Sudan University of Sciences and Technology

College of Graduate Studies

Synthesis of Some Biginelli Compounds from Thiosemicarbazide, Urea and Thiourea

تخليق بعض مركبات البكنلي من الثايوسيميكارباذايد واليوريا الثايويوريا

By:

Hind Abderhman Elmusharaf Mucktar

(B.Sc. Chemistry, M.Sc. Chemistry)

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Supervisor:

Prof. Dr. Ahmed Elsadig Mohammed Saeed

Co. supervisor

Dr. Izeldin. E. Barakat

2015

Dedication

My family

My brothers

My sisters

Acknowledgment

I would like to express my deepest thanks and gratitude to Prof. Dr. Ahmed Elsadig Mohammed Saeed for his valuable guidance and continuous supervision to finish this work. I would like to thank the head department of Chemistry at Faculty of Science Khartoum University Dr. Ali Ahmed Ibrahim for giving me the opportunity to work at their laboratories and run IR and UV- analysis at the central laboratory in university Khartoum. And I would like to thank Dr. Mohammed Refaat Faculty of Pharmacy at University Ain shamss in Egypt for helping me to run ^{1}H NMR and ^{13}C NMR analysis

Abstract

Synthesis of some 1-amino-5-acetyl-6-methyl-4-aryl-3,4-dihydropyrimidine -2-thione and 1-amino arylmethylidiene -5- acetyl -6- methyl -4-aryl-3,4-dihydropyrimidine-2-thione, from reaction of acetyl acetone, thiosemicarbazide and aldehyde was achieved. Synthesis of some 1-amino-5-ethoxycarbonyl-6-methyl-4-aryl-3,4-dihydropyrimidine-2-thione and 1-amino arylmethylidiene-5-ethoxycarbonyl -6-methyl- 4-aryl- 3,4-dihydropyrimidine-2-thione was accomplished by reaction of ethyl acetoacetate, thiosemicarbazide and aldehyde. The reaction was carried out in presence of $ZnCl_2$ as catalyst. Synthesis of 5-acetyl-6-methyl-4-aryl-3,4-dihydropyrimidine-2-one, 5-acetyl-6-methyl-4-aryl-3,4-dihydropyrimidine-2-thione, 5-ethoxycarbonyl-6-methyl -4- aryl -3,4- dihydro pyrimidine-2-one and 5- ethoxycarbonyl-6-methyl-4-aryl-3,4- dihydro pyrimidine-2-thione the reaction was accomplished without catalyst. The reaction progress was followed by TLC analysis and the chemical structure confirmed by spectroscopic analysis (UV, IR, ^{1}HNMR, ^{13}CNMR and MS)

الملخص

تخليق بعض مركبات ١-امينو-٥- استايل -٦- ميثايل-٤- ارايل-٣و٤- ثناي هيدروبيرميدين -٢-ثايون و ١- امينواريل ميثايليدين-٥-استايل-٦-ميثايل-٤-اريل-٣و٤- ثناي هيدروبيرميدين-٢-ثايون من تفاعل استايل استون وثايوسميكارباز ايد و الدهيد و تخليق بعض ١- امينو-٥-اثوكسيكاربونايل-٦- ميثايل-٤- اريل-٣و٤- ثناي هيدروبيرميدين-٢-ثايون و ١-امينو ارايل مثايلدين-٥-اثوكسيكاربونايل-٦-ميثايل-٤-اريل-٣و٤-ثناي هيدروبيرميدين-٢-ثايون مصحوب بتفاعل اثايل اسيتواستيت و ثايوسميكارباز ايد و الدهيد التفاعل تم في وجود كلوريد الزنك كمحفز و تخليق مركبات ٥- استايل-٦-ميثايل-٤-ارايل-٣و٤-ثناي هيدروبيرميدين-٢-اون و ٥- استايل-٦-ميثايل-٤-ارايل-٣و٤-ثناي هيدروبيرميدين-٢-ثايون و ٥-اثوكسيكاربونايل -٦-ميثايل-٤-اريل-٣و٤-ثناي هيدروبيرميدين-٢-اون و ٥-اثوكسكاربونيل -٦-ميثايل-٤-اريل-٣و٤- ثناي هيدروبيرميدين-٢-ثايون وتم التفاعل من غير وجود محفز. تقدم التفاعل كان مصحوبا بتحليل الطبقة الرقيقة من الكروماتوكرافية تم تاكيد البنيه الكيميائيه بالتحاليل الطيفية (الاشعة فوق البنفسجيه والاشعة الحمراء و وبرتون الرنين المغناطيسي النووي وكربون ١٣ الرنين المغناطيسي النووي واطياف الكتلة)٠

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List of Abbreviation

Room temperature	r.t
Multicomponent reactions	MCRs
Proton nuclear magnetic resonance	^{1}HNMR
Carbon thirteen nuclear magnetic resonance.	^{13}CNMR
Ethanol	EtOH
Dihydropyrimidine-2-(H)-one	DHPM
Chiral ionic liquid	CIL
Di methyl furan	DMF
Melting point	m.p
Chemical shift	δ
Thin layer chromatography	TLC
Ultra violet	UV
Infrared	IR
Nanometer	nm
Parts per million	ppm
Fluorescence 254	F_{254}
Mill liter	ml
Mole	ml
Centimeter	cm
Mega hertz	MHz

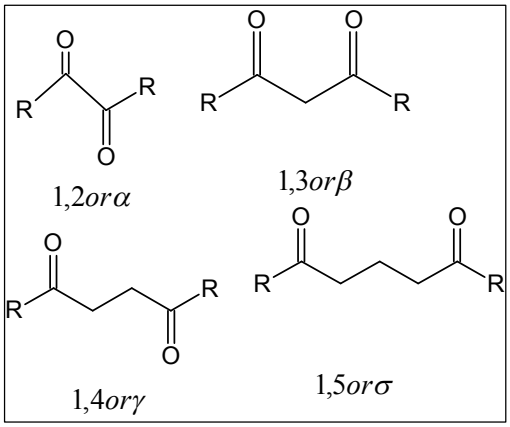
Gram	gm
Tetra methyl silane	TMS
Dimethyl sulfoxide	DMSO

Chapter One

1.Introduction

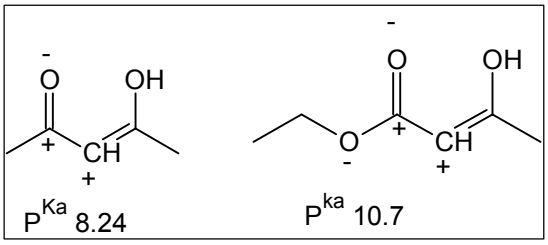
1.1. Dicarbonyl Compounds

The compounds described as dicarbonyl are diketones, keto acids and keto esters, the relative location of two carbonyl group in the carbon chain are designated numerically or by letter Greek alphabet, the alkyl group may be the same or different, the formula are below represent ketoaldehyde and dialdehydes when one or both of the residues (R), are hydrogen (Brain *et.al*, 1948)



Scheme .1.1.dicarbonyl compounds

1.2. Acidity of α-H



Scheme . 1.2. acidity of *α*-H

The presence of carbonyl group facilitates the release of proton from α- carbon atom, in case of β-ketoester the oxygen atom which is more electronegative than carbon make this release of proton more stable, so enol form of β-ketoester is more stable than enol form of β-diketone (Finar, 1951)

1.3. The preparation of 1,3-Dicarbonyl

1,3-Dicarbonyl compound preparation is by condensation of two esters or ester and ketone in presence of sodium ethoxide (Brain *et.al*, 1948)

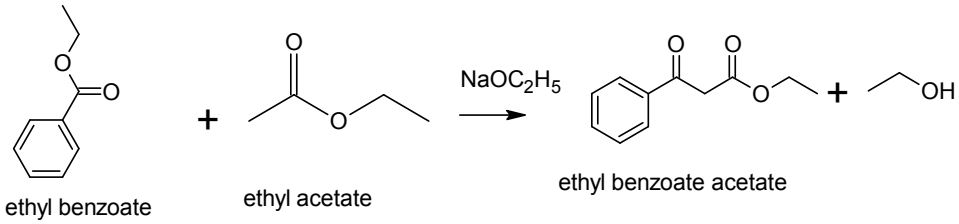


Fig.1.1. two esters Claisen condensation.

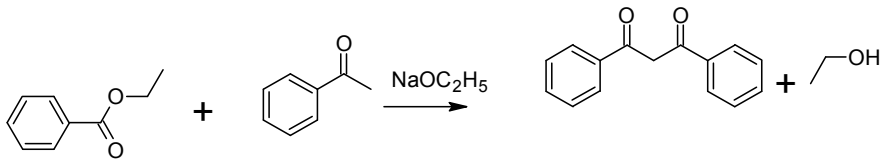


Fig.1.2.ester and ketone , Claisen condensation

Also cyclic dicarbonyl compound can be obtained by condensation of ethyl succinate in the presence of sodium or sodium ethoxide (Finar, 1956)

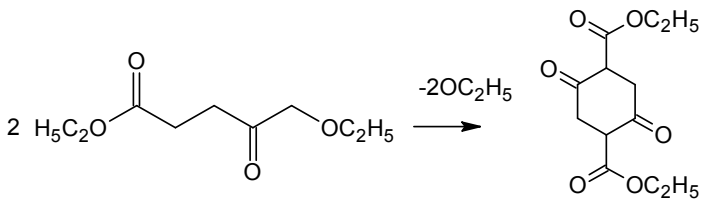


Fig.1.3.succinosuccinic ester.

Benzoylacetone is produced from the reaction of acetophenone with acetic anhydride in the presence of boron trifloride (Durden & Crosby, 1965)

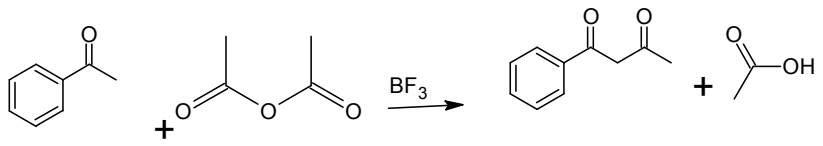


Fig.1.4. synthesis of benzoyl acetone.

Dibenzoyl methane synthesis is from reaction of acetophenone with ethyl benzoate in the presence of sodium ethoxide (Magnani & McElvain, 1938).

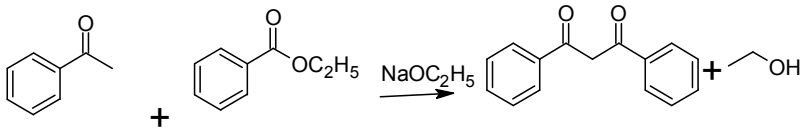


Fig.1.5. synthesis of dibenzoyl methane

1.4. Reaction of 1, 3-Dicarbonyl compounds

1,3-Dicarbonyl compounds react with alkenes and alcohols in the presence of heterogeneous catalyst to give derivative alkanes (Motokura *et.al*, 2006)

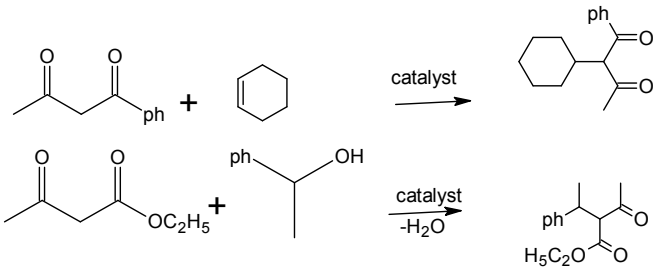


Fig.1.6. addition reaction of 1,3-dicarbonyl compound.

Also 1,3-dicarbonyl compounds react with maleimides in presence of organo cataylic symmetric to give derivative maleimides (Bartoil *et.al*, 2006)

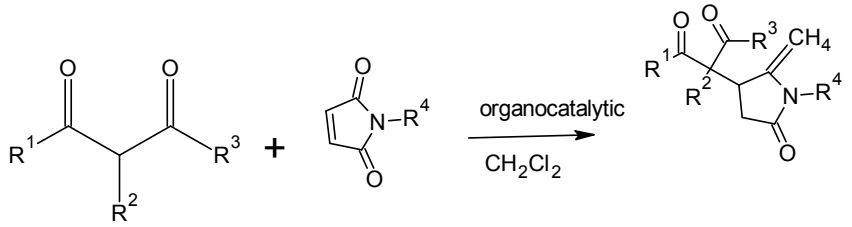


Fig .1.7. organocatalytic catalyzed 1,3-dicarbonyl compound

All the above addition of Michael addition type, Lewis acid catalyzed reaction provided α-halogenation of 1,3-dicarbonyl compound (Yang *et.al*, 2002)

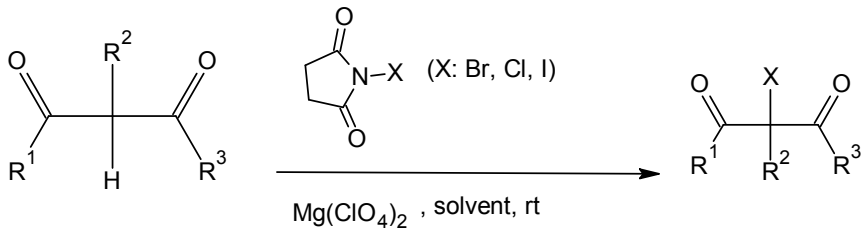


Fig.1.8. α-halogenation of 1,3-dicarbonyl.

The furan can be synthesized from 1,3-dicarbonyl compound, by reaction of propargylic alcohols or acetates with 1,3-dicarbonyl compounds leads to highly substituted furans, use $FeCl_3$ as catalyst (Wen-hua *et.al*, 2008).

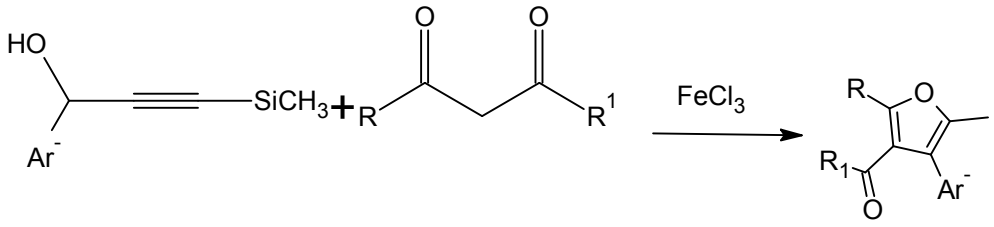


Fig .1.9. synthesis of furan

Or by reaction with nitroolefins, promoted by KOAc (Li *et.al*, 2012)

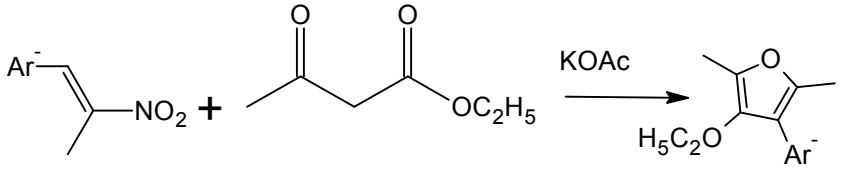


Fig .1.10. reaction with nitroolefins.

1,4-Dihydropyridine is produced from the reaction of acetyl acetone with ammonium acetate and aldehyde (Mathi *et.al*, 2012)

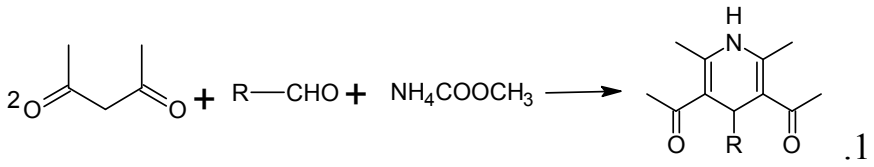


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Fig.1.11. one pot synthesis 1,4-dihydropyridine

1.2. Multicomponent Reactions

Chemical reaction utilizing more than two starting material as the precursors for product formation are usually referred to as multicomponent reactions (MCRs). Three different types of MCRs are distinguished in the literature: Type I when all the participating reactions are reversible: Type Π when the majority of the reactions are reversible but the final product is formed irreversibly: Type ΠI when all the reactions are irreversible. Type I are usually reactions of amines, carbonyl compounds and weak acid all steps of reaction are in equilibrium, the products are generally obtained in low purity and low yield, if one of the substrate is bifunctional compound the reaction is to be type Π MCRs, because of the equilibrium is forced towards the product side such MCRs often give pure products in almost quantitative yield. In case of type ΠI MCRs only a few examples are known in biochemical compound (Tietzer *et al,* 2006).

1.2.1. Biginelli Reaction

Pietro Biginelli who first reported condensation reaction of ethyl acetoacetate, benzaldehyde, and urea promoted by HCl in ethanol solvent at reflux temperature to produce 3,4-dihydropyrimidine-2(H)-one (Kappe, 2000)

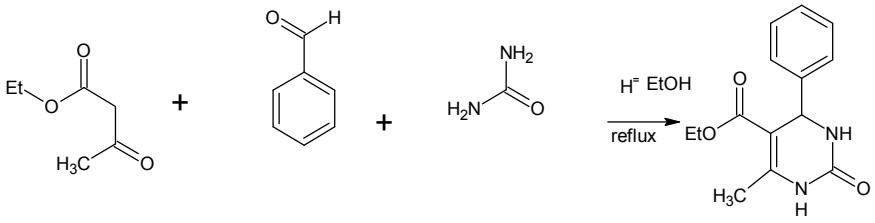


Fig.1 .2.1. Biginelli reaction.

