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SYNTHESIS OF PYRIMIDINE AND PYRIMIDINTHIONE

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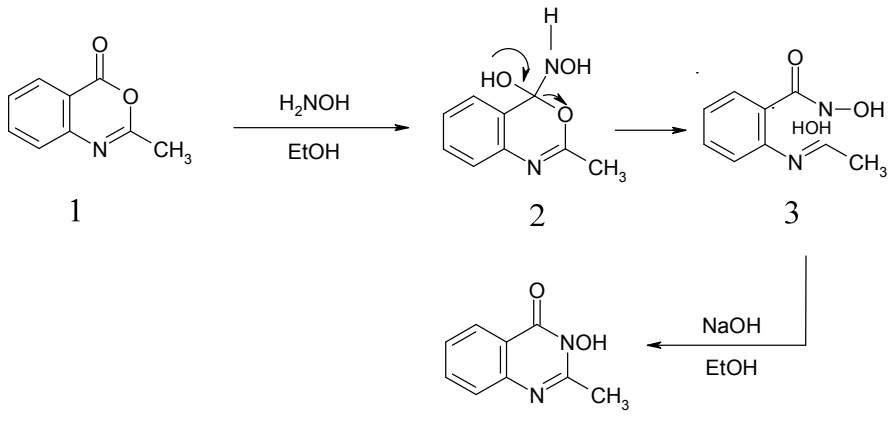
Abstract
The review summarizes literature dealing with the synthesis of pyrimidine and pyrimidinthione Various methods for synthesizing pyrimidine and pyrimidinethione are discussed.

Key words: Pyrimidine, pyrimidinthione , synthesis.

1- PYRIMIDINE

The formation of 3- hydroxyl -2- methyl – benzpyrimidine -4- one, **4** was suggested to proceed via sensitive nucleophelic addition of hydroxyl amine to the quinoxalinone carbonyl group to product the corresponding adduct intermediate **2**. Such intermediate undergo basic hydrolysis in the presence of sodium hydroxide to afford the open structure intermediate compound 3 which under thermal basic condition undergo dehydrated ring closer to give desire compound **4.** Soleiman et al , 2004[1].

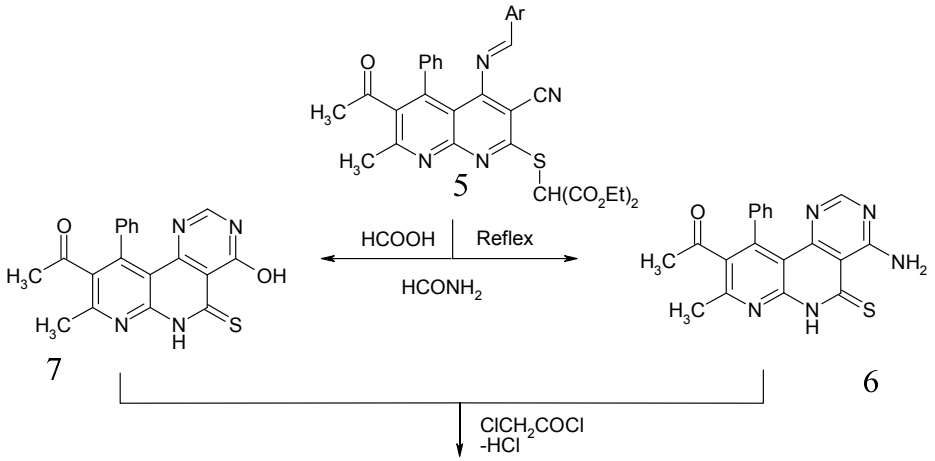


1 2 3

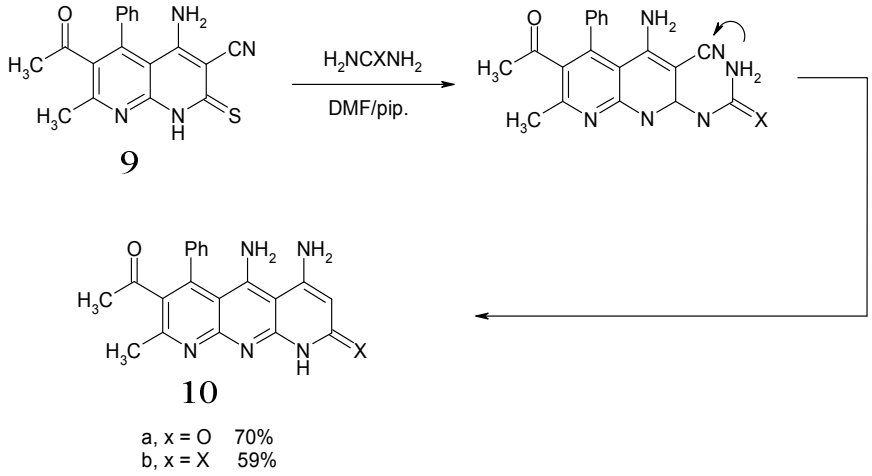
4

Also compound **5** fused with formamide at reflux temperature leading to amino pyrimidine derivative , while the reaction in a mixture of formamide /formic acid gave hydroxyl pyrimidine derivative **7**, the formation of **6** was assumed to by product via intial condensation reaction of the carbonyl group in formamide with the amino function in the naphthpyridine then subsequent

nucleophilic addition of the amino of the formamide into the cyano function in the naphthpyridine **5** yielded the product **6**, further reaction of **6** and **7** with one mole of chloroacetyl chloride in ethanol solution in the presence of triethylamine as catalyst leads to the new thieno derivatives **(8)a,b**.Soleiman et al, 2002[2].

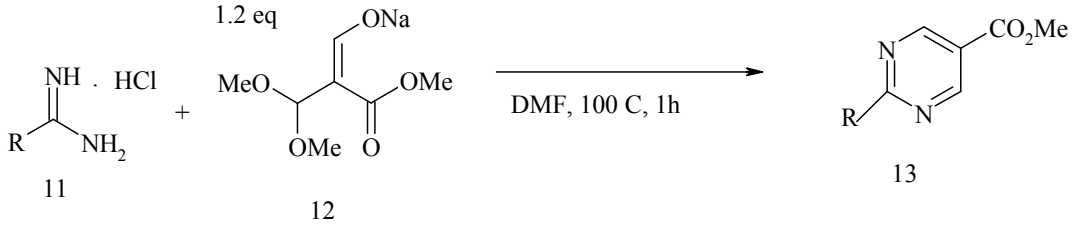


The synthesis of pyrimidine derivatives **10** were achieved through the interaction of **9** with one mole of urea and/or thiourea , respectively in DMF using piperidine as a catalyst at reflux temperature . Soleiman H.A. et al ., 2002[2].



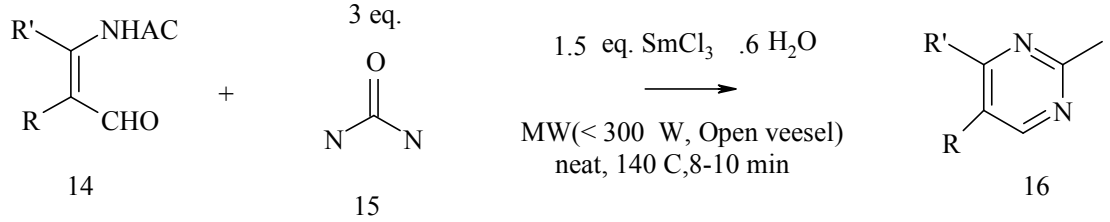
A method for the synthesis of 2-substituted pyrimidine-5-carboxylic esters is described. The sodium salt of 3,3-dimethoxy-2-methoxycarbonylpropen-1-ol has been found to react with a

variety of amidinium salts to afford the corresponding 2-substituted pyrimidine-5-carboxylic esters. Zhichkin, et al, 2002[3].



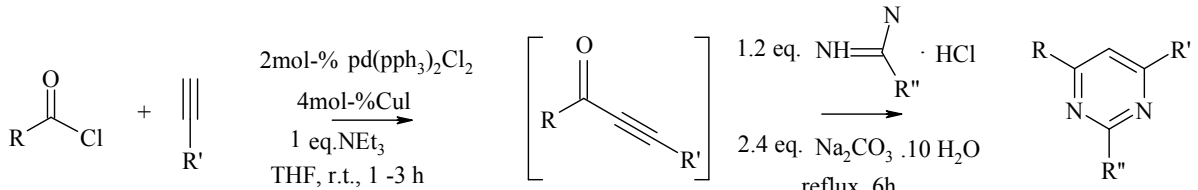
11 12 13

A novel and efficient synthesis of pyrimidine from β-formyl enamides involves samarium chloride catalysed cyclisation of β-formyl enamides using urea as source of ammonia under microwave irradiation. Barthakur, et al, 2007[4]



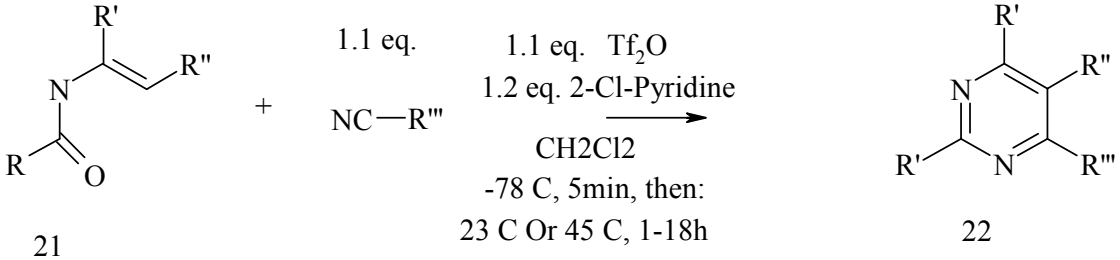
14 15 16

The coupling of acid chlorides with terminal alkynes using one equivalent of triethylamine under Sonogashira conditions followed by subsequent addition of amines or amidinium salts to the intermediate alkynones allows a straightforward access to enaminones and pyrimidines under mild conditions and in excellent yields. Karpov, et al, 2003[5]



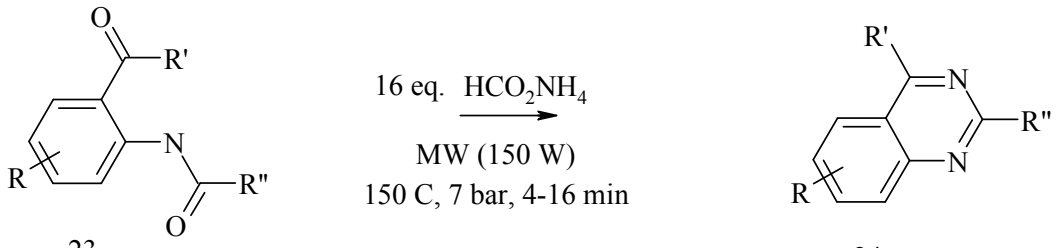
17 18 19 20

A single-step conversion of various *N*-vinyl and *N*-aryl amides to the corresponding pyrimidine and quinazoline derivatives involves amide activation with 2-chloropyridine and trifluoromethanesulfonic anhydride followed by nitrile addition into the reactive intermediate and cycloisomerization. Movassaghi, et al, 2006[6].



