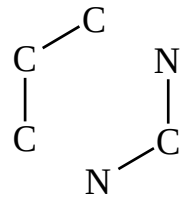
INTRODUCTION

SYNTHESIS OF PYRIMIDINE DERIVATIVES

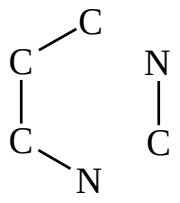
A) Synthesis of pyrimidine nucleus:

Pyrimidines (1,3-diazines) and their fused analogues form a large group of heterocyclic compounds which share in building of nucleic acids, DNA and RNA. These compounds have given attention in the last period due to their interesting biological activities and therapeutic applications.

In fact, there are seven types of pyrimidine ring closure (i-vii) depending upon the nature of fragments that combine together to form the pyrimidine nucleus [(1)]. Also, pyrimidine derivatives can be synthesized by ring transformation and ring expansion.



(i)



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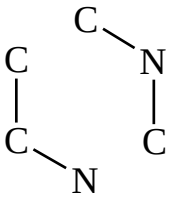

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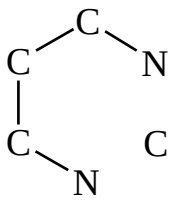

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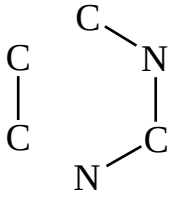

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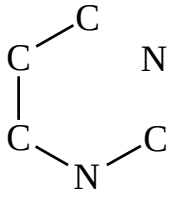

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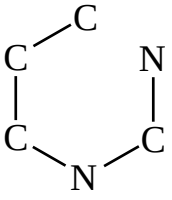
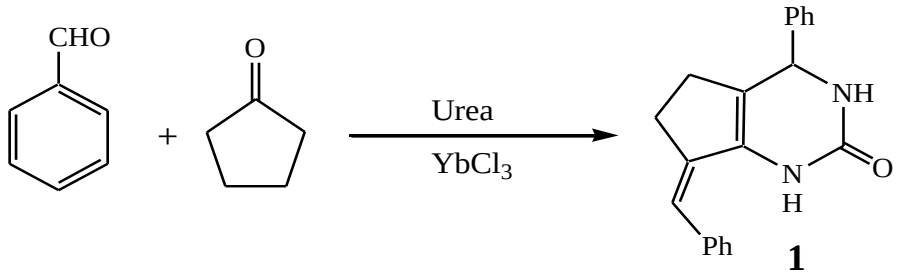


(vii)

i) Synthesis of pyrimidine from C-C-C and N-C-N fragments:

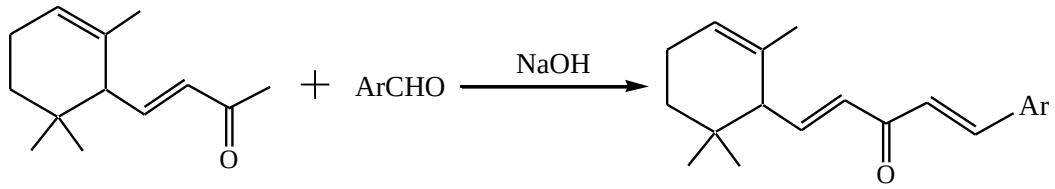
This type is the most useful and widely used one for the construction of a pyrimidine ring from non-heterocyclic precursors. It involves the condensation of an amidine, urea, thiourea, guanidine or their derivatives with 1,3-bifunctional three-carbon fragment.

Condensation of benzaldehyde, cyclopentanone and urea in the presence of $YbCl_3$ (Lewis acid) under free-solvent conditions yielded pyrimidine derivative **(1)** [2].

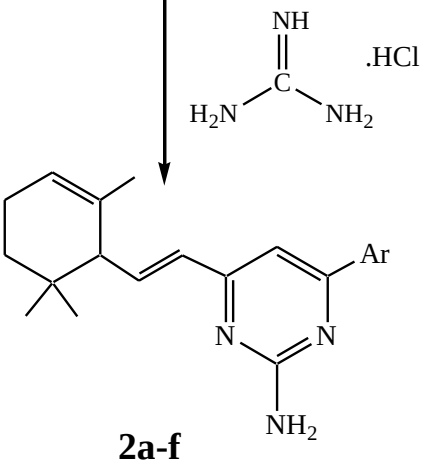


1

α-Ionone was condensed with different aldehydes under phase transfer conditions and the produced chalcones were refluxed with guanidine hydrochloride in isopropanol in the presence of silver oxide to afford the pyrimidine derivatives **(2a-f)** [3].

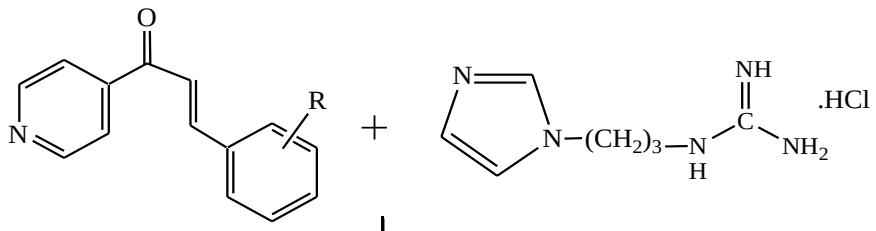


	Ar
a	4-MeO-C_6H_4
b	3-MeO-C_6H_4
c	4-Cl-C_6H_4
d	4-F-C_6H_4
e	4-BnO-C_6H_4
f	4-NO_2-C_6H_4



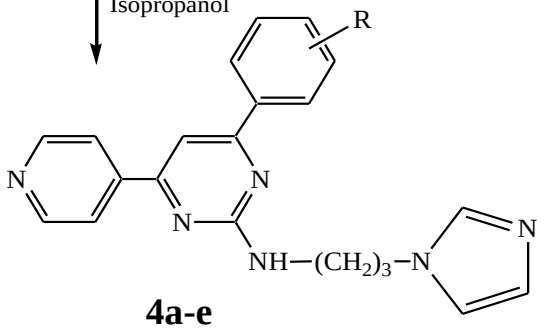
2a-f

The biologically active pyrimidine derivatives **(4a-e)** were produced by the reaction of chalcones **(3a-e)** with guanidine derivative in isopropanol and sodium isopropoxide [4].



3a-e

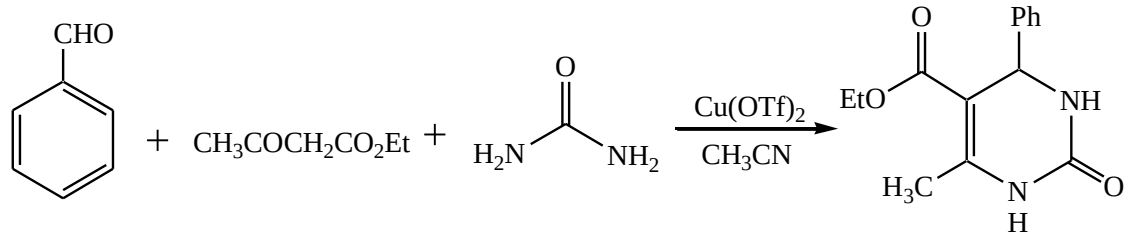
Sodium isopropoxide,
Isopropanol



4a-e

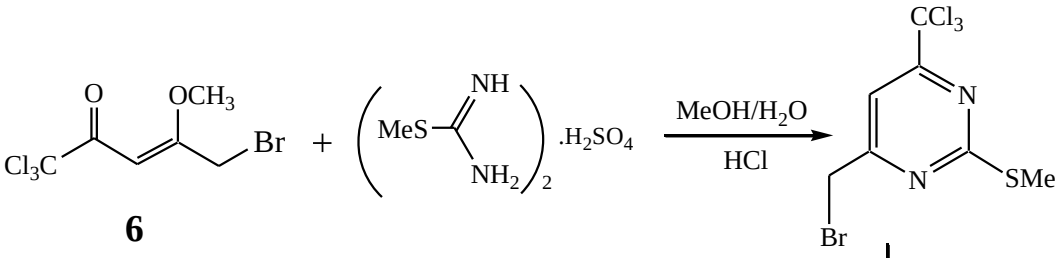
	R
a	H
b	4-SMe
c	4-Me
d	4-Cl
e	4-OMe

High yield of 3,4-dihydropyrimidin-2(*1H*)-one derivative **(5)** was obtained by the three-component condensation reaction of benzaldehyde, ethyl acetoacetate and urea in acetonitrile and employing copper (II) triflate as a reusable catalyst [5].



5

The pharmacologically active 6-methylenesubstituted-4-trichloromethyl-2-methylsulfanylpyrimidines **(7a-d)** were achieved by refluxing the halogenated enone **(6)** with *S*-methylisothiourea sulphate in methanol/water (3:1 v/v) in the presence of hydrochloric acid followed by nucleophilic substitution reactions [6].



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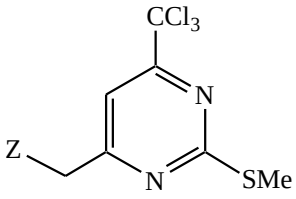
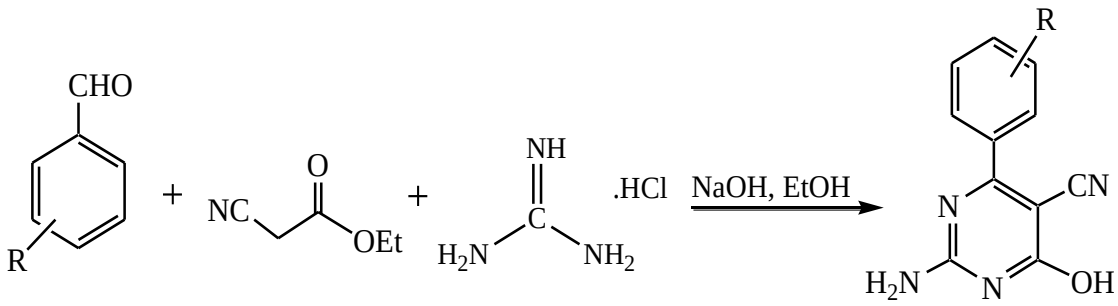


	Z
a	SC_6H_5
b	Morpholin-4-yl
c	Piperidinyl
d	$N(CH_2CH_3)_2$

7a-d

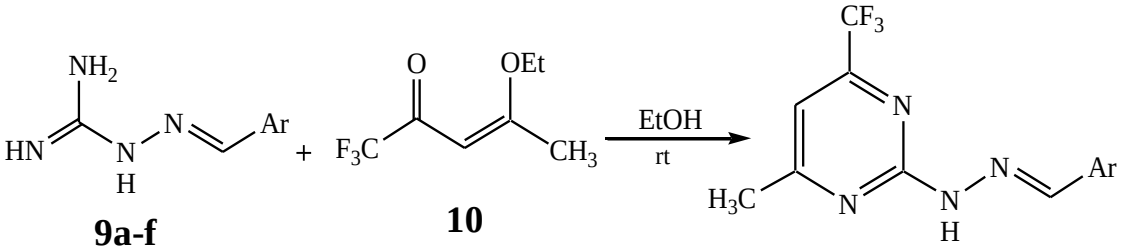
The reaction of aromatic aldehydes, ethyl cyanoacetate and guanidine hydrochloride in alkaline ethanol under reflux afforded 2-amino-5-cyano-6-hydroxy-4-arylpyrimidines **(8a-g)** [7].