Biginelli reaction involve the condensation of β-ketoester with aromatic aldehyde and urea, but now it extended by variation of all the three precursors compounds to formation a large number of dihydro pyrimidine derivatives (Zhu *et al*,2005)

1.2.2. Mechanism of Biginelli Reaction

For many years the mechanism of the Biginelli reaction had been under study, first Folker and Johnson suggested that the first step of the reaction is condensation of benzaldehyde and urea and it is rate determining step of the reaction (Folker & Johnson, 1933). Second Sweet and Fissekis proposed that the interaction of benzaldehyde and catalyst acid give carbonium ion which reacts with ethyl acetoacetate, is the first step in the reaction (Sweet & Fissekis, 1973). At last the mechanism was reinvestigated using ^{1}H / ^{13}C NMR spectroscopy and trapping experiments and found that the acid- catalyzed of an N-acyliminmium ion intermediate from the aldehyde and urea precursor is the first step of the reaction followed by addition of ethyl acetoacetate in enol form produced open chain uried which cyclized by elimination of water to 3,4-dihydropyrimidine-2-(H)-one, DHPM product (Kappe, 1997)

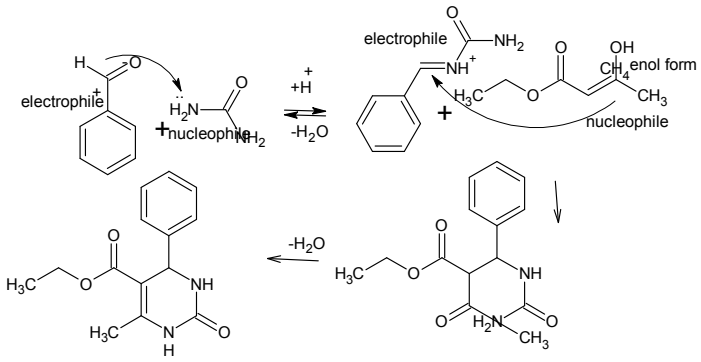


Fig.1. 2.2. mechanism of Biginelli reaction

The "carbonium ion mechanism" is not the major pathway, however, small amounts of enone are sometimes observed as a by product. So this mechanistic formulation, monosubstituted (thio) ureas produce the N1-alkylated DHPMs, where as N,N-disubstituted ureas do not react under reaction conditions. (Yadav *et.al*. 2008)

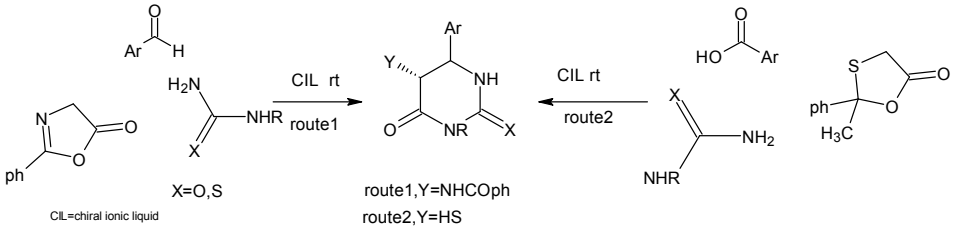
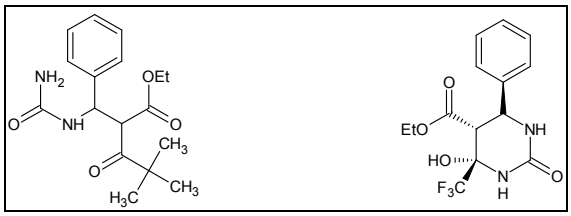


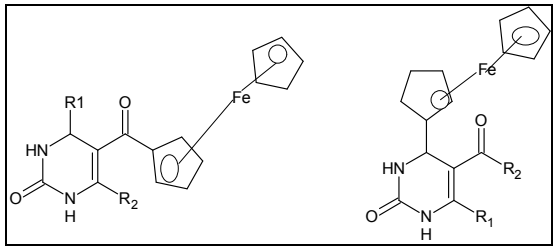
Fig.1.2.3. N,N-disubstituted ureas

To confirm The intermediate, N-acyliuminmium ion are very reactive and cannot be isolated they applied bulky group or electron deficient in ethyl acetoacetate and observed it by X-ray analysis (Jenner, 2004).



Scheme .1.2.1. isolated intermediate .

lewis acids catalyst stabilized N-acyliuminmium ion by coordination to the urea oxygen (Ranu *et.al* 2000), also to stabilized enol form, a chelatin of 1,3 the dicarbonyl component with suitable lewis-acids are used (Fu *et.al* 2003)



Scheme .1.2.2. ferrocenoyl 3,4dihydropyrimidinone and 4- ferrocenoyl - 3,4dihydropyrimidinone.

1.2.3.Reaction Conditions

More than 100 different reaction condition are known for Biginelli reaction (Zhu *et.al,* 2005), Biginelli condensation are carried out in solvent such as water (Suzuki *et.al*, 2006), ionic liquids (Peng & Deng, 2001) ethanol (Holden &Crouch, 2001), or methanol (Lin *et.al,* 2000), but more recently aprotic solvent such as tetrahydrofuran (Huang *et.al* 2005), dioxane (Saha & Moorthy, 2010), toluene (Nikna *et.al,* 2010), acetic acid (Heravi *et.al*, 2006), or acetonitrile (Mait *et.al,* 2003) are also used. A recent trend is to perform the reaction without any solvent(Bigi *et.al*,1999), or with the component either adsorbed on an in organic support (Xia & Wang, 2002). Bignelli reaction depend on the amount of catalyst in the medium (Peng & Deng, 2001), BrØnsted acids such as hydrochloric acid (Kappe, 2000), or sulfuric acid (Saloutin *et.al*, 2000), have been employed, but nowadays the used of lewis acids such as BF_3OEt_2 and CuCl (Dondoni *et.al,* 2001), LaCl3.7H2O and $CoCl_2$.$6H_2O$ (Lu *et,al*, 2000) , $FeCl_3$ and $NiCl_2$ (Lu & Bai, 2002), $ZnCl_2$ (Pasha *et.al*, 2005), $Yb(OTf)_3$, (Dondoni *et,al*, 2002) $La(OTf)_3$, $InCl_3$,(Ranu *et.al*, 2000), $InBr_3$ and $InCl_3$ (Fu *et. al,* 2003), $In(OTf)_3$ (Ghosh, *et,al*, 2004),

LiBr (Mait *et.al*, 2003), ZnI_2 (Liang *et.al*, 2007), $CoCl_2.6\ H_2O$ MnCl2.4H2O and $SnCl_2.2H_2O$ (Kumar *et,al,* 2005),$YbCl_3$ (Zhang, *et.al,* 2009) $BiCl_3$ (Ramalinga *et.al,* 2001) , $LiClO_4$ (Ramalingam, 2001) metal acetate (Karamate *et.al,* 2010), CuI (Kalita & Phukan, 2007), $ZrCl_4$ (Reddy *et.al,* 2002), $SnCl_2.2H_2O$ (Russowsky *et.al*, 2004), Y $(NO_3)_3$ .6 H_2O (Nandurkar *et.al*.2007), Cu $(OTf)_3$ (Paraskar *et.al*, 2003), $Sr(OTf)_2$ (Su *et.al*, 2005), VCl_3 (Sabitha *et.al*, 2003), Zn $(OTf)_3$ (Hui & Guang, 2003), $CuCl_2$ (Singh *et.al*, 2008), $HgCl_2$ (Sachdeva *et.al*, 2011), $SbCl_3$ (Cepanec *et.al*, 2007), $AlCl_3$ (Saini *et.al*, 2006), $TaBr_5$ (Ahmed & Vanlier, 2007), are prevalent. Also solid acid catalyst, such as an acidic clay (Heravi *et.al*, 2005), a zeolite (Tajbakhsh *et.al*, 2005), an ion exchange material such as Amberyst or a heteropoly acid such as $Ag_3PW_{12}O_{40}$ (Rafiee & Shahbazi, 2006), in addition material such as silica / H_2SO_4 (Salehi *et.al*, 2003) or silica aerogel-iron oxide nano composites have been reported as efficient supported catalysts for the Biginelli reaction (Martinez *et.al,* 2003), or reaction mediators cellulose sulfuric acid (Reddy *et.al,* 2009), N-butyl-N,N-dimethyl-*α*-phenylethyl ammonium bromide (Reddy *et.al*, 2003), *p*-toluene sulfonic acid (jin *et.al*, 2002), formic acid (Jiang & You, 2007), TMSCl/NaI (Kamal *et.al*, 2007), Boric acid (Csampai *et.al*, 2009), triphenyl phosphonium perchlorate (Debache *et.al*, 2008), and iodine (Saxena *et.al*, 2005). The reaction also preceded without any catalyst by just mixing and heating the neat reagents (Ranu *et.al*, 2002). Biginelli reaction are slow at room temperature (Li *et.al*, 2010), so activating by heating (Niknam *et.al,* 2010), microwave dielectric heating are used to shorten reaction times (Kidwai *et.al*, 2002), or ultrasound activation (Wang & Pei, 2010), (Zhang *et.al*, 2006), by IR irradiation (Stadler & Kappe, 2001), or by photochemical methods (Foroughifar *et.al*, 2003). The pressure have an affected on Biginelli reaction (Jenner, 2004). The amount of reactants are affected, generally by excess of 1,3-dicarbonyl and urea than aldehyde (Dong *et.al,* 2007), the Biginelli compounds are sparingly soluble in methanol or ethanol at room temperature, so they are separate by

filtration (Holden & Crouch, 2001), of its precipitate by addition of water (Tamaddon *et.al*, 2010)

1.2.4. Reactants of Biginelli Compounds

The aldehyde reactants can be varied to the largest extent, the reaction works best with aromatic aldehydes. These can be substituted in the *o*-position (Li *et.al*, 2010).

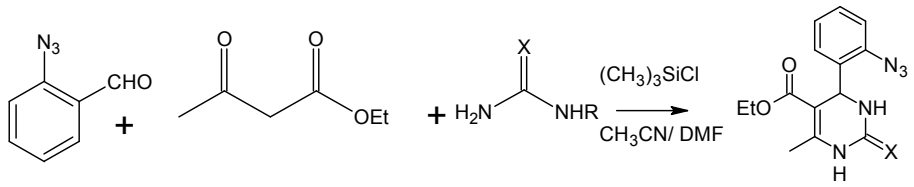


Fig.1.2.4. dihydropyrimidine azides,*o*-position

Or *m*-position (Fu *et.al*, 2003)

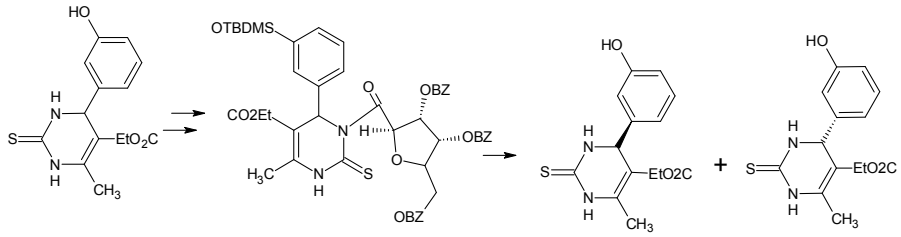


Fig. 1.2. 5. racemic monastrol, aldehyde

Or in *p*-position (Lin *et.al*, 2000).

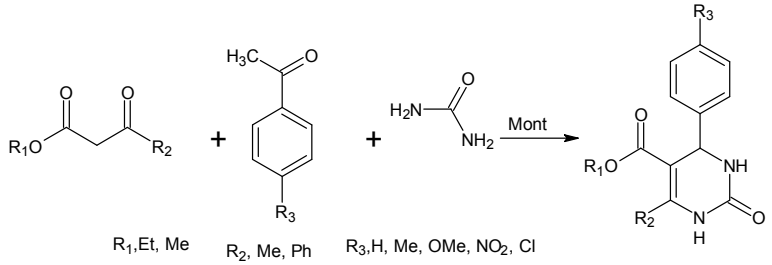


Fig.1.2.6. substituted in *p*-position.

high yields are obtained with *m*- or *p*- substituted aromatic aldehydes carrying electron- withdrawing substituent, for *o*- substituted benz aldehydes having bulky substituent, yield can be lower (Lin,*et.al*, 2000), example salicyaldehyde (Abbas, 2008), heterocyclic aldehydes derived from furan (Lu & Bai, 2002), thiophene (Ramalinga *et.al,* 2001) , pyrazole (Zhang, *et.al*, 2006)

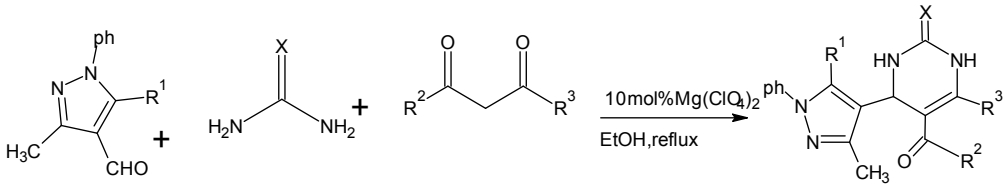
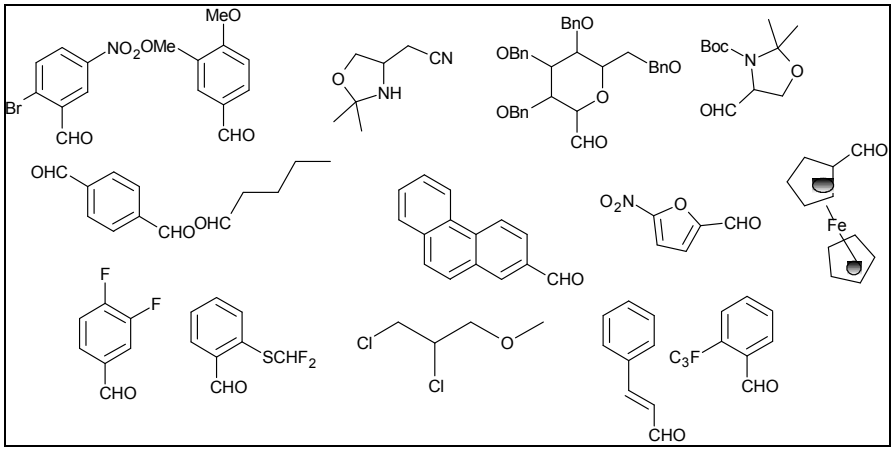


Fig. 1.2.7. substituted pyrazole



Scheme.1.2.3. aldehyde reactants differ at C_4 of DHPMs (Dallinger &Kappe, 2005)

Aliphatic aldehydes provide lower yields in the Biginelli reaction unless special reaction conditions are employed, such as lewis-acid catalysts or solvent-free methods (Slimi *et.al*, 2011), or the aldehydes are used protected form (Kishi,1980)

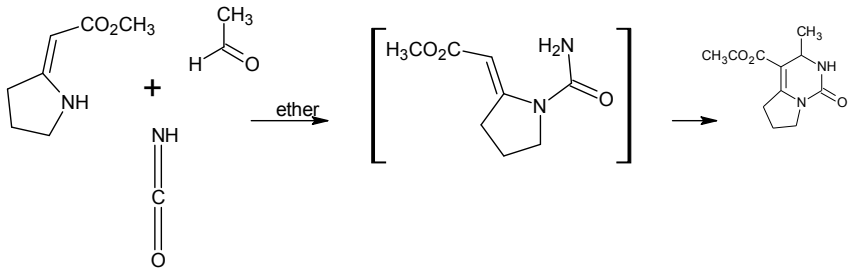
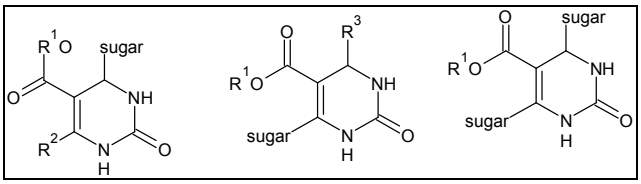


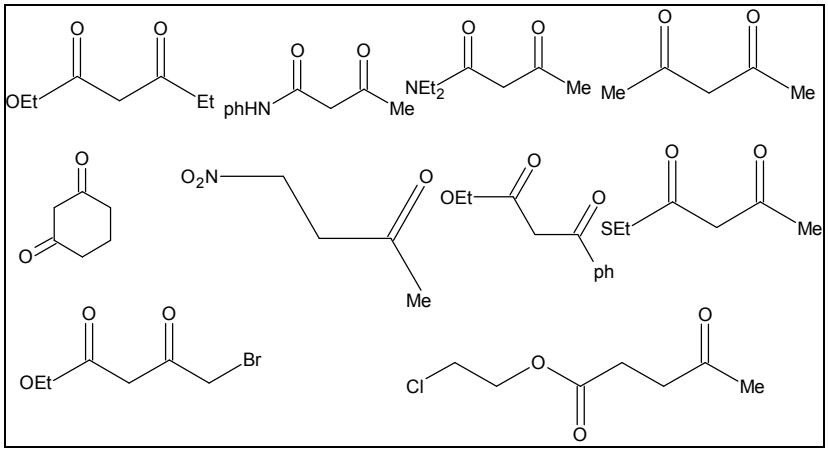
Fig. 1.2.8. protect form of aldehyde

The aldehyde component which is derived from a carbohydrate, can obtain DHPMs having a sugar-like moiety in position 4(C-nucleoside analogues) (Dondoni *et.al,* 2001)



Scheme 1.2.4. C-glycosylated aldehydes

1,3-dicarbonyl compounds employed in Biginelli reaction in many forms (Kappe, 2000).



Scheme .1.2.5. forms of 1,3-dicarbonyl compounds

3-oxoalkanoic esters or thioester (Ryabukhin *et.al*, 2008), Benzoyl acetic esters (Thakur & TrivediI, 2011), 3-ketoamides (Couto *et.al*, 2011), β-diketones, acetyl

acetone (Ramu *et.al,* 2008), cyclic β-diketones (Lin *et.al*, 2007), cyclic ketone and substituted α ketoacid (Abelman. 2003), acetophenone (Liang *et.al,* 2007), all these 1,3-dicarbonyl substrates can be applied in Biginelli reaction.

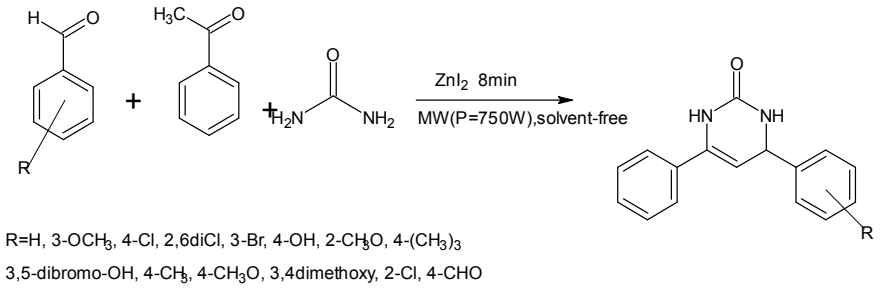


Fig. 1.2.9. acetophenone applied in DHPM synthesis.

Last component in Biginelli condensation is urea which are very restricted, most published literature involves urea or thiourea, However, monosubistituted alkylureas and substituted thioureas are provide Biginelli compound in form of N-substituted DHPMs (Yadav *et.al*, 2008) and (Yadav *et.al,* 2007).