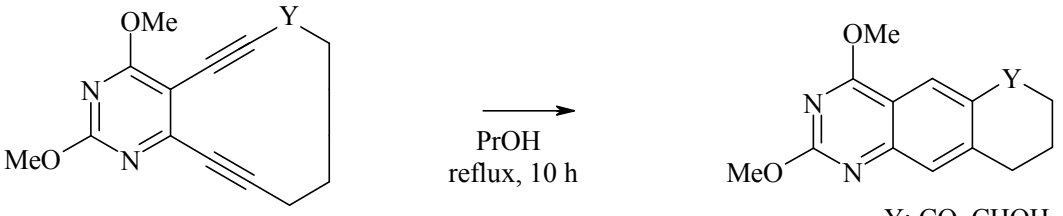
21 22

A photochemically induced Fries rearrangement of anilides gave several *ortho*-aminoacylbenzene derivatives that were acylated. These acylamides underwent rapid microwave-assited cyclization to 2,4-disubstituted quinazolines and benzoquinazolines in the presence of ammonium formate. Ferrini, et al, 2007[7].



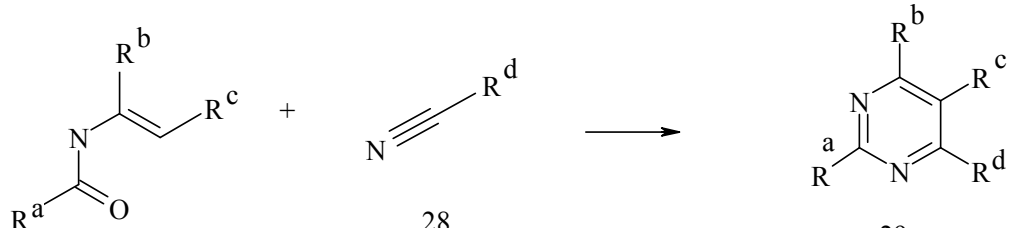
23 24

Novel 10-membered pyrimidine enediynes were synthesized in seven and eight steps, respectively. These compounds were compared for their abilities to undergo Bergman cyclization both thermally and photochemically and to cleave dsDNA under the appropriate conditions.. Choy, et al, 2000[8].



25 26

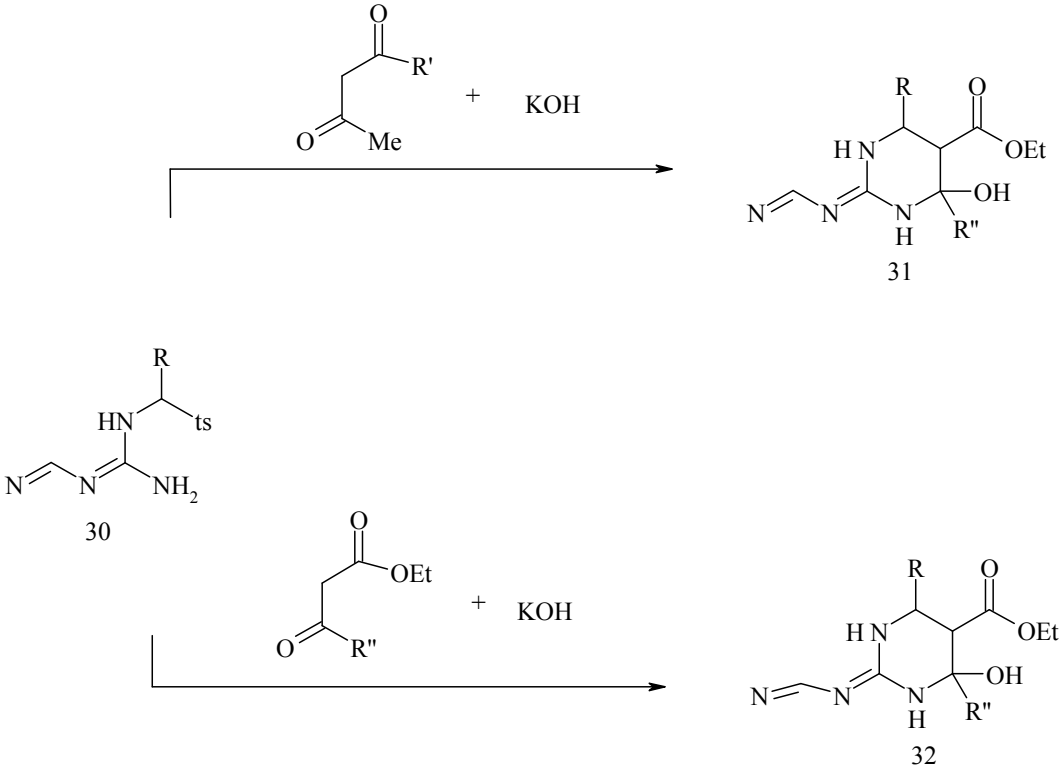
Movassaghi, et al, 2006[6] describe a single-step conversion of various *N*-vinyl and *N*-aryl amides to the corresponding pyrimidine and quinazoline derivatives, respectively. The process involves amide activation with 2-chloropyridine and trifluoromethanesulfonic anhydride followed by nitrile addition into the reactive intermediate and cycloisomerization. In situ nitrile generation from primary amides allows for their use as nitrile surrogates. The use of this chemistry with sensitive *N*-vinyl amides and epimerizable substrates in addition to a wide range of functional groups is noteworthy



27 28 29

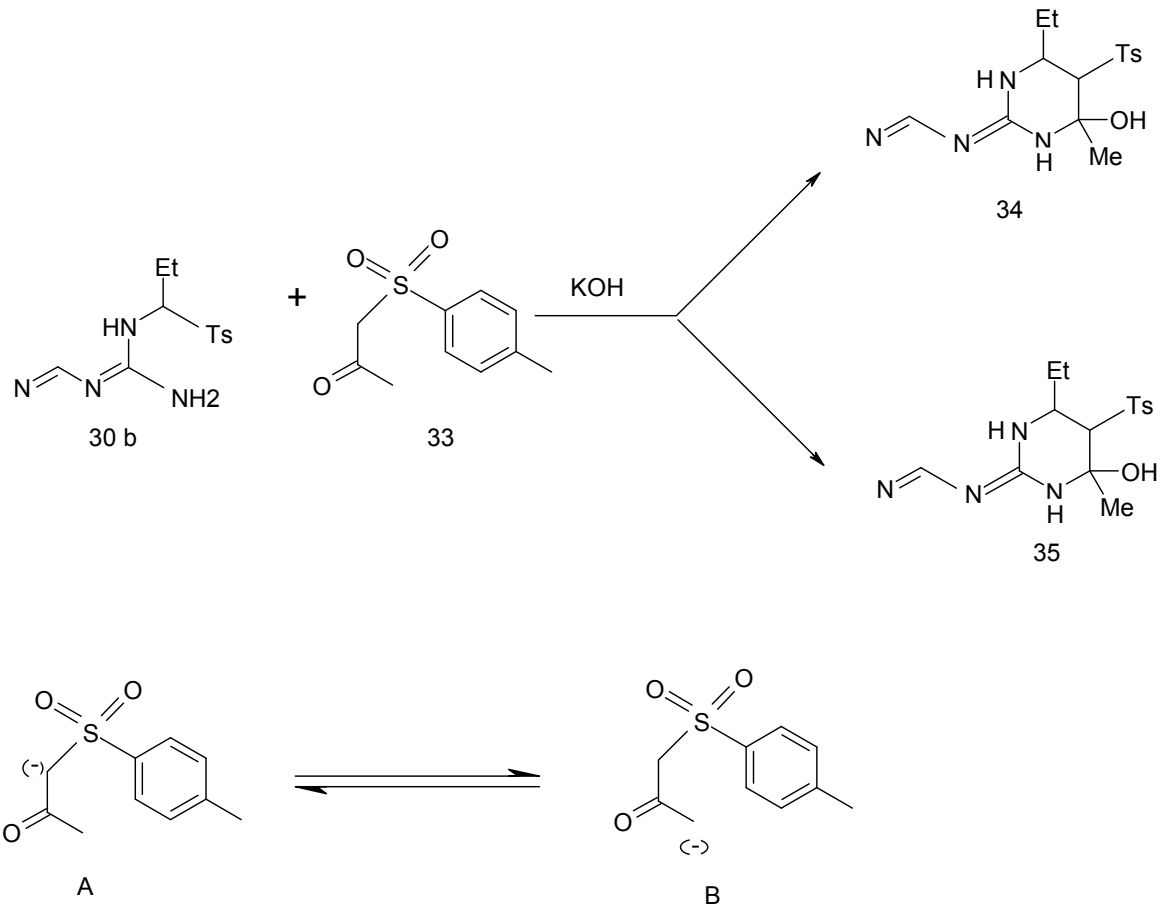
Anatoly et al, 2000[9] reported that compound **30** reacted readily (r.t., 6-7 h) with potassium enolates of 1,3-dicarbonyl compounds (acetylacetone and benzoylacetone) generated *in situ* by treatment of the corresponding CH-acids with KOH in ethanol to give the corresponding5-acyl-2-cyanimino-4-hydroxyhexahydropyrimidines **31** in 72-91 % yields. Analogously, ethyl 2-

cyanimino-4-hydroxyhexahydropyrimidine-5-carboxylates **32** were prepared in 51-80 % yields starting from **30** and oxoesters (ethyl acetoacetate and ethyl butyrylacetate)**.** The pyrimidines **31**, **32** were formed in good diastereomeric purity.

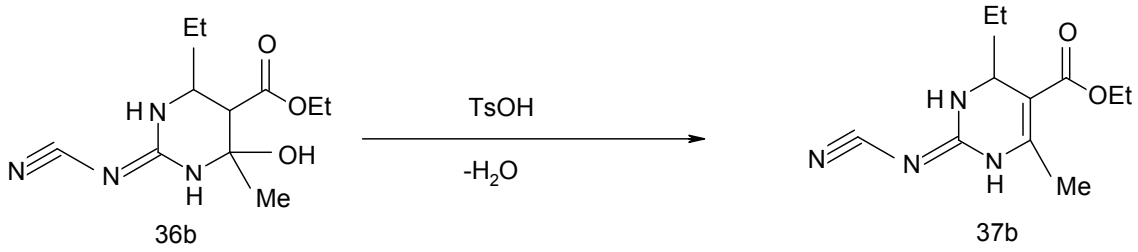


R=Me, Pr. R'=Me, ph; R"=Me, pr

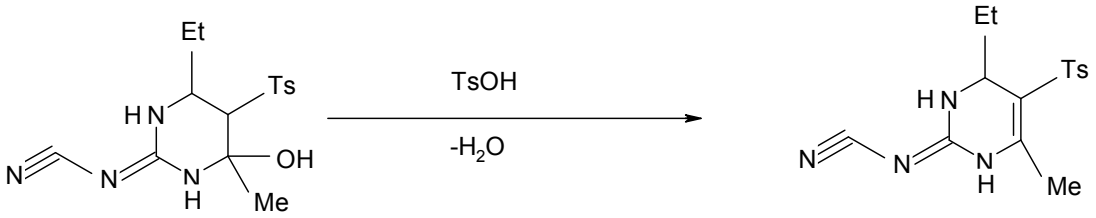
Reaction of **30b** with potassium enolate of tosylacetone**33** (ethanol, r.t., 7.5 h) gave rather unusual result. Instead of obtained a mixture of **34** and **35** in the ratio of 3:1. Probably, formation of **35** can be explained by equilibrium of enolates A and B. Clearly, despite huge predominance of A over B in the equilibrium, reaction rate of **33**b with B is much higher than with A because of steric and electronic factors.



