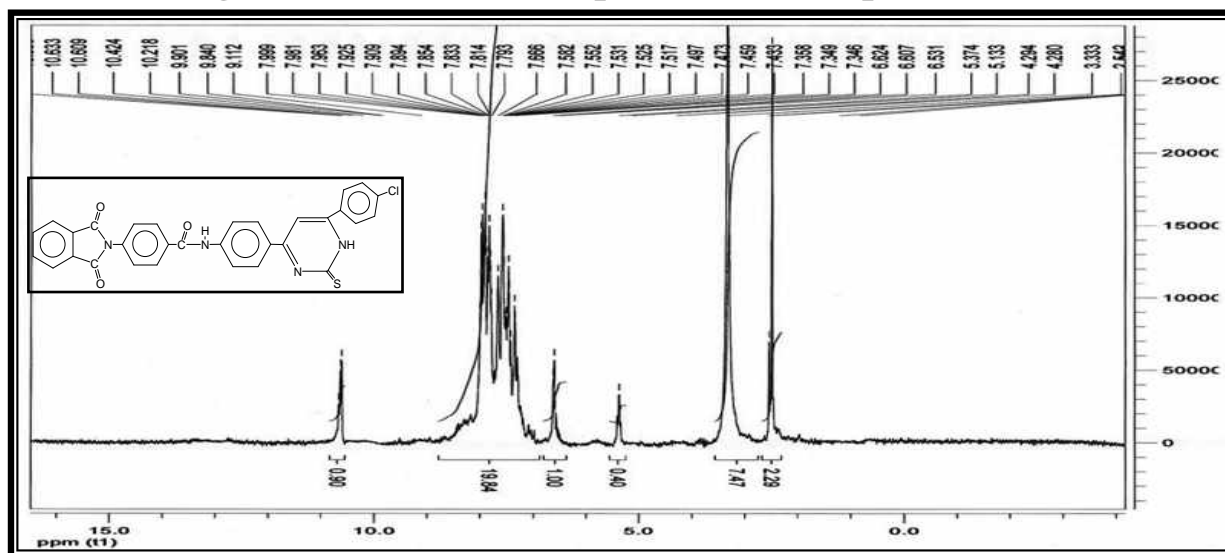
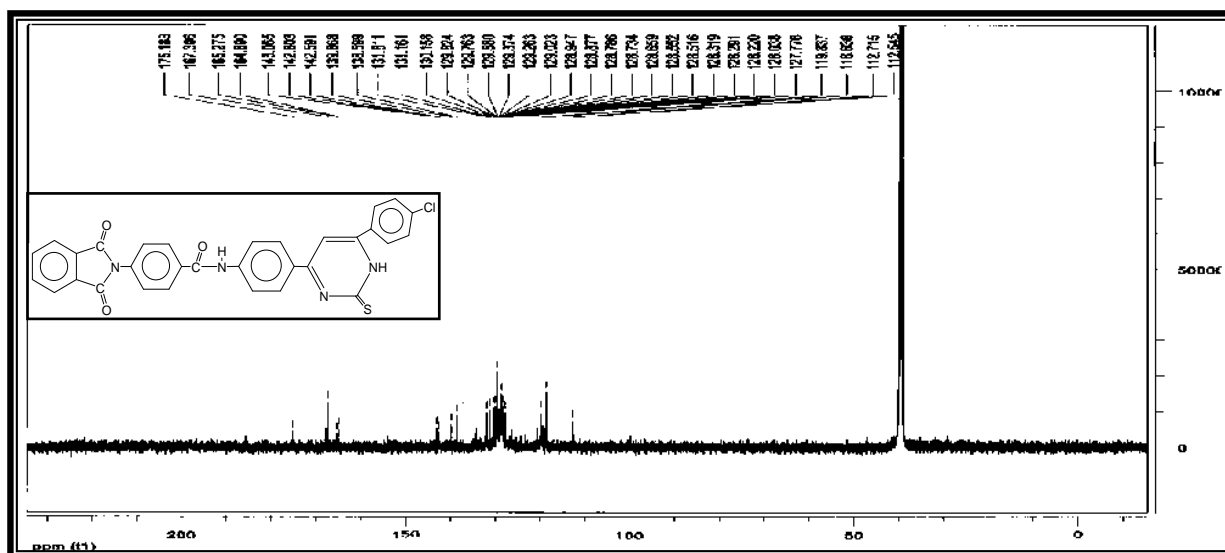


Figure (3-104): FTIR- Spectrum of compound [44a]

Figure (3-105): ¹H NMR- Spectrum of compound [44a]Figure (3-106): ¹³C NMR- Spectrum of compound [44a]

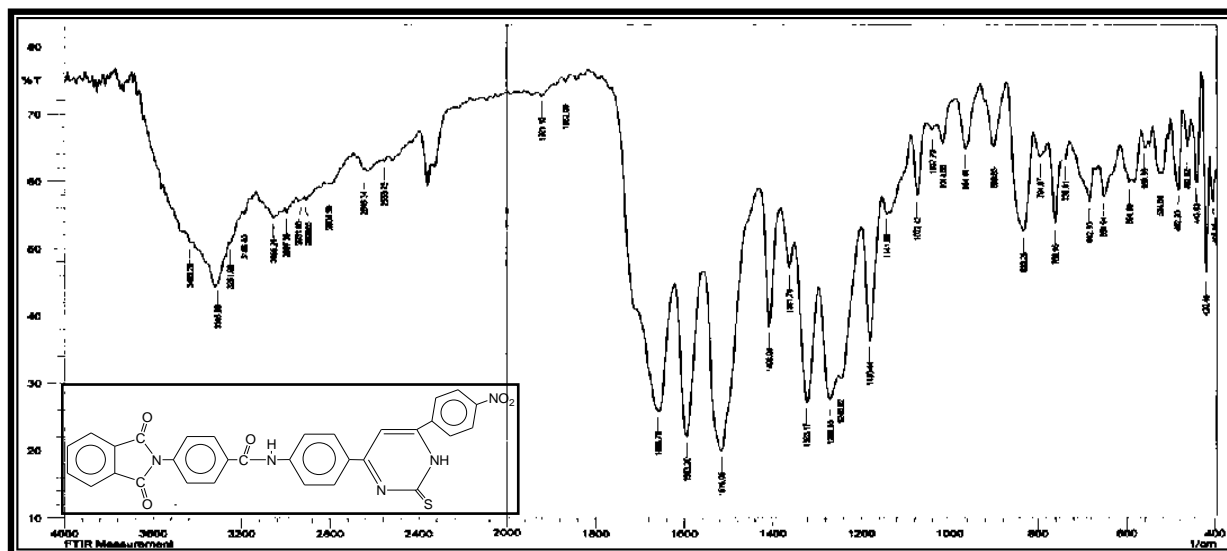


Figure (3-107): FTIR- Spectrum of compound [45a]

Chapter Four
Antimicrobial
Activity

4.1. Antimicrobial evaluation:

Agar well diffusion method^[86,87,121-125] was used to detect antimicrobial activity for the synthesized compounds. Compounds were tested for their antibacterial with Gram–Ve (*Serratia marcescens*, *Pseudomonas aeruginosa*) and Gram+Ve (*Staphylococcus aureus*, *Streptococcus pyogenes*), antifungal with (*Gandida albicans*).

The antimicrobial activity of synthesized compounds [1a–45a] were compared with standard antibiotics Cephalexin, Amoxicillin, Tetracycline Lincomycin, Nystatine and Fluconazol which considered popular for treatment of diseases caused by those five pathogenic species.

4.1.1 Bacterial and fungal cultures:

Four species of pathogenic Bacteria used in this study as tested organisms. These are *Serratia marcescens*, *Pseudomonas aeruginosa* (Gram negative) and *staphylococcus aureus*, *streptococcus pyogenes* (Gram positive). Fungal used *candida albicans*. These bacterial and fungal species were obtained from the central service laboratory in Ibn Al- Haitham advisory office, Baghdad University.

4.1.2 Determination of antimicrobial activity

Fresh bacterial cultures suspension equivalent of 0.5 tube McFarland turbidity standards (10^8 cfu/ μ l) (Colony forming unit/ml) and incubated at 37°C for 24- 48h, 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 30 μ l 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).

4.1.3 Drugs and antibiotics sensitivity test

Antibiotic susceptibility of (*Serratia marcescens*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Streptococcus pyogenes*) 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 *Candida albicans* 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

It is known, that chalcones (1,3-diaryl-2-propene-1-one) have antimicrobial activities against many types of bacteria and fungi^[86,87,121-125]. So, we design to synthesize some certain chalcones containing active antimicrobial groups at positions (1 and 3) in order to extend its antimicrobial activities, like sulphonamido, ureido, N-methylaminophenylazo *p*,N-phthalimido and (N-phthalimido)benzamido at position-1 and chloro or nitro groups at position- 3, as in following scheme.

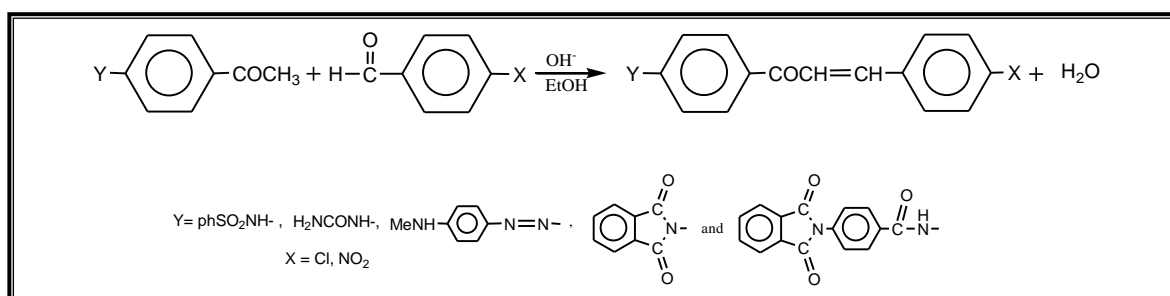


Table (4–1) showed antimicrobial activities data of chalcones [2a, 3a, 11a, 12a, 20a, 21a, 29a, 30a, 38a and 39a] and synthetic *p*-substituted acetophenones [A, 1a, 10a, 19a, 28a and 37a] which were used in synthesis of these chalcones, against some (G-Ve and G+Ve) bacteria like (*Serratia marcescens*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Streptococcus pyogenes*) and (*Candida albicans*) fungi, in comparison with antimicrobial activities of some pharmaceutical antibiotics like Cephalexin, Amoxicillin, Tetracycline and Lincomycin and antifungal Nystatine and Fluconazole treatments.

Antimicrobial data as in Table (4-1), showed:

First: *p*-substituents at acetophenone ring, have better effect than used antibiotics in this study and are in rank [10a] (ureido) >

[1a] (sulphonamido) > [19a] (N-methylaminophenylazo) > [A] > [28a], [37a] on *Serratia marcescens* and *Pseudomonas aeruginosa* (G-Ve) bacteria.

Second: Also chalcones have much better effect than antibiotics used in this study, but showed small increasing affect then *p*-substituted acetophenones, on *Serratia marcescens* and *Pseudomonas aeruginosa* (G-Ve) bacteria, with rank are [11a], [29a], [38a] > [2a], [20a]. In case of chalcones containing *p*-nitrophenyl group at position-3, [21a] showed, much better effect then other chalcones [3a], [12a], [30a], [39a].

Third: Also chalcons give good inhibition effect, on *Candida albicans* fungi, better than *p*-substituted acetophenons, specially, that chalcones [21a] containing *p*(N-methylamino)phenylazo phenyl group at position- 1 and *p*-nitrophenyl group at position-3.