1.2.5. Modification of the Biginelli Reaction

The Atwal modification of the Biginelli reaction that an enone is first condensed with a suitable protected urea or thiourea derivative under almost neutral condition (O'Reilly & Atwal, 1987)

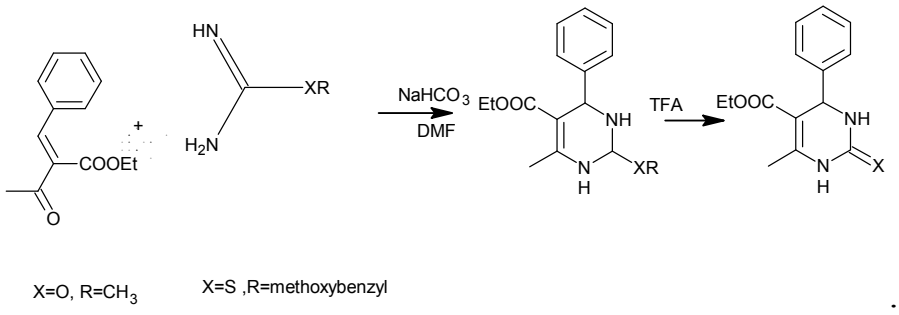


Fig. 1.2. 10. Atwal modification of the Biginelli reaction.

Another conception are the condensation of α-Tosyl-substituted (thio) ureas with the (insitu prepared) enolates of acetoacetates or 1,3-dicarbonyl compounds this for aliphatic aldehydes and thioureas (Shutalev, 1998)

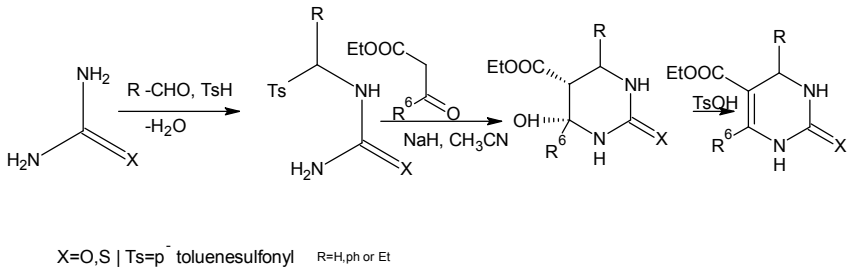


Fig. 1.2.11. the Shutalev modification

Another approach to Biginelli developed by Kishi is the trimolecular of an enamine, acetaldehyde, and isocyanic acid which produces the bicyclic dihydropyrimidine derivative at room temperature.

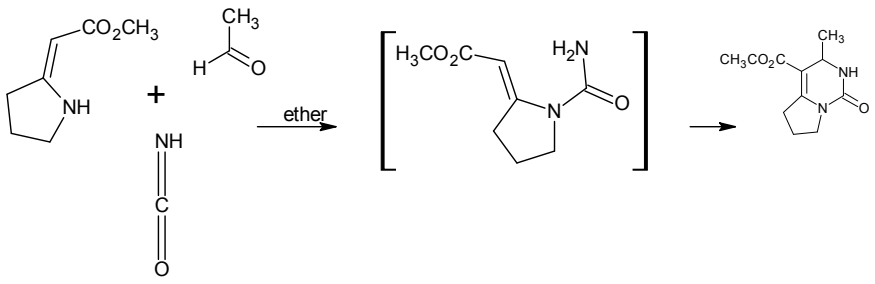


Fig. 1.2.12. Kishi bicyclic dihydropyrimidine derivative.

Chapter Two

Material & Methods

2. Materials and Methods

2.1.Chemicals

Acetyl acetone, Benzaldehyde, Cinnamaldehyde, Ethyl acetoacetate, Ethanol, Furfuraldehyde, *P*-dimethylamino benzaldehyde, Salicyaldehyde, Thiourea, Thiosemicarbazide. Urea and Zinc chloride, all these chemical from ALPHA CHEMIKA company, INDIA

2.2.Instruments

2-2-1- TLC 20 x 20cm plates of aluminium precoating silica gel G F_{254} (magnesium activated zinc silicate) s d fine-chem limited

2-2-2- Fourier transform infrared (FTIR) spectrometer 4800s instrument (Shimadzu,Japan)

2.2-3- UV spectrophotometer, source of radiation Deuterium arc lamp (190 - 400nm), single beam instrument (Shimadzu, Japan)

2.2.4- Gas Chromatography- Mass Spectroscopy. (Shimadzu, Japan)

2.2.5- Mass spectrometer, ionization source of energy electron- impact (Shimadzu,Japan)

2.2.4- ^{1}HNMR spectra were recored on BRUKER spectrometer at 400MH_Z

2.2.5-^{13}CNMR spectra were recored on BRUKER spectrometer at 400MH_Z

2.3.General Equipment

Electrothermal melting point apparatus, Hot plate with magnetic stirrer, sensitive Balance, oven. Round bottom flask, (capacity 250 ml)with glass stopper and fitted condenser, Rectangular glass tank, Cylinders Beakers, Funnel and Conical flask.

2.4.1. General Procedure for Synthesis of 1-amino-5- acetyl -6-methyl-4-aryl-3,4-dihydropyrimidine-2-thione (I, III, V, VII & IX) and 1-amino arylmethylidiene-5-acetyl-6-methyl-4-aryl-3,4-dihydropyrimidine-2-thione (II, IV, VI, VIII & X)

In a 250 ml round bottom flask equipped with a reflux condenser were placed 0.01mol of the required aromatic aldehyde, (1.0gm, 1.0ml, 0.01mol) acetyl acetone, (0.9 gm, 0.01mol) thiosemicarbazide and (1.36 gm, 0.01 mol) zinc chloride as catalyst, the mixture was heating with stirring under reflux for 10 hours, after the reaction completed monitored by TLC, the resulting mixture kept overnight in refrigerator and then poured in 15ml cool water with shaking to precipitate the product. The product was dissolved in hot ethanol and allowed to precipitate and then separated into two components by TLC method using plates of aluminium precoating silica gel G F_{254} the developing system are chloroform : methanol (9.2:0.8)

2.4.2. General Procedure for Synthesis of 1-amino-5-ethoxy carbonyl -6-methyl -4-aryl- 3,4-dihydropyrimidine-2-thione (XI, XIII, XV & XVII) and 1-amino arylmethylidiene -5-ethoxycarbonyl -6-methyl -4-aryl- 3,4-dihydro pyrimidine-2-thione (XII, XIV, XVI &XVIII)

In a 250 ml round bottom flask equipped with a reflux condenser were placed 0.01mol of the required aromatic aldehyde, (1.3gm, 1.3 ml, 0.01mol) ethyl acetoacetate, (0.9gm, 0.01mol) thiosemicarbazide and (1.36gm, 0.01mol) zinc chloride as catalyst, the mixture was heated with stirring under reflux for 10 hours, after the reaction completed monitored by TLC, the resulting mixture kept overnight in refrigerator and then poured in 15ml cool water with shaking to precipitate the product. The product was dissolved in hot ethanol, and allowed to precipitate and separated into two components by TLC method using plates of aluminium precoating silica gel G F_{254} the developing system are chloroform: methanol (9.5 : 0.5).

2.4.3. General Procedure for Synthesis of 5-acetyl-6-methyl-4-aryl-3,4-dihydropyrimidine-2-one (XIX, XX, XXI, XXII & XXIII).

In a 250 ml round bottom flask equipped with a reflux condenser were placed 0.01mol of the required aromatic aldehyde (1.0gm, 1.0ml, 0.01mol) acetyl acetone, (0.6gm, 0.01mol) urea, the mixture was heated with stirring under reflux for 5 hours, after the reaction completed monitored by TLC developing system methanol : chloroform (2:8), the resulting mixture kept overnight in refrigerator and then poured in 15ml cool water with shaking to precipitate the product and crystallized by ethanol

2.4.4. General Procedure for Synthesis of 5-acetyl-6-methyl-4-aryl-3,4-dihydropyrimidine-2-thione (XXIV, XXV, XXVI, XXVII & XXVIII)

In a 250 ml round bottom flask equipped with a reflux condenser were placed 0.01mol of the required aromatic aldehyde, (1.0gm, 1.0ml, 0.01mol) acetyl acetone, (0.76gm, 0.01mol) thiourea, the mixture was heated with stirring under reflux for 5 hours, after the reaction completed monitored by TLC developing system methanol :chloroform (1:9), the resulting mixture kept overnight in refrigerator and then poured in 15ml cool water with shaking to precipitate the product, and crystallized by ethanol

2.4.5. General Procedure for Synthesis of 5- ethoxycarbonyl-6-methyl -4- aryl -3,4-dihydropyrimidine-2-one. (XXIX, XXX, XXXI, XXXII & XXXIII)

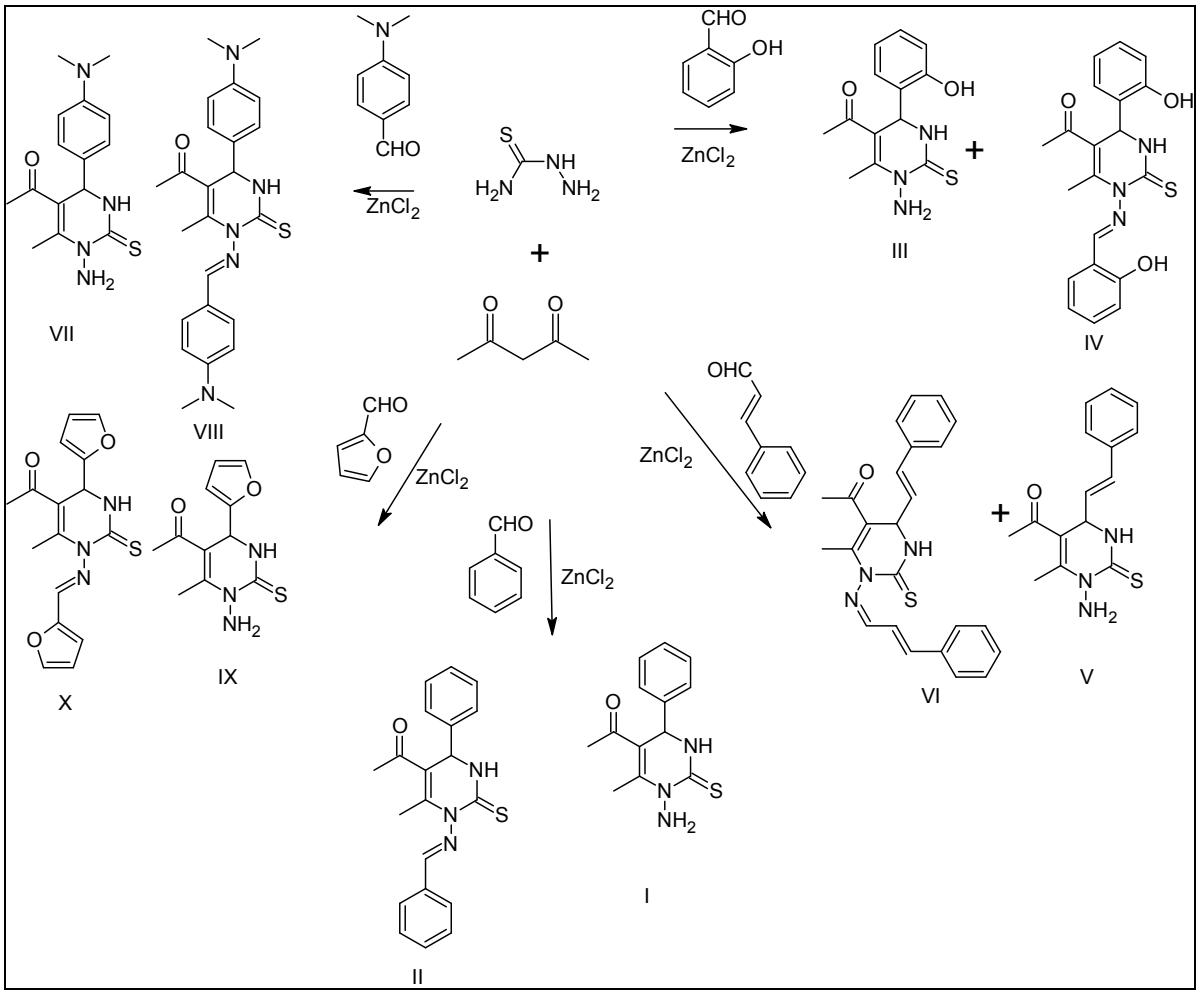
In a 250 ml round bottom flask equipped with a reflux condenser were placed 0.01mol of the required aromatic aldehyde, (1.3gm, 1.3ml, 0.01mol) ethyl acetoacetate, (0.6gm, 0.01mol) urea, the mixture was heated with stirring under reflux for 5 hours, after the reaction completed monitored by TLC developing system methanol : chloroform (2:8) the resulting mixture kept overnight in refrigerator and then poured in 15ml cool water with shaking to precipitate the product and crystallized by ethanol

2.4.6. General Procedure for Synthesis of 5- ethoxycarbonyl-6-methyl-4-aryl-3,4- dihydropyrimidine-2-thione (XXXIV ,XXXV, XXXVI, XXXVII & XXXVIII)

In a 250 ml round bottom flask equipped with a reflux condenser were placed 0.01mol of the required aromatic aldehyde, (1.3gm, 1.3ml, 0.01mol) ethyl acetoacetate, (0.76gm, 0.01mol) thiourea, the mixture was heated with stirring under reflux for 5 hours, after the reaction completed monitored by TLC developing system methanol :chloroform (1:9), the resulting mixture kept overnight in refrigerator and then poured in 15ml cool water with shaking to precipitate the product and crystallized by ethanol

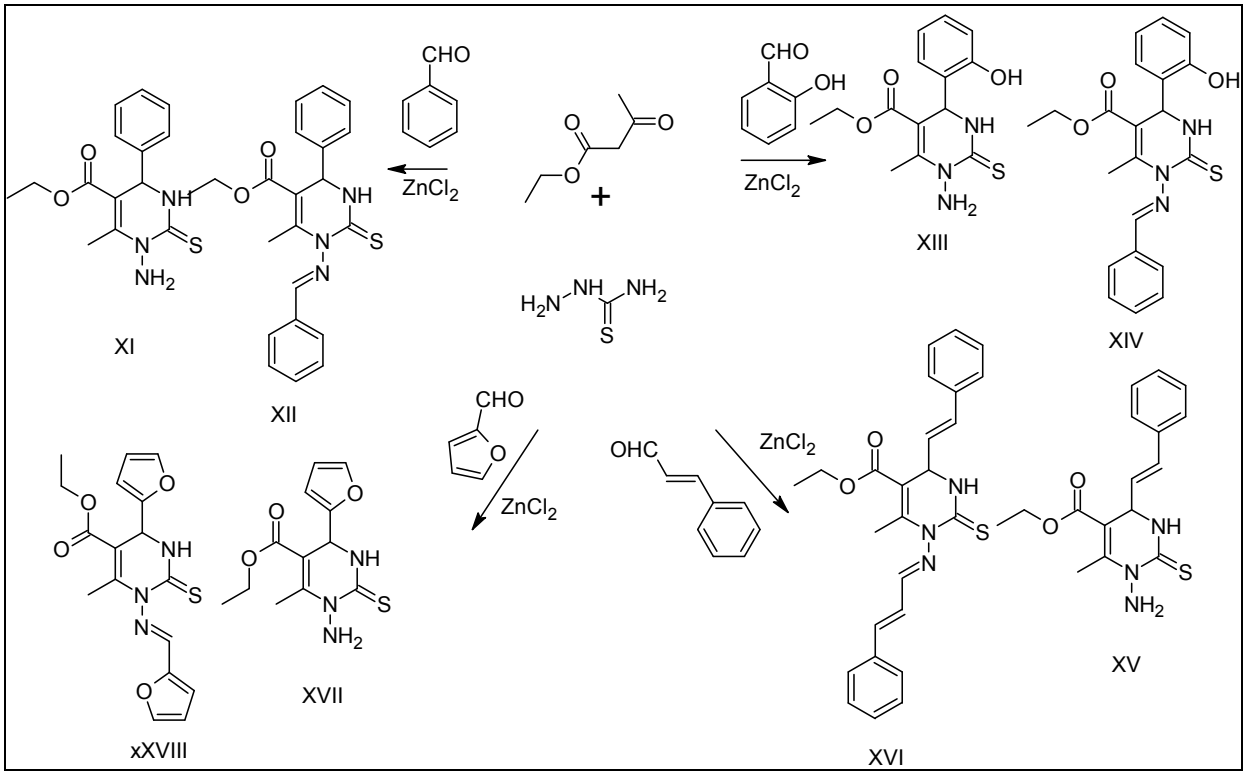
2.5. Synthetic methods

2.5.1. Synthesis of 1-amino-5-acetyl -6-methyl -4-aryl- 3,4-dihydropyrimidine-2-thione (I, III, V, VII & IX) and 1-amino arylmethylidiene-5-acetyl-6-methyl-4-aryl-3,4-dihydropyrimidine-2-thione (II, IV ,VI, VIII & X) from acetyl acetone with thiosemicarbazide and different aldehyes in the presence of zinc chloride as catalyst. (Scheme.2.5.1).