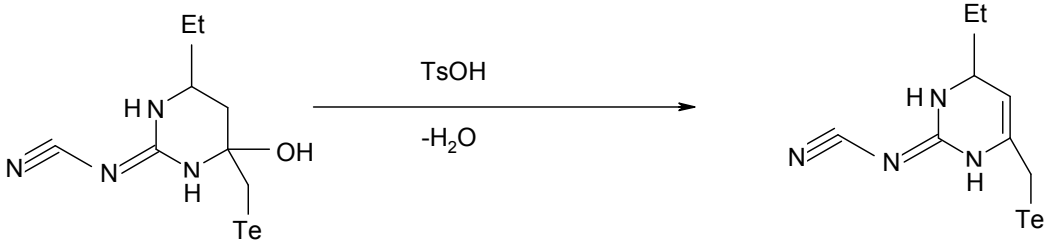
The obtained 2-cyanimino-4-hydroxypyrimidines **31**, **32**, **34**, **35** can be easily dehydrated in the presence of acids to produce the corresponding 2-cyanimino-1,2,3,4-tetrahydropyrimidines **37-41**. Really, refluxing **36b** and TsOH (0.2 equiv.) in ethanol for 1.2 h gave the tetrahydro-pyrimidine**37b** in 73 % yield. Analogously, a mixture of **39** and **41** in the ratio of 3:1 was prepared starting from the mixture of **38** and **40** (3:1)**.** The pyrimidine **41** was easily separated by recryctallization from ethanol.



36b 37b

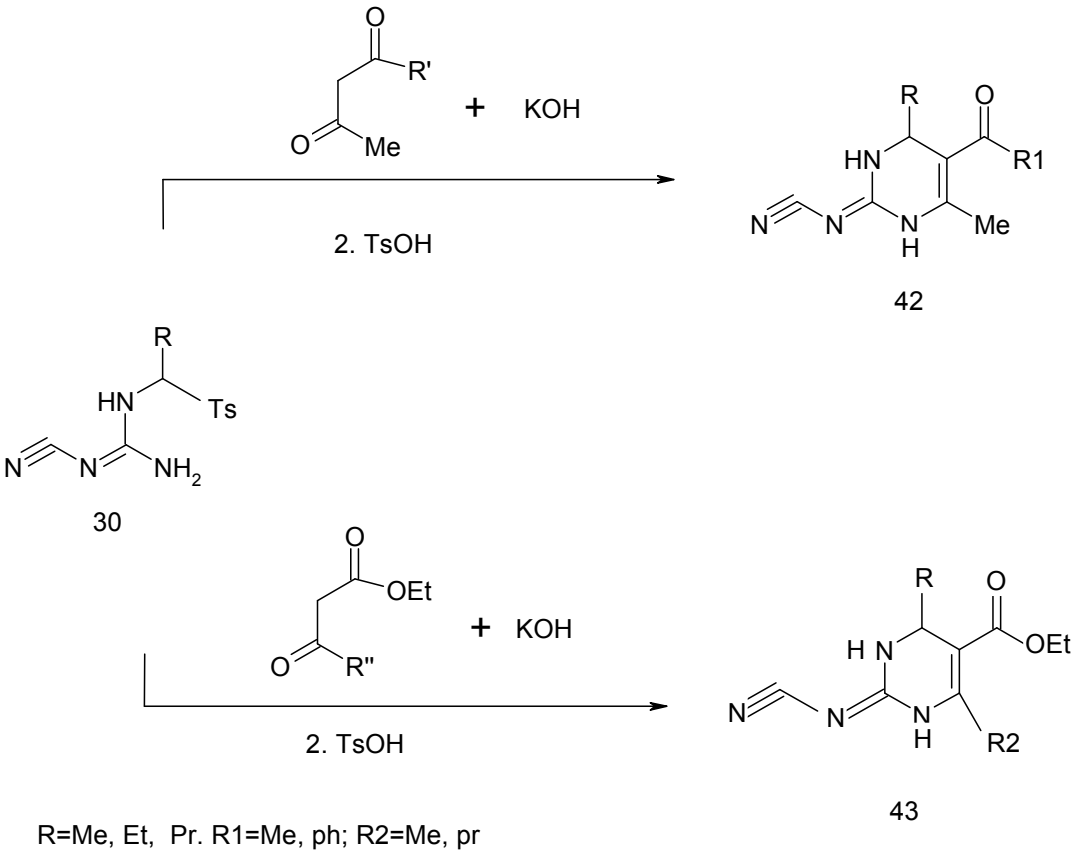


38b 39b



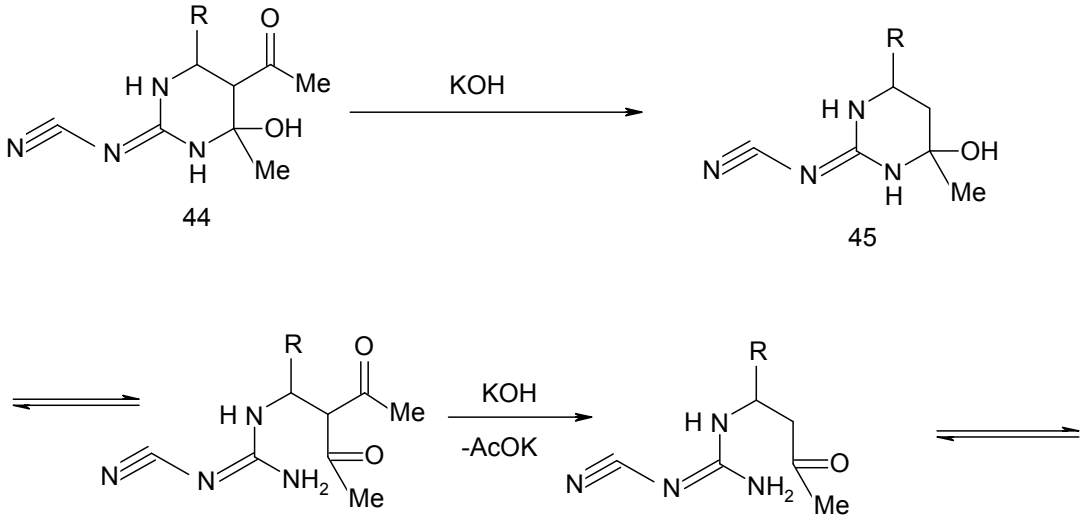
40b 41b

Mainly,however,2-cyanimino-1,2,3,4-etrahydropyrimidines **37 b** were synthesized by convenient one-pot procedure starting directly from N-tosyl substituted N-cyanoguanidines**30 a-b**. According to this procedure, **30 a-c** reacted (r.t., 6-7 h) with potassium enolates of 1,3-dicarbonyl compounds or **β**-oxoesters to afford **31**, **32** which without isolation were dehydrated after addition of TsOH (0.2 equiv.) to the reaction mixtures and subsequent refluxing for 1-2 h to afford **42**, **43** in 46-73 % overall yields .



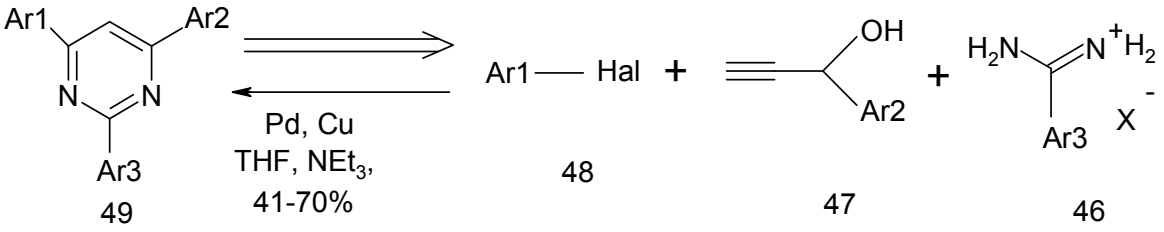
R=Me, Et, Pr. R1=Me, ph; R2=Me, pr

5-acetyl-4-hydroxypyrimidines **44** (R^1 = Me)reacted with aq. KOH at r.t. give 4-hydroxypyrimidines **45** (27-82 % yields) in result of removing the acetyl group in 44.Probably, this transformation proceeds *via* the retro-Claisen reaction in the acyclic isomeric form of **44**.



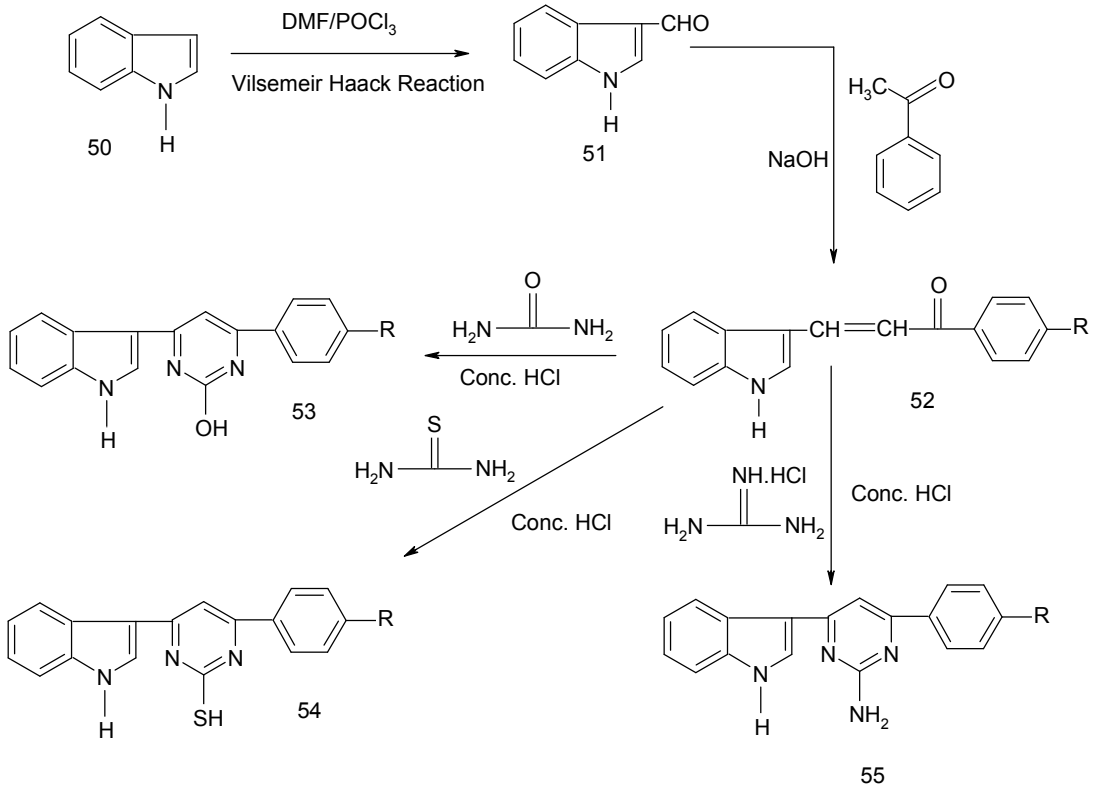
2,4,6-Tri(hetero)aryl-substituted pyrimidines can be readily synthesized in a three-component one-pot process based upon a coupling−isomerization sequence of an electron-poor (hetero)aryl

halide and a terminal propargylalcohol subsequently followed by a cyclocondensation with amidiniumsalts.Thomas et al, 2000[10].