8a-g

	R
a	H
b	3-NO_2
c	2-Cl
d	4-OMe
e	3-Cl
f	4-OH
g	2-NO_2

Novel 2-(*N*'-benzylidenehydrazino)-4-trifluoromethylpyrimidines **(11a-f)** were produced by the cyclocondensation reaction of *N*-guanidino-benzylimines **(9a-f)** with enone **(10)** through stirring in ethanol at room temperature [8].

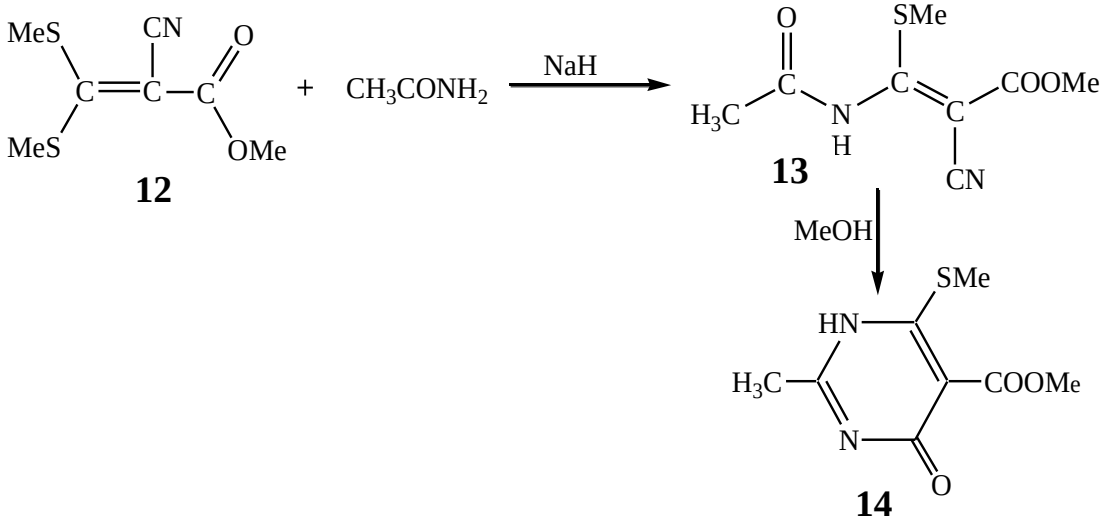


9a-f **10** **11a-f**

	Ar
a	C_6H_4
b	2-HO-C_6H_4
c	4-Me-C_6H_4
d	4-Cl-C_6H_4
e	4-MeO-C_6H_4
f	4-NO_2-C_6H_4

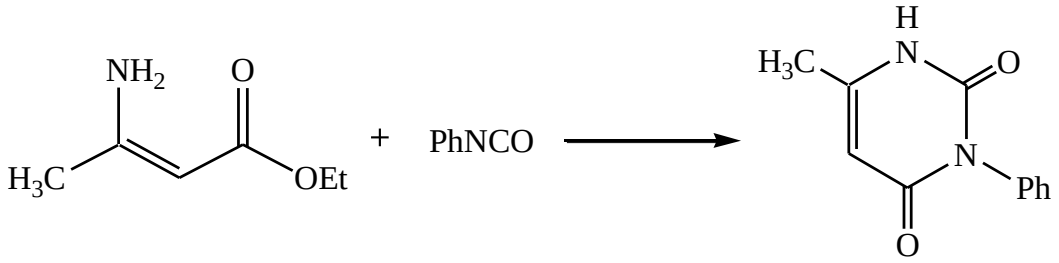
ii) Synthesis of pyrimidine from C-C-C-N and C-N fragments:

Ketenethioacetal **(12)** was reacted with acetamide in the presence of sodium hydride in a mixture of benzene and DMA to give **(13)**, which cyclized on refluxing in methanol to the pyrimidine derivative **(14)** [9].



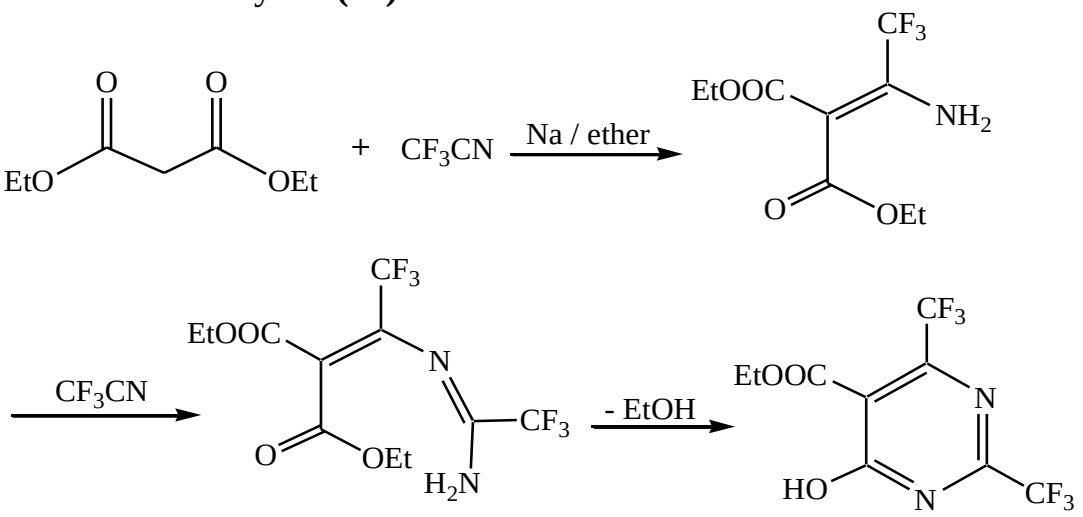
12 **13** **14**

6-Methyl-3-phenyluracil **(15)** was obtained by the reaction of ethyl β-aminocrotonate with phenylisocyanate [10].



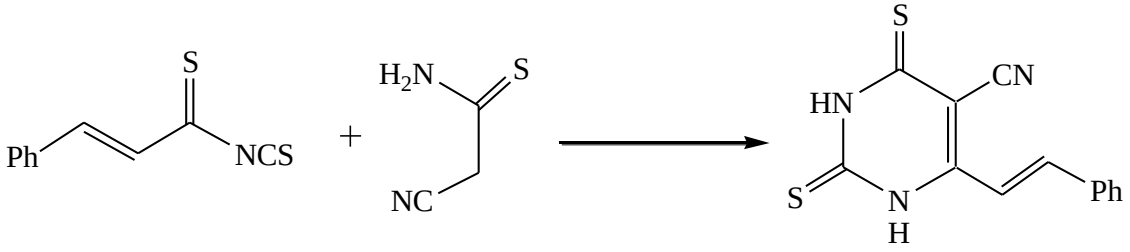
15

The condensation reaction of diethyl malonate and two molecules of trifluoroacetonitrile furnished ethyl 2,6-bis(trifluoromethyl)-4-hydroxy-pyrimidine-5-carboxylate **(16)** [11].



16

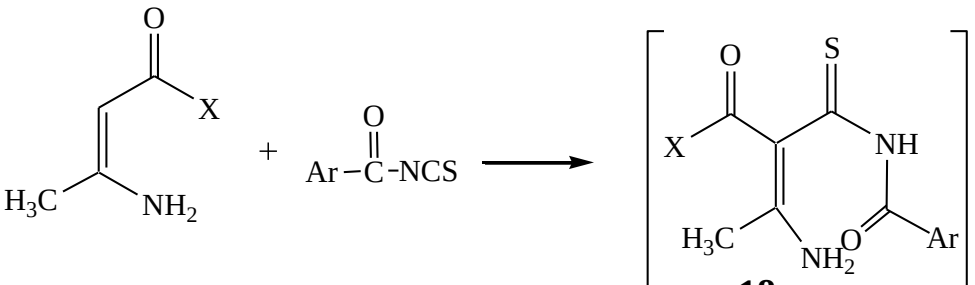
3-Phenylthioacryloylisothiocyanate was reacted with 2-cyanothio-acetamide and yielded 6-styryl-2,4-dithioxo-1,2,3,4-tetrahydropyrimidine-5-carbonitrile **(17)** [12].



17

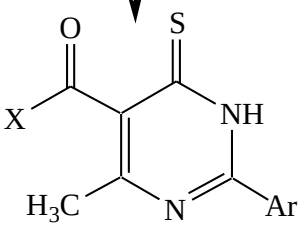
iii) Synthesis of pyrimidine from C-C-N and C-N-C fragments:

Addition of enaminoketone or enaminoester to aroylisothiocyanate provided the intermediate **(18)**, which undergoes cyclodehydration in basic medium to give the corresponding pyrimidine derivative **(19a-d)** [13-15].



18

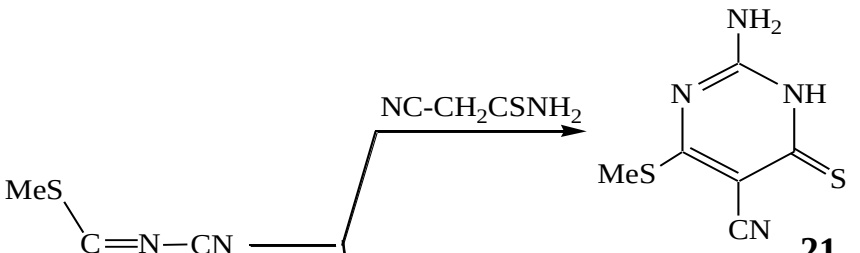
- H_2O



19a-d

	X	Ar
a	OEt	C_6H_5
b	OEt	4-MeO-C_6H_4
c	OEt	4-Cl-C_6H_4
d	CH_3	C_6H_5CH=CH

Cycloaddition of chalcogen **(20)** with 2-cyanothioacetamide in sodium ethoxide afforded pyrimidine derivative **(21)** [16], while cycloaddition of the same compound with 3-aminoacrylonitrile derivatives in DMSO and anhy. K_2CO_3 at room temperature yielded the derivatives **(22a,b)** [17].



20

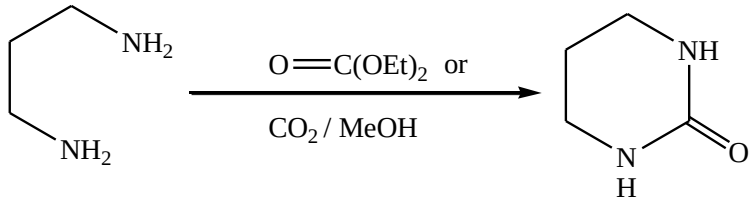
21

22a,b

	X
a	Pyrrolidinyl
b	Morpholin-4-yl

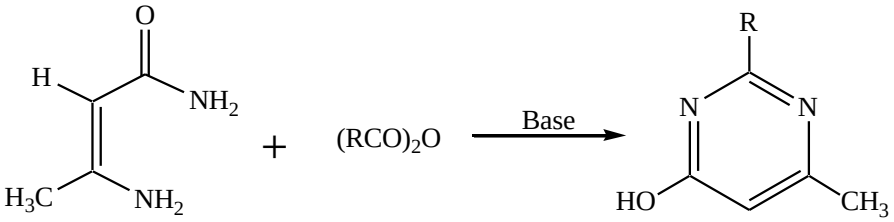
iv) Synthesis of pyrimidine from N-C-C-C-N and C fragments:

1,3-Diaminopropane was reacted with diethyl carbonate [18] or carbon dioxide in methanol [19] and yielded perhydropyrimidin-2-one **(23)**.