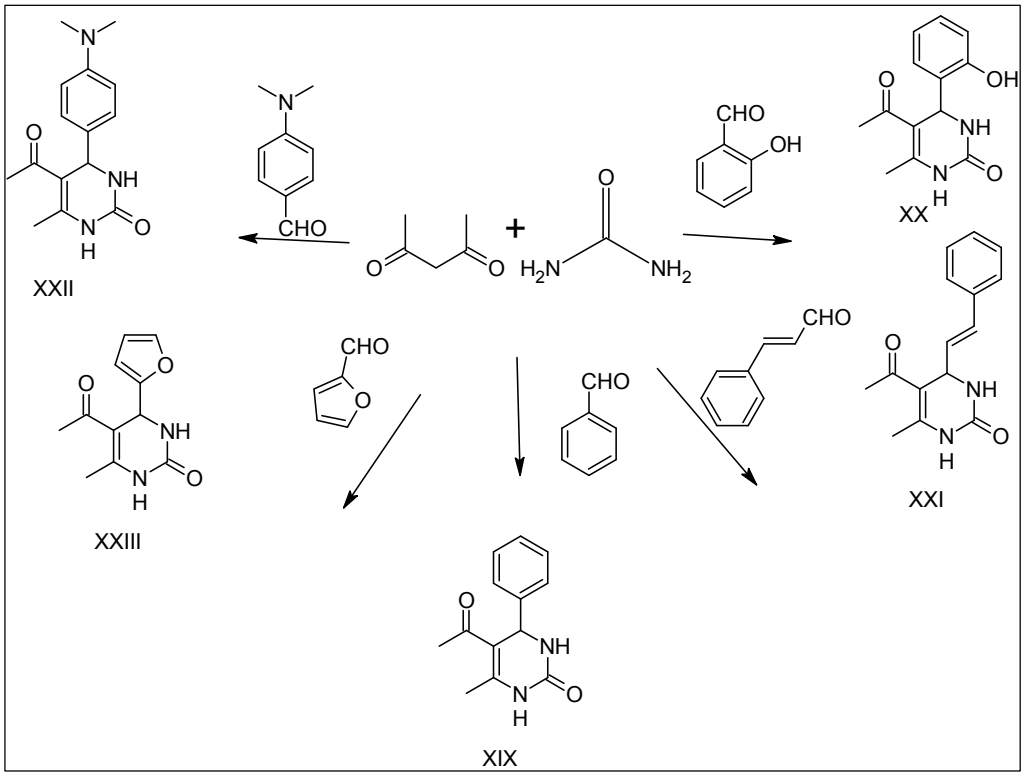
Scheme.2.5.1. chemical reaction of acetyl acetone with thiosemicarbazide and different aldehydes in the presence of zinc chloride as catalyst

2.5.2. Synthesis of 1-amino-5-ethoxycarbonyl-6-methyl-4-aryl-3,4-dihydro pyrimidine-2-thione (XI, XIII, XV & XVII) and 1-amino aryl methylidiene-5-ethoxycarbonyl-6-methyl-4-aryl-3,4-dihydropyrimidine -2-thione (XII, XVI, XIV & XVIII) from ethyl acetoacetate with thiosemicarbazide and different aldehydes in the presence of zinc chloride as catalyst. (Scheme.2.5.2)



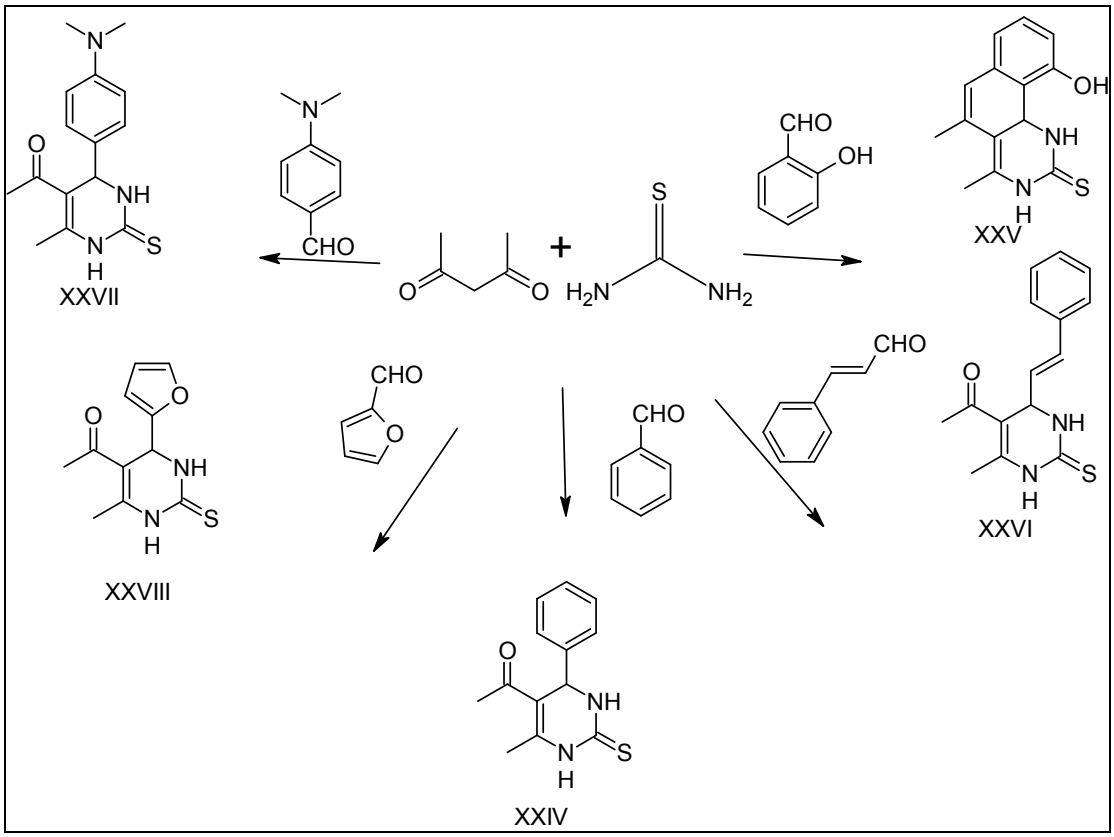
Scheme.2.5.2.chemical reaction of ethyl acetoacetate with thiosemicarbazide and different aldehydes, in the presence of zinc chloride as catalyst

2.5.3. Synthesis of 5-acetyl-6-methyl-4-aryl-3,4-dihydropyrimidine-2-one (XIX, XX, XXI, XXII & XXIII) from acetyl acetone with urea and different aldehydes. (Scheme. 2.5.3)



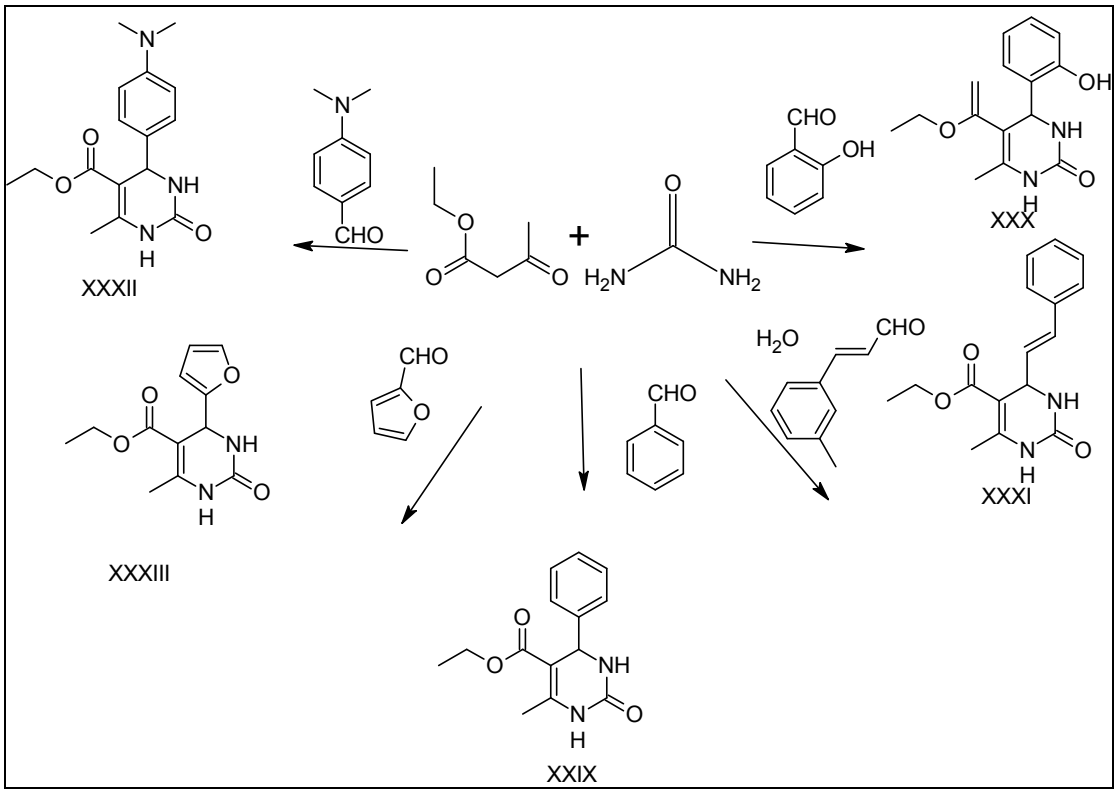
Scheme.2.5.3. Chemical reaction of acetyl acetone with urea and different aldehydes

2.5.4. Synthesis of 5-acetyl-6-methyl-4-aryl-3,4-dihydropyrimidine-2-thione (XXIV, XXV, XXVI, XXVII & XXVIII) from acetyl acetone with thiourea and different aldehydes (Scheme.2.5.4).



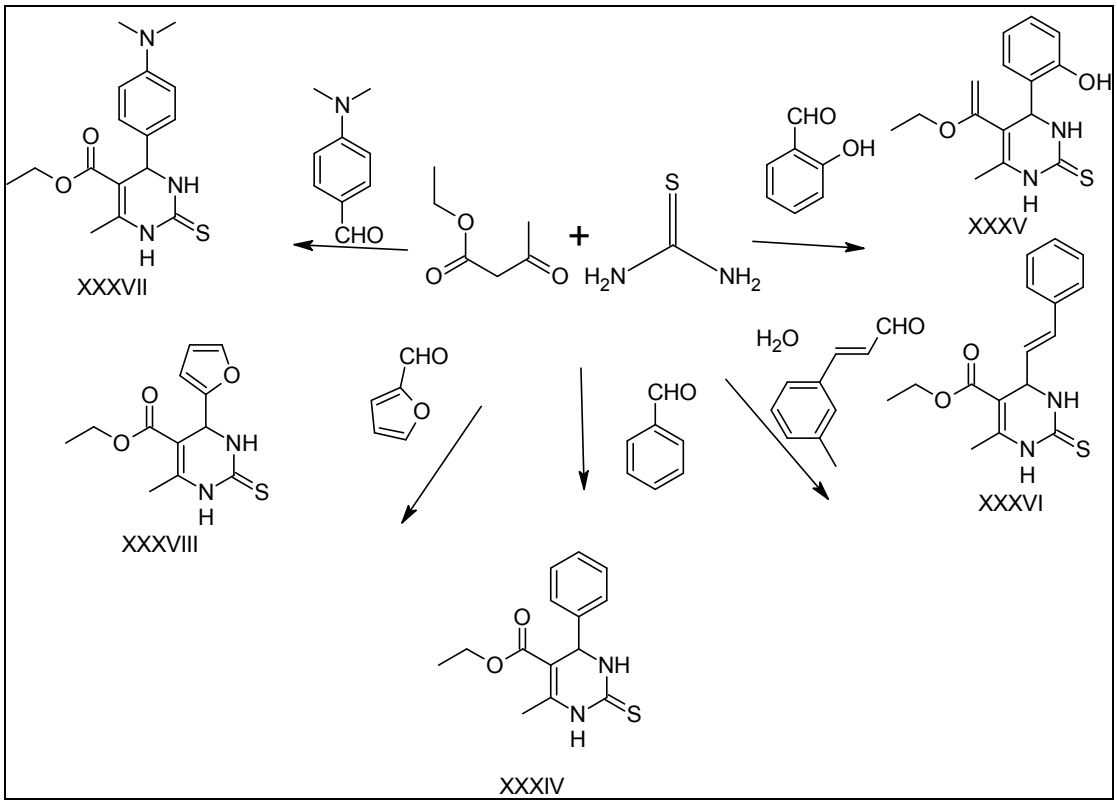
Scheme.2.5.4.Chemical reaction of acetyl acetone with thiourea and different aldehydes

2.5.5. Synthesis of 5-ethoxycarbonyl -6- methyl -4- aryl-3,4- dihydro pyrimidine-2-one (XXIX, XXX, XXXI, XXXII & XXXIII) from ethyl acetoacetate with urea and different aldehydes (Scheme.2.5.5)



Scheme.2.5.5.Chemical reaction of ethyl acetoacetate with urea and different aldehydes.

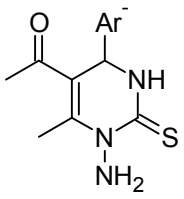
2.5.6. Synthesis of 5-ethoxycarbonyl- 6-methyl - 4-aryl-3,4-dihydropyrimidine -2-thione (XXXIV, XXXV ,XXXVI ,XXXVII & XXXVIII) from ethyl acetoacetate with thiourea and different aldehydes (Scheme.2.5.6)



Scheme.2.5.6. Chemical reaction of ethyl acetoacetate with thiourea and different aldehydes

2.6. Chemical Names of Synthesized Compounds

Table. 2.6.1. Chemical names of 1-amino-5-acetyl-6-methyl-4-aryl-3,4-dihydro pyrimidine-2-thione (I, III,V, VII & IX)



I,III.V,VII.IX

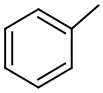
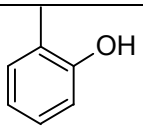
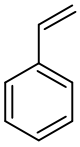
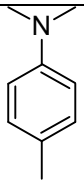
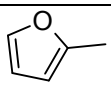
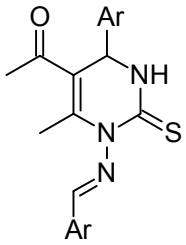
No	Ar	Chemical name
I		1-amino-5-acetyl-6-methy-4-phenyl-3,4-dihydro pyrimidine-2-thione
III		1-amino-5-acetyl-4-(2-hydroxy phenyl)-methyl-3,4-dihydropyrimidine-2-thione
V		1-amino-5-acetyl-6-(cinnamyl)-6-methyl-3,4-dihydropyrimidine-2-thione
VII		1-amino-5-acetyl-4-(4-dimethylamino- phenyl)-6-methyl-3,4-dihydro pyrimidine-2-thione
IX		1-amino-5-acetyl-4-(furyl)-6-methyl-3,4-dihydropyrimidine-2-thione

Table. 2.6.2. Chemical name of 1-amino arylmethylidiene-5-acetyl-6-methyl-4-aryl-3,4-dihydropyrimidine-2-thione (II, IV,VI,VIII & X).



II,IV,VI,VIII,X

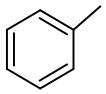
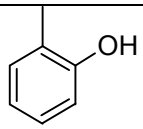
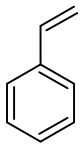
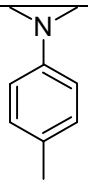
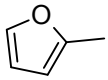
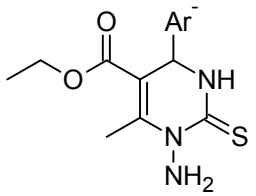
No	Ar	Chemical name
II		1-amino phenyl methylidiene-5-acetyl-6-methyl-4-phenyl-3,4-dihydropyrimidine-2-thione.
IV		1-(amino(2-hydroxy-phenyl methylidiene) -5-acetyl -4-(2-hydroxy phenyl)-6-methyl-3,4-dihydro pyrimidine -2-thione
VI		1-amino phenyl prop-2-en-1-ylidiene-5-acetyl-4-(cinnamyl)-6-methyl-3,4-dihydropyrimidine-2-thione
VIII		1-amino (4-dimethylamino-phenyl methylidiene)-5-acetyl-4-(4-dimethylamino-phenyl)-6-methyl-3,4-dihydropyrimidine-2-thione
X		1-amino furan-2-yl methylidiene-5-acetyl-4-(furyl)-6-methyl-3,4-dihydropyrimidine-2-thione

Table. 2.6.3. Chemical names of 1-amino-5-ethoxycarbonyl-6-methyl-4-aryl-3,4-dihydrop yrimidine-2-thione (XI, XIII, XV& XVII).



XI,XIII,XV,XVII

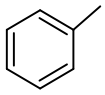
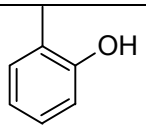
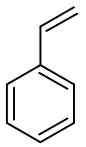
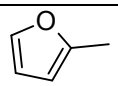
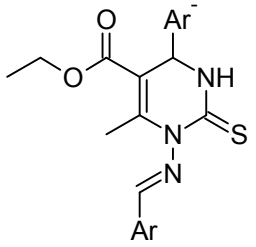
No	Ar	Chemical name
XI		1-amino-5-ethoxy carbony-6-methy-4-phenyl-3,4-dihydro pyrimidine-2-thione
XIII		1-amino-5-ethoxy carbony-6-methy-4-(2-hydroxy-phenyl)-3,4-dihydropyrimidine-2-thione
XV		1-amino-5-ethoxy carbony-6-methy-4-(cinnamyl)-3,4-dihydropyrimidine-2-thione
XVII		1-amino-5-ethoxy carbony-6-methy-4-(furyl)-3,4-dihydropyrimidine-2-thione

Table .2.6.4. Chemical names 1-amino arylmethylidiene-5-ethoxy carbonyl-6-methyl-4-aryl-3,4-dihydropyrimidine-2-thione (XII, XVI, XIV &XVIII)



XII,XIV,XVI,XVIII

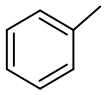
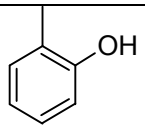
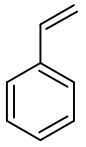
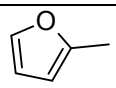
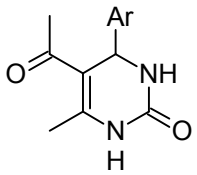
No	Ar	Chemical name
XII		1-amino phenyl methyl idiene-5-ethoxycarbony-6-methy-4-phenyl-3,4-dihydropyrimidine-2-thione
XIV		1-(amino(2-hydroxy- phenyl methylidiene)-5-ethoxycarbonyl-4-(2-hydroxy phenyl)-6-methyl-3,4-dihydro pyrimidine-2-thione
XVI		1-amino phenyl prop-2-en-1-ylidiene -5-ethoxy carbony-6-methy-4-(cinnamyl)-3,4-dihydro pyrimidine-2-thione
XVIII		1-amino(furan-2-yl methylidiene)-5-ethoxycarbonyl-4-(furyl)-6-methyl-3,4-di hydropyrimidine-2-thione

Table .2.6.5. Chemical names of 5-acetyl-6-methyl-4-aryl-3,4-dihydropyrimidine-2-one (XIX, XX, XXI, XXII & XXIII)



XIX,XX,XXI,XXII&XXIII

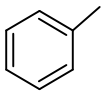
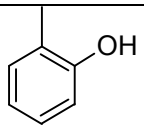
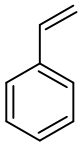
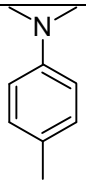
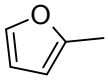
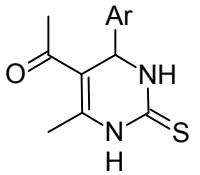
No	Ar	Chemical name
XIX		5-acetyl-6-methyl-4-phenyl-3,4-dihydro pyrimidine-2-one
XX		5-acetyl-6-methyl-4-(2-hydroxy-phenyl)-3,4-dihydropyrimidine-2-one
XXI		5-acetyl-6-methyl-4-(cinnamyl)-3,4-dihydro pyrimidine-2-one
XXII		5-acetyl-6-methyl-4-(4-dimethylamino- phenyl)-3,4-dihydropyrimidine-2-one
XXIII		5-acetyl-6-methyl-4-furyl-3,4-dihydro pyrimidine-2-one

Table. 2.6.6. Chemical names of 5-acetyl-6-methyl-4-aryl-3,4-dihydro pyrimidine-2-thione (XXIV, XXV, XXVI, XXVII & XXVIII).