Also, it is known that pyrimidine (1,3-diazines) have antimicrobial activities against some types of bacteria and fungi^[90-91]. So, for this purposes, we design to synthesize some certain pyrimidine containing active antimicrobial group at positions-2, 4, 6 in order to improve its antimicrobial activities, like *p*-benzene-sulphonamidophenyl, *p*-ureidophenyl *p*,N-methylaminophenylazo-phenyl *p*-phthalimidophenyl and *p*-amidophenylphthalimidophenyl groups at position- 1, *p*-chloro or *p*-nitro phenyl group at postion-6 and oxo, imino and thioxo groups at position-2, as in the following Scheme:

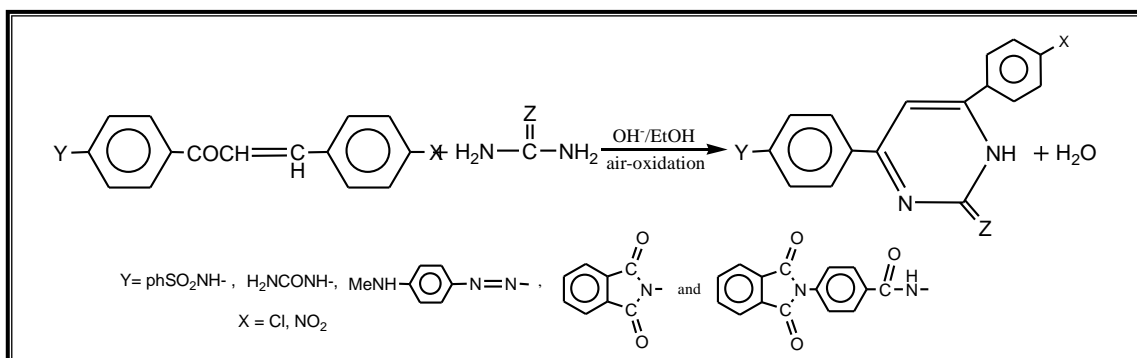


Table (4-1), Figs. (4-1), (4-2), (4-3), (4-4) and (4-5) showed antimicrobial activities data of some synthesized pyrimidines [4a to 9a, 13a to 18a, 22a to 27a and 31a to 36a] against some of (G-Ve and G+ve) bacteria like (*Serratia marcescens*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Streptococcus pyogenes*) respectively and (*Candida albicans*) fungi, in comparison with antimicrobial activities of some pharmaceutical antibiotics Cephalexin, Amoxicillin, Tetracycline and Lincomycin and antifungal Nystatine and Fluconazole treatments.

Antimicrobial data as in Table (4-1) showed:

First: pyrimidine containing benzenesulphonamido group [4a to 9a] have much better effect than used antibiotics in these studies, on both types of (G-Ve) bacteria, specially that pyrimidines group containing imino [6a and 7a] and thioxo groups [8a and 9a] at position-2.

Second: pyrimidine containing ureido group [13a to 18a] have better effect than used antibiotic on both (G+Ve) *Staphylococcus aureus* and (G-Ve) *Serratia marcescens* and *Pseudomonas aeruginosa*, specially that pyrimidines containing imino group [15a and 16a] and thioxo group [17a] at position-2.

Third: pyrimidines containing N-methylaminophenylazo phenyl group [22a to 27a] have strong inhibition effect more than used antibiotics in this study, on both types of (G-Ve and G+Ve) bacteria (*Serratia marcescens*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Streptococcus pyogenes*) respectively, specially that pyrimidines containing imino group [24a and 25a], thioxo group [26a and 27a] at position- 2.

Fourth: While pyrimidines containing *p*-phthalimido group [31a to 36a], showed also better effect than used antibiotic in this study, on both (G+Ve) *Staphylococcus aureus* and (G-Ve) *Serratia marcescens*, *Pseudomonas aeruginosa*, specially that pyrimidine containing imino group [33a and 34a] and thioxo group [35a and 36a] at position- 2.

Fifth: while pyrimidines containing *p*-amidophenyl phthalimidophenyl group [40a to 45a] showed also better effect than used antibiotic in this study, on both (G+Ve) *Staphylococcus aureus* and (G-Ve) *Serratia marcescens*, *Pseudomonas aeruginosa*, specially that pyrimidine containing imino group [42a and 43a] and thioxo group [44a and 45a] at position- 2.

Sixth: Also all synthesized pyrimidines [4a to 45a] showed good effect on (*Candida albicans*) fungi, in comparison with pharmaceutical antifungal treatment specially that pyrimidine [22a], containing N-methylaminophenylazo phenyl group at position- 4 and oxo group at position- 2, showed strong effect more than antifungal Nystatine and fluconazole treatments.

Table (4–1): Antimicrobial activity of compounds [1a– 45a]

Comp. No.	Structure	Mean of Inhibition zone Diameter (mm)				
		<i>Staphylococcus aureus</i>	<i>Streptococcus pyogenes</i>	<i>Serratia marcescens</i>	<i>Pseudomonas aeruginosa</i>	<i>Candida albicans</i>
[A]		–	–	13	–	–
[1a]		–	–	15	–	13
[2a]		–	–	15	–	14
[3a]		–	–	16	13	13
[4a]		–	–	16	–	15
[5a]		–	–	–	17	–
[6a]		15	–	21	13	–
[7a]		–	–	20	12	–
[8a]		–	–	18	15	–
[9a]		15	–	19	–	13
[10a]		–	–	16	–	–
[11a]		15	–	18	17	13
[12a]		–	–	16	15	–
[13a]		12	–	18	17	13
[14a]		17	–	–	16	8
[15a]		15	–	–	18	14
[16a]		–	–	–	13	14

Comp. No.	Structure	Mean of Inhibition zone Diameter (mm)				
		<i>Staphylococcus aureus</i>	<i>Streptococcus pyogenes</i>	<i>Serratia marcescens</i>	<i>Pseudomonas aeruginosa</i>	<i>Candida albicans</i>
[17a]		—	—	—	16	12
[18a]		—	—	—	—	12
[19a]		—	—	14	—	19
[20a]		—	—	15	13	28
[21a]		—	—	19	—	Large inhibition zone
[22a]		11	—	20	13	=
[23a]		—	—	19	18	14
[24a]		24	20	12	23	13
[25a]		26	38	28	19	12
[26a]		35	35	25	25	10
[27a]		38	24	—	26	14
[28a]		—	—	—	—	19
[29a]		—	—	16	—	16
[30a]		15	—	19	11	18
[31a]		15	—	17	11	15
[32a]		17	—	15	12	15
[33a]		—	17	19	18	13

Comp. No.	Structure	Mean of Inhibition zone Diameter (mm)				
		<i>Staphylococcus aureus</i>	<i>Streptococcus pyogenes</i>	<i>Serratia marcescens</i>	<i>Pseudomonas aeruginosa</i>	<i>Candida albicans</i>
[34a]		–	–	17	11	13
[35a]		11	–	16	18	12
[36a]		–	–	–	–	17
[37a]		–	–	–	–	10
[38a]		10	–	10	19	14
[39a]		–	–	11	8	9
[40a]		–	–	11	11	12
[41a]		–	–	13	15	11
[42a]		–	–	18	17	11
[43a]		–	–	19	15	11
[44a]		–	–	16	14	8
[45a]		–	–	20	16	13

Drugs	Mean of Inhibition zone Diameter (mm)				
	<i>Staphylococcus aureus</i>	<i>Streptococcus pyogenes</i>	<i>Serratia marcescens</i>	<i>Pseudomonas aeruginosa</i>	<i>Candida albicans</i>
Cephalexin	–	–	13	–	–
Amoxicillin	–	12	–	–	–
Tetracycline	25	25	–	12	–
Lincomycine	17	30	–	21	–
Nystatine	–	–	–	–	29
Fluconazole	–	–	–	–	–
Dimethyl-sulphoxide	–	–	–	–	–

A= *p*-aminoacetophenone

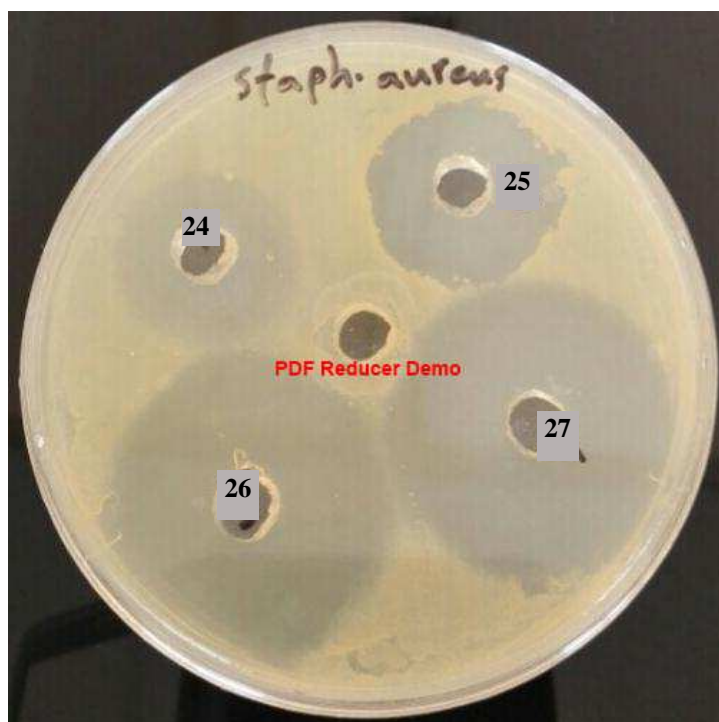


Figure (4-1): The antibacterial activity of compounds [24a, 25a, 26a and 27a] against *Staphylococcus aureus*

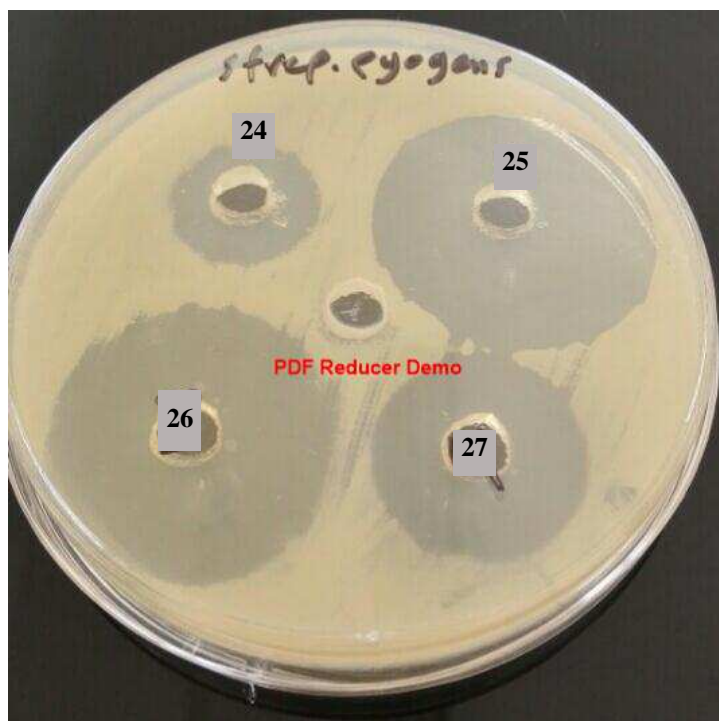


Figure (4-2): The antibacterial activity of compounds [24a, 25a, 26a and 27a] against *Streptococcus pyogenes*