23

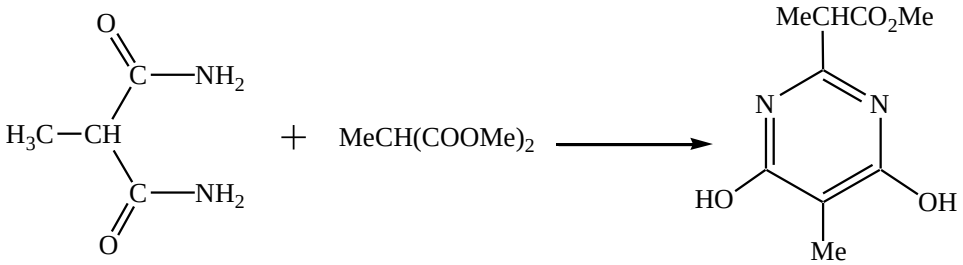
2-Alkenyl-6-methyl-4-hydroxypyrimidines **(24a,b)** were produced by the reaction of β-aminocrotonamide with α,β-unsaturated acid anhydride followed by cyclization in basic medium [20].



24a,b

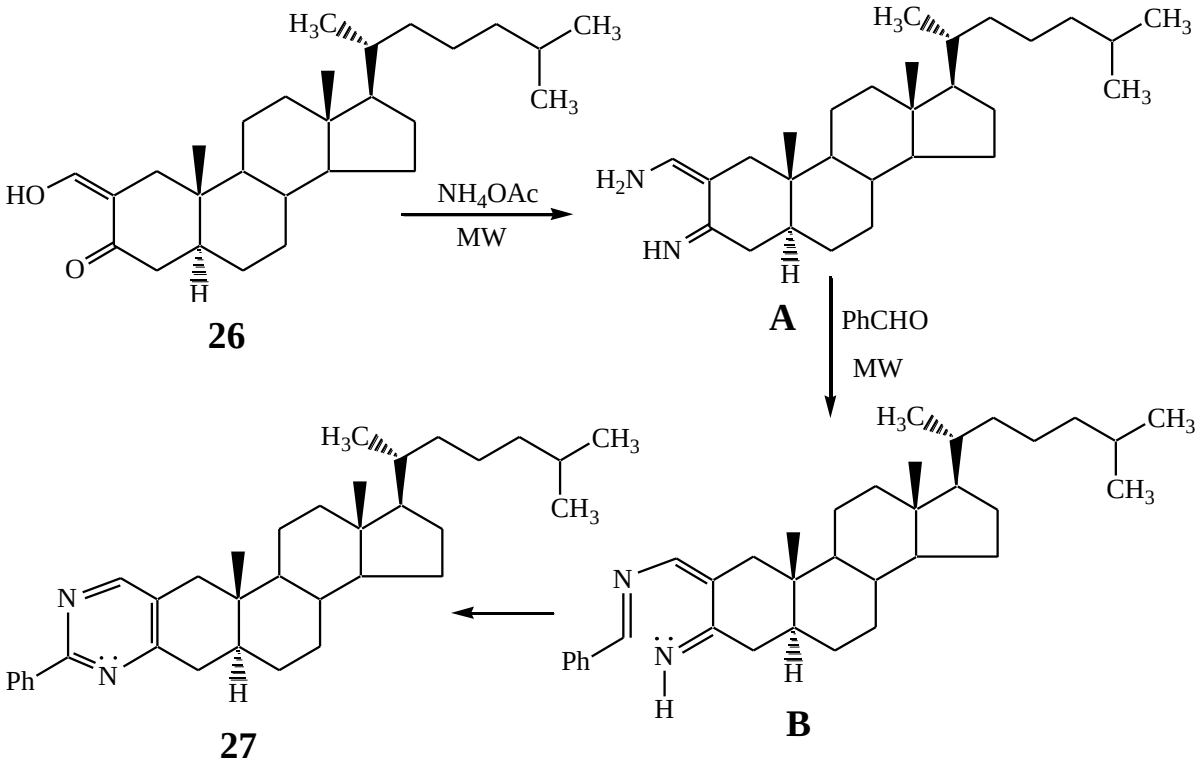
	R
a	CH_2=CH
b	CH_3-CH=CH

The reaction of 2-methylmalonodiamide with an ester such as 2-methylmalonic ester afforded 4,6-dihydroxypyrimidine derivative **(25)** [21].



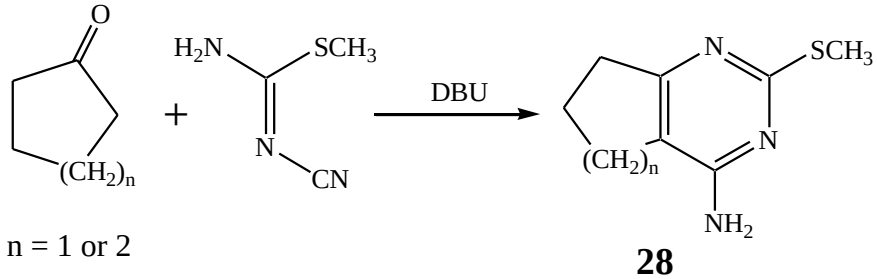
25

Steroidal pyrimidine **(27)** was prepared through microwave-assisted three-component reaction of 2-hydroxymethylene-3-ketocholestan **(26)**, benzaldehyde and ammonium acetate for 6 min. The mechanism involves the formation of β-aminoketoimine intermediate **(A)**, which condensed with benzaldehyde led to diimine intermediate **(B)**. Then the latter was cyclized and auto-oxidized to the product [22].

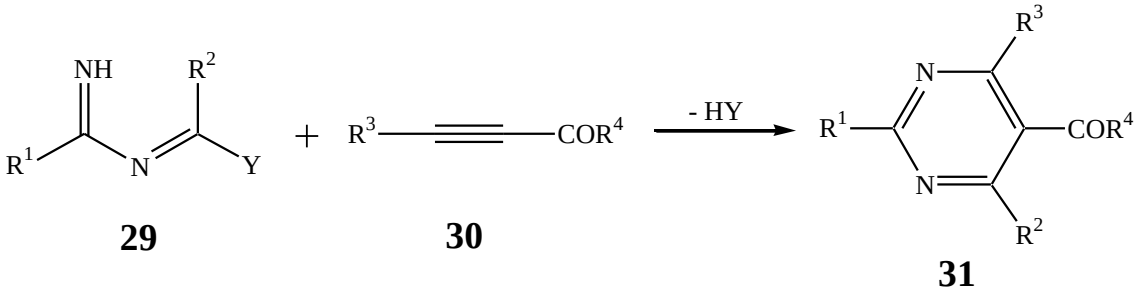


v) Synthesis of pyrimidine from C-N-C-N and C-C fragments:

The reaction of cyclopentanone or cyclohexanone with 3-cyano-2-methylisothiourea in the presence of DBU as base catalyst afforded 4-aminopyrimidine derivatives **(28)** [23].



1,3-Diaza-1,3-butadienes **(29)** were reacted with electron-deficient acetylenes **(30)** under mild conditions to provide pyrimidine derivatives **(31)** [24].



29 **30** **31**

R^1 = Ph, EtO_2C, $(EtO)_2CH$, Cl_3C

R^2 = H, Me, Ph, 4-Me-C_6H_4

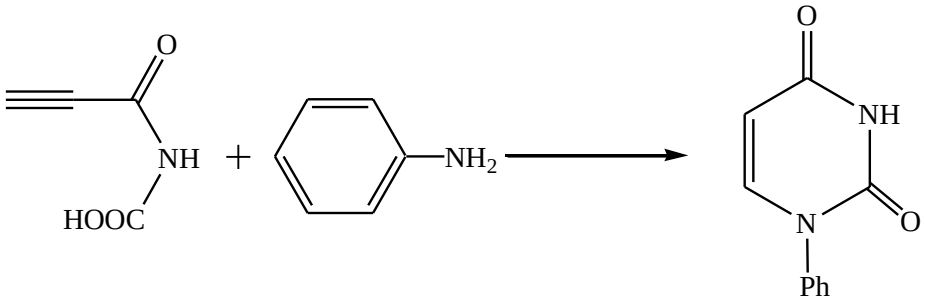
R^3 = H, Me, Ph, MeO_2C

R^4 = H, OMe, OEt

Y = OR, SMe, NMe_2

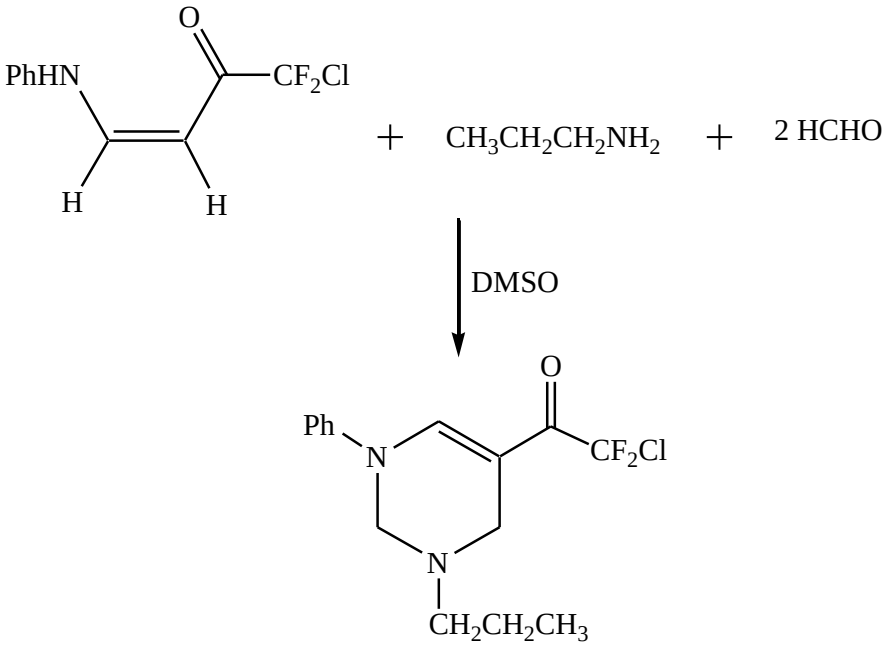
vi) Synthesis of pyrimidine from C-C-C-N-C and N fragments:

N-phenyluracil **(32)** was prepared by the addition of aniline to *N*-propynoylcarbamic acid [25].



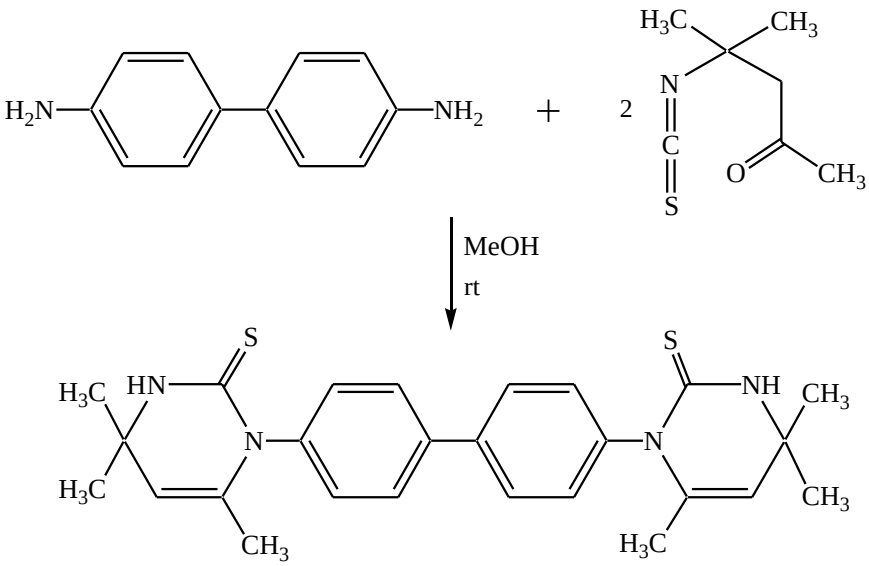
32

1-Chloro-1,1-difluoro-4-phenylaminobut-3-en-2-one was reacted with *n*-propylamine and formaldehyde in DMSO under mild conditions and the corresponding pyrimidine derivative **(33)** was obtained [26].