XXIV,XXV,XXVI,XXVII&XXVIII

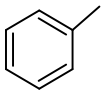
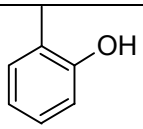
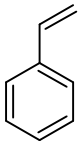
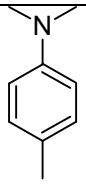
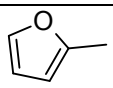
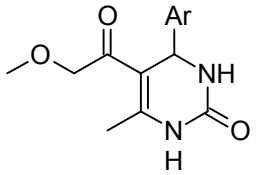
No	Ar	Chemical name
XXIV		5-acetyl-6-methyl-4-phenyl-3,4-dihydro pyrimidine -2-thione
XXV		5-acetyl-6-methyl-4-(2-hydroxy-phenyl)-3,4-dihydropyrimidine-2-thione
XXVI		5-acetyl-6-methyl-4-(cinnamyl)-3,4-dihydro pyrimidine-2-thione
XXVII		5-acetyl-6-methyl-4-(4-dimethylamino -phenyl)-3,4-dihydropyrimidine-2-thione
XXVIII		5-acetyl-6-methyl-4-furyl-3,4-dihydropyrimidine-2-thione

Table .2.6.7. Chemical names of 5-ethoxycarbonyl-6-methyl-4-aryl-3,4-dihydro pyrimidine-2-one (XXIX, XXX, XXXI, XXXII &XXXIII)



XXIX,XXX,XXXI,XXXII&XXXIII

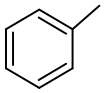
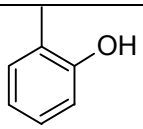
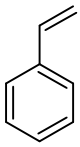
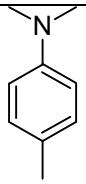
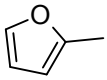
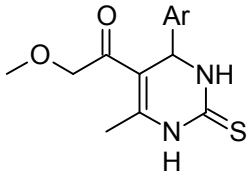
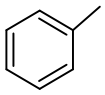
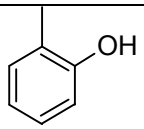
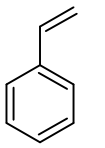
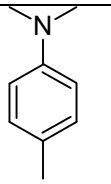
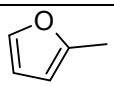
No	Ar	Chemical name
XXIX		5- ethoxycarbonyl-6-methyl-4-pheny-3,4- dihydro pyrimidine-2-one
XXX		5- ethoxycarbonyl-6-methyl-4-(2-hydroxy-phenyl)-3,4- dihydropyrimidine-2-one
XXXI		5- ethoxycarbonyl-6-methyl-4-cinnamyl-3,4-dihydropyrimidine-2-one
XXXII		5- ethoxycarbonyl-6-methyl-4-(4-dimethylamino-phenyl)-3,4- dihydropyrimidine-2-one
XXXIII		5- ethoxycarbonyl-6-methyl-4-furyl-3,4-dihydropyrimidine-2-one

Table .2.6.8. Chemical names of 5- ethoxycarbonyl-6-methyl-4-aryl-3,4- dihydro pyrimidine-2-thione. (XXXIV ,XXXV ,XXXVI, XXXVII & XXXVIII)



XXXIV, XXXV, XXXVI, XXXVII &XXXVIII

No	Ar	Chemical name
XXXIV		5- ethoxycarbonyl-6-methyl-4-pheny-3,4-dihydropyrimidine-2-thione
XXXV		5- ethoxycarbonyl-6-methyl-4-(2-hydroxy-phenyl)-3,4- dihydropyrimidine-2-thione
XXXVI		5- ethoxycarbonyl-6-methyl-4-cinnamyl-3,4-dihydropyrimidine-2-thione
XXXVII		5- ethoxycarbonyl-6-methyl-4-(4-dimethyl amino- phenyl)-3,4- dihydropyrimidine-2-thione
XXXVIII		5- ethoxycarbonyl-6-methyl-4-furyl-3,4-dihydropyrimidine-2-thione

2.7. Reaction Conditions

Table. 2.7.1. Reaction condition of 1-amino-5-acetyl-6-methyl-4-aryl-3,4-dihydro pyrimidine-2-thione (I, III,V,VII & IX) and 1-amino aryl methylidiene-5-acetyl-6-methyl-4-aryl-3,4-dihydropyrimidine-2-thione (II, IV,VI,VIII &X)

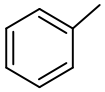
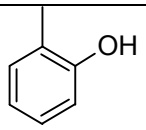
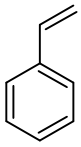
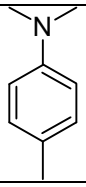
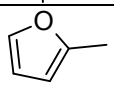
No	Ar	Reaction temp.	Reaction time	Yield gm	Yield %	m.p
I&II		100	10h	2.5076	95%	150-152^{O}C
III&IV		130	10h	I.916	69%	135-137^{O}C
V& VI		120	10h	2.151	74%	139-140^{O}C
VII&VIII		105	10h	2.0005	65%	159-162^{O}C
IX&X		80	10h	1.8245	72%	Viscous

Table.2.7.2. Reaction condition of 1-amino-5-ethoxycarbonyl-6-methyl-4-aryl-3,4-dihydropyrimidine-2-thione (XI, XIII, XV & XVII) and 1-amino arylmethylidiene-5-ethoxycarbonyl-6-methyl-4-aryl-3,4-dihydropyrimidine-2-thione (XII, ,XVI , XIV &XVIII).

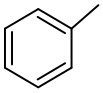
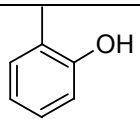
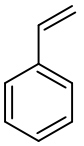
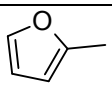
No	Ar	Reaction temp.	Reaction time	Yield gm	Yield %	m.p
XI&XII		100	10h	2.5076gm	81,3%	194-196^{O}C
XIII&XIV		110	10h	3.1795gm	98%	135-136^{O}C
XV&XVI		120	10h	2.5410gm	75,9%	152-154^{O}C
XVII&XVIII		70	10h	2.5019gm	62.8%	209-211^{O}C

Table .2.7.3. Reaction condition of 5-acetyl -6- methyl -4- aryl-3,4-dihydro pyrimidine-2-one (XIX, XX, XXI, XXII &XXIII).

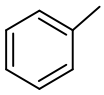
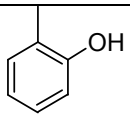
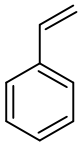
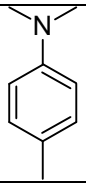
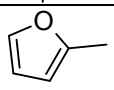
No	Ar	Reaction temp.	Reaction time.	Yield gm	Yield %	m.p.
XIX		120°C	5h	1.401 gm	95.5 %	246 -245°C (lit,228-229°C. Ramu.*et.al*.2008., 236-238 °C . Debache.*et.al*.2012.,233-235°C. Kundu.*et.al*.2009.,235-236°C. Bahekar.*et.al*.2004.,207-210°C. Kumar.*et.al*.2005)
XX		120°C	5h	1.201 gm	80%	209-207°C(lit.204-208°C. Ramu.*et.al*.2008.
XXI		110°	5h	0.901 gm	61%	222-225°C.(lit.230-232°C. Ramu.*et.al*. 2008
XXII		120°C	5h	1.3o1 gm	92%	220-221°C.(lit.213-214°C. Ramu.*et.al*. 2008.
XXIII		80°C	5h	1.00 gm	68%	216-217°C(lit.210-212 °C .Ramu.*et.al*.2008., 210 212°C.Kundu.*et.al*. 2009.

Table .2.7.4. Reaction condition of 5-acetyl -6-methyl- 4-aryl-3,4-dihydro pyrimidine-2-thione (XXIV, XXV, XXVI, XXVII &XXVIII).

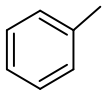
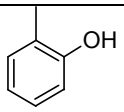
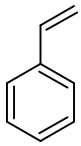
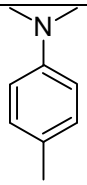
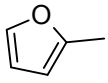
No	Ar	Reaction temp.	Reaction time.	Yield gm	Yield %	m.p.
XXIV		120°C	5h	1.801 gm	88%	234-235°C. (lit.220-221°C.Ramu.*et.al*.2008.,224-226°C. Debache.*et.al*.2012.,219-220°C. Kundu.*et.al*.2009.
XXV		120°C	5h	1.701 gm	84%	210-211°C.(lit.240-243°C.Ramu.*et.al*.2008.
XXVI		130°C	5h	1.00 gm	48%	240-241°C.(lit.160-162°C.Ramu.*et.al*.2008.
XXVII		140°C	5h	0.701 gm	34%	228-229°C.(lit.152-155°C.Ramu.*et.al*.2008.
XXVIII		70°C	5h	1.401 gm	70%	244-245°C.(lit.240-242°C. Ramu.*et.al*.2008.

Table .2.7.5. Reaction condition of 5- ethoxycarbonyl -6-methyl -4-aryl-3,4-dihydropyrimidine-2-one (XXIX, XXX, XXXI, XXXII & XXXIII).

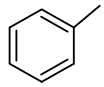
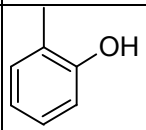
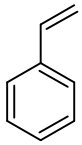
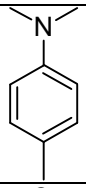
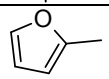
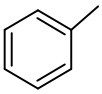
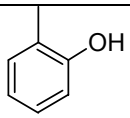
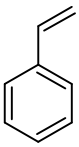
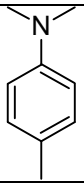
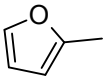
No	Ar	Reaction temp.	Reaction time.	Yield gm	Yield %	m.p.
XXIX		120°C	5h	2.301 gm	88%	210-212°C.(lit.212.5-213.5°C.Shutalev.*et.al*. 1998.202°C. Ramu. *et.al*. 2008. 203-204°C. Debache.*et.al*.2012.
XXX		120°C	5h	2.501 gm	89%	207-209°C.(lit. 201°C.Ramu.*et.al*.2008.
XXXI		120°C	5h	2.501 gm	89%	240-242°C.(lit. 234-235°C.Ramu.*et.al*.2008.
XXXII		120°C	5h	1.501 gm	50%	248-250°C.(lit.230-234°C.Ramu.*et.al*.2008.
XXXIII		80°C	5h	1.501 gm	51%	203-205°C.(lit.208-209°C.Ramu.*et.al*.2008

Table .2.7.6. Reaction condition of 5- ethoxycarbonyl-6-methyl-4-aryl-3,4-dihydro pyrimidine-2-thione (XXXIV ,XXXV ,XXXVI, XXXVII &XXXVIII)

No	Ar	Reaction temp.	Reaction time.	Yield gm	Yield %	m.p.
XXXIV		120°C	5h	2.501 gm	89%	208-210°C.(lit.212-213°C.Shutalev.*et.al*.1998. ,202°C. Ramu.*et.al*.2008.,200-202°C. Debache.*et.al*.2012.,202-204°C.Kundu.*et.al*.2009.
XXXV		120°C	5h	2.601 gm	86.5%	198°C.(lit.204-206°C.Ramu.*et.al*.2008.
XXXVI		120°C	5h	1.800 gm	60%	166°C.(lit.163-165°C.Ramu.*et.al*.2008.
XXXVII		120°C	5h	1.601 gm	50%	207-209°C.(lit.210-212°C.Ramu.*et.al*.2008.
XXXVIII		80°C	5h	1.901 gm	73%	206-208°C.(lit.234-236°C.Ramu.*et.al*.2008

2.8. UV of Synthesized Compounds

Table. 2.8.1.UV-data of 1-amino-5-acetyl-6-methyl-4-aryl-3,4-dihydro pyrimidine-2-thione (I, III, V, VII & IX) and 1-amino aryl methylidiene -5-acetyl-6-methyl-4-aryl-3,4-dihydropyrimidine-2-thione (II, IV, VI, VIII & X) , solvent methanol, the absorbance maxima ,wavelength λ_{max} nm

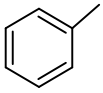
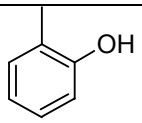
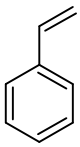
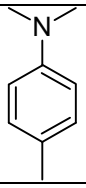
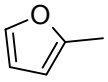
No	Ar	λ_{max} nm	No	λ_{max} nm
I		273.6, 265.6, 250.8, 223.2	II	310.4, 232.2
III		328.5	IV	331.0
V		265.5	VI	266
VII		355.5, 236.5	VIII	236.5
IX		319	X	274.5

Table. 2.8.2. UV-data of 1-amino-5-ethoxycarbonyl-6-methyl-4-aryl -3,4-dihydro pyrimidine-2-thione (XI, XIII, XV &XVII) and 1- amino arylmethylidiene -5-ethoxycarbonyl -6-methyl -4-aryl -3,4-dihydropyrimidine-2-thione (XII, ,XVI, XIV & XVIII), solvent methanol, the absorbance maxima wavelength λ_{max} nm.

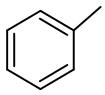
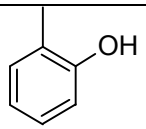
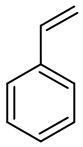
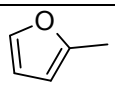
No	Ar	λ_{max} nm	No	λ_{max} nm
XI		267, 227	XII	329
XIII		317	XIV	331, 230.5
XV		342 , 264	XVI	330
XVII		317.5, 268	XVIII	255.5, 317 268.

Table. 2.8.3. UV- data of 5-acetyl-6-methyl-4-aryl-3,4-dihydropyrimidine -2-one (XIX, XX, XXI, XXII &XXIII). solvent ethanol, the absorbance maxima ,wavelength λ_{max} nm.

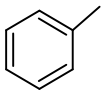
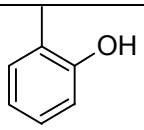
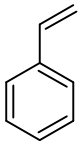
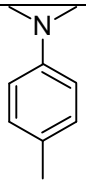
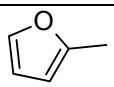
No	Ar	λ_{max} nm
XIX		323
XX		252.5
XXI		256, 321
XXII		260, 322.
XXIII		324

Table. 2.8.4. UV-data of 5-acetyl-6-methyl-4-aryl-3,4-dihydropyrimidine -2-thione (XXIV, XXV, XXVI, XXVII & XXVIII)**,** solvent ethanol, the absorbance maxima ,wavelength λ_{max} nm.

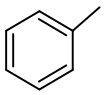
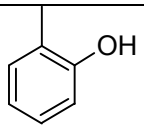
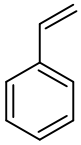
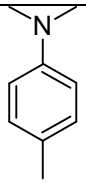
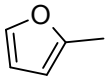
No	Ar	λ_{max} nm
XXIV		300
XXV		288
XXVI		255, 285, 293.
XXVII		259, 300
XXVIII		296

Table. 2.8.5. UV-data of 5-ethoxycarbonyl-6- methyl -4-aryl- 3,4-dihydro pyrimidine-2-one (XXIX, XXX, XXXI, XXXII & XXXIII), solvent ethanol, the absorbance maxima ,wavelength λ_{max} nm

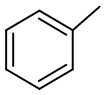
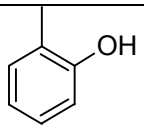
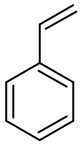
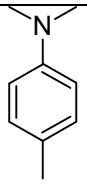
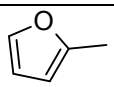
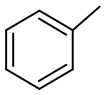
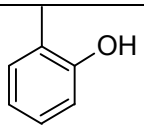
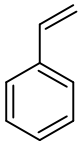
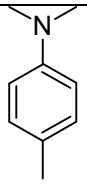
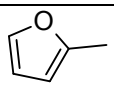
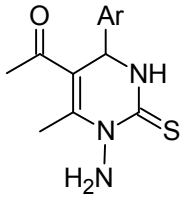
No	Ar	λ_{max} nm
XXIX		337, 240.
XXX		254
XXXI		330
XXXII		274
XXXIII		258, 281.

Table. 2.8.6. UV-data of 5- ethoxycarbonyl -6-methyl -4-aryl-3,4- dihydro pyrimidine-2-thione (XXXIV ,XXXV ,XXXVI, XXXVII & XXXVIII) solvent ethanol, the absorbance maxima ,wavelength λ_{max} nm

No	Ar	λ_{max} nm
XXXIV		216, 296
XXXV		257, 306
XXXVI		253
XXXVII		308
XXXVIII		257, 308

2.9. IR of Synthesized Compounds

Table. 2.9.1. IR-data of 1-amino-5-acetyl-6-methyl-4-aryl-3,4-dihydro pyrimidine-2-thione (I, III, V, VII & IX) IR absorption spectra, wave number cm^{-1} of synthesized compounds were obtained by preparing KBr pellet



I, III, V, VII & IX

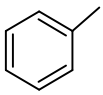
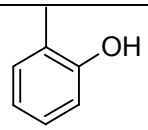
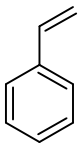
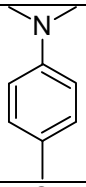
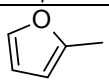
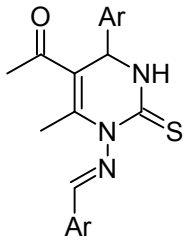
No	Ar	Ar-H_b	N-H_s	C-H_s	C-H_s	C=O_s	N-H_b	C=S_s
I		871&757	3394	3159&3242	2921&2852	1733	1535	1103
III		O-H_s 3425			2923&2852	1733	1566	1137
V		C=C_s 981	3265	3157	2923&2856	1726	1591	1105
VII		C-N_s 1421	3433	3305	2921&2856	1731	1569	1110
IX		C-O_s 1227	3411	3278&3145	2921&2850	1731	1585	1107

Table.2.9.2. IR-data of 1-amino arylmethylidiene-5-acetyl-6-methyl-4-aryl-3,4-dihydropyrimidine-2-thione (II, IV, VI, VIII & X). IR absorption spectra, wave number cm-[1], of synthesized compounds were obtained by preparing KBr pellet



II,IV,VI,VIII & X

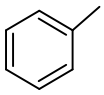
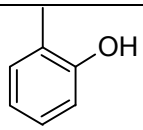
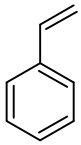
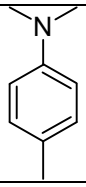
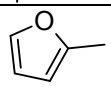
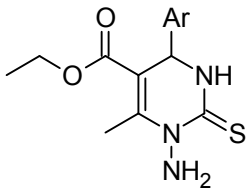
No	Ar	N-H_s	C-H_s	C=O_s	N=C_s	C=S_s	Others
II		3427	2923&2852	1735	1560	1107	
IV		O-H 3442	2925&2856	1730	1569	1110	
VI		3446	29250&2858	1731	1556	1101	C=C_s 800
VIII		3413	2923&2858	1731	1517	1114	C-N_s 1365
X		3436	2925&2852	1731	1566	1137	C-O_s 1413

Table. 2.9.3. IR-data of 1-amino5-ethoxycarbonyl-6-methyl-4-aryl-3,4-dihydro pyrimidine-2-thione (XI, XIII, XV & XVII). IR absorption spectra, wave number cm-[1], of synthesized compounds were obtained by preparing KBr pellet



XI,XIII,XV &XVII

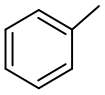
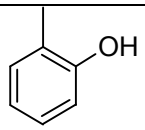
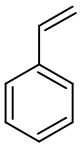
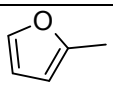
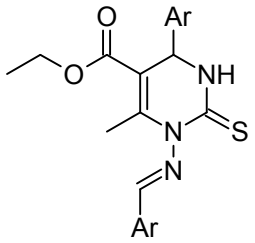
No	Ar	N-H_s	C-H_s	C-H_s	C=O_s	C-O_s	N-H_b	C=S_s
XI		3542	3197 & 3298	2979 & 2829	1706	1303	1625	1182
XIII		O-H_s 3446		2923 & 2854	1733	1224	1637	1112
XV		3419	3159	2923 & 2852	1731	1371	1587	1099
XVII		3442		2923 & 2856	1373	1301	1566	1139

Table. 2.9.4. IR-data of 1-amino arylmethylidene-5-ethoxycarbonyl-6-methyl -4-aryl-3,4-dihydropyrimidine-2-thione (XII, XIV, XVI & XVIII). IR absorption spectra, wave number cm-[1] of synthesized compounds were obtained by preparing KBr pellet.