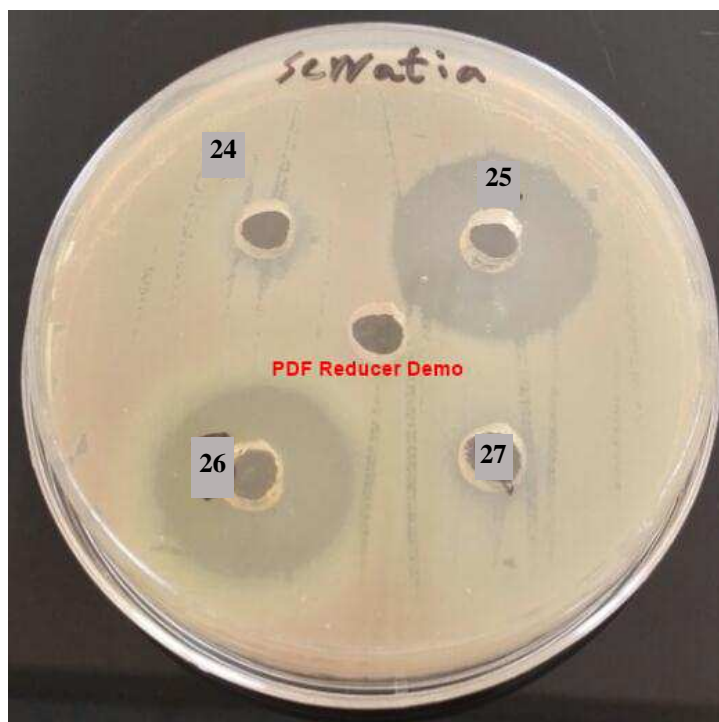


Figure (4-3): The antibacterial activity of compounds [24a, 25a, 26a and 27a] against *Serratia marcescens*

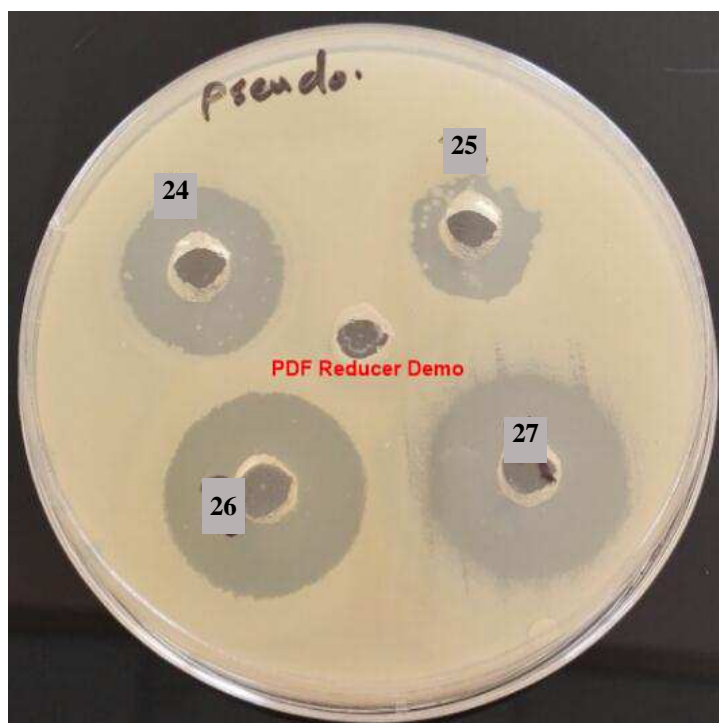


Figure (4-4): The antibacterial activity of compounds [24a, 25a, 26a and 27a] against *Pseudomonas aeruginosa*



Figure (4-5): The antibacterial activity of compounds [10a, 11a, 12a, 13a, 14a, 15a, 16a, 17a, 32a, 33a, 34a and 35a] against *Pseudomonas aeruginosa*

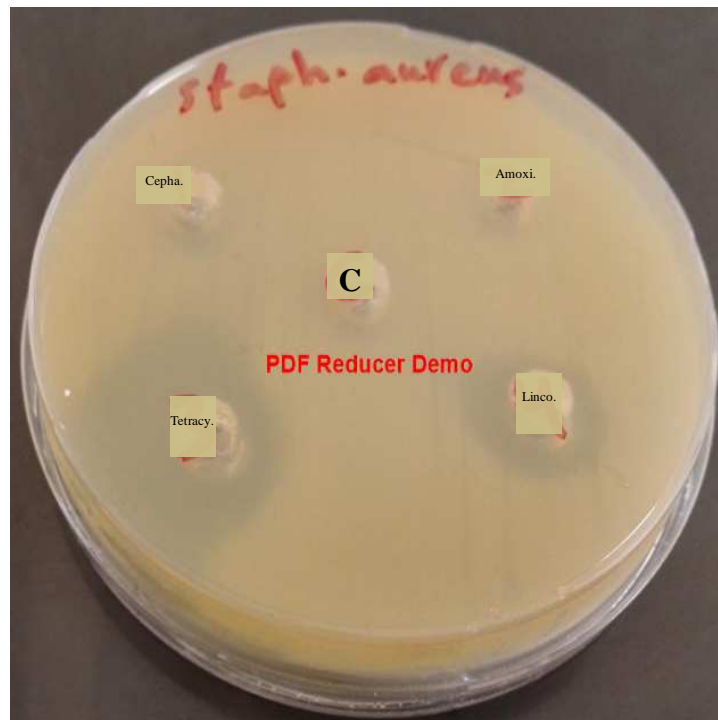


Figure (4-6): The antibacterial activity of antibiotics drugs against *Staphylococcus aureus*

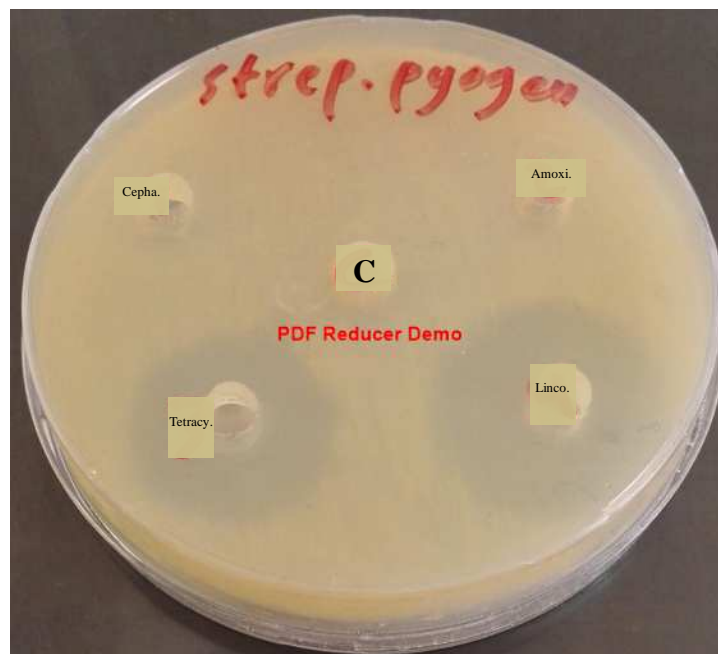


Figure (4-7): The antibacterial activity of antibiotics drugs against *Streptococcus pyogenes*

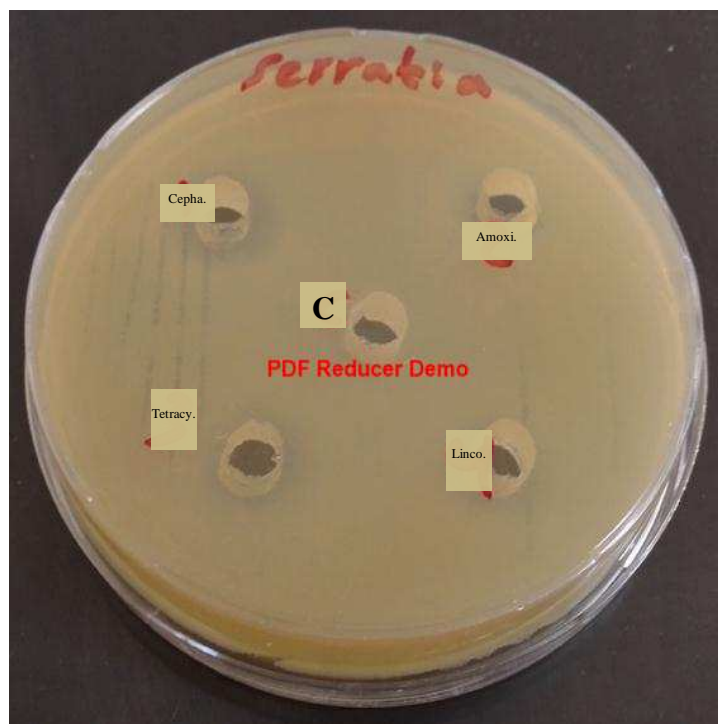


Figure (4-8): The antibacterial activity of antibiotics drugs against *Serratia marcescens*

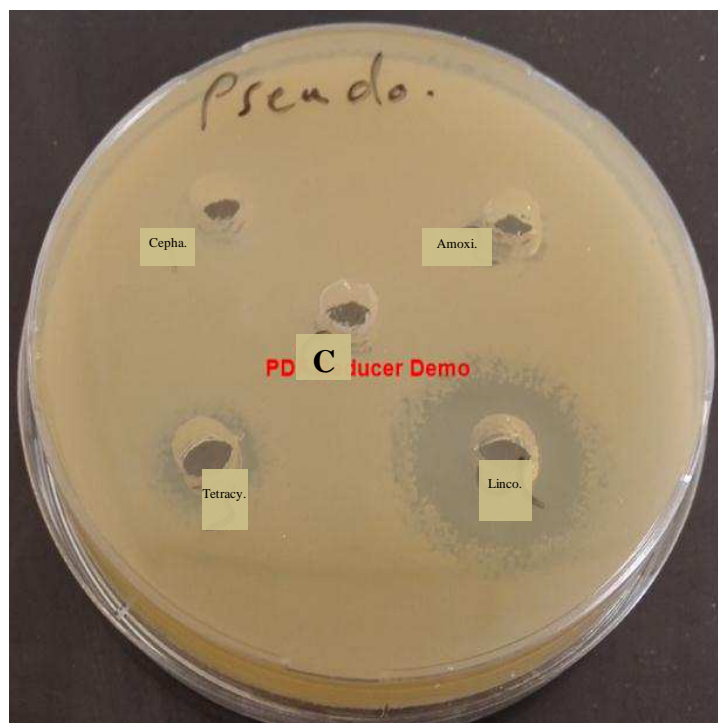


Figure (4-9): The antibacterial activity of antibiotics drugs against *Pseudomonas aeruginosa*

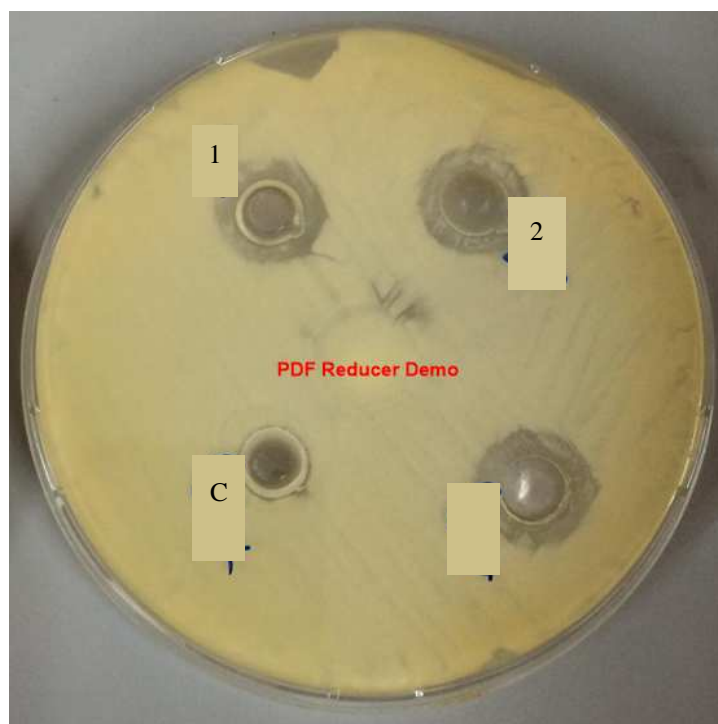


Figure (4-10): The antifungal activity of compounds [1a] and [2a] against *Candida albicans*