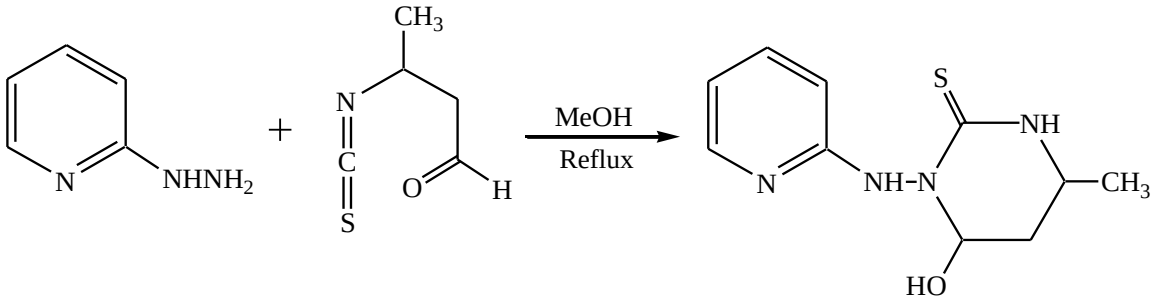
33

4-Isothiocyanato-4-methyl-2-pentanone was reacted with benzidine in methanol at room temperature with two to one molar ratio and yielded bis(2-thioxopyrimidin-1-yl) biphenyl derivative **(34)** [27].



34

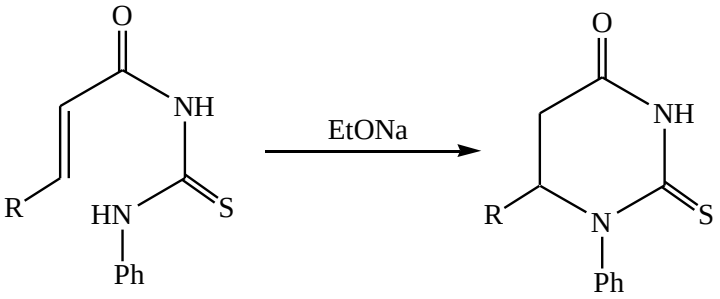
Pyrimidine-2-thione derivative **(35)** was obtained by refluxing 2-hydrazinopyridine with 3-isothiocyanatobutanal in methanol [28].



35

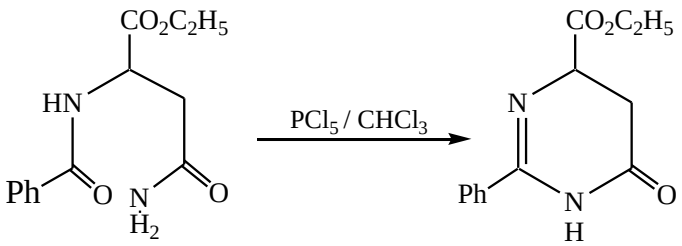
vii) Synthesis of pyrimidine from N-C-C-C-N-C fragment:

N-propenoylthiourea derivatives **(36)** were cyclized in sodium ethoxide to 2-thioxoperhydropyrimidin-4-ones **(37)** [29].



36 **37**

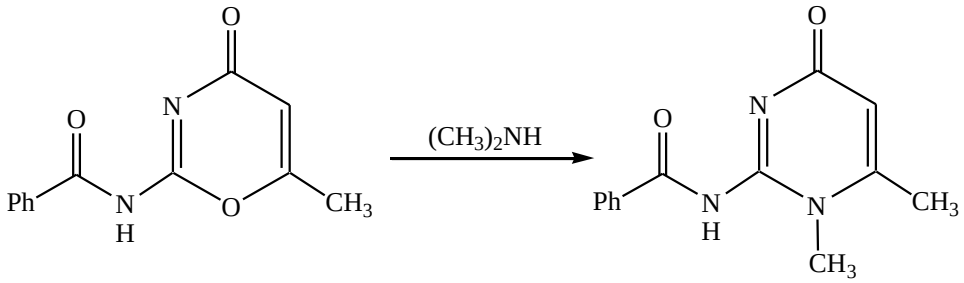
Oxidative cyclization of ethyl ester of benzoyl asparagine by using phosphorus pentachloride in chloroform yielded ethyl 2-phenyl-6-oxotetrahydropyrimidine-5-carboxylate **(38)** [30].



38

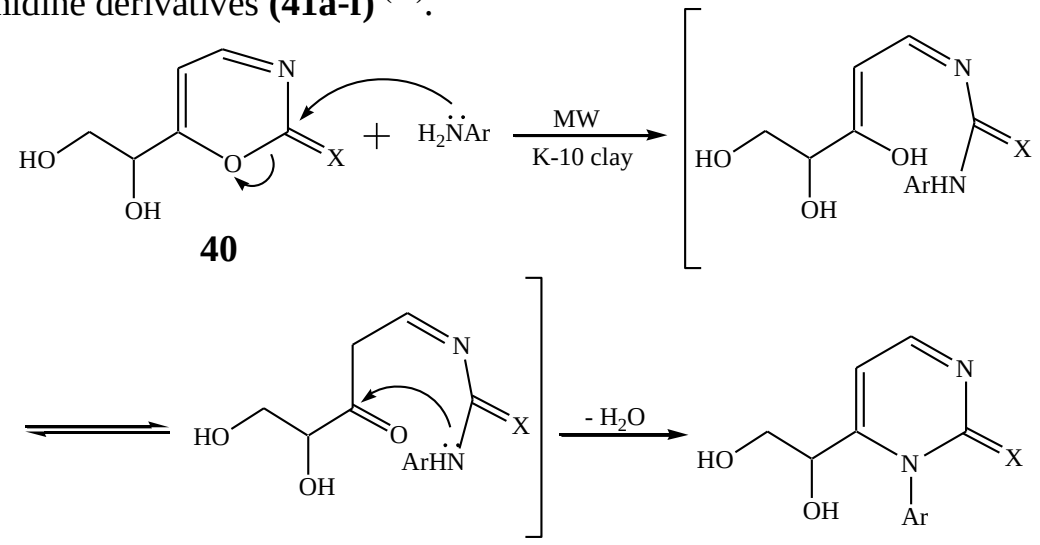
viii) Synthesis of pyrimidine by ring transformation and ring expansion:

2-Benzoylamino-6-methyl-1,3-oxazin-4-one was transformed into pyrimidine derivative **(39)** via the reaction with dimethylamine [31].



39

Solvent-free microwave irradiation of a mixture of 1,3-oxazin-2-ones (thiones) **(40)** and aromatic amines in the presence of K-10 clay through amine-driven dehydrative ring transformation result in formation of pyrimidine derivatives **(41a-f)** [32].

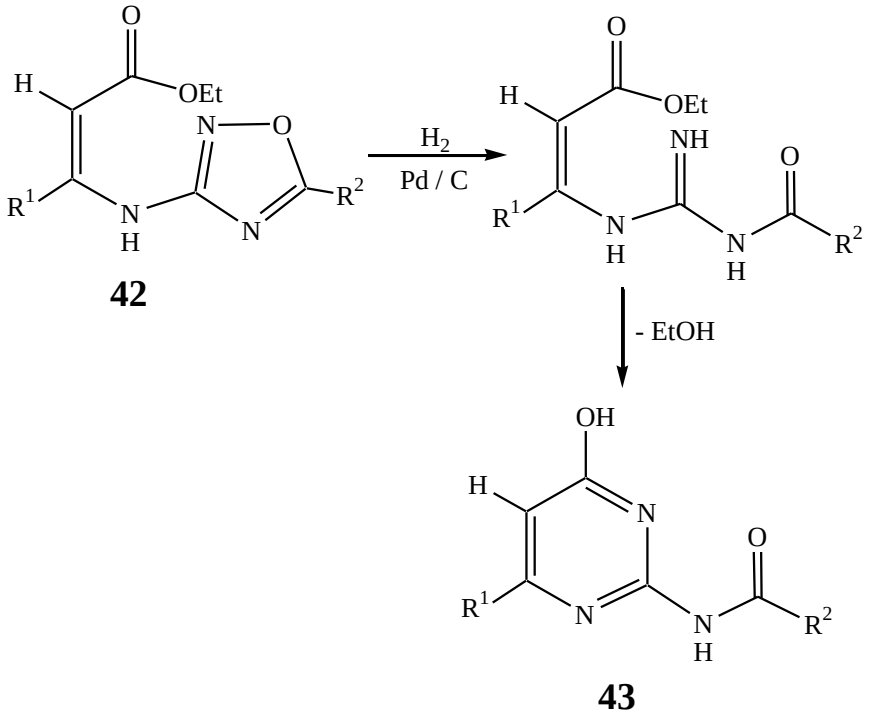


40

41a-f

	X	Ar
a	O	C_6H_5
b	O	4-Cl-C_6H_4
c	O	4-MeO-C_6H_4
d	S	C_6H_5
e	S	4-Cl-C_6H_4
f	S	4-MeO-C_6H_4

The hydrogenation of 1,2,4-oxadiazole derivatives **(42)** lead to the reductive cleavage of N-O bond followed by cyclization to give the pyrimidine derivatives **(43)** [33].



42

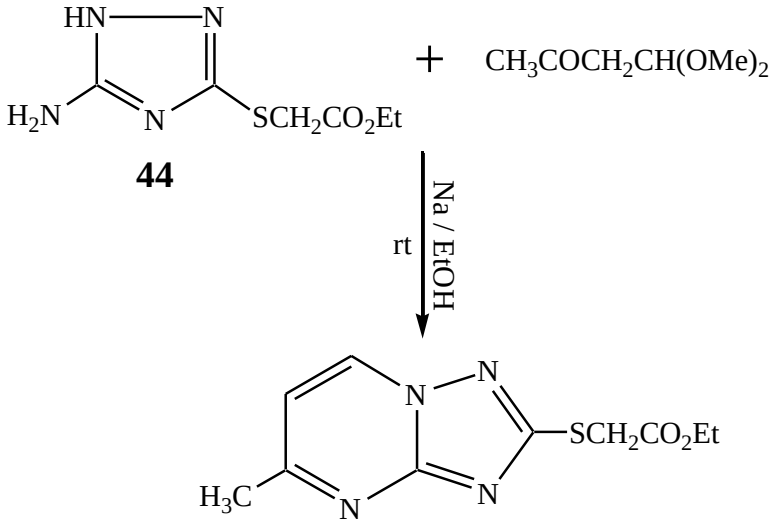
43

B) Synthesis of fused pyrimidines:

1. Synthesis of triazolopyrimidines:

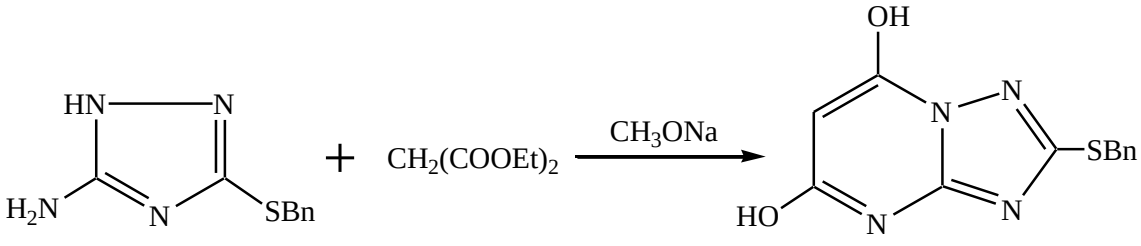
1.1. ***From triazole derivatives:***

The aminotriazole derivative **(44)** was cyclized with acetylacetaldehyde dimethylacetal in Na / EtOH at room temperature to give ethyl 2-(5-methyl-1,2,4-triazolo[1,5-a]pyrimidin-ylthio)acetate **(45)** [34].