XII, XIV, XVI &XVIII

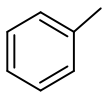
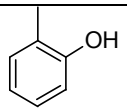
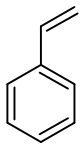
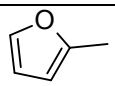
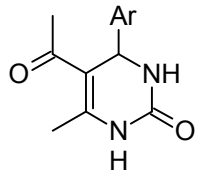
No	Ar	N-H_s	C=N_s	C-H_s	C-H_s	C=O_s	C-O_s	C=S_s
XII		3400	1602	3242& 3157	2923& 2854	1726	1284	1101
XIV		O-H_s 3444	1629		2925	1841		1108
XVI		3452	1637		2923& 2854	C=C_s 798	1415	1101
XVIII		3419	1647		2925&2 842		1107	1016

Table. 2.9.5. IR-data of 5-acetyl-6-methyl-4-aryl-3,4-dihydropyrimidine-2-one (XIX, XX, XXI, XXII & XXIII). IR absorption spectra, wave number cm^{-1} ,of synthesized compounds were obtained by preparing KBr pellet



XIX,XX,XXI,XXII&XXIII

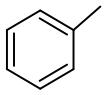
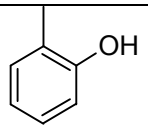
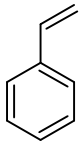
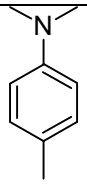
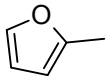
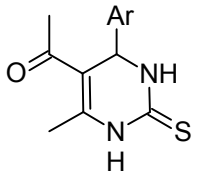
No	Ar	N-H_s	C-H_s	C-H_s	C=O_s	C=C_s	Ar-H_b
XIX		3257	3124	2920	1701	1598	705
XX		3110	3024	2941	1712	1508	O-H 3236
XXI		3278	3116	2945	1695	1608	C=C_s 999
XXII		3294	3114	2900	1697	1610	C-N_s 1236
XXIII		3334	3101	2952	1693	1620	C-O_s 1234

Table. 2.9.6. IR-data of 5-acetyl-6-methyl-4-aryl-3,4-dihydropyrimidine-2-thione (XXIV, XXV, XXVI, XXVII & XXVIII). IR absorption spectra, wave number cm-^{1} of synthesized compounds were obtained by preparing KBr pellet



XXIV,XXV,XXVI,XXVII&XXVIII

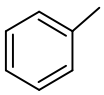
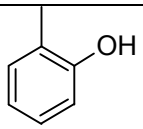
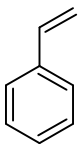
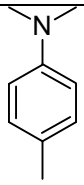
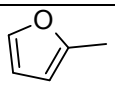
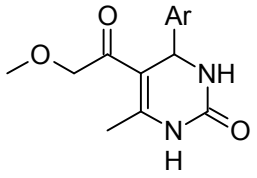
No	Ar	N-H_s	C-H_s	C-H_s	C=O_s	C=C_s	C=S_s	Ar-H_b
XXIV		3296	3199	2993	1608	1577	1180	757
XXV		3145		2954	1714	1568	1089	O-H_s 3226
XXVI		3280	3170	2995	1616	1573	1186	C=C_s 1014
XXVII		3286	3180	2887	1612	1579	1188	C-N_s 1235
XXVIII		3286	3193	2987	1610	1573	1180	C-O_s 1112

Table. 2.9.7. IR-data of 5-ethoxycarbonyl -6-methyl -4-aryl -3,4-dihydro pyrimidine-2-one (XXIX, XXX, XXXI, XXXII &XXXIII). IR absorption spectra , wave number cm-[1], of synthesized compounds were obtained by preparing KBr pellet.



XXIX,XXX,XXXI,XXXII&XXXIII

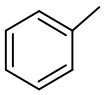
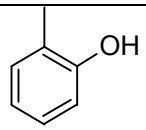
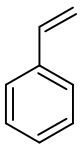
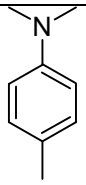
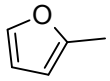
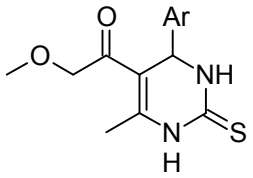
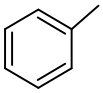
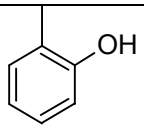
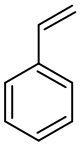
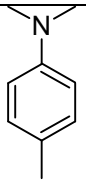
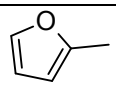
No	Ar	N-H_s	C-H_s	C-H_s	C=O_s	C=C_s	Ar-H_b	C-O_s
XXIX		3440	3344	2804	1681	1623	788	1153
XXX		3330	3074	2941	1749	1508	O-H_s 3238	1244
XXXI		3242	3110	2975	1720	1650	C=$C_{s,cis}$ 779	1286
XXXII		3448	3244	2925	1701	1598	C-N_s 1166	1230
XXXIII		3452		2920	1654	1546		1230

Table. 2.9.8. IR-data of 5- ethoxycarbonyl-6-methyl-4-aryl-3,4-dihydro pyrimidine-2-thione (XXXIV, XXXV, XXXVI, XXXVII &XXXVIII). IR absorption spectra, wave number cm-^{1}, of synthesized compounds were obtained by preparing KBr pellet

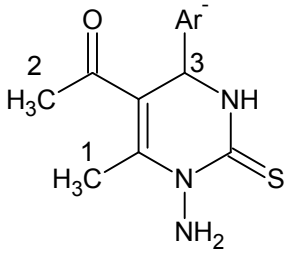


XXXIV, XXXV, XXXVI, XXXVII &XXXVIII

No	Ar	N-H_s	C-H_s	C-H_s	C=O_s	C=C_s	C=S_s	Others
XXXIV		3328	3174	2979	1670	1573	1118	Ar-H_b 761
XXXV		3365	3170	2705	1728	1564	1087	O-H_s 3278
XXXVI		3161		2979	1706	1595	1191	C=C_s, cis 752
XXXVII		3326	3172	2981	1670	1577	1182	C-N_s 1116
XXXVIII		3311	3176	2983	1662	1575	1186	C-O_s 1112

2.10. ^{1}H NMR of Synthesized Compounds

Table. 2.10.1. ^{1}H NMR-data, chemical shift ppm δ of protons of 1-amino-5-acetyl-6-methyl-4-aryl-3,4-dihydropyrimidin2-thione (I, V, VII & IX), synthesized compound dissolved in deuterated DMSO and TMS for calibrating chemical shift, frequency, 400MH$_z$, intensity ,s-sharp, m-medium, w-weak, multiplicity: s-singlet, d-doublet, t-triplet ,q-quartet, qu-quintet, se-sextet, **J**-spin- coupling constant by H$_z$.



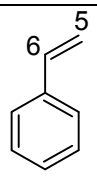
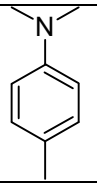
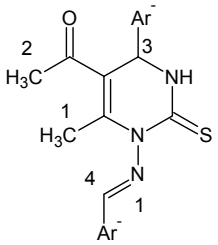
No	Ar	CH_3[1]	CH_3[2]	CH[3]	HAr		
I		2.50(s,s,3H)	3.50(s,s,3H)	1.30(d,m, 1H,1.68, 0.39,J)	7.40-8.30 (q,m, 5H,1.00,0.62,1.00J)		
V		2.50(s,s,3H)	3.50(s,s,3H, 1.00,2.59J)	1.30(d,m, 1H,- 2.80,J)			
VII		2.40(s,s,3H	3.50(s,s,3H)	1.30(d,w, 1H)	$CH_3$5 2.80(d,s, 3H)	$CH_3$6 2.80(d, s,3H)	6.60,7.00(q, w,4H)
IX		2.50(s,s,3H)	3.50(s,s,3H4 9.28J)	1.20(d,w, 1H- 1.51J)	7.10-8.50 (3H, 0.04,0.98J)		

Table. 2.10.2. [1]H NMR-data of 1-amino arylmethylidene-5-acetyl-6-meth yl -4-aryl-3,4-dihydropyrimidine-2-thione (II, IV, VI, VII,VIII & X)



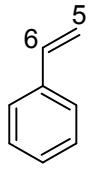
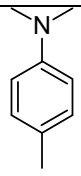
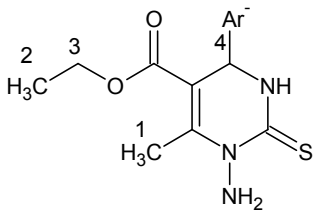
No	Ar	CH_3[1]	CH_3[2]	CH[3]	CH4	HAr	
II		2.50(s,s, 3H)	3.50(s,s,3 H)	1.20(d,s1H,20.79J)	2.00(s,s,1H,2.74J)	6.50-8.50(w,10H,0.29,1.00J)	
IV		2.50(s,s, 3H)	3.50(s,s,3H,0.41J)	1.20(d,m, 1H,0.48, 0.9J)	1.70(s,m,1H,0.47,0.83)	HAr´ 6.80-7.40 (t,s.3H,0.92,1.05,1.40 ,2.49J)	HAr 7.50-8.50(t,s,3H,2.22 ,1.07,1.10,1.00J)
VI		2.50(s,s, 3H)	2.50(s,s,3 H,2.87J)	CH[3] 1.30(d,m, 1H,0.8J)	CH4 2.00(s,w ,1H)	CH5&CH 6´ 1.60(d,s,1 H4.53J)& 1.40(d,w, 1H,2.85J)	CH6&C H6´ 1.10(d,w ,1H,0.52 J)&0.8(d ,w,1H0. 78	HAr´ 6.70-7.30(t,m,5 H,1.35,1.2 9,1.05J)	HAr 7.80-8.50(t,m,5H,1.0 0,0.76,1..84J)
VIII		2.50(s,s, 3H)	3.50(s,s,3 H)	CH[3] 1.30(d,m,1 H,1.28J)	CH4 1.60(s, w,1H)	CH53.00 (d,s,3H,2 .89J)	CH6 3.20(d,m, 3H,0.44J)	HAr&HAr´ 6.80-8.50 (q, m, ,0.48,0.57,48,1.00,1.05J)	
X		2.50(s,s, 3 H)	3.50(s,s,3 H,3.69J)	1.30(s,m,1H,2.09J)	1.60(s,m,1H,1.20J)	HAr&HAr´ 6.60-8.50 (sep ,m, 6H ,0,83,0.93,0.87,0.71,0.82,0.84 J)	

Table. 2.10.3. [1]H NMR-data of 1-amino-5-ethoxycarbonyl-6-methyl-4-aryl-3,4-dihydropyrimidine-2-thione (XI, XIII, XV & XVII) synthesized compound dissolved in deuterated DMSO and TMS for calibrating chemical shift, radiofrequency400MHz.



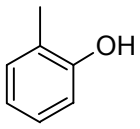
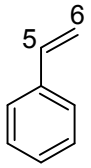
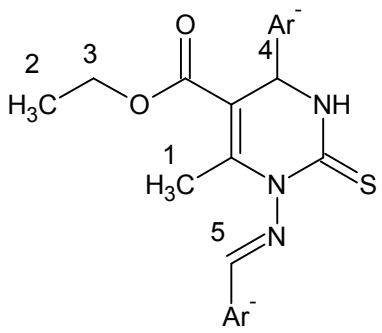
No	Ar	CH_3[1]	CH_3[2]	CH_2[3]	CH4		HAr
XI		2.50(s,s,3H)	3.50(t,s,3H,)	1.20(q,m,1H,1.18)1.30(q,m,2H,1.50J)	0.80(s,w,1H)		7.00-8.50 (m,5H,J)
XIII		2.50(s,s,3H)	3.50(t,s,3H,1.19J)	1.30(q,m,2H,2.23,2.20J)	1.60(s,m,1H,1.77J)		6.80-8.50 (m,4H 0.22,0.77,1.00,2.19,2.36, 1.33,1.13.122J)
XV		2.50(s,s,3H)	3.50(t,s,3H,34.01,14.16J)	1.30(q,s,2H,56.95J)	CH5 1.70(d,m,1H,8.79J)	CH6 0.80(d,w,1H,15.29J)	6.80-8.50-(10H,1.00J)
XVII		2.50(s,s,3H)	3.50(t,s,3H,5.08J)	1.30(q,s,2H7.89,5.30J)	CH4 0.80(d,w,1H,3.65J)		7.00-8.5(w,3H,1.00,0.89,1.15J)

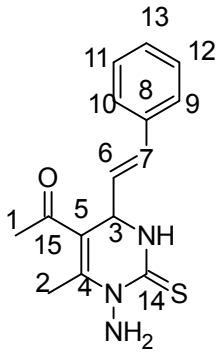
Table 2.10.4. ^{1}H NMR-data of 1-amino arylmethylidene -5- ethoxy carbonyl-6-methyl-4-aryl-3,4-dihydropyrimidine-2-thione (XII, XVI & XVIII) synthesized compound dissolved in deuterated DMSO and TMS for calibrating chemical shift, radiofrequency 400MHz



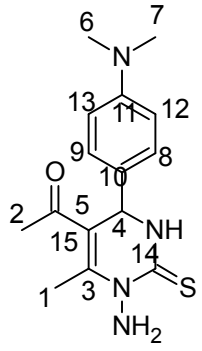
No	Ar	CH_3^1	CH_3^2	CH_2^3	CH4	CH5	H Ar&HAr´
XII		2.50(s,s,1H)	3.50(t,s,3H, 0.46 26.84J)	1.30(q,m, 2H,1.50J)	2.00(d,w,1H, 0.48,174J)	0.8(d,m,1H, 1.50J)	7.50-8.50(0.04,0.98 J)
XIV		2.50(s,s,1H, 6.29)	3.50(t,s,3H,97. 19,0.56J)	1.30(q,m, 2H,4.71J)	2.20(s,m,1H, 1.07J)	0.80(d,w,1H, 0.83J)	6.80-8.50 (o,m,10H,1.02 ,1.13,3.49,3.8 0,1.14.1.05J)
VXIII		2.50(s,s,1H)	3.50(t,s,3H,95, 15J)	1.30(q,w,2 H3.56J)			6.00-8.00(6H,1.29)

2.10.^{13}CNMR of Synthesized Compounds

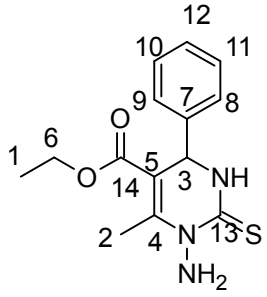
Table. 2.10.5. ^{13}C NMR-data of 1-amino -5- acetyl -6- (cinnamyl)-6-methyl-3,4-dihydropyrimidine-2-thione, -V-, 1-amino-5-acetyl-4-(4-dimethyl amino phenyl)-6-methyl-3,4-dihydropyrimidine-2-thione, -VII- and 1-amino phenyl methylidene 5-ethoxycarbony-6-methy-4-phenyl-3,4-dihydropyrimidine-2-thione-XII



-V-

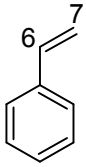
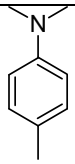


-VII-



XII

Table.2.10.5. ^{13}C NMR.

No	Ar	$CH_3$1	$CH_3$2	CH3	C4	CH5	CH6	CH7	CAr	C=S	C=O
V		39.31	39.52	39.73	39.94	40.15	40.36	40.57	125.56, 127.39, 129.31, 129.36 136.35, 139.33	145.21	178.17
VII		38.49	39.31	39.52	39.73	39.94	40.65	40.51	40.67 40.57 112.92 123.96 128.1 130.59	144.09	197.68
XI		39.32	39.53	39.73	39.94	40.15	40.36		40.57, 127.26 129.13, 130.44, 134.75	142.80	185.90

2.11. MS of Synthesized Compounds

Table. 2.11.1. of MS-data of 1-amino -5- acetyl -6-methyl -4-aryl-3,4-dihydro pyrimidine2-thione.(I, III, V, VII & IX)

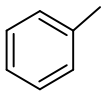
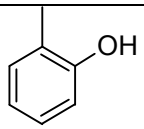
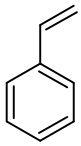
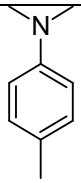
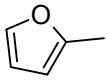
No	Ar	Base peak(m/z)	Fragments(m/z)
I		179	35,43, 60, 76, 93, 119, 162, 185.
III		35	35, 42, 63, 71, 84, 99, 112, 126, 141, 329, 340.
V		195	35, 43, 60, 77, 91, 102, 120, 132,147, 161, 178,219, 239.
VII		35	35,46, 63, 71,85, 99, 113, 127, 332, 343.
XI		130	35,43, 69, 77, 91, 103, 115, 145, 171, 205

Table.2.11.2.of MS-data of 1-amino arylmethylidiene -5- acetyl-6-methyl -4- aryl -3,4-dihydropyrimidine-2-thione (II, IV, VI, VIII & X)

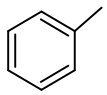
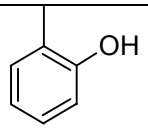
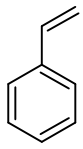
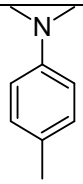
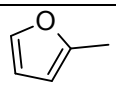
No	Ar	Base peak(m/z)	Fregments(m/z)
II		43	35,41, 57, 83, 96, 98, 121, 129, 147, 157, 171, 183.
IV		54	35, 56, 70, 84, 98, 112, 252, 254, 271.
VI		49	35, 56, 70, 84, 98, 209, 216, 225.
VIII		311	35,41, 43, 60, 77, 91, 105, 120, 149, 192, 227, 253, 269, 295.
X		43	35,41, 57, 73, 97, 105, 129, 147, 185.