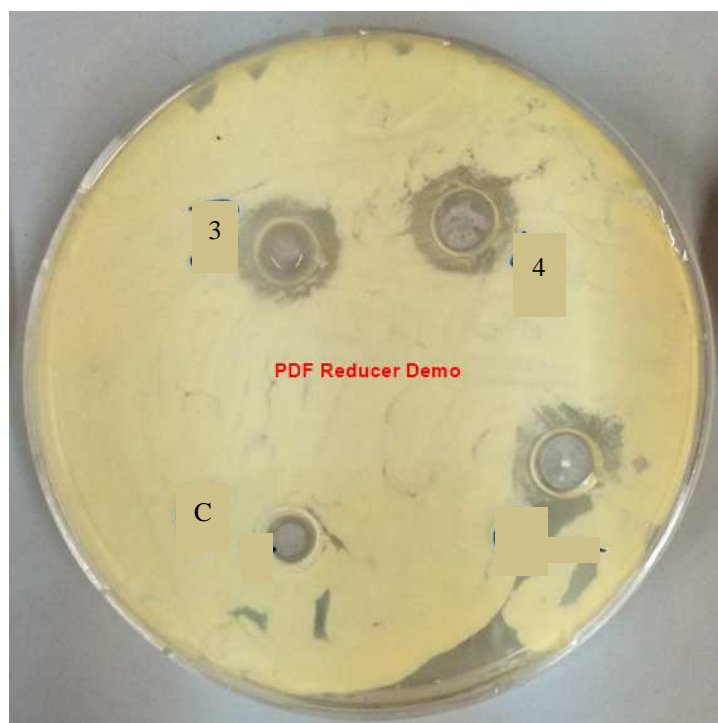


Figure (4-11): The antifungal activity of compounds [3a] and [4a] against *Candida albicans*

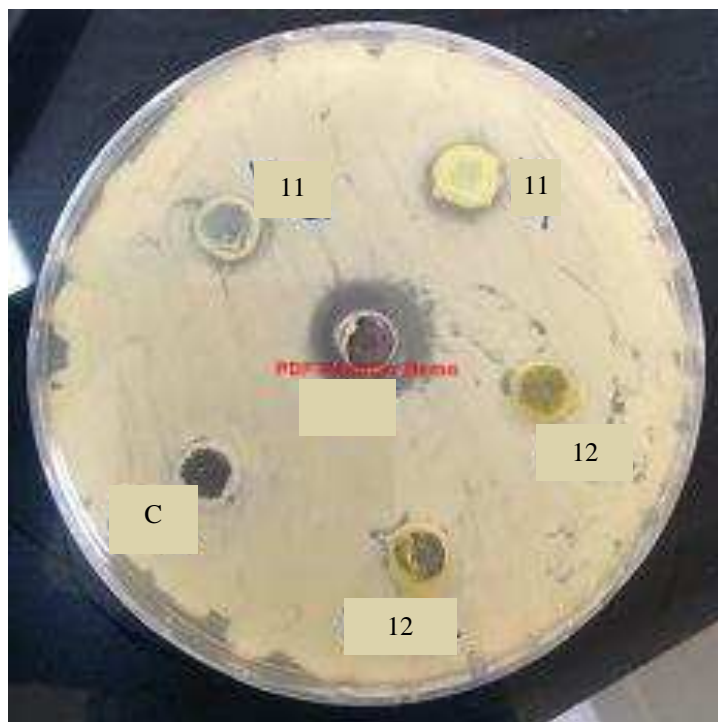


Figure (4-12): The antifungal activity of compounds [11a] and [12a] against *Candida albicans*

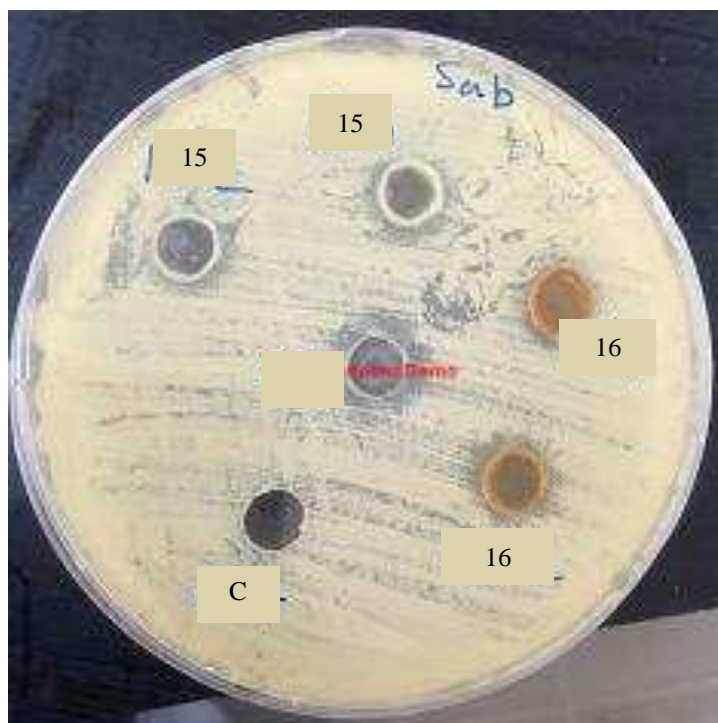


Figure (4-13): The antifungal activity of compounds [15a] and [16a] against *Candida albicans*

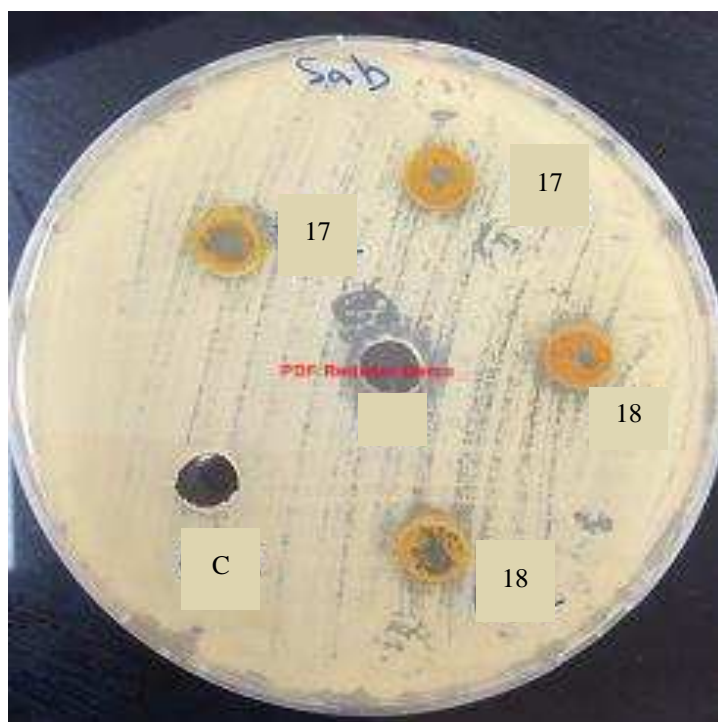


Figure (4-14): The antifungal activity of compounds [17a] and [18a] against *Candida albicans*

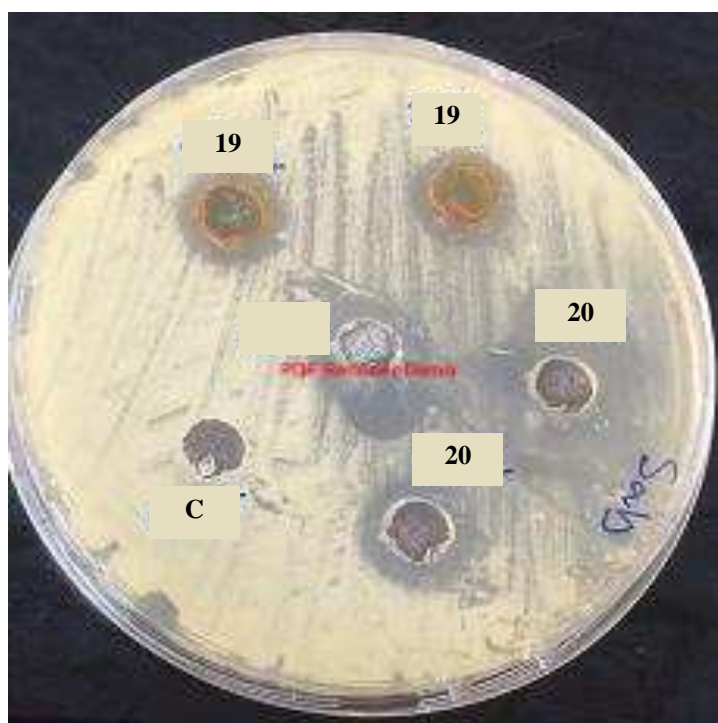


Figure (4-15): The antifungal activity of compounds [19a] and [20a] against *Candida albicans*

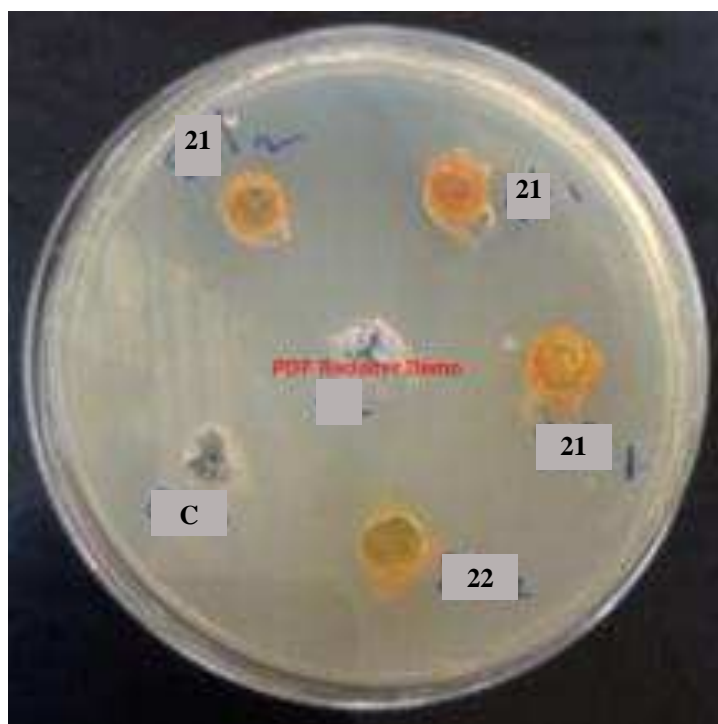


Figure (4-16): The antifungal activity of compounds [21a] and [22a] against *Candida albicans*