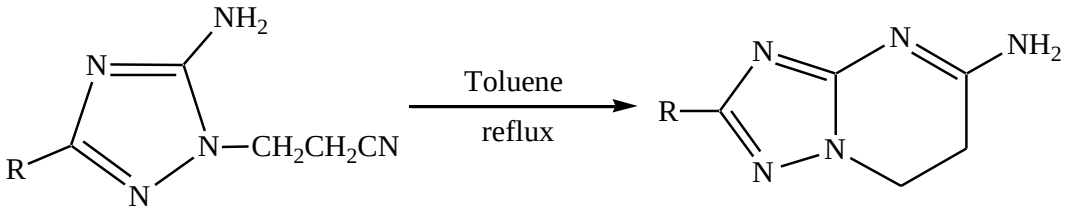
44 **45**

2-Benzylthio-5,7-dihydroxy-1,2,4-triazolo[1,5-a]pyrimidine **(46)** was prepared by the cyclization reaction of 3-amino-5-benzylthio-*2H*-1,2,4-triazole with diethyl malonate in sodium methoxide [35].



46

Cyclization of 3-amino-2-(cyanoethyl)-5-substituted-1,2,4-triazoles **(47a-c)** by refluxing in toluene for 48 hours afforded 5-amino-1,2,4-triazolo-[1,5-a]pyrimidine derivatives **(48a-c)** [36].

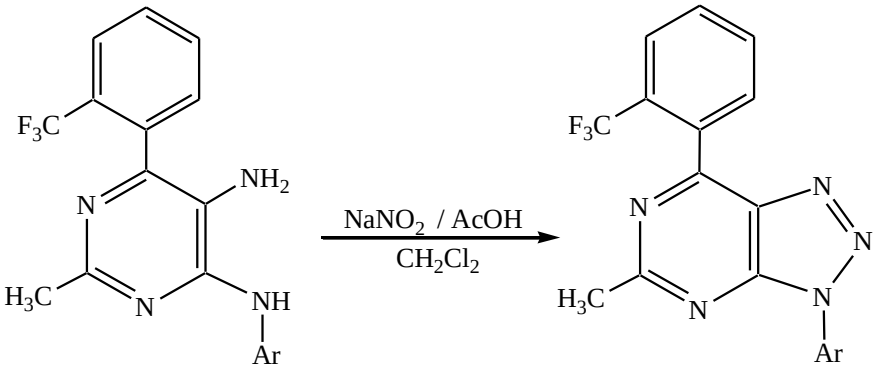


47a-c **48a-c**

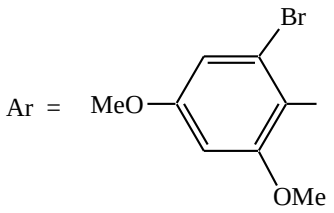
	R
a	CH_3
b	C_2H_5
c	Ph

1.2. ***From pyrimidine derivatives:***

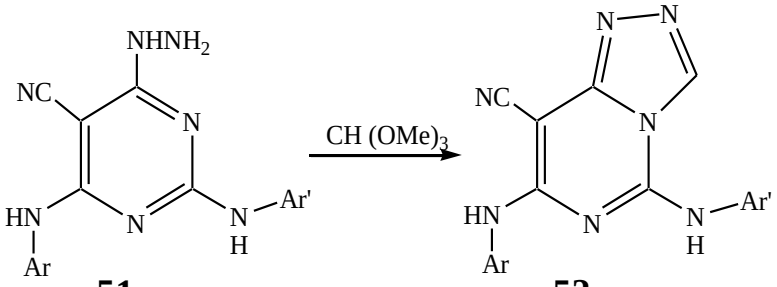
Triazolo[4,5-d]pyrimidine derivative **(50)** was achieved by the diazotization of the pyrimidine derivative **(49)** with sodium nitrite and acetic acid in methylene chloride [37].



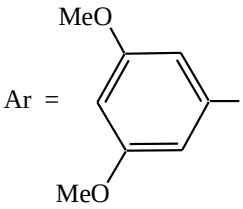
49 **50**



The reaction of 4-hydrazinopyrimidine derivatives **(51a-c)** with trimethylorthoformate in THF afforded the triazolo[4,3-c]pyrimidine derivatives **(52a-c)** as novel Syk inhibitors [38].



51a-c **52a-c**

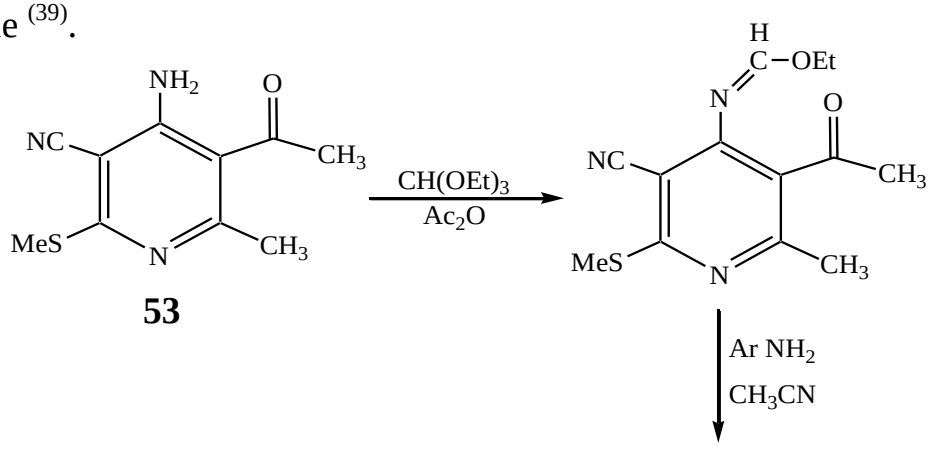


	Ar’
a	CH_2CH_2OTBS
b	$CH_2CO_2Bu^t$
c	CH_2CH_2NHBoc

2. Synthesis of pyridopyrimidines:

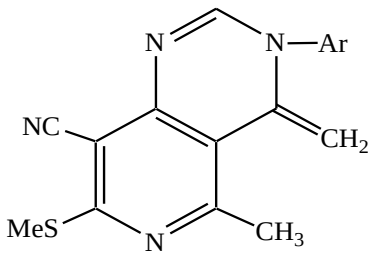
2.1. ***From pyridine derivatives:***

Pyrido[4,3-d]pyrimidine derivative **(54a-d)** was produced by the reaction of 4-aminopyrimidine derivative **(53)** with triethyl orthoformate using acetic anhydride as catalyst followed by treatment with different amines in acetonitrile [39].



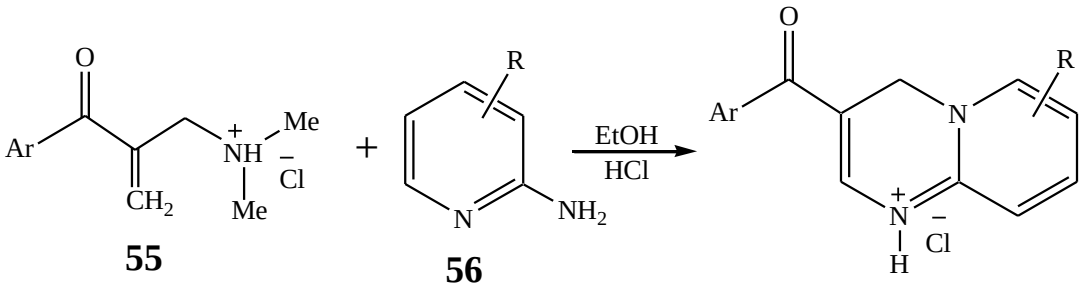
53

	Ar
a	$C_6H_5CH_2$
b	2-F-$C_6H_4CH_2$
c	4-F-$C_6H_4CH_2$
d	4-F-$C_6H_4CH_2CH_2$



54a-d

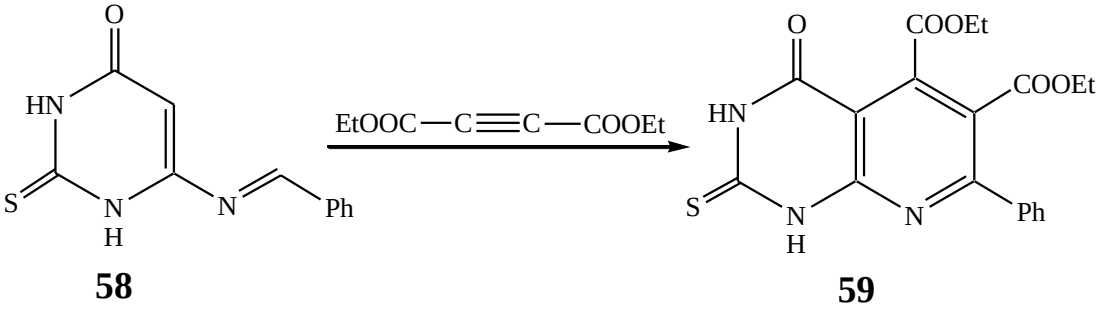
Condensation of 2-aminopyridines **(56)** with enone Mannich bases **(55)** in ethanol and the presence of hydrochloric acid afforded pyrido[1,2-a]-pyrimidines **(57a-c)** [40].



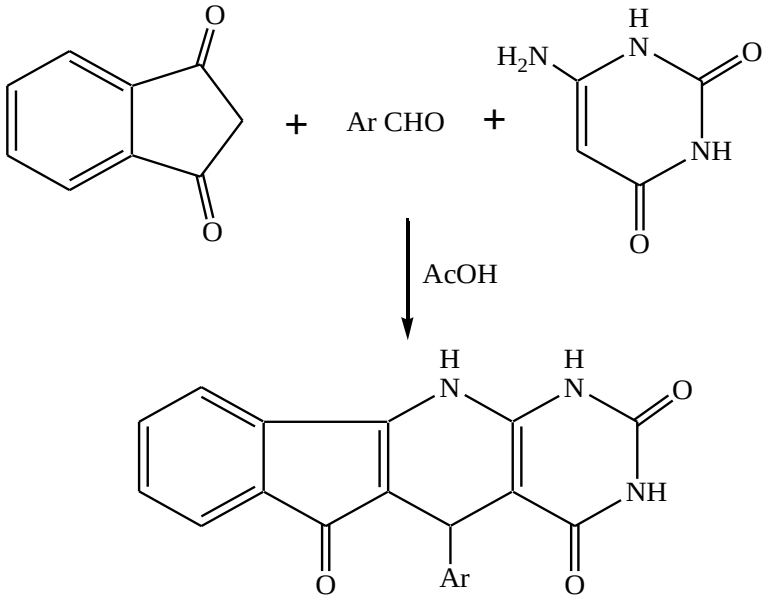
	R	Ar
a	H	4-Br-C_6H_4
b	3-Me	C_6H_5
c	6-Me	$C_6H_5CH_2O$

2.2. ***From pyrimidine derivatives:***

Cycloaddition reaction of azadiene **(58)** with diethyl acetylene-dicarboxylate yielded pyrido[2,3-d]pyrimidine derivative **(59)** [41].