Table. 2.11.3. of MS-data of 1-amino- 5-ethoxycarbonyl-6- methyl -4-aryl-3,4-dihydropyrimidine-2-thione (XI, XIII, XV & XVII).

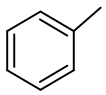
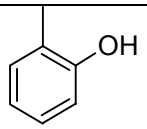
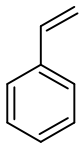
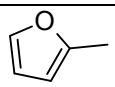
No	Ar	Base peak(m/z)	Fragments (m/z)
XI		43	35,39, 60, 76, 93, 104, 119, 145, 179.
XIII		130	35,43, 69, 76, 91, 103, 115, 145, 163, 172, 189, 205.
XV		47	35, 56, 70, 84, 182, 183, 197..
XVII		427	35,41,43, 57, 77, 91, 115, 129, 144, 155, 177, 185,387, 401, 473.

Table. 2.11.4. of MS-data of 1-amino arylmethylidene-ethoxycarbonyl-6-methyl-4-aryl-3,4-dihydropyrimidine-2-thione(XII, XIV, XVI &XVIII)

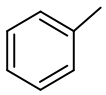
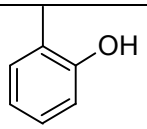
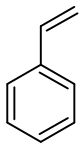
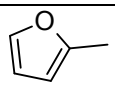
No	Ar	Base peak(m/z)	Fragments(m/z)
XII		35	35,55,57, 71, 85, 99, 113, 251, 253.
XIV		133	35, 41, 43, 69, 91, 103, 119, 145, 177, 205
XVI		43	35,41,57, 71,85, 111, 113, 129,147, 169..
XVIII		195	35, 39, 43, 60, 77, 91, 102, 120, 135, 178, 196.

Table. 2.11.5. of MS-data of 5-acetyl -6-methyl -4-aryl -3,4-dihydropyrimidine -2-one (XIX, XX, XXI, XXII & XXIII).

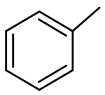
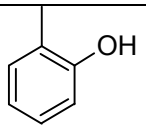
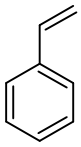
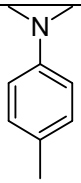
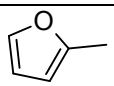
No	Ar	Molecular ion(m/z)	Base peak(m/z)	Fragments (m/z)
XIX		229	153(M+-Ar)	50, 68, 77, 91, 110, 131, 153, 169, 187, 215.
XX		246	203(M+-CH_3CO	50, 57, 77, 91, 111, 144, 160, 189,
XXI		257	196(M+-ph)	50, 63, 77, 115, 141, 168, 211.
XXII			177	50, 65, 77, 94, 106, 122, 134, 149, 166, 191, 203, 220.
XXIII		220	177	50, 68, 77, 94, 106, 122, 134, 149, 166, 191,203.

Table. 2.11.6. of MS- data of 5- acetyl -6-methyl -4-aryl -3,4-dihydro pyrimidine-2-thione (XXIV, XXV, XXVI, XXVII & XXVIII).

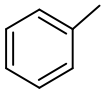
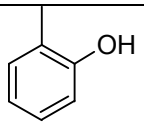
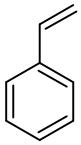
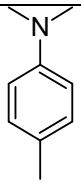
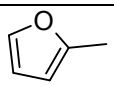
No	Ar	Molecular ion(m/z)	Base peak(m/z)	Fragments (m/z)
XXIV			274	50, 67, 77, 91, 110, 120, 137, 144, 155, 175, 230, 239, 288, 303.
XXV		261	220	50, 65, 77, 91, 104, 120, 127, 145, 160, 205,
XXVI		271	245	51, 68, 77, 91, 110, 115, 130, 144, 160, 169, 187, 202, 219, 261.
XXVII			181	7250, 68, 77, 91, 110, 128, 153, 196, 212, 229, 239, 255, 272.
XXVIII		236	236	51, 65, 77, 94, 106, 121,134, 162, 176, 193, 203, 219.

Table. 2.11.7. of MS-data of 5- ethoxycarbonyl -6-methyl -4-aryl -3,4- dihydro pyrimidine-2-one (XXIX, XXX, XXXI, XXXII & XXXIII).

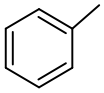
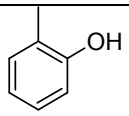
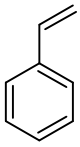
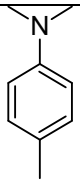
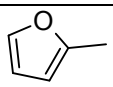
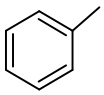
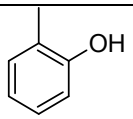
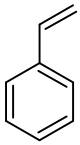
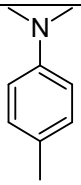
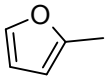
No	Ar	Molecular ion(m/z)	Base peak(m/z)	Fragments (m/z)
XXIX		260	183	51, 67, 77, 96, 110, 137, 144, 155, 172, 214, 231, 245.
XXX			193	50, 65, 77, 94, 106, 121, 134, 153, 178, 237, 266.
XXXI			73	51, 55, 69, 85, 98, 115, 130, 149, 207.
XXXII			257	50, 67, 77, 91, 110, 137, 151, 155, 183, 213, 240, 286.
XXXIII		250	177	52, 65, 77, 94, 110, 124, 137, 150, 162, 193, 203, 221, 233.

Table. 2.11.8. of MS-data of 5-ethoxycarbonyl-6-methyl-4-aryl-3,4-dihydro pyrimidine-2-thione (XXXIV, XXXV, XXXVI, XXXVII &XXXVIII)

No	Ar	Molecular ion(m/z)	Base peak(m/z)	Fragments(m/z)
XXXIV		276	199	50, 67, 77, 91, 103, 115, 128, 153, 171, 230, 247, 261.
XXXV			328	51, 67, 77, 91, 105, 115, 127, 152, 167, 221, 239, 267, 295, 315
XXXVI			60	55, 73, 95, 98, 129, 207.
XXXVII			193	50, 53, 65, 77, 94, 106, 121, 134, 153, 178, 237, 266,
XXXVIII		266	193	50, 65, 77, 94, 106, 221, 237.

2.12. Retention factor for synthesized compounds

Table. 2.12.1. TLC-data of 1-amino -5- acetyl -6-methyl -4-aryl -3,4-dihydro pyrimidin-2-thione (I, III, V, VII & IX) and 1-amino aryl methylidiene-5-acetyl-6-methyl-4-aryl-3,4-dihydropyrimidine-2-thione (II, IV, VI, VIII & X) by thin layer chromatography 20 x 20cm plates of aluminium precoating silica gel G F_{254} (magnesium activated zinc silicate)

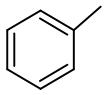
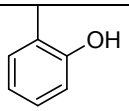
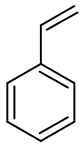
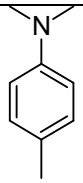
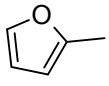
No	Ar	Solvent system	Retention factor	No	Retention factor
I		Chloroform: methanol 9.2 : 0.8	0.68	II	0.7
III		Chloroform: methanol 9.2 : 0.8	0.65	IV	0.6
V		Chloroform: methanol 9.2 : 0.8	0.7	VI	0.8
VII		Chloroform: methanol 9.2 : 0.8	0.7	VIII	0.8
IX		Chloroform: methanol 9.2 : 0.8	0.75	X	0.8

Table. 2.12.2. TLC-data of 1-amino-5-ethoxy carbonyl -6-methyl-4-aryl-3,4-dihydropyrimidin2-thione (XI, XIII, XV &XVII) and 1-amino arylmethylidene -5- ethoxycarbonyl -6-methyl -4-aryl -3,4-dihydropyrimidin2-thione (XII, XIV, XVI & XVIII). by thin layer chromatography 20 x 20cm plates of aluminium precoating silica gel GF_{254} (magnesium activated zinc silicate)

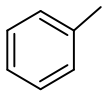
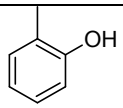
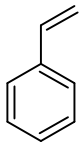
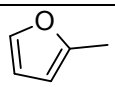
No	Ar	Solvent system	Retention factor	No	Retention factor
XI		Chloroform: methanol 9.5 : 0.5	0.65	XII	0.7
XIII		Chloroform: methanol 9.5: 0.5	0.3	XIV	0.3
XV		Chloroform: methanol 9.5 : 0.5	0.6	XVI	0.7
XVII		Chloroform: methanol 9.5 : 0.5	0.5	XVIII	0.6

Table. 2.12.3. TLC-data of 5-acetyl -6-methyl -4-aryl -3,4-dihydro pyrimidine-2-one (XIX, XX, XXI, XXII & XXIII).by thin layer chromatography 20 x 20cm plates of aluminium precoating silica gel G F_{254} (magnesium activated zinc silicate)

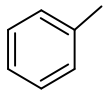
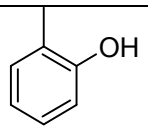
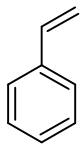
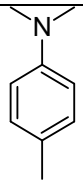
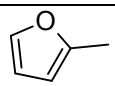
No	Ar	Solvent system	Retention factor
XIX		Chloroform: methanol (8:2)	0.5
XX		Chloroform: methanol (8:2)	0.8
XXI		Chloroform: methanol (8:2)	0.7
XXII		Chloroform: methanol(8:2)	0.8
XXIII		Chloroform: methanol (8:2)	0.7

Table. 2.12. 4.TLC-data of 5-acetyl -6-methyl -4-aryl- 3,4-dihydro pyrimidine-2-thione (XXIV, XXV, XXVI, XXVII & XXVIII) by thin layer chromatography 20 x 20cm plates of aluminium precoating silica gel GF_{254} (magnesium activated zinc silicate).

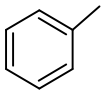
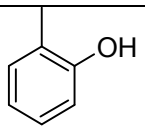
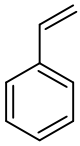
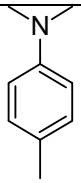
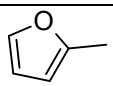
No	Ar	Solvent system	Retention factor
XXIV		Chloroform: methanol (9:1)	0.8
XXV		Chloroform: methanol (9:1)	0.7
XXVI		Chloroform: methanol (9:1)	0.6
XXVII		Chloroform: methanol (9:1)	0.5
XXVIII		Chloroform: methanol (9:1)	0.8

Table.2.12.5.TLC-data of 5-ethoxycarbonyl -6-methyl -4-aryl -3,4-dihydropyrimidine-2-one (XXIX, XXX, XXXI, XXXII & XXXIII) by thin layer chromatography 20 x 20cm plates of aluminium precoating silica gel GF_{254} (magnesium activated zinc silicate)

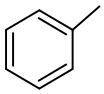
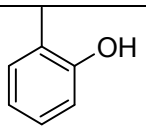
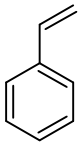
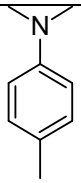
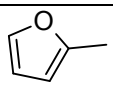
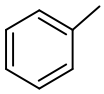
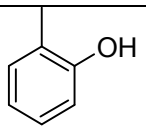
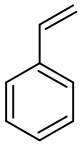
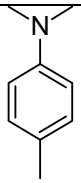
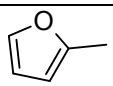
No	Ar	Solvent system	Retention factor
XXIX		Chloroform: methanol (8:2)	0.7
XXX		Chloroform: methanol(8:2)	0.5
XXXI		Chloroform: methanol(8:2)	0.6
XXXII		Chloroform: methanol (8:2)	0.5
XXXIII		Chloroform: methanol (8:2)	0.7

Table.2.12.6.TLC-data of 5- ethoxycarbonyl -6-methyl -4-aryl -3,4-dihydropyrimidine-2-thione (XXXIV, XXXV, XXXVI, XXXVII &XXXVIII) by thin layer chromatography 20 x 20cm plates of aluminium precoating silica gel G F_{254} (magnesium activated zinc silicate)

No	Ar	Solvent system	Retention factor
XXXIV		Chloroform: methanol (9:1)	0.8
XXXV		Chloroform: methanol (9:1)	0.2
XXXVI		Chloroform: methanol (9:1)	0.3
XXXVII		Chloroform: methanol (9:1)	0.9
XXXVIII		Chloroform: methanol (9:1)	0.8

Chapter Three

Discussion

3. Discussion

3.1.Reaction Mechanism

Biginelli reaction belongs to the second type of multicomponent reactions, which mean that the majority of reaction are reversible but the final product is irreversible, the first step in the mechanism is believed to be the condensation between the aldehydes and thiosemicarbazide in nucleophilic addition forming two N - acyliuminmium intermediates one from one aldehyde and other from two aldehydes molecule, this N - acyliuminmium ions acts as electrophile for the nucleophilic addition of the diketone enol form, lewis acids catalyst $ZnCl_2$ stabilized N - acyliuminmium ion intermediate which is very reactive by coordination to the thiosemicarbazide sulphur and the equilibrium of the reaction is forced towards the product by coordination the catalyst with water oxygen which produced from first step, also lewis acid stabilized the enol form. The resulting adduct undergoes condensation with the thiosemicarbazide′s NH to give the cyclized product

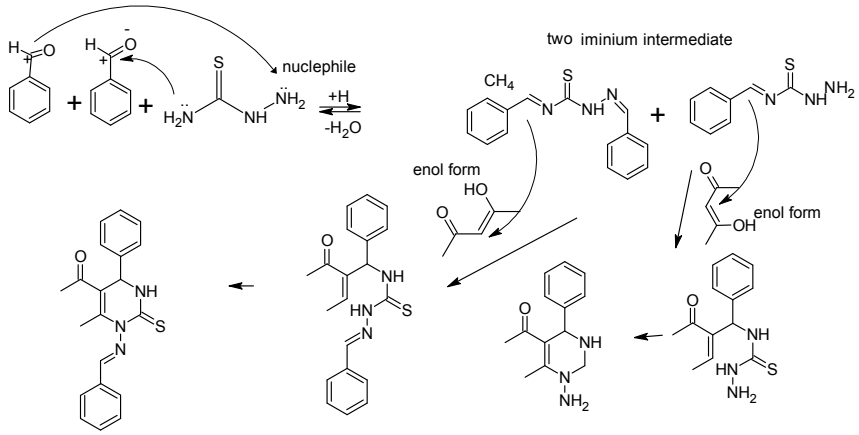
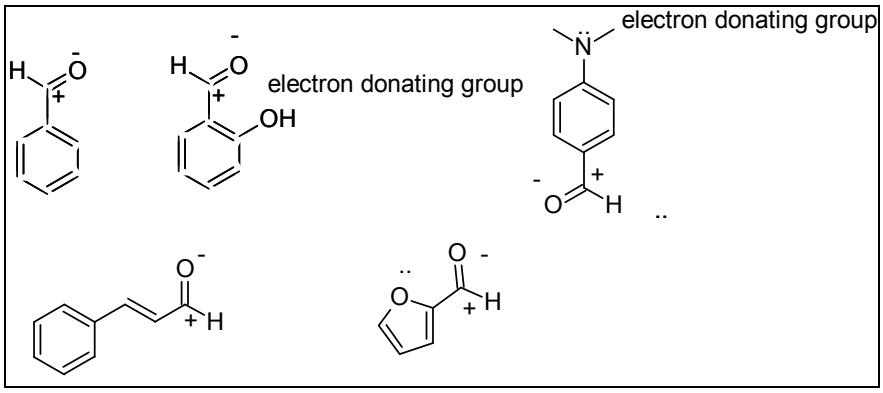


Fig. 3.1. mechanism of the Biginelli reaction

In respect of aldehydes, for benzaldehyde the thiosemicarbazide′s NH_2 acts as nucleophile and attacks benzaldehyde on the electron deficient carbon cation of carbonyl group and form N-acyliuminmium ion, but in case of salicyaldehyde and

p-dimethylamino benzaldehyde which is considered as benzaldehyde with electron donating group (OH) and $N(CH_3)_2$) the OH group decreases the electron deficient carbon cation on the carbonyl group of aldehyde so as not to facilities the reaction also the $N(CH_3)_2$ group through resonance decrease the electron deficient carbon cation on the carbonyl group of aldehyde, in case of cinnamaldehyde the conjugated π system decrease electron deficient carbon cation through resonance, for furfuraldehyde the lone pair of electron on oxygen is delocalized into the ring, creating a 4n+2 aromatic system (Hückle's rule) similar to benzene so act like benzaldehyde.



Scheme. 3.1. reactivity of different aldehydes

The next step of formation of Biginelli compounds is that the active methylene group on acetyl acetone and ethyl acetoacetate adds onto the intermediate N-acyliuminmium ion through its enol form produces open-chain compound which subsequently cyclized to the dihydropyrimidin-2-thione by elimination of water, the ethyl acetoacetate enol form is more stable than acetyl acetone enol form. Thin-layer chromatography used to monitor the progress of the reaction, and the structures of the synthesized compounds confirmed by comparison TLC with authentic starting material, and the retention factor of the synthesized compounds are identified by dividing the distance the product traveled by the distance the solvent front traveled. TLC used to separated synthesized compounds into two components, all the synthesized compounds visualized their spots under UV-lamp

and the stationary phase use are incorporate with fluorescence 254 nm means spots occur due to quenching the plate fluorescence and all synthesis compounds are colorless.