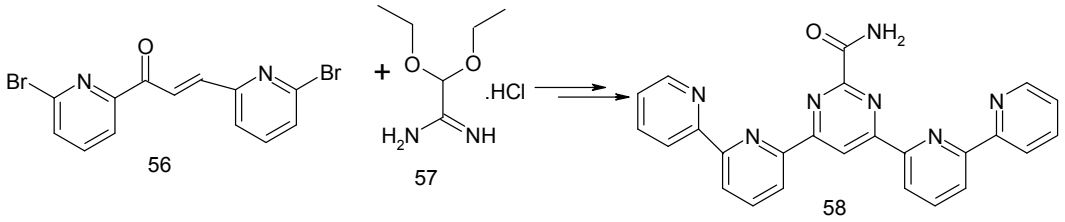


Ar1=elecctron deficient (hetero)aryl
Ar2, Ar3=(hetero)aryl

A number of chalcones were synthesized by reacting indole-3-aldehyde, prepared by VilsemeirHaack reaction with 4-substituted acetophenone in NaOH solution in ethanol. These chalcones were immediately reacted with urea, thiourea and guanidine hydrochloride in presence of concentrated hydrochloric acid as reagent to obtain the corresponding hydroxy, thio and amino pyrimidines. The synthesized heterocyclics were characterized on the basis of physical, chemical tests and spectroscopic data and were tested for the acute antiinflammatory activity, antioxidant, antibacterial activity using carragenan-induced rat paw oedema method, DPPH (diphenylpicrylhydrazyl) radical scavenging method and cup plate method using Muller-Hinton agar media respectively. Evaluation of the compounds revealed remarkable antiinflammatory activity reflected by their ability to reduce the carragenan-induced inflammation in rats, appreciable antioxidant activity and also antibacterial activity was observed**.** Panda et al, 2008[11].



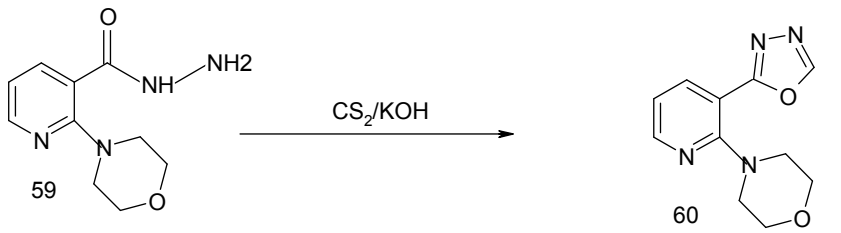
A convenient synthesis of a pyrimidine based bis-tridentate metal ligand is presented. The pyrimidine core is constructed via cyclization of an amidine and a substituted propenone. A Stille coupling appends the terminal pyridyl units. The general methodology presented is amenable to functionality at several positions on the ligand framework**.** Paul et al. 2001[12].



2-Amino-4-(2,4-dichloro-5-fluoro phenyl)-6-(aryl)-pyrimidine 64

A mixture of **62**, guanidine nitrate and sodium methoxide in methanol was refluxed for six hours. After the completion of reaction, the resultant mixture was cooled to room temperature. Separated product was filtered, washed with water, dried and crystallized from methanol. Chikhalia et al, 2007[13]**.**

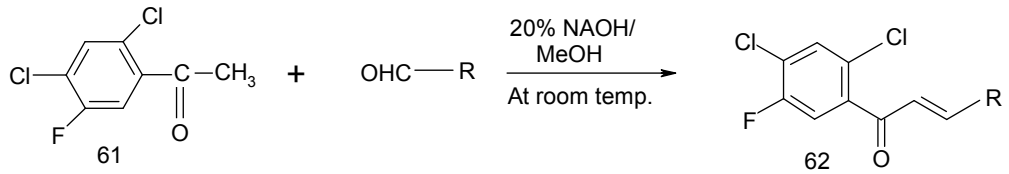
Step 1



2-Morpholino-3-pyridinylic acid hydrazide

2-(2-(Morpholino)-3-pyridinyl)-5-Mercapto-1,2,3-oxadiazole:A

Step 2

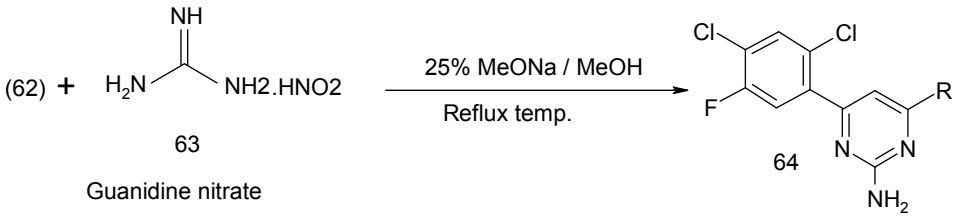


2,4-dichloro-5-fluoro-Acetophenone

Aromatic aldehyde

1-(2,4-Dichloro-5-fluoro phenyl)-3-(aryl)-2-propane-1-one:(B)

Step 3



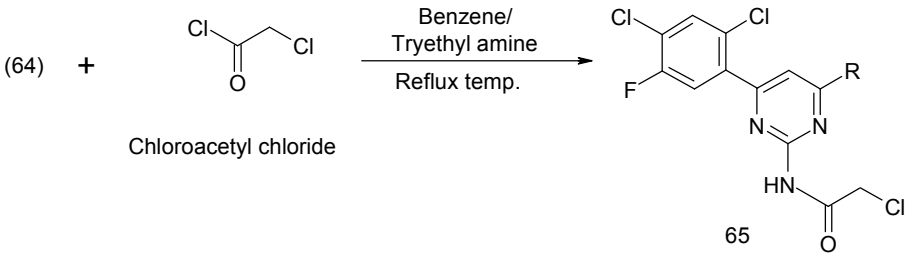
Guanidine nitrate

2-Amino-4-(2,4-dichloro-5-fluoro phenyl)-6-(aryl)-pyrimidine:(c)

N-chloro acetyl- 2-amino-4-(2,4-dichloro-5-fluoro phenyl)-6- (aryl)-pyrimidine was prepared according to the following method

In benzene , chloro acetyl chloride and 2-3 drops of TEA were added and the mixture was stirred in water bath for 10 mins. The solution of **64** in benzene was added drop wise and refluxed for two hours. Then cooled the reaction mixture. The resulting white precipitates were filtered and washed with benzene purified by recrystallization from lcohol. Chikhalia et al, 2007[13].

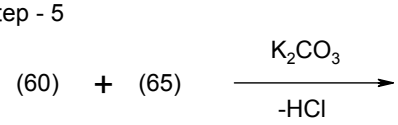
Step-4



N-Cloro acetyl-2-amino-4-(2,4-dichloro-5-fluoro phenyl)-6-(aryl)-pyrimidine

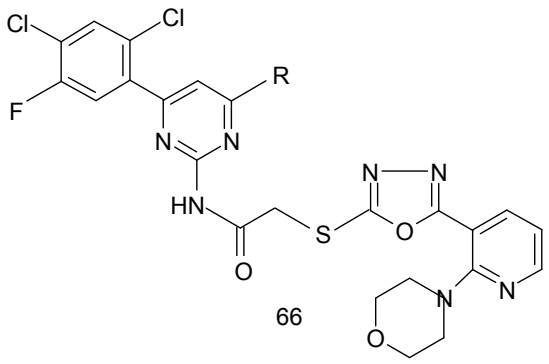
2-[{2-(Morpholino)-3-pyridinyl-5-thio}-2-oxoethyl oxadiazoly]] -amino-4-(2,4-dichloro-5-fluoro phenyl)-6-(aryl)-pyrimidine was prepared as follow:
To a solution of **60** in acetone, **65** and KOH solution in acetone was added and refluxed for two hours. After the completion of reaction, the resultant mixture was poured in to crushed ice. Product was filtered, washed with water and crystallized from ethanol. Chikhalia et al, 2007[13].