5-Aryl-5,11-dihydro-*1H*-indeno[2',1':5,6]pyrido[2,3-d]pyrimidine-2,4,6-triones **(60a-e)** were prepared by Hantzsch cyclization of indan-1,3-dione with aromatic aldehyde and 6-aminouracil in acetic acid [42].



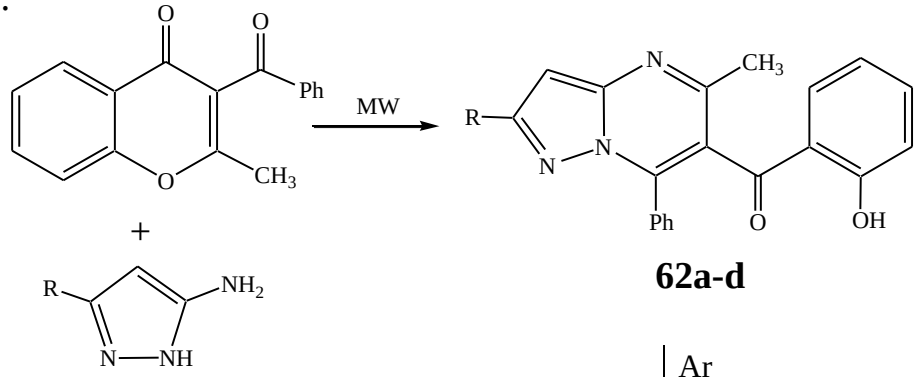
	Ar
a	C_6H_5
b	3-F_3C-C_6H_4
c	3-Br-C_6H_4
d	3-CN-C_6H_4
e	3-F-C_6H_4

60a-e

3. Synthesis of pyrazolopyrimidines:

3.1. ***From pyrazole derivatives:***

6-(2-Hydroxybenzoyl)-5-methyl-7-phenylpyrazolo[1,5-a]pyrimidines **(62a-d)** were achieved by regioselective microwave-assisted reaction of 5-aminopyrazole derivatives **(61a-d)** with 3-benzoyl-2-methyl-*4H*-chromen-4-one [43].

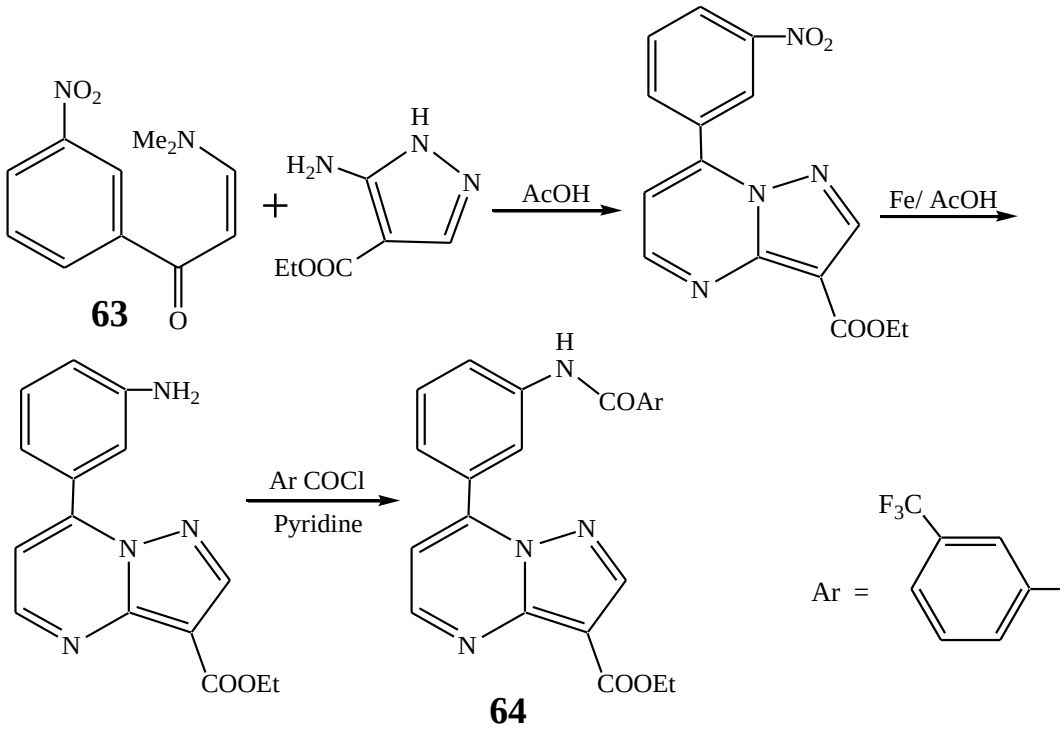


61a-d

62a-d

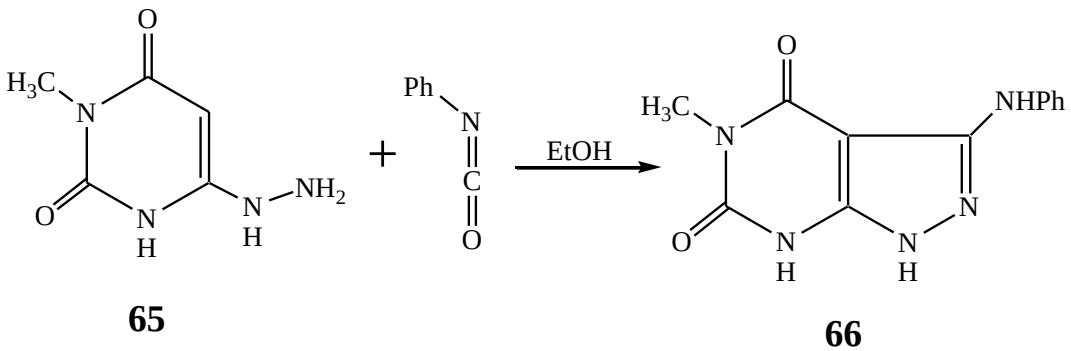
	Ar
a	CH_3
b	Bu^t
c	4-Br-C_6H_4
d	4-NO_2-C_6H_4

The B-Raf kinase inhibitor pyrazolo[1,5-a]pyrimidine-3-carboxylate derivative **(64)** was synthesized from the reaction of 5-amino-*1H*-pyrazole-4-carboxylate with compound **(63)** in acetic acid followed by reduction and aroylation [44].



3.2. ***From pyrimidine derivatives:***

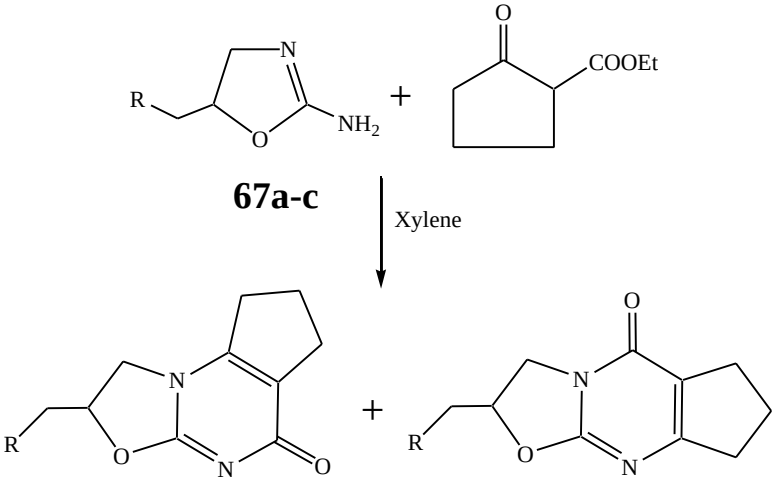
6-Hydrazinouracil **(65)** was reacted with phenylisocyanate at room temperature then refluxed in ethanol to furnish the corresponding pyrazolo[3,4-d]pyrimidine **(66)** [45].



4. Synthesis of oxazolopyrimidines:

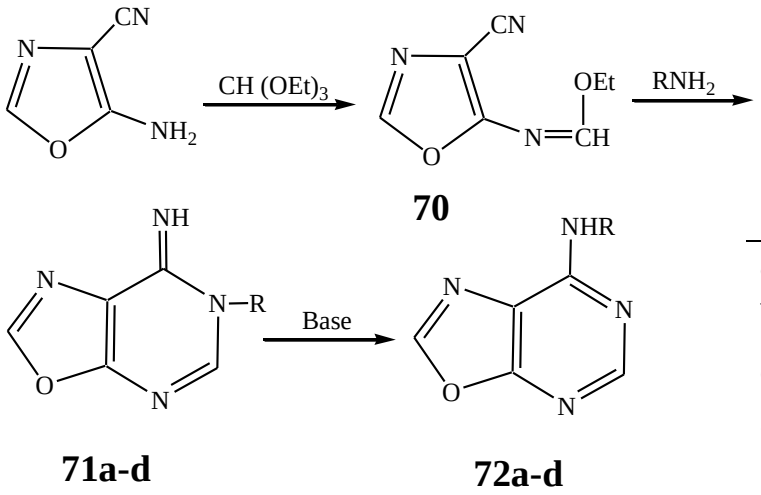
4.1. ***From oxazole derivatives:***

2-Amino-5-substituted-2-oxazolines **(67a-c)** were refluxed with ethyl 2-oxocyclopentane carboxylate in xylene to afford a mixture of isomeric oxazolo[3,2-a]pyrimidines **(68a-c)** and **(69a-c)** [46].