3.2. Spectroscopic analysis of synthesized compounds

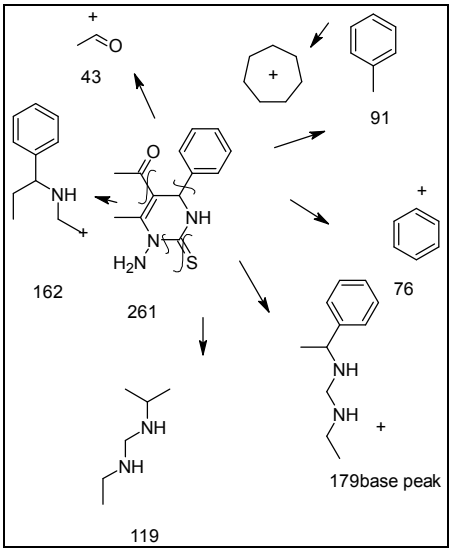
UV spectraphotometer, source of radiation Deuterium arc lamp (190-400nm), single beam instrument samples are placed in a transparent cell, Cuvettes, are rectangular in shape, with an internal width of 1 cm, made of quartz glass. The UV absorption spectrum absorbance on the vertical axis vs wavelength, all synthesized compound shown that electronic transition of the (π-π*) and (n-π*) eg, compound -1- give absorption at wavelength 223.5 and 250nm, compound,-VII- give absorption at wavelength 236.5 and 355.5nm and compound,-XV- give absorption at wavelength 264 and 364nm, spectrum of some compounds synthesized from salicyldehyde show longer wavelength than those synthesized from benzaldehyde due to the present of OH group, auxochrome, which enhance the absorption, resulting from interaction of unshared pair electron with the π electron in chromophore, n-π conjugation, also spectrum of some compounds synthesized from cinnamaldehyde give stronger band long with wavelength, which consider as conjugated system, some p-dimethylamino benzaldehyde compounds have longer wavelength, bathchromic effect.

The IR spectrum absorbance on the vertical axis vs. wavenumbers, all compounds showed absorption bands at wave number in cm^{-1} of $N\text{-}H_s$,(3242 -3452 cm^{-1}) $C{=}O_s$ (1706 -1841cm^{-1}) and $C{=}S_s$ (1099 -1139 cm^{-1}) stretching vibration, chang in distance between two atoms, the compounds have 1-amino-5-acetyl-6-methyl-4-aryl-3,4-dihydropyrimidine-2-thione and 1-amino-5-ethoxycarbonyl-6-methyl-4-aryl-3,4-dihydropyrimidine-2-thione general structure show very strong absorption at wave number in cm^{-1} (1535 -1687 cm^{-1}), N-H bending vibration ,change in

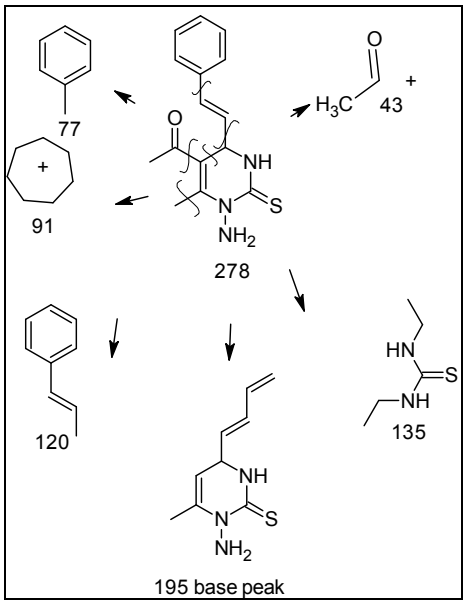
bond angles, due to the presence of NH_2 group, the compounds have 1-amino arylmethyldiene-5-acetyl-6- methyl-4-aryl-3,4-dihydropyrimidine-2-thione and 1-amino arylmethylidene-5-ethoxycarbonyl-6-methyl-4-aryl-3,4- dihydropyrimidine-2 - thione general structure show very strong absorption at wave number in cm^{-1} $C=N_s$ (1517- 1647cm^{-1}) due to the presence of C=N group, all compounds synthesized from salicyaldehyde show broaden band of O-H at wave number in cm^{-1} (3226-3446 cm^{-1}), some compounds show absorption bands at wave number in cm^{-1} (2360-2366cm^{-1}) result from presence of CO_2, or combination bands, all the compounds showed absorption bands at wave number in cm^{-1} (700-954cm^{-1}) this indicated that the substituent on the Ar ring are out of plane or in other words the pyrimidine ring are perpendicular to the Ar ring

Mass spectroscopy, ionization source of energy electron- impact, mass spectrum relative abundance in vertical axis vs mass/charge ratio m/z, all the compounds synthesized from thiosemicarbazide and most compound synthesized from thiourea give no molecular ions in their spectrum this indicates that all these compounds are not stable and fragmented to small molecular ions and most of them give fragment molecular ion of value +43 which indicated that fragment of acylium ion $(CH_3CO)+$ and in some compounds this fragment ion appear as base peak, high abundance, also sulphur compounds have low ionization energy of non bonding sulphur electrons, all the compounds synthesis from thiosemicarbazide showed fragment ion with value 35, this fragment ion appear as base peak in some compounds, also the compounds number VI, V, VI, VII, XIII & XVII showed broader peaks extending over several mass units, meta stable ion peaks, result from these compounds undergo fragmentation during ionization, which mean the kinetic energy of ions converted to the internal energy. While most compounds synthesized from urea showed molecular ion in their spectrum, and all synthesized compounds give fragment ion of value 50,60,68,76,77,91,93 indicating presence of

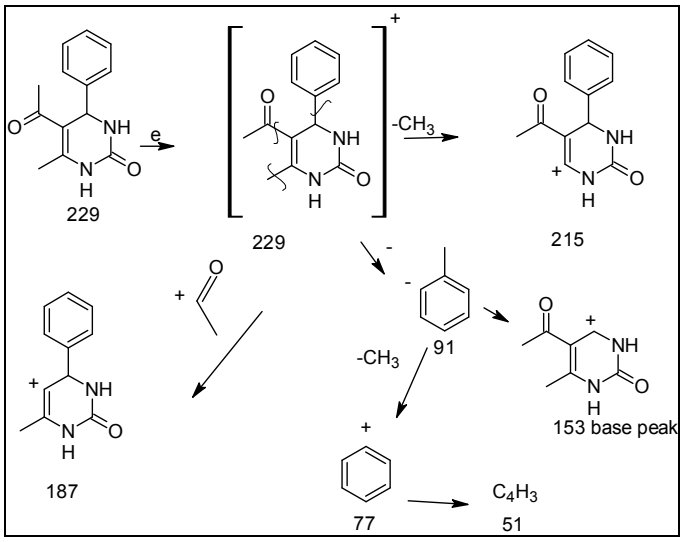
C_6H_6+ fragmentes, here are a fragmentation pattern of some synthesized compounds.



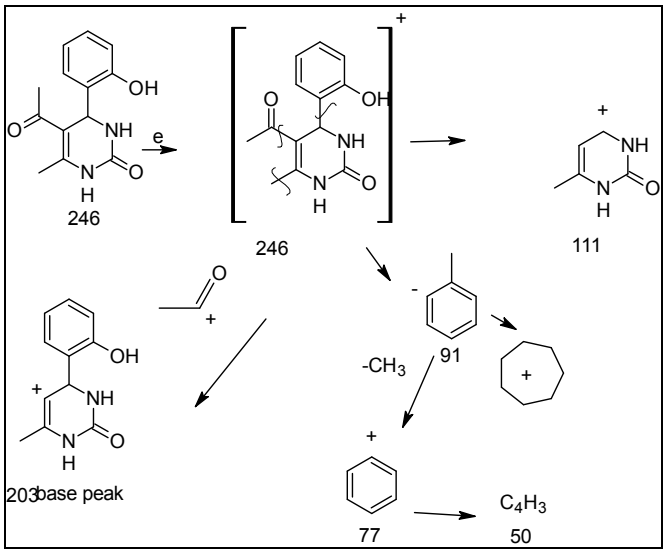
Scheme .4.1. Fragmentation pattern of 1-amino-5-acetyl-6-methy-4- phenyl-3,4-dihydropyrimidine-2-thione.



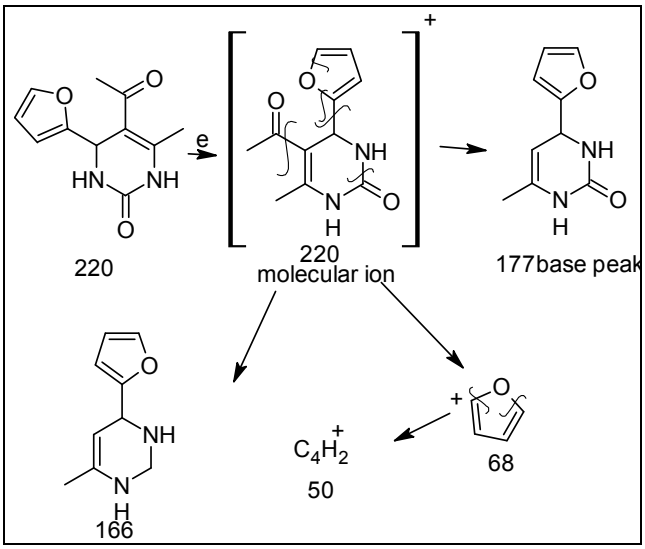
Scheme 4.2. Fragmentation pattern of 1- amino- 5-acetyl -4- (cinnamyl) -6-methy -3,4-dihydropyrimidine -2- thione.



Scheme.4.3. Fragmentation pattern of 5-acetyl-4-phenyl-6-methyl-3,4-dihydropyrimidine-2-one.



Scheme .4.4 fragmentation pattern of 5- acetyl -4-(2-hydroxyl-phenyl)-6-methyl-3,4-dihydropyrimidine-2-one.



Scheme .4.5. Fragmentation pattern of 5-acetyl-4-fury-6-methyl-3,4-dihydropyrimidine-2-one.

The ^{1}HNMR technique uses a continuous wave nuclear magnetic resonance, at 400MH_z frequency and varied magnetic field (field sweep), synthesized compounds dissolved in deuterated dimethyl sulfoxide, and use tetramethyl silane (TMS) as an internal standard for calibrating the chemical shifts. ^{1}HNMR spectrum signal intensity vs. chemical shift δppm, of all the synthesized compounds showed in spectrum singlet peak at (2.50) ppm for three protons of CH_3, three proton in same environment, and all the compounds have 1-amino-5-acetyl-6-methyl-4-aryl-3,4-dihydropyrimidine-2-thione and 1-amino arylmethylidene-5- acetyl -6-methyl -4-aryl-3,4-dihydropyrimidin-2-thione of a general structure showed singlet peak for three protons of CH_3 proton at (3.50ppm) the higher value due to the chemical shift and magnetic anisotropy from neighboring group ,carbonyl group, deshielding effect, downfield, also these compounds not give chemical shift for labile protons in NH_2 group, or the proton on NH group or OH group, hetero atom attached proton, these atom cause higher deshield so proton signal appear offset, and compound number –I-, showed five peaks for five protons of benzene ring three peak due to the di-ortho protons 7.50, 8.00, 8.20ppm and another peak due to the para protons 7.80ppm and the one peak due to the di-meta proton 7.40ppm this

multiples from coupling between neighboring nuclei, spin system, and the higher value due to anisotropy effect of benzene ring, the compounds number VII & VIII showed sharp signal at (3.20-2.60ppm) for six protons on $N(CH_3)_2$ which are structurally indistinguishable, compound number -VII showed doublet doublet peaks for four proton on benzene ring, AA′,BB′ spin system, compounds number-V, VI &XV, which contain CH=CH in their structure showed chemical shift in higher value for these protons because double bonds are magnetically anisotropic, all the compound having 1-amino -5- ethoxycarbonyl -6- methyl -4- aryl-3,4-dihydro pyrimidin-2-thione and 1-amino arylmethylidene-5-ethoxy carbonyl-6-methyl-4- aryl-3,4-dihydropyrimidin-2-thione general structure showed triplet peaks and quarter peaks for CH_3-CH_2 protons resulting from spin-spin coupling of CH_3-CH_2 according to (n+1) multiplicity rule, the J coupling constant of compounds number –II , IX,XII,XIV&XVIII be substantially great this lead to a distortion of the multiplicity, resulting from inner peaks (here peak of CH_3-CH_2) which increase in intensity of absorption while the outer peaks decrease the intensity of absorption (here peaks of benzene and furyl rings), compound number-V spectrum show negative value of J coupling which mean the chemical schif difference become less to the value of the coupling constant and the first order analysis of spin-spin coupling is breaks down completely. The ^{13}C NMR the normal reference compound is TMS and synthesized compound dissolved in DMSO dimethyl sulfoxide, spectrum signal intensity vs. chemical shift δppm, spectrum for compound number V appear the sp^3 hybridized carbons of CH_3 at 39.31, 39.52 & 39.73 ppm upfield than the sp^2 hybridized carbon which appear at 39.94, 40.15, 40.36 & 40.57 and showed six absorption for Ar carbon atoms at 125.56, 127.39, 129.31, 129.36, 136.35 and 139.33 ppm one of these carbon is quaternary, not attach to any proton, longer relaxation time, no nuclear overhauser effect so give lower intensity in spectrum than other carbons, and carbon of C=O appear at 178.17ppm (because the external magnetic field experienced by the

carbon nuclei is affected by the electronegativity of the atoms attached to carbon, so the chemical shift of the carbon increases if it attach an atom like oxygen, down field, (the larger chemical shift) and of C=S appear at145.21ppm, compound number VII appear the effect of substituent on the benzene ring, ($N(CH_3)_2$ in which carbon chemical shift further upfield (40.67, 40.57,112.92, 123.69 128.17 and 130. 59 ppm), the spectrum of compound number XI not showed all the carbon atom as we expect this may be related to that one of these carbons is ^{13}C isotope.

Conclusions and recommendation

The following points may be concluded and recommended according to the results of this study

*Most published of Biginelli reaction involved urea or thiourea as one component of these reaction the modified in this research is use thiosemicarbazide as building block.

* Biginelli compounds from urea and thiourea can be synthesized without catalyst and under solvent free condition but for thiosemicarbazide use catalyst is a must and long reaction time compared to urea and thiourea.

* One reaction of thiosemicarbazide provided two type of Biginelli compounds.

*In summary, hardly a month goes by without the publication of an impoved Biginelli procedure appearing in the primary literature, because Biginelli compounds have many pharmacetial application, such as calcium channel modulators, analgesic, anticancer, antioxidant agents, anti-flammatory, antimicrobial and neuropeptide antagonists. Perform Biginelli reaction by use thiosemicarbazide as precursor leads to synthesis Biginelli compounds having variety structures depend on the aldehydes use in the reaction.

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Appendixes

5.Appendixes

5.1.IR spectrum of synthesized compounds

5.1.1. IR spectrum of 1-amino-5-acetyl-6-methyl-4-aryl-3,4-dihydropyrimidin2-thione (I,III,V,VII&IX)

5.1.2. IR spectrum of 1-amino arylmethylidiene-5-acetyl-6-methyl-4-aryl-3,4-dihydropyrimidin2-thione (II,IV,VI,VIII&X).

5.1.3. IR spectrum of 1-amino5-ethoxycarbonyl-6-methyl-4-aryl-3,4-dihydropyrimidin2-thione (XI,XIII,XV&XVII).

5.1.4. IR spectrum of 1-amino arylmethylidene-5-ethoxycarbonyl-6-methyl-4-aryl-3,4-dihydropyrimidin-2-thione (XII,XIV,XVI&XVIII)

5.1.5. IR spectrum of 5-acetyl-6-methyl-4-aryl-3,4-dihydropyrimidine-2-one (XIX, XX, XXI, XXII &XXIII)

5.1.6. IR spectrum of 5-acetyl-6-methyl-4-aryl-3,4-dihydropyrimidine-2-thione (XXIV, XXV, XXVI, XXVII &XXVIII)

5.1.7. IR spectrum of 5- ethoxycarbonyl-6-methyl-4-aryl-3,4-dihydropyrimidine-2-one (XXIX, XXX, XXXI, XXXII &XXXIII)

5.1.8. IR spectrum of 5- ethoxycarbonyl-6-methyl-4-aryl-3,4-dihydropyrimidine-2-thione (XXXIV, XXXV, XXXVI, XXXVII &XXXVIII)

5.2.Mass spectrum of the synthesized compounds

5.2.1. mass spectrum of 1-amino-5-acetyl-6-methyl-4-aryl-3,4-dihydropyrimidin2-thione (I,III,V,VII&IX).

5.2.2. mass spectrum of 1-amino arylmethylidiene-5-acetyl-6-methyl-4-aryl-3,4-dihydropyrimidin2-thione (II,IV,VI,VIII&X).

5.2.3. mass spectrum of of 1-amino-5-ethoxycarbonyl-6-methyl-4-aryl-3,4-dihydropyrimidin2-thione (XI,XIII,XV&XVII).

5.2.4. mass spectrum of 1-amino arylmethylidene-5-ethoxycarbonyl-6-methyl-4-aryl-3,4-dihydropyrimidin-2-thione(XII,XIV,XVI&XVIII).

5.2.5. mass spectrum of 5-acetyl-6-methyl-4-aryl-3,4-dihydropyrimidine-2-one (XIX, XX, XXI, XXII &XXIII).

5.2.6. mass spectrum of 5-acetyl-6-methyl-4-aryl-3,4-dihydropyrimidine-2-thione (XXIV, XXV, XXVI, XXVII &XXVIII)

5.2.7. mass spectrum of 5- ethoxycarbonyl-6-methyl-4-aryl-3,4- dihydro pyrimidine-2-one (XXIX, XXX, XXXI, XXXII &XXXIII)

5.2.8. mass spectrum of 5- ethoxycarbonyl-6-methyl-4-aryl-3,4- dihydro pyrimidine-2-thione (XXXIV, XXXV, XXXVI, XXXVII &XXXVIII)

5.3. ^{1}HNMR of the synthesized compounds

5.3.1. ^{1}HNMR spectrum of 1-amino-5-acetyl-6-methyl-4-aryl-3,4-dihydro pyrimidin2-thione (I,III, VII&IX)

5.3.2. ^{1}HNMR spectrum of 1-amino arylmethylidiene-5-acetyl-6-methyl-4-aryl-3,4-dihydropyrimidin2-thione (II,IV,VI,VIII&X).

5.3.3. ^{1}HNMR spectrum1-amino-5-ethoxycarbonyl-6-methyl-4-aryl-3,4-dihydropyrimidin2-thione (XI,XIII,XV&XVII).

5.3.4. ^{1}HNMR spectrum1-amino arylmethylidene-5-ethoxycarbonyl-6-methyl-4-aryl-3,4-dihydropyrimidin-2-thione (XII,XVI&XVIII)

5.4-^{13}CNMR

5.4.1. ^{13}CNMR spectrum of 1-amino -5-acetyl-4-(cinnamyl)-6-methyl-3,4-dihydropyrimidine-2-thione of(V),

5.4.2. ^{13}CNMR spectrum 1-amino-5-acetyl-4-(4-dimethyl aminophenyl)-6-methyl-3,4-dihydropyrimidine-2-thione (VII).

5.4.3. ^{13}CNMR spectrum 1-amino -5-ethoxycarbony-6-methy-4-phenyl-3,4-dihydropyrimidine-2-thione (XI).