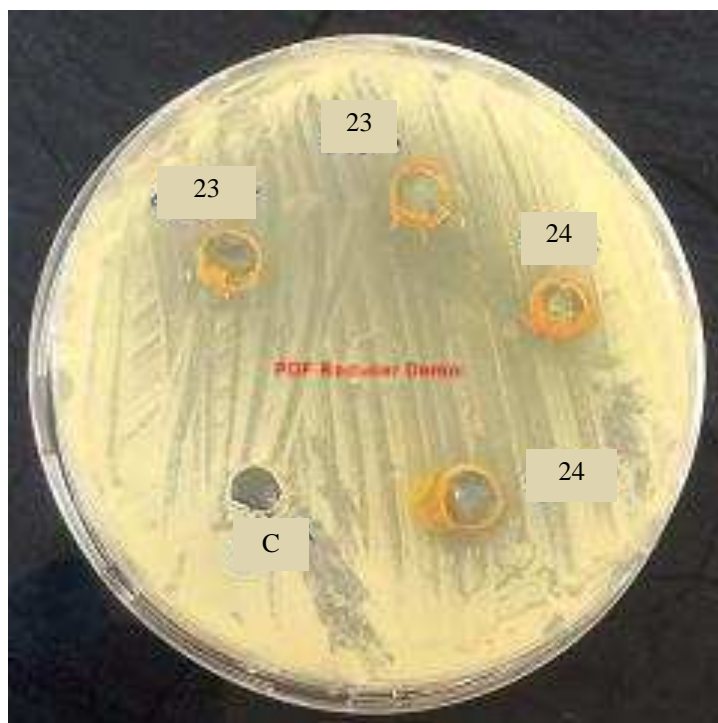


Figure (4-17): The antifungal activity of compounds [23a] and [24a] against *Candida albicans*

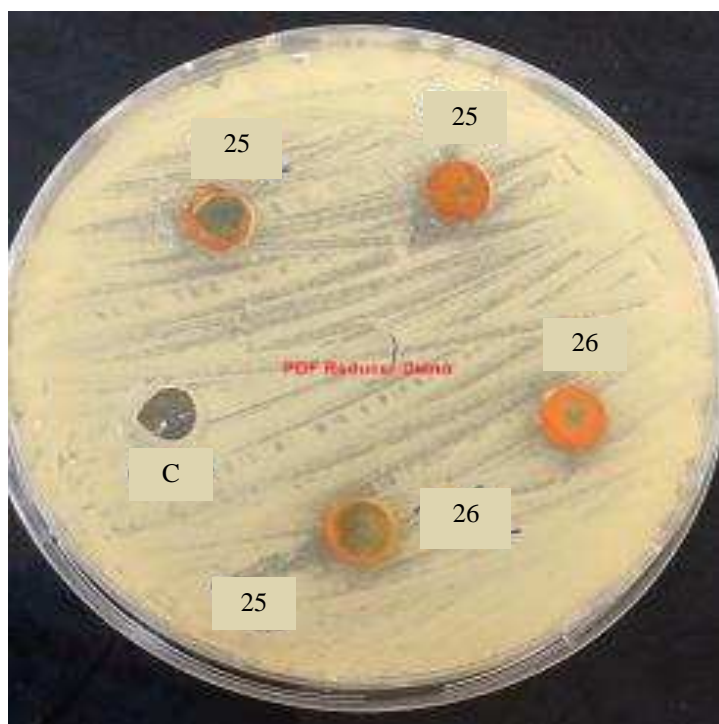


Figure (4-18): The antifungal activity of compounds [25a] and [26a] against *Candida albicans*

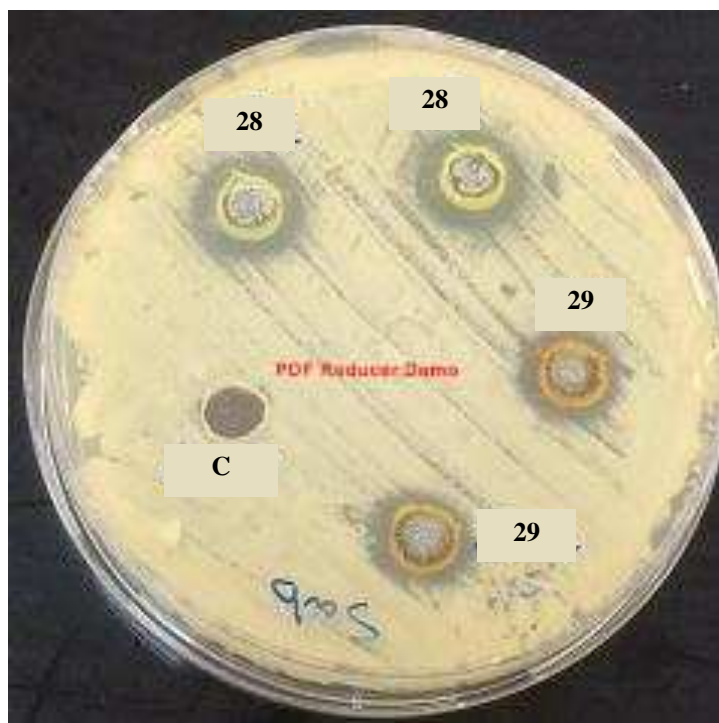


Figure (4-19): The antifungal activity of compounds [28a] and [29a] against *Candida albicans*

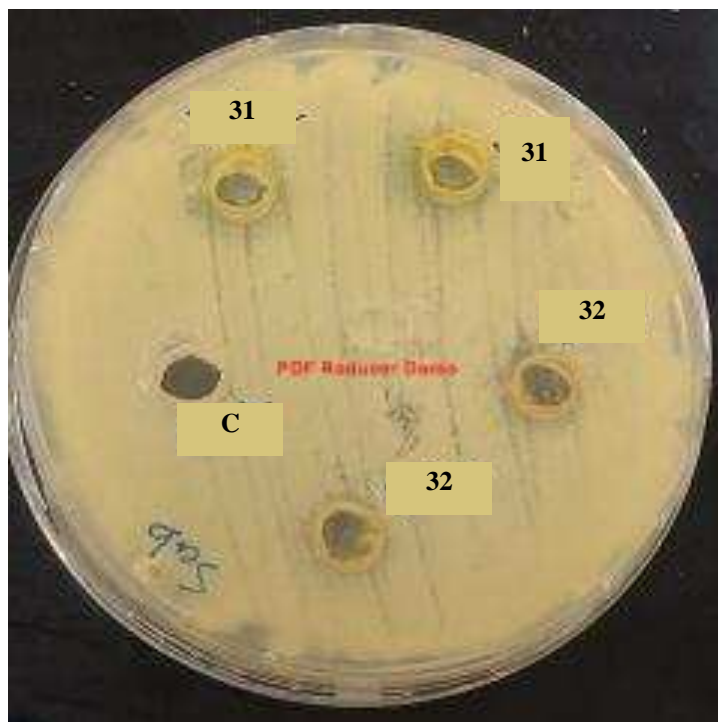


Figure (4-20): The antifungal activity of compounds [31a] and [32a] against *Candida albicans*



Figure (4-21): The antifungal activity of compounds [29a], [30a], [31a] and [32a] against *Candida albicans*



Figure (4-22): The antifungal activity of compounds [33a], [34a], [35a] and [36a] against *Candida albicans*



Figure (4-23): The antifungal activity of compounds [38a], [39a], [40a] and [41a] against *Candida albicans*



Figure (4-24): The antifungal activity of compounds [42a], [43a], [44a] and [45a] against *Candida albicans*



Figure (4-25): The antifungal activity of drug (Nystatine) against *Candida albicans*



Figure (4-26): The antifungal activity of drug (Fluconazole) against *Candida albicans*

Conclusions:

Because of importance of pyrimidine and its derivatives in the field of antimicrobial studies.

- I- We design synthesis of some pyrimidine derivatives containing some biological active groups at positions 2,4 and 6 of pyrimidine ring, like 4(benzenesulphonamido)-phenyl, 4-uriedophenyl, 4[*p*(N-methylamino)phenylazo]phenyl, *p*,N-phthalimidophenyl, *p*(N-phthalimido)benzamido-N'-phenyl, 6(*p*-chloro)phenyl, 6(*p*-nitro)phenyl and 2(oxo), 2(imino), 2(thioxo).
- II- Antimicrobial examination study of those synthesized pyrimidine derivatives, showed good extension 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) bacteria (*Serratia marcescens*, *pseudomonas aeruginosa*); (Gram+Ve) bacteria (*Staphylococcus aureus*, *Streptococcus pygense*) and *candida albicans* fungi.

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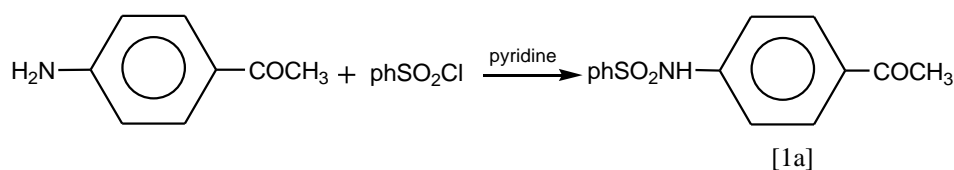
الخلاصة

الكثير من العلماء اهتموا بتحضير البريميدينات ودراسة فعاليتها البيولوجية، والصيدلانية. لهذا السبب في هذا البحث قمنا بتصميم وتحضير مركبات تحتوي على وحدة البريميدينات والتي تحتوي على بعض المجاميع الفعالة بايولوجياً في مواقع ٢، ٤ و٦ من اجل زيادة التوسع في تأثير الفعالية البيولوجية، مثل بارا-بنزين سلفون أميدو فنيل، بارا-يوريدو فنيل بارا-(ن-ميثيل أمينو) فنيل آزوميثيل، بارا،ن-فيثالاميدو فنيل وبارا(ن-فيثالاميدون)بنزميدون-فنيل في موقع ٤، بارا-كلوروفنيل وبارا-نايترو-فنيل في موقع ٦، ومجاميع أوكسو، إمينو، ثايوكسو في موقع ٢.

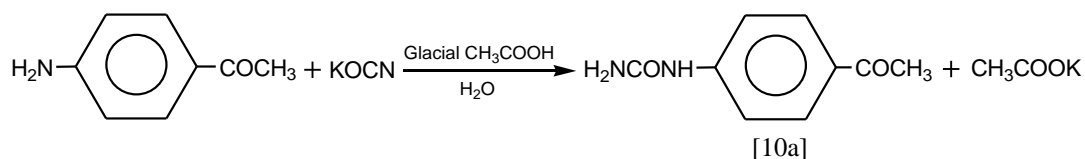
لأجل بناء مثل هذه المشتقات للبريميدينات تتطلب خطوات التي تتضمن:

١- تحضير لـ:

أ- بارا-اسيتايل فينايل بنزين سلفون أميد [1a]، من تكاثف البنزين سلفونيل كلورايد مع بارا-امينواسيتوفينون بوجود البريدين.

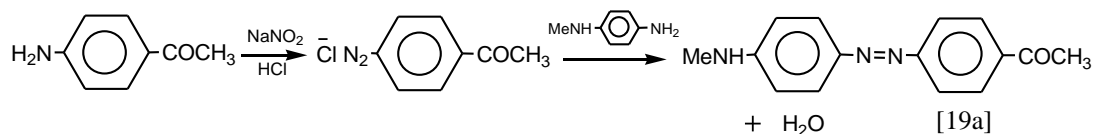


ب- بارا-اسيتايل فنيل يوريا [10a]، من تفاعل سيانات الصوديوم مع بارا-امينواسيتوفينون في محلول مائي يحتوي حامض الخليك.

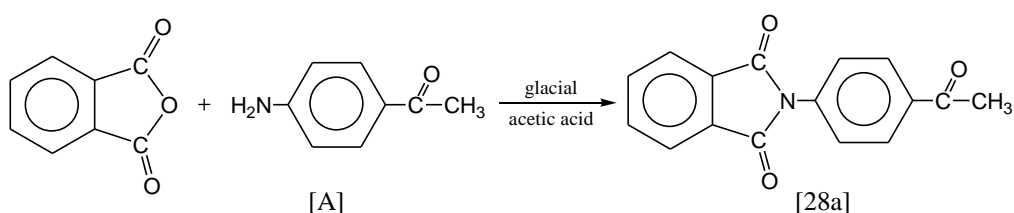


ج- بارا-استيل بارا(ن-أمينومثيل) أزوبنزين [19a]، من تفاعل (الديازونيوم) لبارا-امينواسيتوفينون مع نترت الصوديوم بوجود حامض الهيدروكلوريك المركز

للحصول على ملح بارا-اسيتايل فينيل ديازونيوم، الذي فُوعِل بازدواج مع بارا-
(ن-أمينومثيل) انيلين.