	R
a	C_6H_5O
b	Piperidinyl
c	4-Et-C_6H_4O

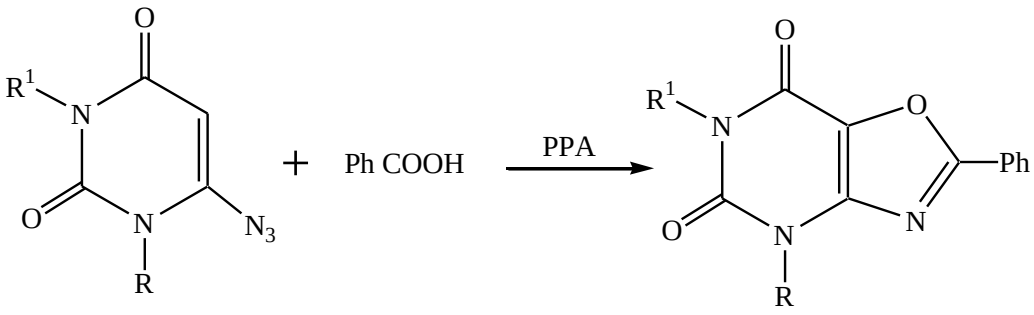
Reaction of 5-aminooxazole-4-carbonitrile with triethyl orthoformate gave an ethoxymethyleneamino derivative **(70)** which cyclized with the appropriate amine to the isolable 7-iminooxazolo[5,4-d]pyrimidine derivatives **(71a-d)**. However, the latter underwent a Dimorth rearrangement under basic conditions to7-amino derivatives **(72a-d)** [47]



	R
a	Me
b	Et
c	Pr^n
d	$PhCH_2$

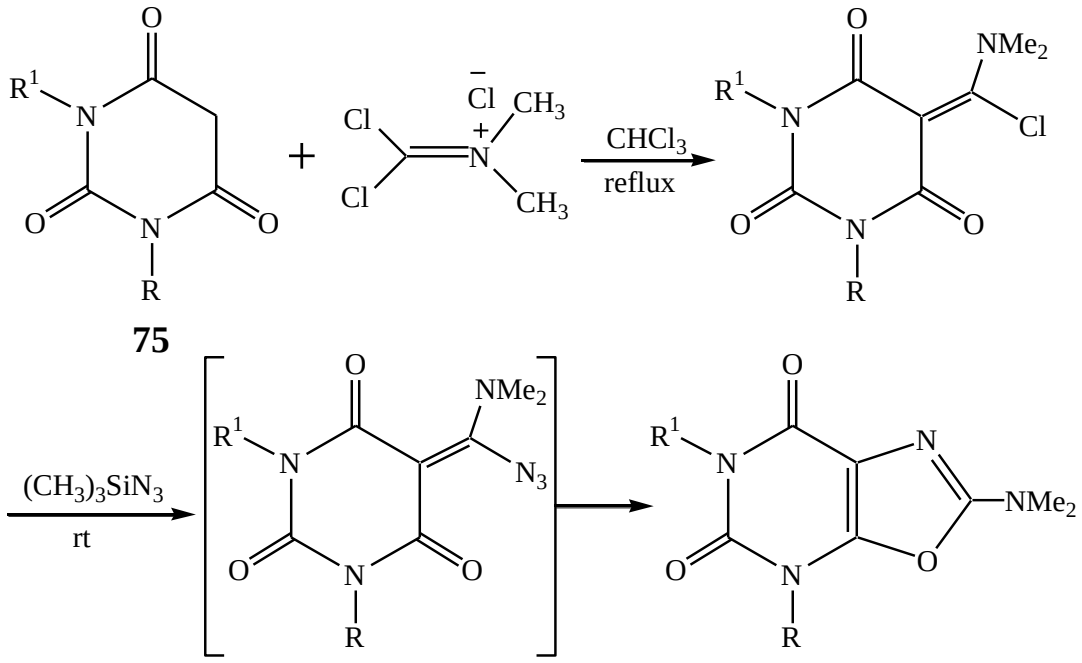
4.2. ***From pyrimidine derivatives:***

Oxazolo[5,4-d]pyrimidine-5,7-diones **(74)** were produced by thermolytic reaction between 6-azidouracils **(73)** and benzoic acid in the presence of PPA [48].



73 **74**

Condensation of 1,3-disubstitutedbarbituric acid **(75)** with dimethyl-dichloromethyleniminium chloride and subsequent treatment with trimethyl-silylazide afforded **(77)** through the rearrangement of the highly unstable α-azidoenamines **(76)** [49].

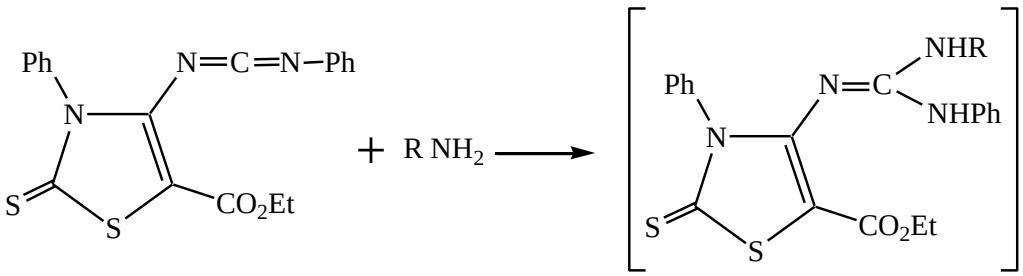


75 **76** **77**

5. Synthesis of thiazolopyrimidines:

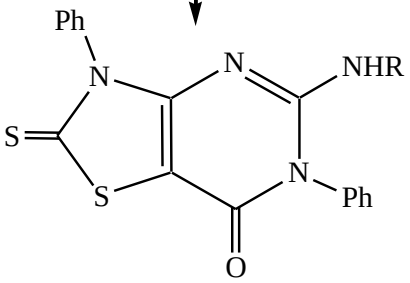
5.1. ***From thiazole derivatives:***

Thiazolo[4,5-d]pyrimidines **(79a-e)** were obtained by the reaction of thiazole carbodiimide derivative **(78)** with different amines followed by cyclization in sodium ethoxide and ethanol [50].



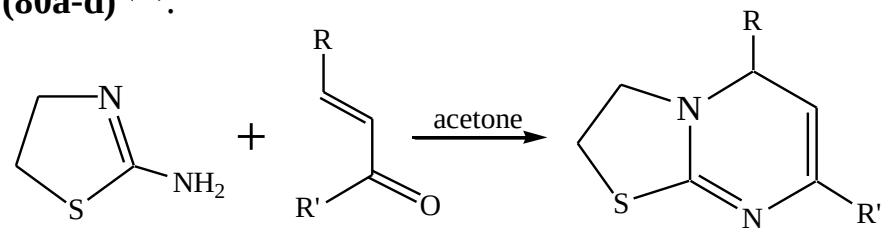
78

	R
a	3-MeBn
b	2-FBn
c	4-FBn
d	Bu^{i}
e	Bu^{t}



79a-e

The reaction of 2-aminothiazoline with α,β-unsaturated carbonyl compounds under mild conditions yielded dihydrothiazolo[2,3-a]pyrimidines **(80a-d)** [51].

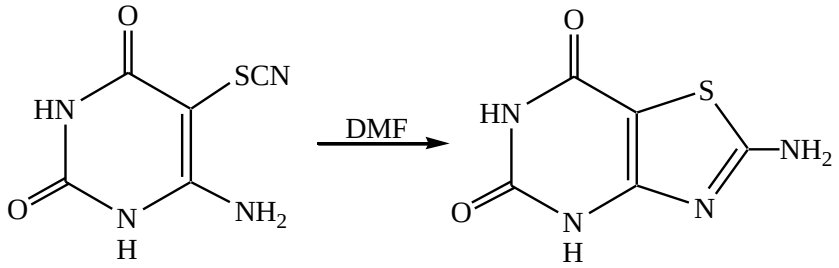


80a-d

	R	R’
a	Me	H
b	Ph	Me
c	Ph	Et
d	Ph	Ph

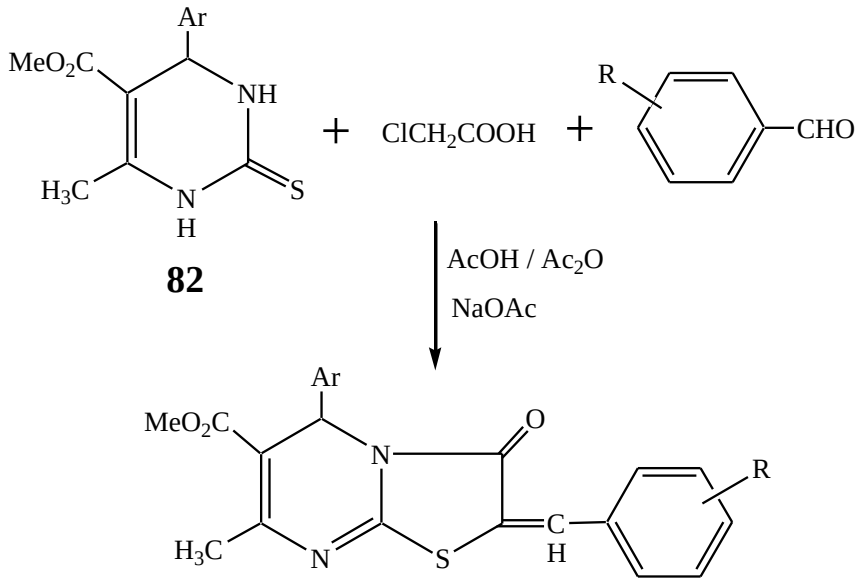
5.2. ***From pyrimidine derivatives:***

Preparation of 2-aminothiazolo[4,5-d]pyrimidine-5,7-dione **(81)** was achieved via thermal cyclization of 4-aminouracil-5-thiocyanate in DMF [52].



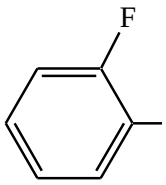
81

Three-component reaction of pyrimidine derivative **(82)**, chloroacetic acid and aromatic aldehyde produced thiazolo[3,2-a]pyrimidines **(83a-d)** [53].



82

83a-d

Ar = 

	R
a	H
b	4-Me
c	4-MeO
d	4-Cl

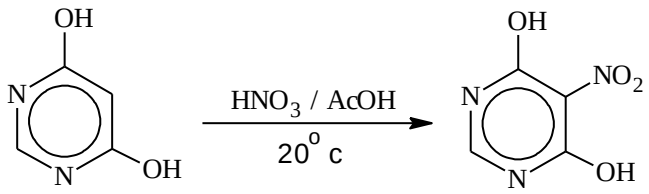
REACTIONS OF PYRIMIDINES

1) Electrophilic substitution:

Formal replacement of a CH unit in pyridine by a nitrogen atom reduces the capacity of corresponding diazine towards electrophilic substitution. Electrophilic substitution is difficult in simple inactivated diazine because of both extensive protonation under strongly acidic conditions and the inherent lack of reactivity of the free base. For these reasons, one strongly electron-releasing group, at least, must be present to make the reaction successful.

a) Nitration:

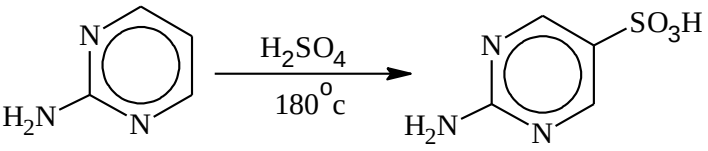
Pyrimidines normally require the presence of at least two electron-releasing groups for successful nitration. Thus, 4,6-dihydroxypyrimidine was nitrated using nitric acid in acetic acid at 20°c to give the 5-nitroderivative **(84)** [54].



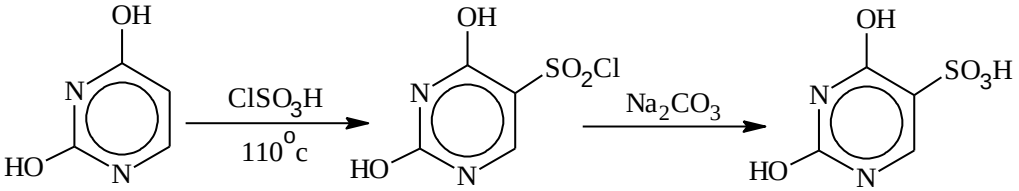
84

b) Sulphonation:

Contrary to nitration, sulphonation needs only one electron releasing group and takes place at position 5. Sulphonation of 2-aminopyrimidine using fuming sulphuric acid at 180°c gave 2-amino-5-sulphopyrimidine **(85)** [55], while chlorosulphonation of 2,4-dihydroxypyrimidine at 110°c gave 5-(chlorosulphonyl)-2,4-dihydroxypyrimidine **(86)** which reacted with sodium carbonate to give 2,4-dihydroxy-5-sulphopyrimidine **(87)** [56].