Step - 5



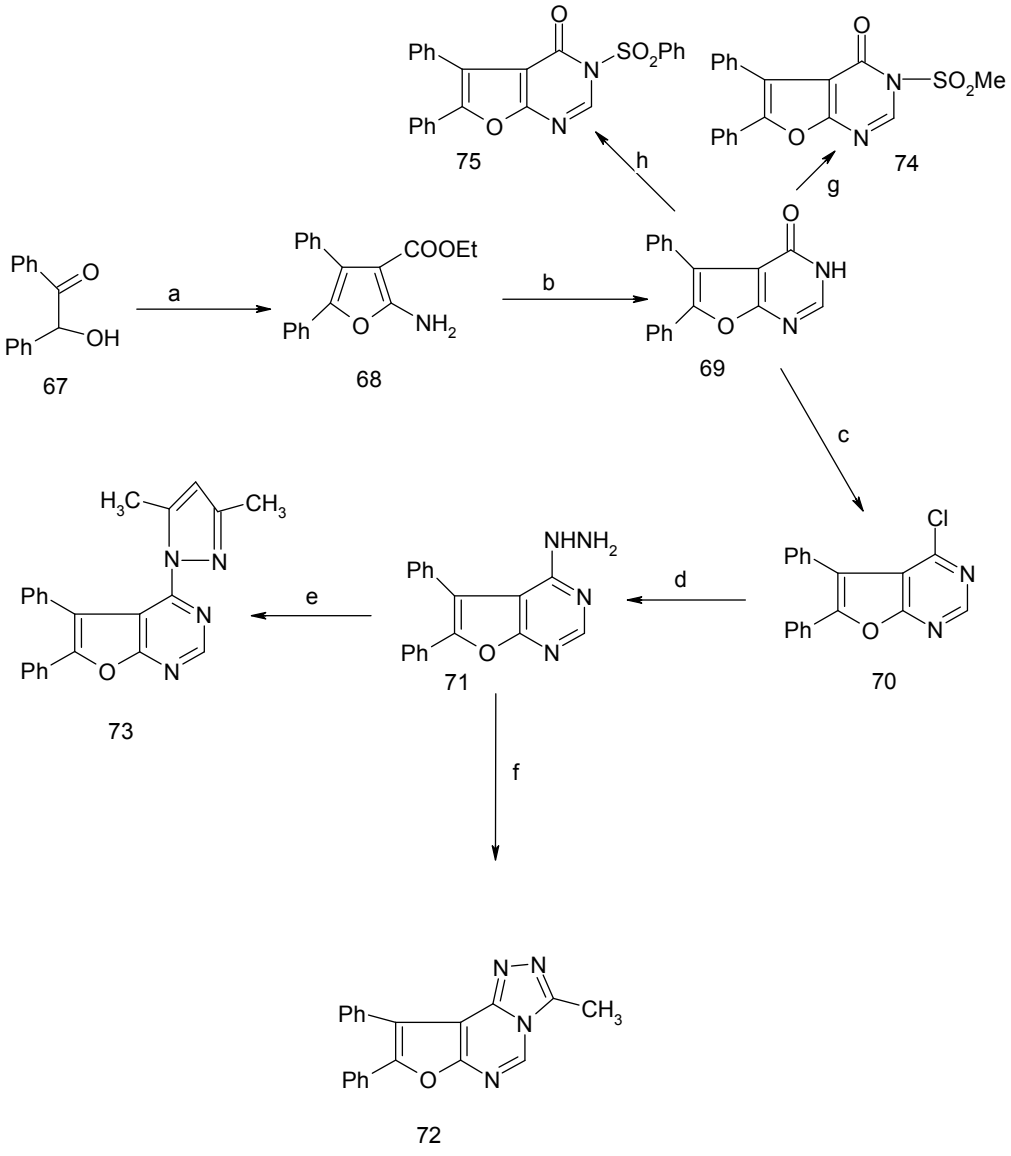
(TN-1 to TN-10)

4- $CH_3C_6H_4$	-NT-1
4- $N(CH_3)_2C_6H_4$	-NT-2
2- OHC_6H_4	-NT-3
4- OHC_6H_4	-NT-4
4- $Cl.C_6H_4$	-NT-5
2,4- $(Cl_2)C_6H_3$	-NT-6
4- $F\text{-}C_6H_4$	-NT-7
2- $OCH_3\text{-}C_6H_4$	-NT-8
4- $OCH_3C_6H_4$	-NT-9
3,4,5- $(OCH_3)_3C_6H_2$	-NT-10

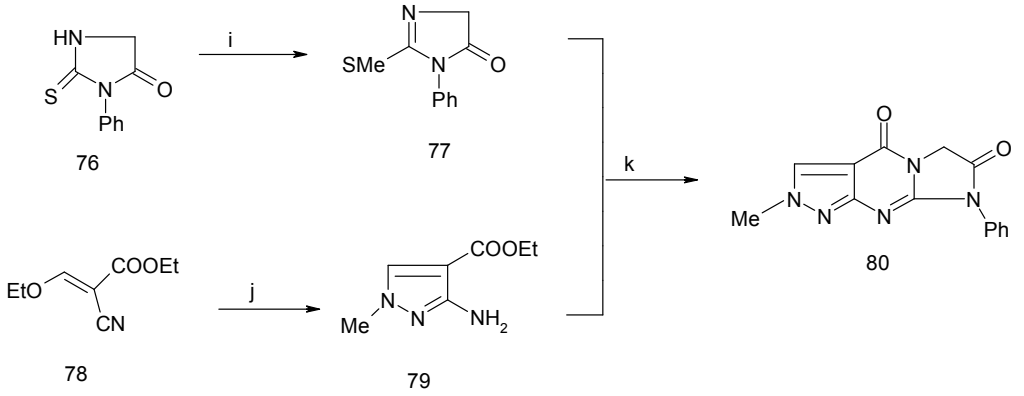


2-[{2-(Morpholino)-3-pyridinyl-5-thiol} -2-oxoethyl oxadiazolyl]-amino-4-(2,4-dichloro-5-fluoro phenyl)-6-(aryl)-pyrimidines

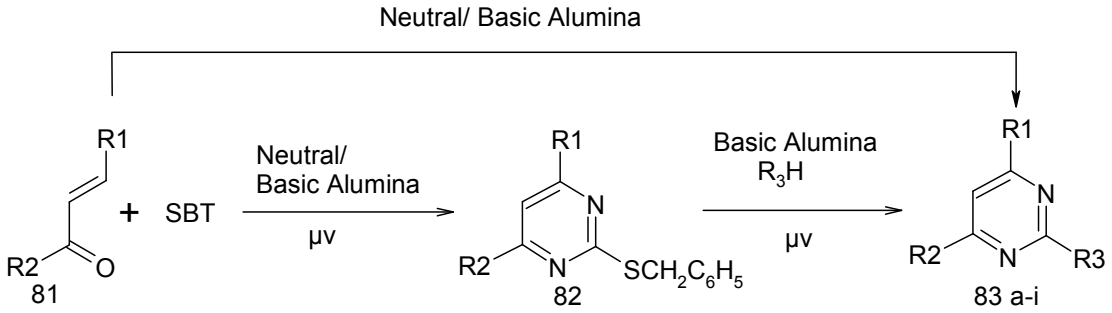
Treatment of amino carboxylate **68** with formamide under reflux afforded.5,6-diphenylfuro[2,3-d]pyrimidin-4(3H)-one **69** in goodyield. Compound **69** was then chlorinated by $SOCl_2$ to afford 4-chloro-5,6-diphenylfuro[2,3-d]pyrimidine **70** in78% yield. Moreover, compound **69** reacted with methanesulphonyl chloride and benzene sulphonylchloride to form 4-oxo-5,6-diphenylfuro[2,3-d]pyrimidin-3-methylsulphonate ester **74** and 4-oxo-5,6-diphenylfuro[2,3-d]pyrimidin-3-phenylsulphonate ester **75** respectively. A nucleophilic substitution reaction of the chlorinated compound **70** with hydrazine hydrate indioxane under reflux afforded 4-hydrazino-5,6-diphenylfuro[2,3-d]pyrimidine **71**. Compound **71** was then treated with acetic anhydride under reflux to give 3-methyl-8, 9-diphenylfuro[3, 2-e][1, 2,4]triazolo[4, 3- c]pyrimidine **72** as yellow crystals in 72%. The hydrazino compound **71**, on reaction with acetylacetone under reflux, also afforded 4-(3,5-dimethylpyrazolyl)-5,6-diphenylfuro[2,3-d]pyrimidine **73** as a pale yellow crystal in 68% yield.



2-Methylthio-1-phenyl-5-oxoimidazoline 77 was prepared from 1-phenyl-5-oxo-2-imidazolidinethione **76** followed by methylation with MeI. The annelating substrate, ethyl 3-amino-1-methylpyrazole-4-carboxylate **79** was prepared by the condensation of ethyl (ethoxymethylene)cyanoacetate and methyl hydrazine as shinning white plates, yield 70%. The annelating reagent **77** and the annelatingsubstrate **79** were cyclisized in dry acetic acid under reflux at 116°C form 1-phenyl-7-methylpyrazolo [3,4-d] imidazo[1,2-a]pyrimidin-2,5(1H,3H)-dione**80** as white crystal, yield 72.29%, Bhuiyan et al, 2005[14].

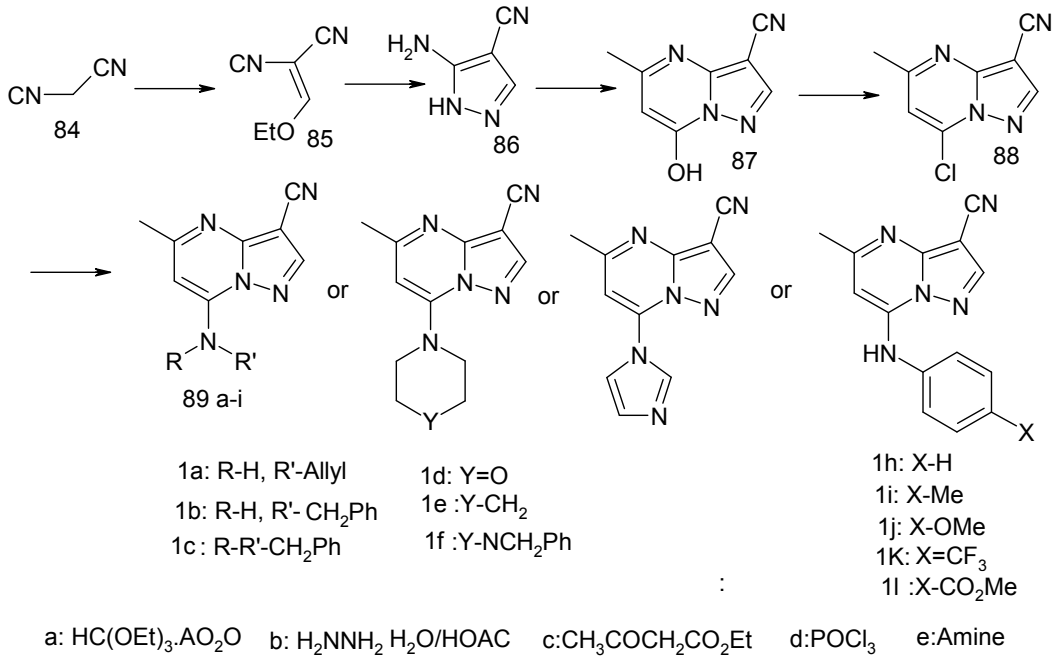


Synthesis of 4,6-diaryl-2- (4-morpholinyl/1-piperidinyl/1-pyrrolidinyl)-pyrimidines**(83a-i)**. Classically**,(82)** 2,4,6-trisubstituted pyrimidines are obtained by refluxing α,β-unsaturated ketones **(81)** with SBT and heterocyclic secondary amines in ethanol (20 mL) for 10-18h. Kidwai, et al, 2003[15]**.**