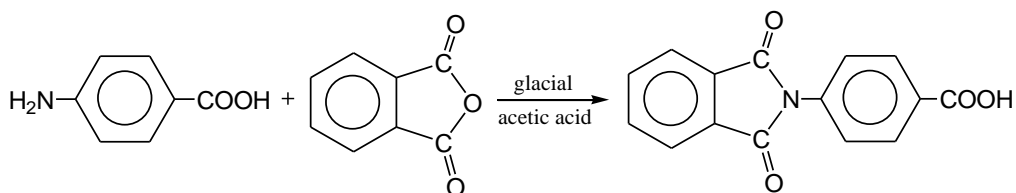


د-ن (٤-استيل) فنيل فيثاليميديد [28a]، من تفاعل بارا أمينو اسيتوفينون مع انهديرد
الفيثاليك بوجود حامض الخليك الثلجي.

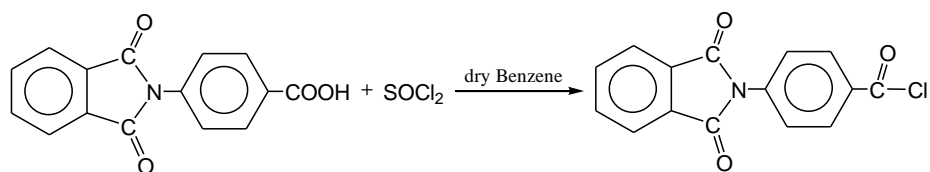


ه-ن (٤-استيل فنيل) بارا (ن-فيثالاميدو) بنزمايد [37a] هذا المركب حُضر بثلاثة
خطوات:

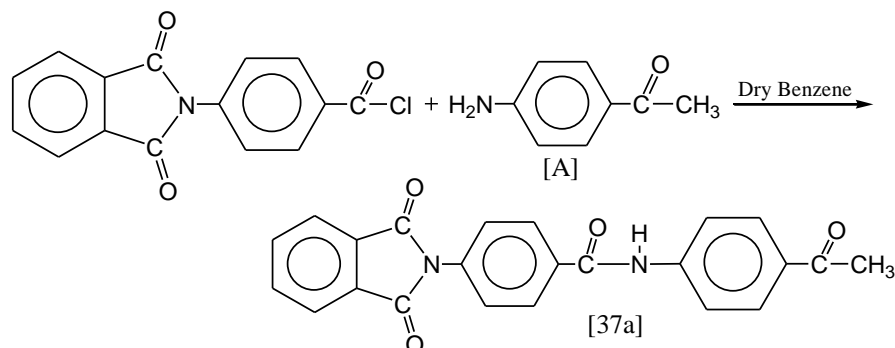
الخطوة I: تحضير المركب ٤ (ن-فيثالاميدو بنزويك أسد، من تفاعل انهديرد
الفيثاليك مع بارا- أمينو بنزويك أسد بوجود حامض الخليك الثلجي.



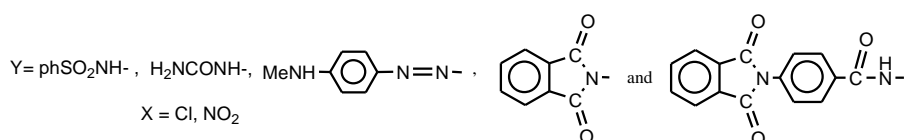
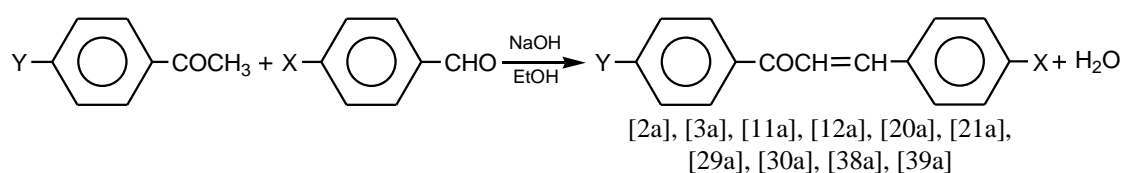
الخطوة II: تحضير المركب ٤ (ن-فيثالاميدو بينزوايل كلورايد)، من تفاعل
المركب ٤ (ن-فيثالاميدو بنزويك أسد) مع كلوريد الثايوتيل بوجود بنزين مجفف.



الخطوة III: تحضير المركب ٤ (٤-استيل فنيل أميدو) فنيل فيثاليميد [37a]، من تفاعل المركب ٤ (ن-فيثالاميدو بينزوايل كلورايد) مع بارا أمينو اسيتو فينون بوجود بنزين مجفف.



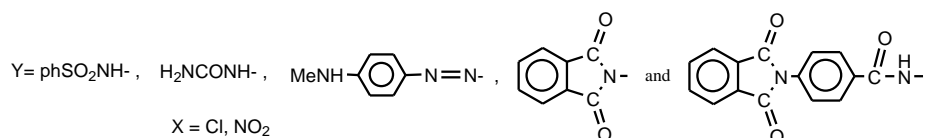
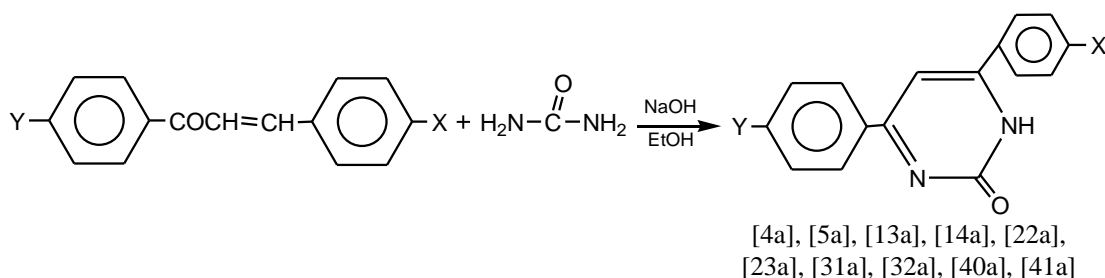
٢- تفاعل تحضير الجالكونات، تتضمن تكاثف متساوي النسب المولية للمركبات [1a]، [10a]، [19a]، [28a] و [37a] مع بارا-كلوروبنزولديهايد وبارا-نايتروبنزولديهايد بوجود هيدروكسيد الصوديوم للحصول على مركبات (بارا-معوض-١-٣-داي أريل بروبين-٢-١-ون) [2a]، [3a]، [11a]، [12a]، [20a]، [21a]، [29a]، [30a]، [38a] و [39a] من خلال المعادلة الآتية:



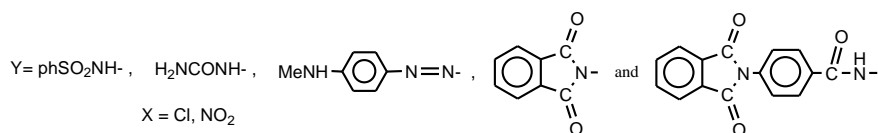
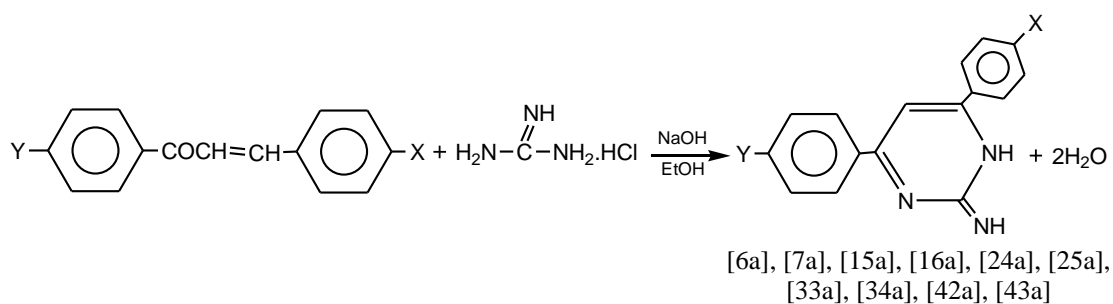
٣- تحضير البريميدينات المعوضة في موقع ٢، ٤ و ٦

أ- من تكثيف المواد المتساوية في النسب المولية من الجالكونات [2a]، [3a]، [11a]، [12a]، [20a]، [21a]، [29a]، [30a]، [38a] و [39a] مع اليوريا بوجود هيدروكسيد الصوديوم لاعطاء ٤ (بارا-معوض) مثيل-٦ (بارا-معوض) فنيل-٢-

او كسو (١ بروتون) البريميدينات [4a], [5a], [13a], [14a], [22a], [23a], [31a], [32a], [40a] و [41a].

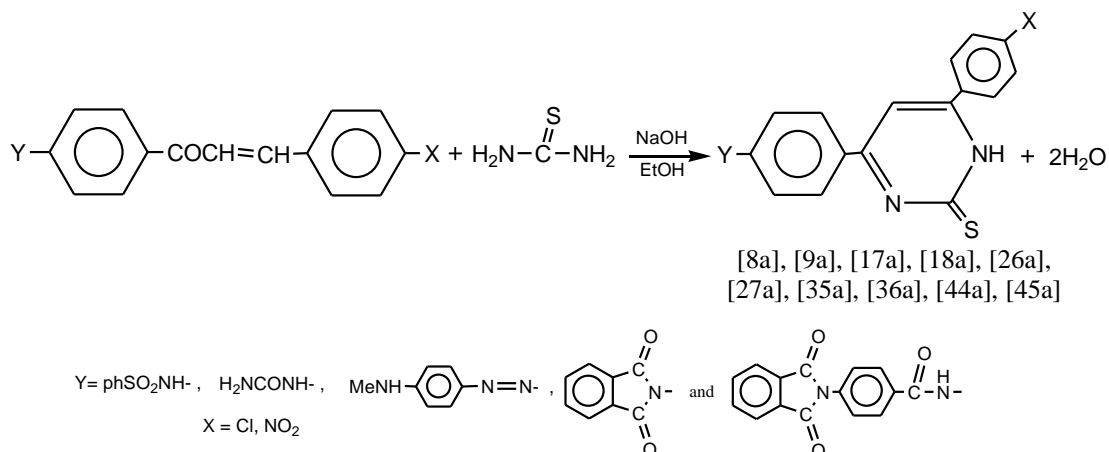


ب- عند التكتيف المتساوي في النسب المولية من تفاعل الجالوكونات [2a], [3a], [11a], [12a], [20a], [21a], [29a], [30a], [38a] و [39a] مع مركب هايدروكلوريد الكواندين بوجود القاعدة هيدروكسيد الصوديوم بنسبة مولية مضاعفة لاعطاء المركبات ٤ (بارا-معوض) فينيل-٦- (بارا-معوض) فينيل-٢- إمينو (١ بروتون) البريميدينات [6a], [7a], [15a], [16a], [24a], [25a], [33a], [34a], [42a] و [43a].



ج- من تكتيف المواد المتساوية في النسب المولية للجالوكونات [2a], [3a], [11a], [12a], [20a], [21a], [29a], [30a], [38a] و [39a] مع الثايوبوريا بوجود القاعدة هيدروكسيد الصوديوم، لاعطاء المركبات ٤ (بارا-معوض) فينيل-٦- (بارا-معوض) فينيل-

معووض) فينيل-٢-ثايوكسو (١ بروتون) البريميدينات [8a]، [8a]، [17a]، [18a]، [26a]، [27a]، [35a]، [36a]، [44a] و [45a].