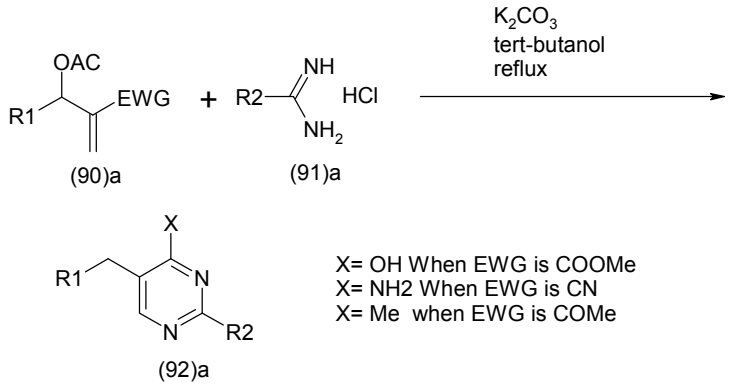


81a $R_1 = R_2$ =Phenyl, R_3 = Morpholinyl
81b R_1 = PiPeronyl, $R_2 = {}_4$-Br-C_6H_4 R_3 = Morpholinyl
81c $R_1 = {}_2$-Furyl, $R_2 = CH_3 R_3$ = Morpholinyl
81d $R_1 = {}_3$-Indolyl, $R_2 = {}_4$Br-C_6H_4, R_3 = Morpholinyl
81e $R_1 = R_2$ = Phenyl , R_3 = Pyrroolhdhnyl
81f R_1 = Pipeonyl , $R_2 = {}_4$- Br-C_6H_4, R_3 = Pyrrolidinyl
81g $R_1 = {}_2$- Furyl, $R_2 = CH_3$, R_3 = Pyrrolidinyl
81h $R_1 = {}_3$-Idolyl, $R_2 = {}_4$-BrC_6H_4, R_3 = Pyrrolidinyl
81i $R_1 = R_2$ = Phenyl, R_3 = Piperidinyl
81j R_1 = Piperonyl , $R_2 = {}_4$-Brc_6h_4 = Piperidinyl
81k $R_1 = {}_2$-Furyl, $R_2 = CH_3$, R_3 = Piperidinyl
81l $R_1 = {}_3$- Indolyl, $R_2 = {}_4$- Br C_6H_4 = Piperidinyl

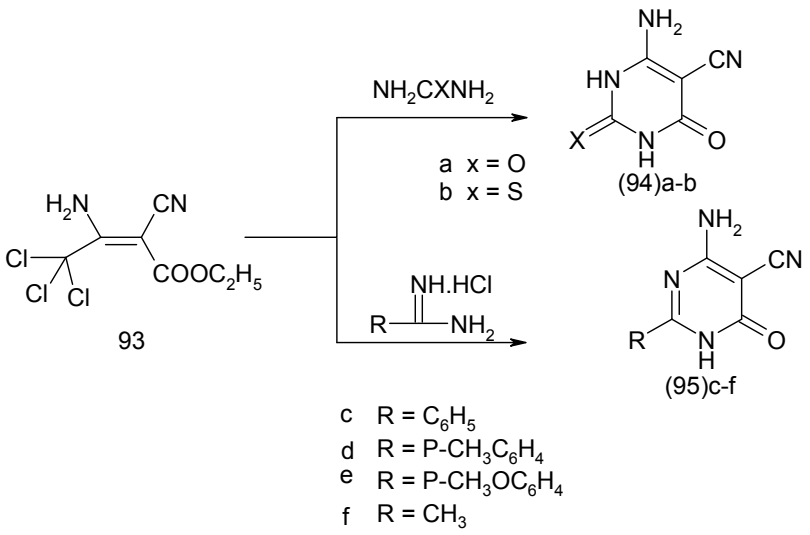
Reaction of methane dinitrile**84** with triethyl orthormate**85** in acetic anhydride gave the condensation product **86**, which was reacted with hydrazine for the formation of cyclic compound **87**. The second ring was easily constructed by reacting **86** with ethyl acetoacetate to give **87**, which was converted to chloride **88**. Replacement the halide of **88** with amines produced the desired products **89a-i** in good yield.Song et al, 2004[16]**.**



The reaction of the Baylis-Hillman acetate **90a** and benzamidine hydrochloride **91a** in tert-butanol in the presence of K_2CO_3 produced desired compound **92a** in 91% isolated yield. Jeong et al. 2007[17].

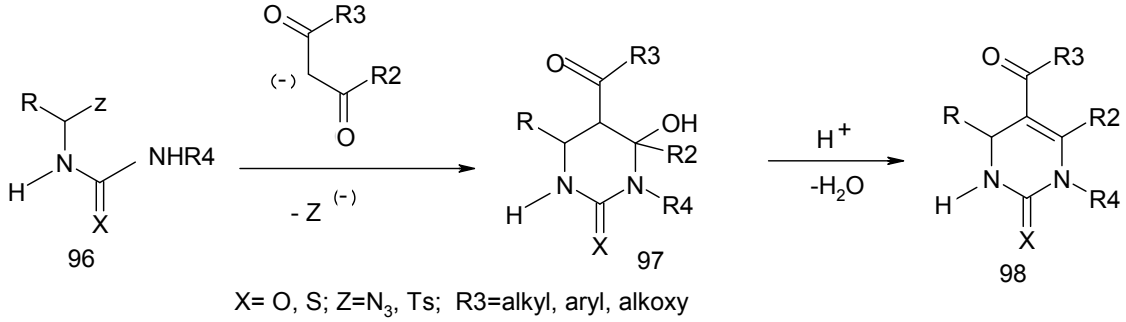


The reaction of ethyl 2-amino-2-trichloromethylcrotonate **93** with urea , thiourea or some amidines via nucleophilicvinylic substitution , elimination of chloroform followed by cyclization and elimination of ethanol to yield (1,3H)-4-amino -5-cyanopyrimidine-2,6-dione**94a-b,95c-f**Abdel-Razik et al, 2004[18]**.**



2-Pyrimidinthiones:

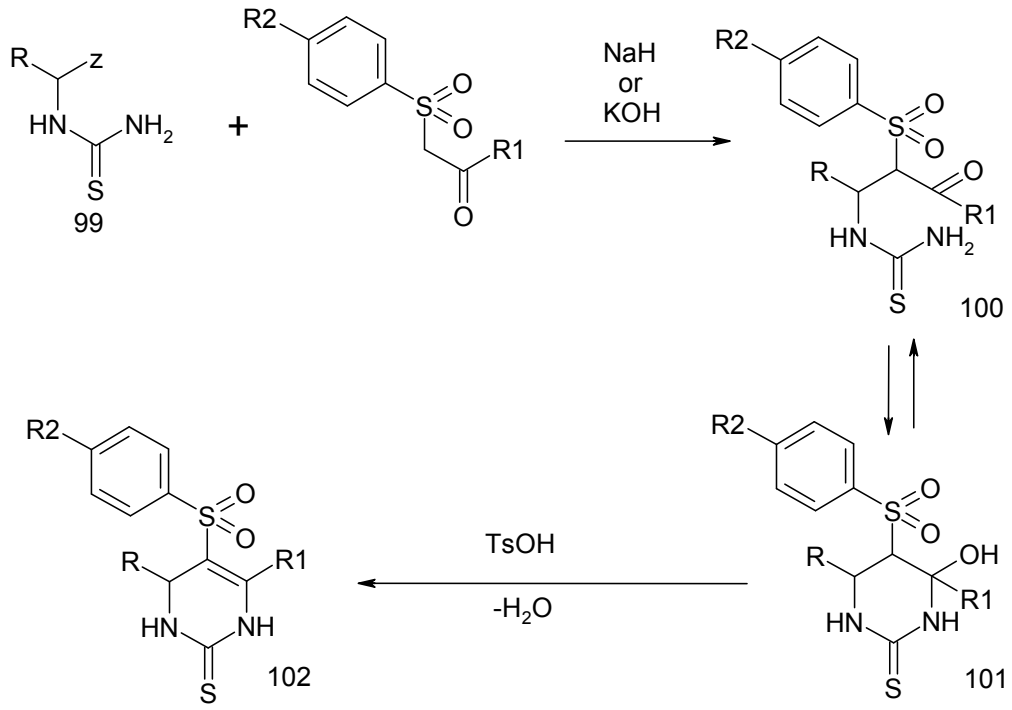
The synthesis of various 5-acyl-and 5-alkoxycarbonyl substituted pyrimidine-2-thiones/ones]. This approach is based on the reaction of azido or tosyl substituted thioureas and ureas with sodium enolates of oxoesters and 1,3-dicarbonyl compounds followed by acid-catalyzed dehydration of the obtained 4-hydroxyhexahydropyrimidine-2-thiones/ones**.** Anatoly et al, 2004[19]**.**



We found that tosyl substituted thioureas**99** or N-(azidomethyl)thiourea readily reacted with enolates of α-(arylsulfonyl)acetones generated by treatment of the corresponding *CH*-acids with NaH in acetonitrile or KOH in ethanol to produce the corresponding 5-arylsulfonyl-4-hydroxyhexahydropyrimidine-2-thiones **101** in good yields and high diastereoselectivity. Clearly, the pyrimidines**101** are products of spontaneous heterocyclization of the intermediate N-[2-(arylsulfonyl)-3-oxopropyl]thioureas (**100** R1 = Me). In contrast, the reaction of **99** with enolates of α-(arylsulfonyl)acetophenones failed to give 5-arylsulfonyl-4-hydroxyhexahydropyrimidine-2-thiones **101**. The obtained products were N-[2-(arylsulfonyl)-3-oxopropyl]thioureas (**100** R1 = Ph), both in solid state and in solutions. This fact could be explained by scarce electrophilicity of carbonyl group of **100** (R1 = Ph) as well as steric hindrances for heterocyclization into **101**.

The hydroxypyrimidines**101** (R1 = Me) were dehydrated by refluxing in acetonitrile in the presence of *p*-toluenesulfonic acid to furnish 5-arylsulfonyl-1,2,3,4-tetrahydropyrimidine-2-thiones (**102** R1 = Me) in excellent yields. Dynamic equilibrium between **100** and **101** (R1 = Ph)

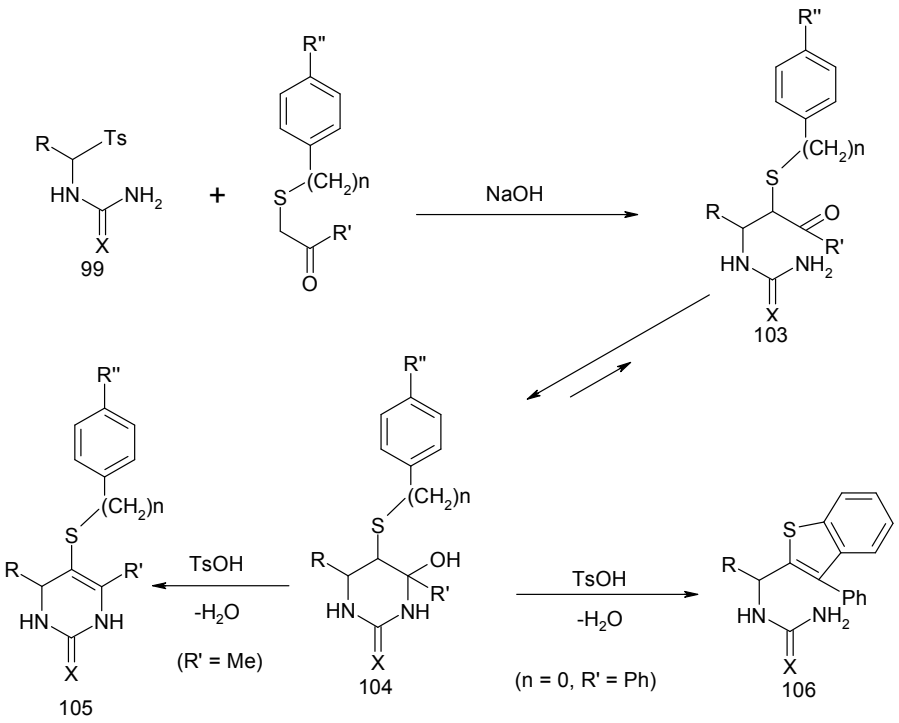
in solutions gave also possibility to convert **100** into **102** (R1 = Ph). This reaction took place by refluxing **100** (R1 = Ph) in acetonitrile in the presence of TsOH (> 50 mol%) in very good yields.Anatoly et al, 2004[19].



Z=Ts, N_3; R =H, alkyl, aryl; R1= Me, Ph; R2= H, Me

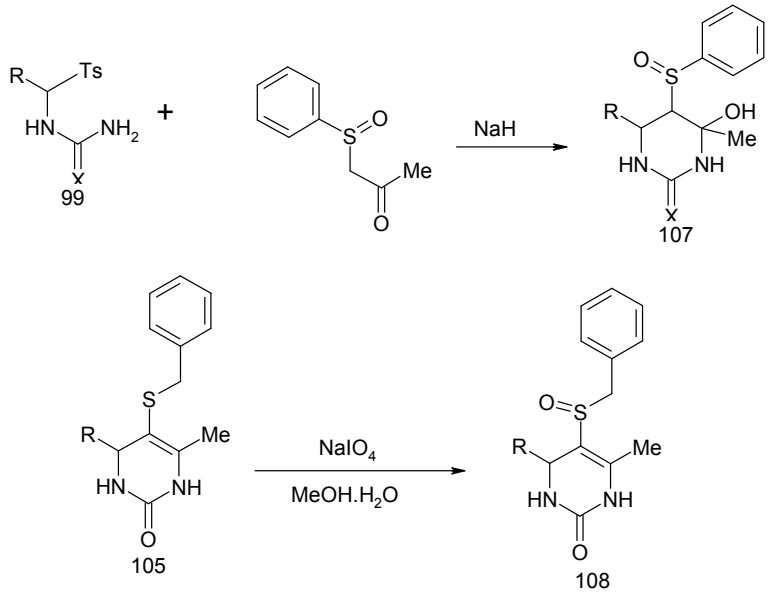
The reaction of α-substituted N-(tosylmethyl)thioureas and ureas**99** with α-phenylthio and α-benzylthio ketones proceeded in acetonitrile at 20 °C with the use of NaH as a base. In that way, the corresponding 5-phenylthio- and 5-benzylthio-4-hydroxyhexahydropyrimidine-2-thiones **104** were obtained in good yields and high diastereoselectivity. It should be noted that in contract to α-(arylsulfonyl)acetophenones (R1 = Ph), the reaction of α-(phenylthio)acetophenone (6 n = 0, R1 = Ph) with **99** gave only cyclic products **104** but not acyclic ones **103**.

The dehydration of 4-hydroxy-4-methyl-5-(R-thio)hexahydropyrimidine-2-thiones (**104** R1 = Me) (30 mol% of TsOH, acetonitrile, reflux) led to formation of the expected 5-(R-thio)-1,2,3,4-tetrahydropyrimidine-2-thiones (**105** R1 = Me). To the contrary, treatment of 4-hydroxy-4-phenylpyrimidines (**104** R1 = Ph) with 1 equiv. of TsOH in boiling acetonitrile gave 2,3-disubstituted benzothiophenes**106** which were products of intramolecular electrophilic substitution in the acyclic isomeric forms of **104**, namely in **103**. Anatoly et al, 2004[19]**.**



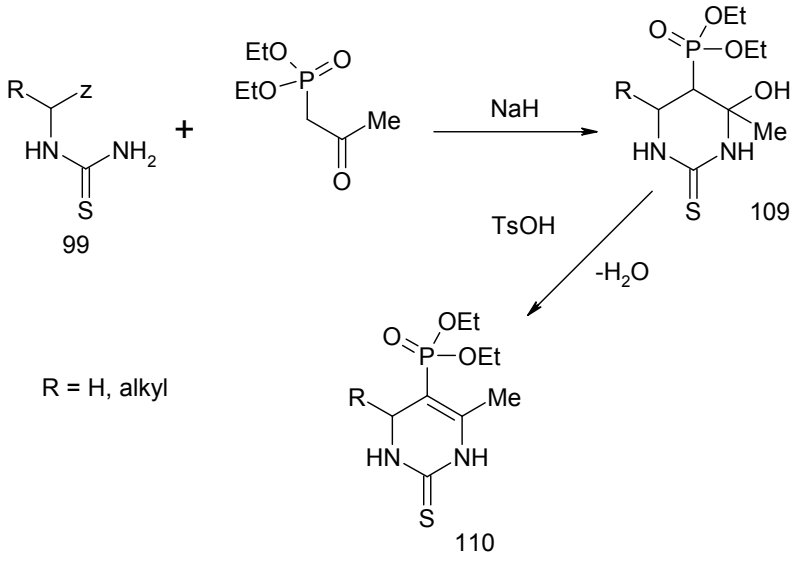
n = 0,1; X = O,S; R = alkyl, aryl; R' = Me, Ph; R'' = H, Me, OMe

The described above method was applied also to the synthesis of hydrogenated pyrimidine-2-thiones/ones bearing phenylsulfinyl group at the C(5). Reaction of **99** with **α**-phenylsulfinylacetone in the presence of NaH provided 4-hydroxy-5-phenylsulfinylpyrimidines **107** as mixtures of diastereomers. 5-Benzylsulfinyl-1,2,3,4-tetrahydropyrimidin-2-ones **108** were obtained by oxidation of the corresponding 5-benzylthiopyrimidines **105** with $NaIO_4$ in aqueous methanol. Anatoly et al, 2004[19]**.**

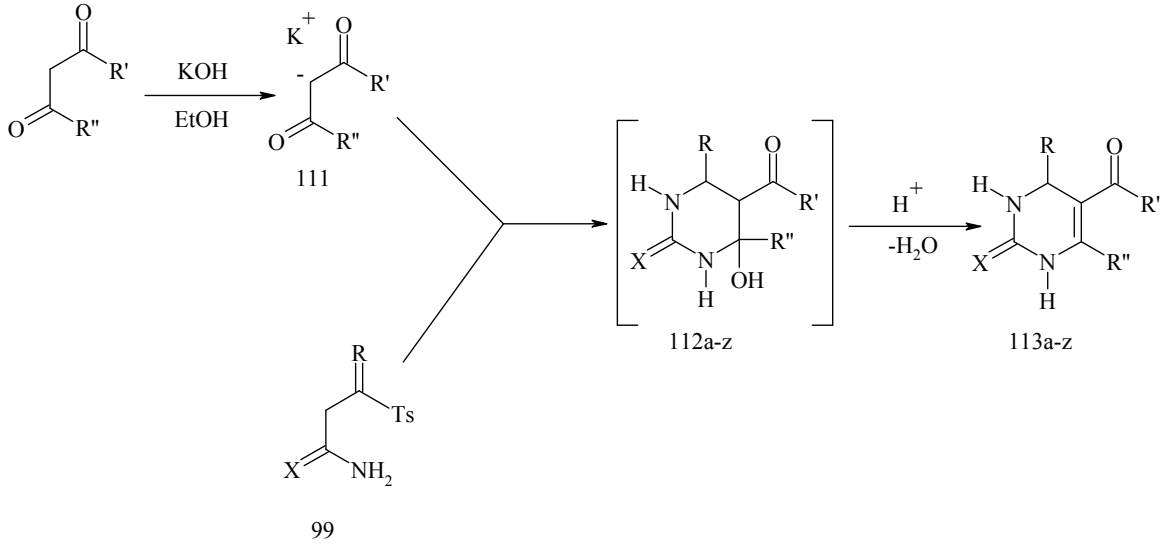


X = O, S; R = aryl

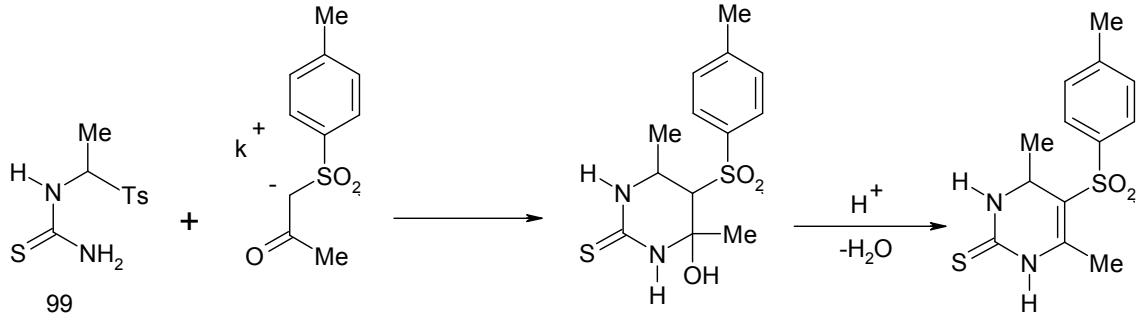
The reaction of α-substituted N-(tosylmethyl)thioureas**99** with sodium enolate of diethyl (2-oxopropyl)phosphonate . The products of this reaction, namely diethyl (4-hydroxy-2-thioxohexahydropyrimidin-5-yl)phosphonates**109** were dehydrated without their isolation in the presence of TsOH to give diethyl (2-thioxo-1,2,3,4-tetrahydropyrimidin-5-yl)phosphonates**110.** Anatoly et al, 2004[19]**.**



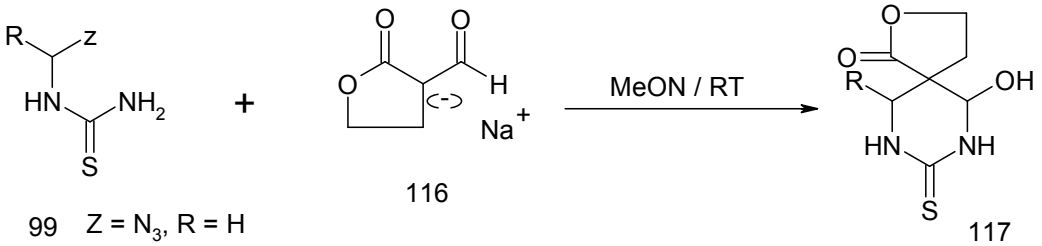
The synthesis of the 4-alkyl substituted 1,2,3,4-tetrahydropyrimidine-2-thiones **113** and 4-aryl substituted 1,2,3,4-tetrahydropyrimidine-2-thiones **113a,z** by reaction of the corresponding thioureas **99a,z** with the potassium enolates of **111a,z** in ethanol (r.t., 4.5-6 h) followed by acidification and refluxing of the reaction mixtures. The yields of the pyrimidines **113a,z**were 46-98 %. Similarly, starting from the α-aryl substituted (tosylmethyl)ureas obtained the corresponding 5-acyl-4-aryl-1,2,3,4-tetrahydropyrimidine-2-ones **113a,z** in 40-85 % yields. Anatoly et al.2001[20]



The proposed method for the one-pot pyrimidine synthesis is general and very flexible. This approach was successfully used by us in the cases when the Biginelli reaction and the Atwal procedure failed to give the disired products. Moreover, this method can be applied not only for preparation of Biginelli compounds but also for synthesis of a large variety of hydrogenated pyrimidines. For example, reaction of N-(1-tosylethyl)thiourea**99** with the potassium enolate of tosyl acetone (r.t., 4.5 h) generated by treatment of the CH acid with KOH in ethanol gave the 4-hydroxy-5-tosylhexahydropyrimidine-2-thione **114** which was dehydrated without isolation after addition of TsOH to the reaction mixture and subsequent refluxing for 1 h. Thus we obtained 4,6-dimethyl-5-tosyl-1,2,3,4-tetrahydropyrimidine-2-thione **115** in 55 % yield**.** Anatoly et al,2001[20].