لقد تم تشخيص جميع المركبات الجديدة من [1a-45a] بواسطة التقنيات الفيزيائية الطيفية مثل (الاشعة تحت الحمراء، الرنين النووي المغناطيسي للبروتون 1، الرنين النووي المغناطيسي للكربون 13 وقياس الطيف الكتلي).

لقد تم دراسة الفعالية المايكروبية لجميع المركبات المحضرة [1a-45a] والبارامينواسيتوفينون ضد اصناف البكتريا (الكرام- سالب) والتي هي (سيرشا مارسنس وبسيدومونس أرنوزا) والبكتريا (الكرام- موجب) والتي هي (ستافيلوكوكس أوربوس وستربتوكوكس بايوجينس) ومع الفطر (كانددا اليكانس) بالمقارنة مع المضادات المايكروبية والتي تعرف الانتيبايك الصيدلاني مثل سيفالكيس، اموكسلين، تتراسايكلين و لنكوميسين ومضادات الفطريات مثل النستاتين وفلوكانزول، وهذه الدراسة اعطت النتائج التالية:

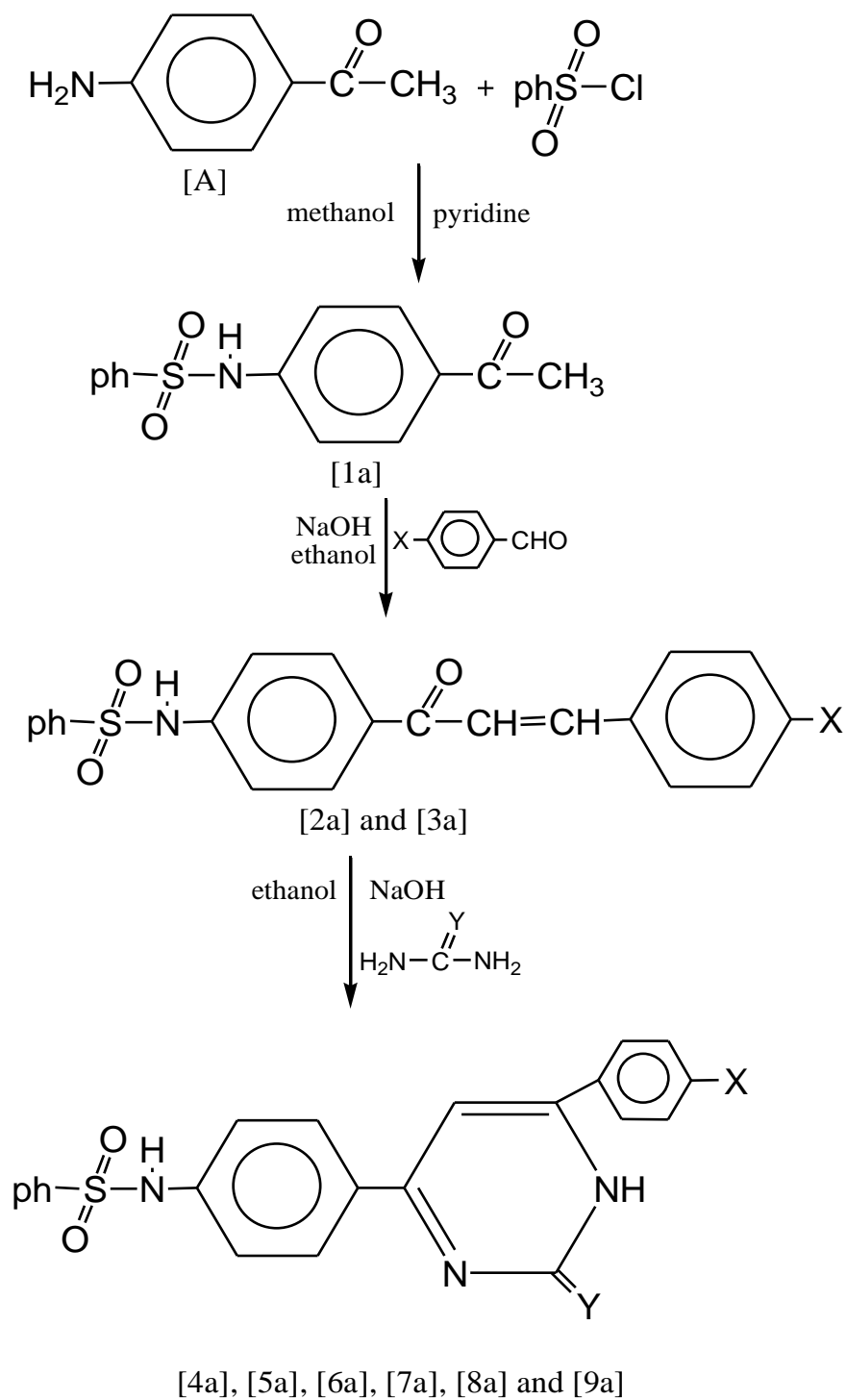
أولاً: مركبات الاسيتوفينون المعوضة المحضرة والتي هي [1a]، [10a]، [19a]، [28a] و [37a] والبارامينواسيتوفينون، أظهرت فعالية حيوية جيدة ضد البكتريا (الكرام- سالب) (سيرشيا مارسنس وبسيدومونس ارنوزا) افضل بالمقارنة مع

الادوية الانتيبايوتك المستخدمة وحسب التصنيف الآتي [10a] < [1a] < [19a] < (بارالامينو استيوفينون) < [28a]، [37a].

ثانياً: الجالكونات المحضرة اعطت فعالية حيوية أفضل من الادوية الانتيبايوتك المستخدمة، مع زيادة قليلة بالتأثير من مركبات الاسيتوفينون المعوضة، فكانت تأثيرها على البكتريا (الكرام- سالب) وهي (سيرشيا مارسنس وبسيديمونس ارجنوزا) وحسب التصنيف الآتي: [11a]، [29a]، [38a] < [2a]، [20a]، ولكن في حالة الجالكون [21a] والذي يحتوي مجموعة الناييترو، شهد له تأثير أفضل من المركبات المحضرة من نفس مجموعة الناييترو.

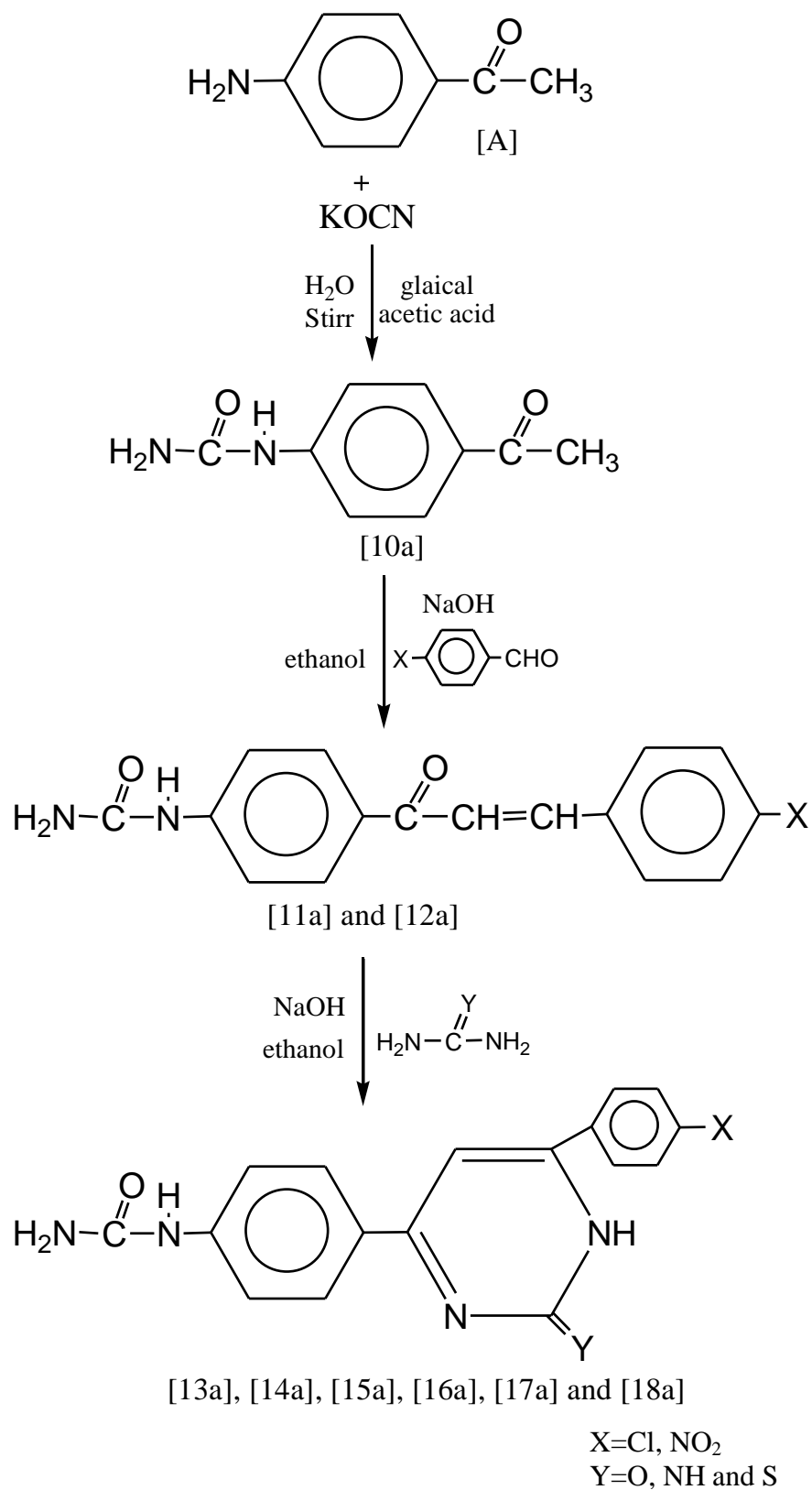
ثالثاً: جميع البريميدينات المحضرة [4a]، [5a]، [6a]، [7a]، [8a]، [9a]، [13a]، [14a]، [15a]، [16a]، [17a]، [18a]، [22a]، [23a]، [24a]، [25a]، [26a]، [27a]، [31a]، [32a]، [33a]، [34a]، [35a]، [36a]، [40a]، [41a]، [42a]، [43a]، [44a] و [45a]. شهدت لها فعالية حيوية جيدة وأفضل من المضادات الحيوية المستعملة في هذه الدراسة، خصوصاً البريميدينات التي تحتوي على مجاميع الثايوكسو والإمينو في موقع ٢.

رابعاً: جميع المركبات المحضرة، مشتقات الاسيتوفينون المعوضة في موقع بارا، الجالكونات والبريميدينات التي هي من [1a-45a]، شهدت تأثير تثبيط جيد جداً ضد الفطر كانددا البيكانس، خصوصاً الجالكون [21a] والبريميدين [22a] والتي تحتوي على مجموعة الازو.

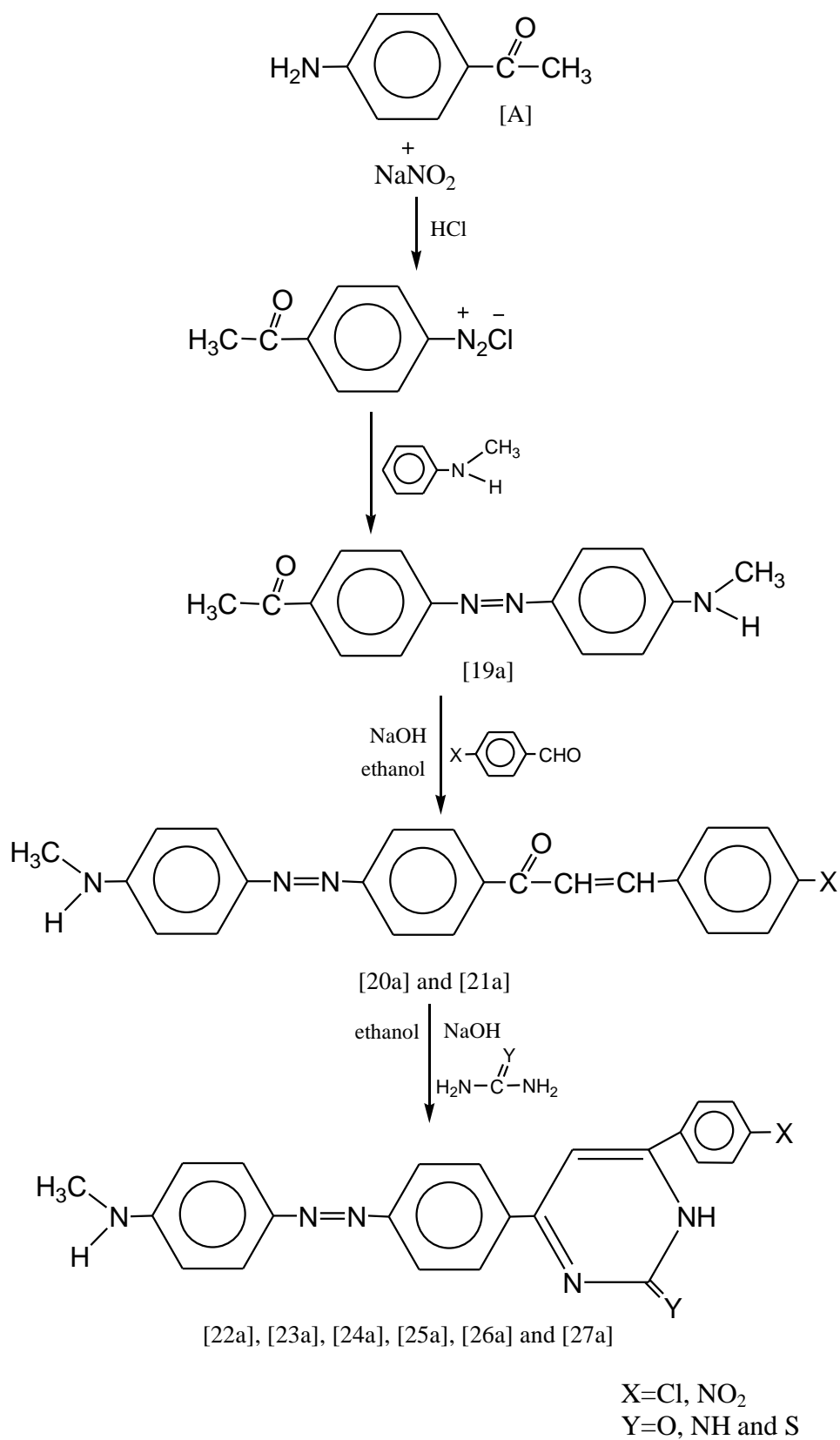


X=Cl, NO₂
 Y=O, NH and S

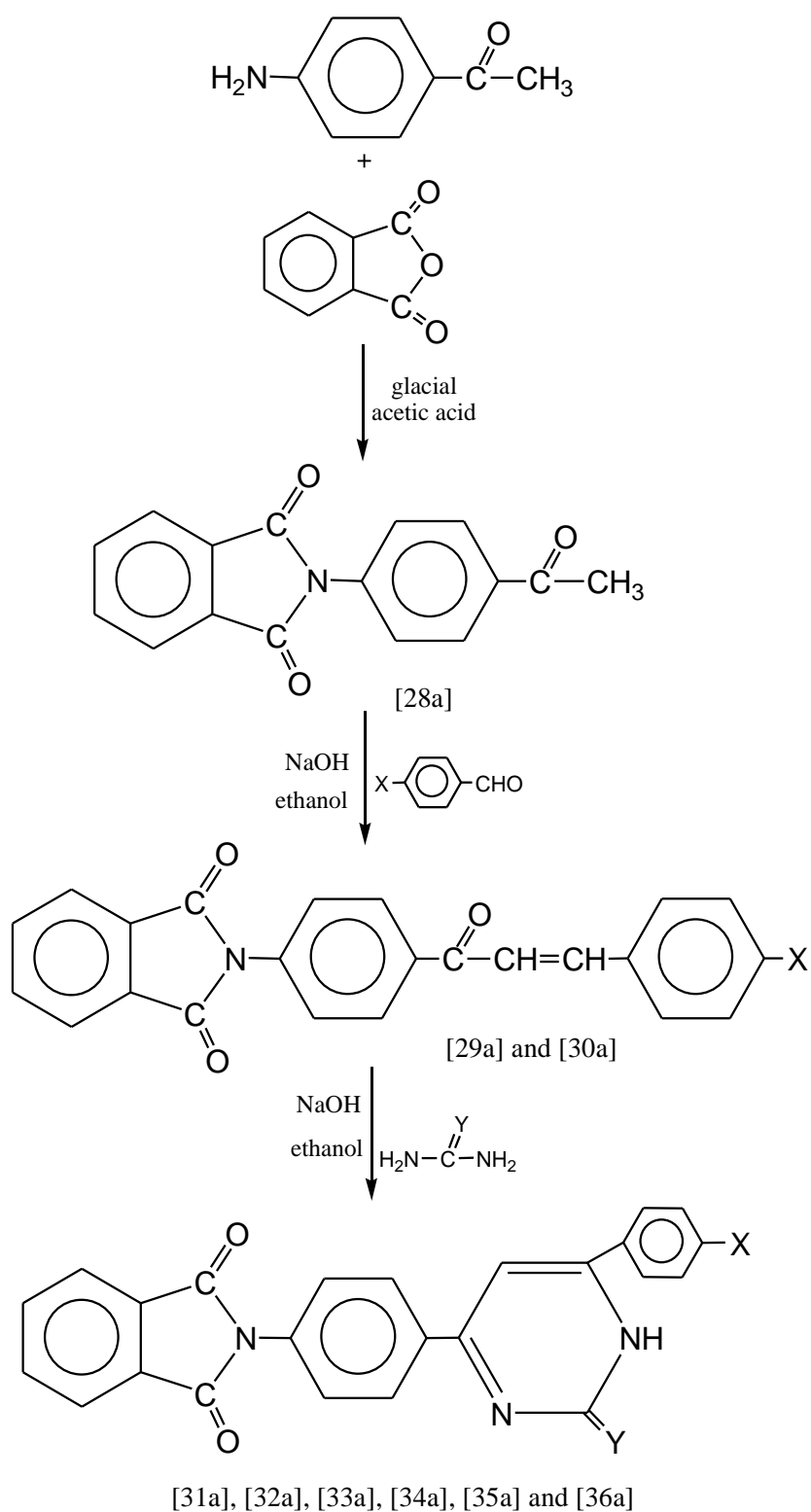
مخطط (١) تفاعلات السلسلة الأولى



مخطط (٢) تفاعلات السلسلة الثانية

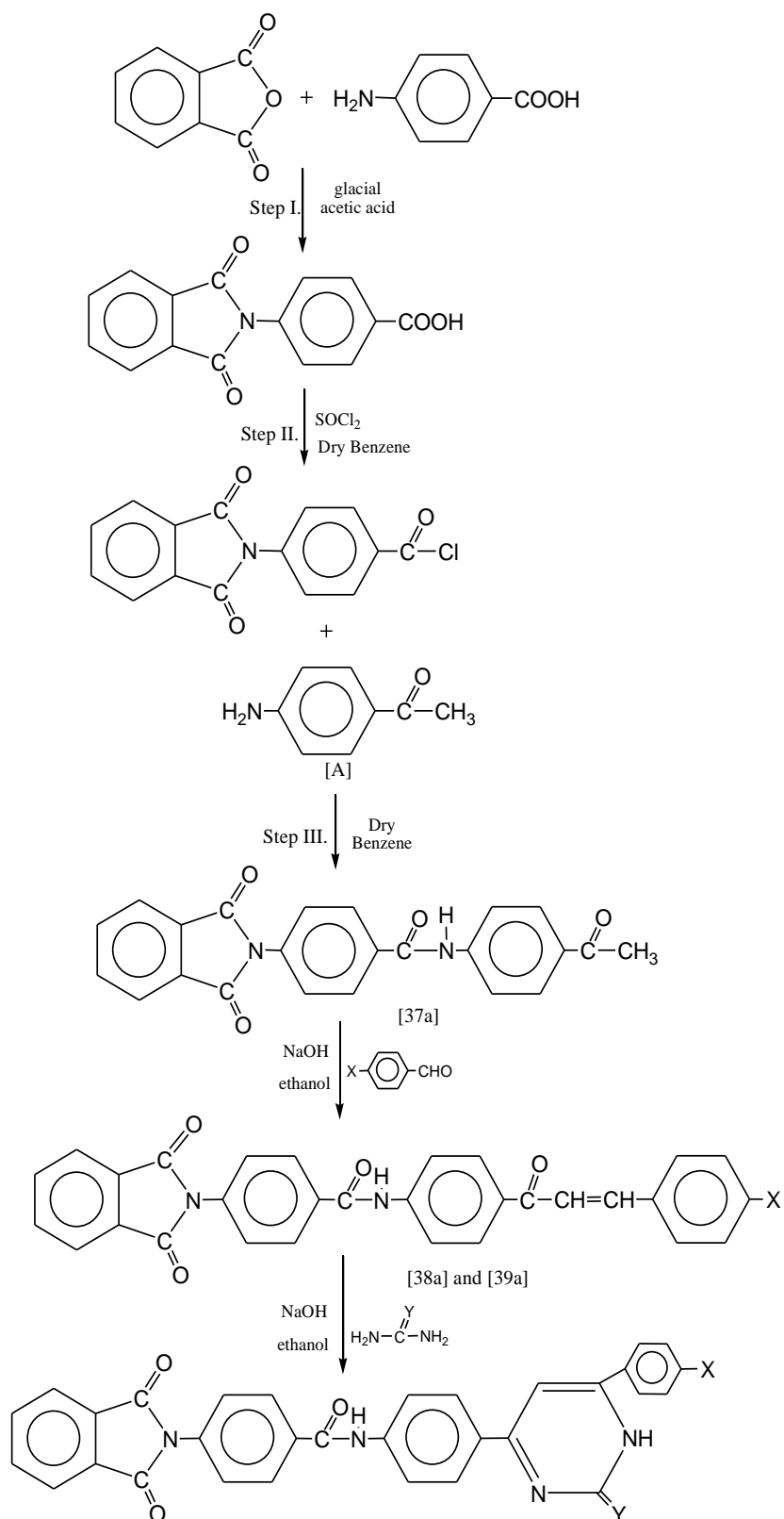


مخطط (٣) تفاعلات السلسلة الثالثة



$X = \text{Cl}, \text{NO}_2$
 $Y = \text{O}, \text{NH}$ and

مخطط (٤) تفاعلات السلسلة الرابعة



[40a], [41a], [42a], [43a], [44a] and [45a]

X=Cl, NO_2

Y=O, NH and

مخطط (٥) تفاعلات السلسلة الخامسة



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

تحضير وتشخيص وقياس تأثير الفعالية الحيوية لمشتقات الجالكون والبريميدين الجديدة المعوضة في المواقع ٢ ، ٤ ، ٦

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

إسراء شكيب عبد الرزاق القاضي

بكلوريوس علوم كيمياء- ٢٠٠١- جامعة بغداد

ماجستير علوم كيمياء- ٢٠٠٥- جامعة بغداد

بإشراف

أ.م.د. علي حمادي سمير

٢٠١٧م

أ.م.د. زكريا هادي أيوب

١٤٣٨هـ