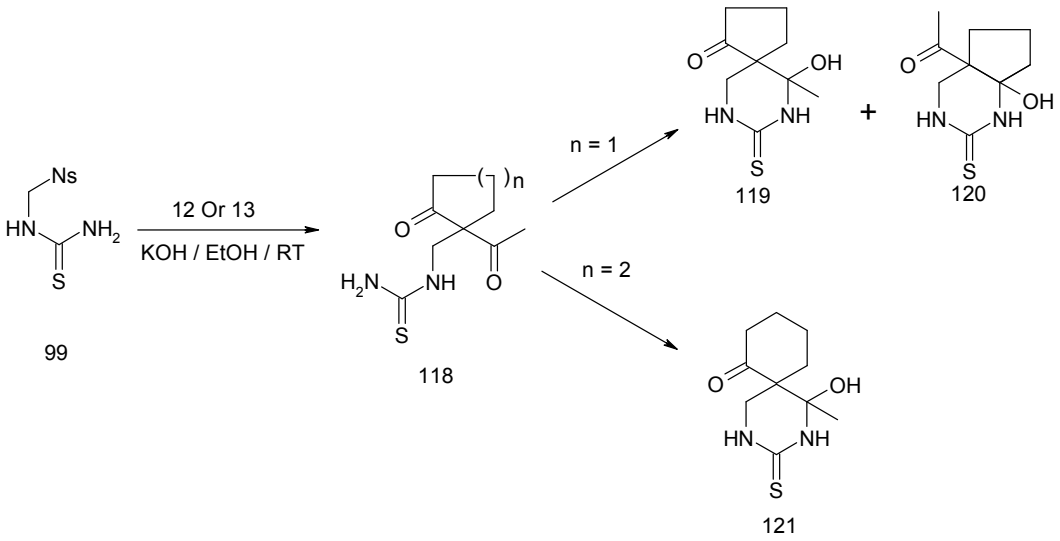
The reaction of **99a** and **99b** with lactone containing exocyclic aldehydo group proceed as follow . a sodium salt of **116** was reacted with **99** to give the expected spiroheterocycle**117a** in good isolated yields**.** Similarly, the sulfone**99b** reacted with **116** to form **117b**. Anatoly et al, 2001[20]**.**



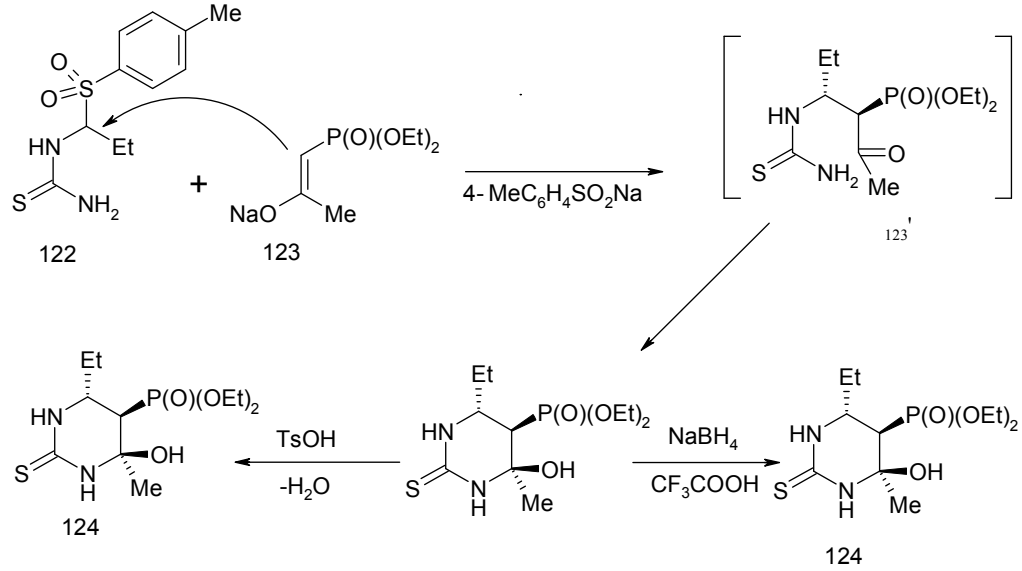
99 Z = N_3, R = H
99a Z = Ts, R = H
99b Z = Ts, R = Me

117a R = H
117b R = Me

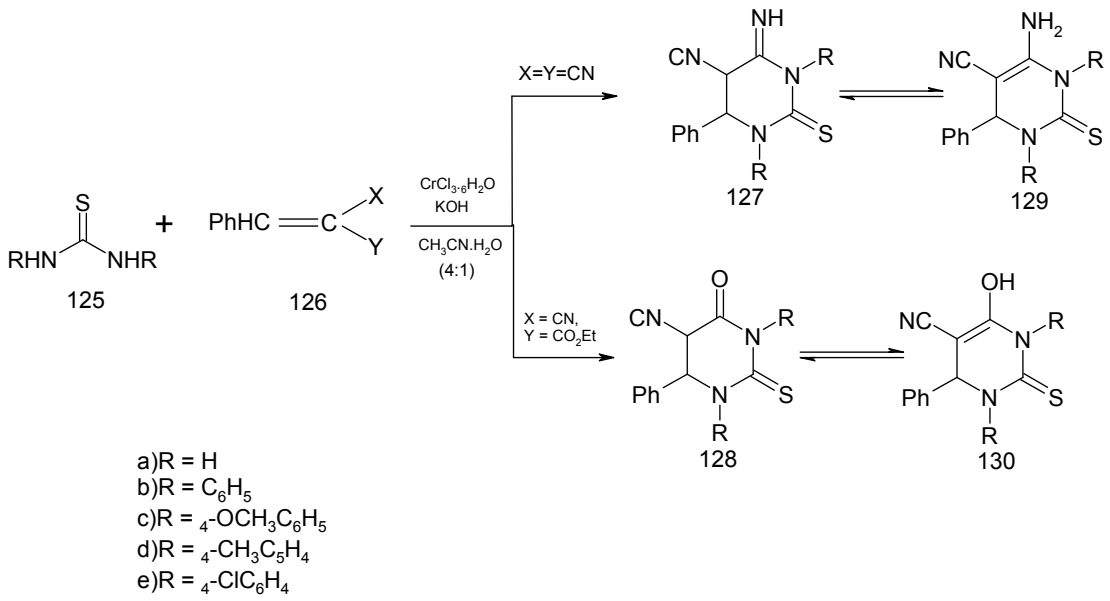
The reactivity of **99** towards enolates of cyclic 1,3-diketones followed a somewhat more complex pattern. In this case, initial thioureidomethylation of 1,3-diketones would lead to an intermediate **123**\ where the electrophilicity of the endo- and exocyclic carbonyl groups might be very similar **.** Hence, in the next step, both spiroheterocyclic and fused heterocyclic products might be formed. Anatoly et al, 2001[20].



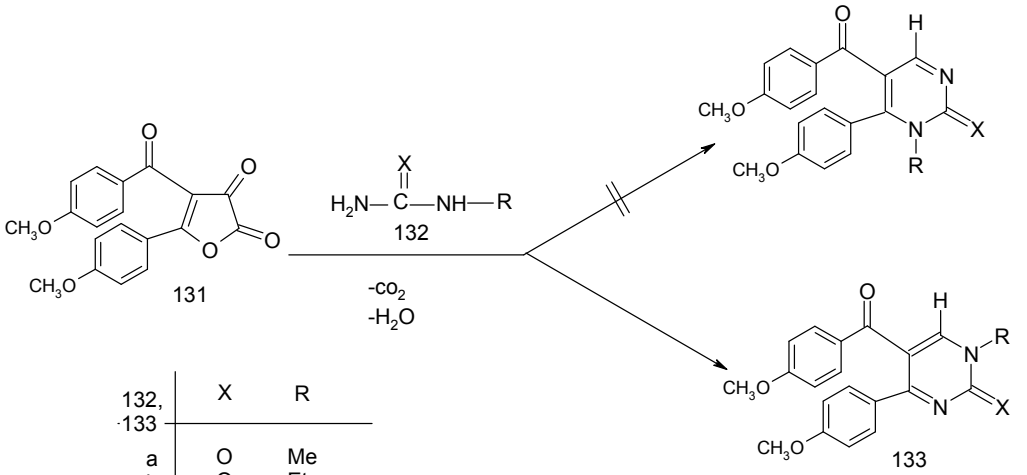
The enolate**123** reacted with readily available *N*-(1-tosylprop-1-yl)thiourea **122** in dry THP for 8 hr at r.t. to produce the expected hydroxypyrimidine**124** in 81 % yield**.** Anastasia et al, 2007[21]**.**



Ethyl phenylmethylenemalononitrile reacted with N-arylthioureas to give excellent yields of 4-amino-5- cyano-6-phenyl-pyrimidine-2-thiones **129**, which are derived from the intermediates 6-phenyl-2-thio- cytosines**127**. However, when ethyl phenylmethylene- cyanoacetate was allowed to react with the above thioureas, the products were not 5-carbethoxy-6- phenyl-2-thiocytosines but an equally good yield of 4- hydroxy-5-cyano-6-phenyl-pyrimidine-2-thiones **130**, which are derived from 6-phenyl-2-thiouracils 4, were obtained**.** Nimalini et al, 2009[22].



The reactions of 4-p- anisoyl-5-p-anisyl-2,3-furandione **131** with monosubstitutedureas and thioureas **132a-g** gave N-alkyl pyrimidine derivatives **133a-g**, with loss of carbon dioxide and water. These new heterocyclic compounds **133a-g** were obtained in moderate to excellent yields 40-96%. The compound **131** was easily prepared by the reaction of dianisoylmethane with oxalyl dichloride. Ismail et al, 2002[23].



132, 133	X	R
a	O	Me
b	O	Et
c	O	n-Bu
d	O	Allyl
e	S	Me
f	S	Et
g	S	Allyl

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