85

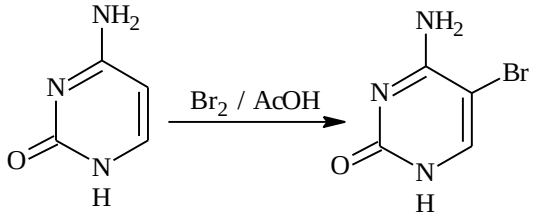


86 **87**

c) Halogenation:

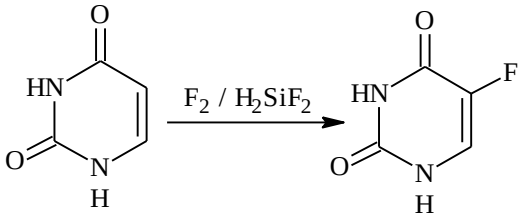
Typically, pyrimidines having at least one electron-releasing substituent may be halogenated at position 5 by chorine or bromine in aqueous solution or by bromine in acetic acid. *N*-chlorosuccinimide, *N*-bromosuccinimide, phosphoryl chloride, phosphoryl bromide and phosphorous pentachloride have been used for the 5-halogenation of some pyrimidines.

The reaction of cytosine **(88)** with bromine in acetic acid provided 5-bromocytosine **(89)** as a major product [57].



88 **89**

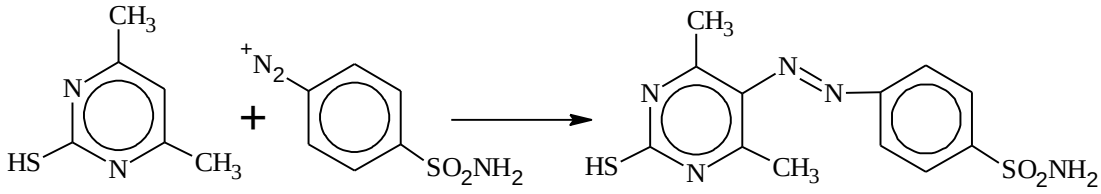
5-Fluorouracil **(90)** was prepared by the interaction of uracil with fluorine in 40% H_2SiF_2 at 70°c [58].



90

d) Diazo-Coupling:

Pyrimidines may be coupled with diazotized amines to give 5-arylazo-derivatives. Thus, treatment of 4,6-dimethyl-2-mercaptopyrimidine **(91)** with diazotized *p*-aminobenzenesulphonamide leads to the formation of 4,6-dimethyl-5-(sulphamylbenzeneazo)-2-mercaptopyrimidine **(92)** [59].

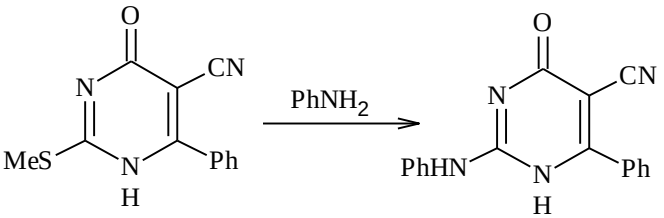


91 **92**

2) Nucleophilic substitution:

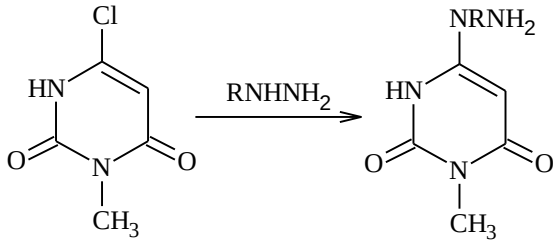
a) Reaction with amines and hydrazines:

5-Cyano-2-methylthio-6-phenylpyrimidine-4-one **(93)** was reacted with aniline to give 5-cyano-2-(phenylamino)-6-phenylpyrimidine-4-one **(94)** [60].



93 **94**

6-Chloro-3-methyluracil **(95)** was reacted with hydrazine, methyl-hydrazine and benzylhydrazine to give the corresponding hydrazino-pyrimidines **(96a-c)** [61].

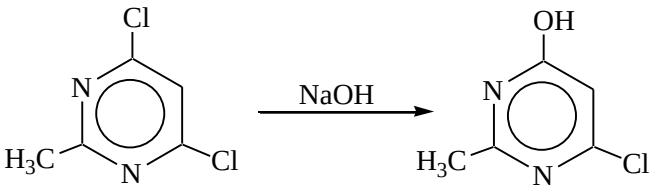


95 **96a-c**

	R
a	H
b	Me
c	Bn

b) Hydrolysis:

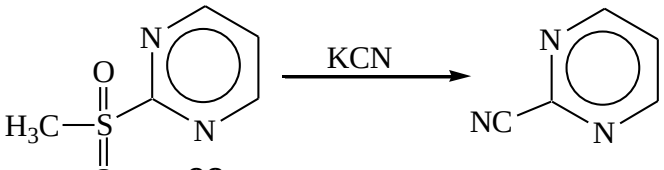
The reaction of 4,6-dichloro-2-methylpyrimidine with sodium hydroxide provided 4-chloro-6-hydroxy-2-methylpyrimidine **(97)** [62].



97

c) Cyanation:

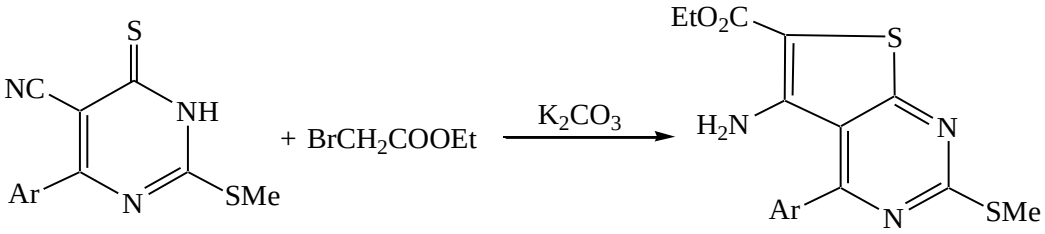
Treatment of 2-pyrimidinyl-methylsulfone **(98)** with potassium cyanide afforded 2-cyanopyimidine **(99)** [63].



98 **99**

3) Alkylation and acylation:

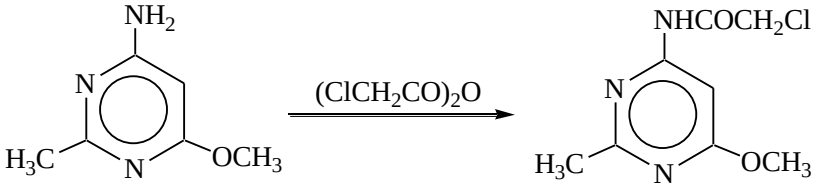
2-Methylthio-4-thioxopyrimidines **(100a-c)** were treated with ethyl bromoacetate and potassium carbonate in ethanol to give thieno[2,3-d]-pyrimidines **(101a-c)** [64].



100a-c **101a-c**

	Ar
a	C_6H_5
b	4-MeO-C_6H_4
c	4-Cl-C_6H_4

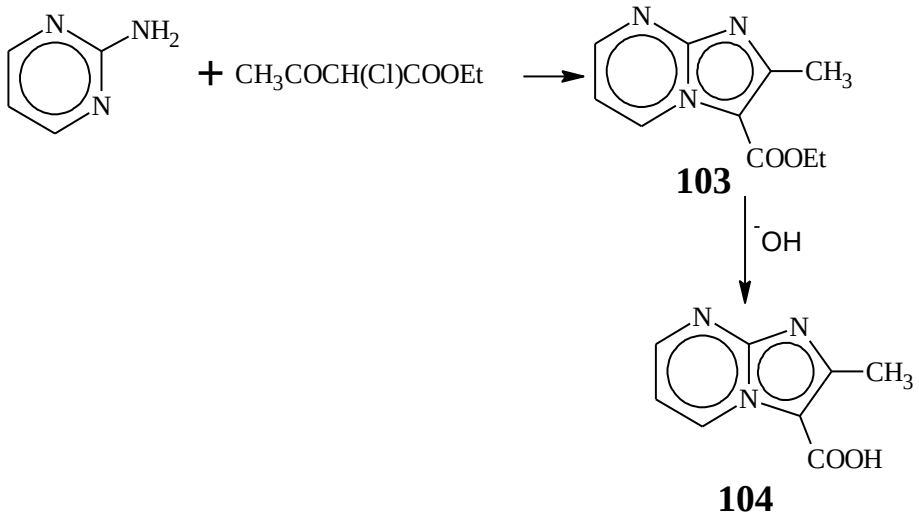
2-Chloroacetamido-4-methoxy-6-methylpyrimidine **(102)** was obtained by acylation of 2-amino-4-methoxy-6-methylpyrimidine with $(ClCH_2CO)_2O$ in dioxane [65].



102

4) Reaction with active methylene group containing compounds:

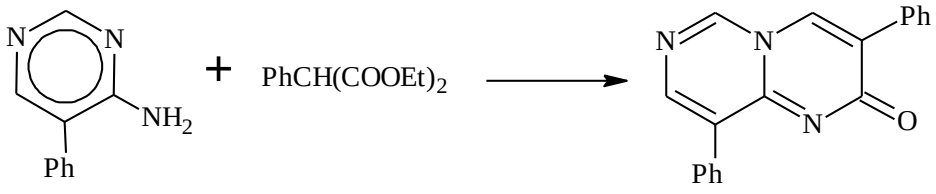
2-Aminopyrimidine was reacted with ethyl 2-chloroacetoacetate and furnished ethyl imidazo[1,2-a]pyrimidine-5-carboxylate **(103)** which was converted into the corresponding carboxylic acid **(104)** by alkaline hydrolysis [66].



103

104

Reaction of 4-amino-5-phenylpyrimidine with diethyl phenylmalonate gave pyrimido[1,6-a]pyrimidine derivative **(105)** [67].

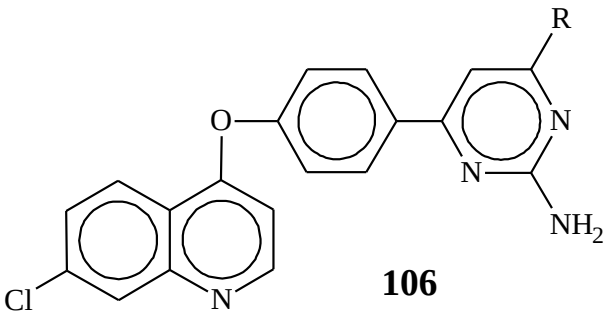


105

BIOLOGICAL ACTIVITY OF PYRIMIDINE DERIVATIVES

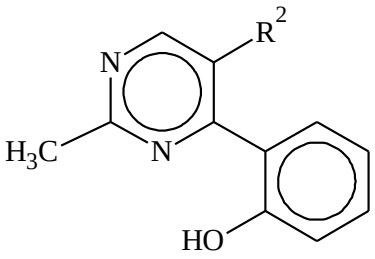
Condensed and non-condensed pyrimidines are biologically interesting molecules that have established utility in the pharmaceutical and the agrochemical industries. Compounds with these ring systems have diverse pharmacological activity such as anticancer [68], anti-inflammatory [69,70], antitumor [17,71], antibacterial [72-74], antimalarial [75] and antifungal [76].

A number of substituted quinolinyl pyrimidines **(106)** were synthesized as a new class of anti-infective agents and showed a good antitubercular and antimalarial activities [77].



106

A series of novel 2,4,5-trisubstituted pyrimidine derivatives **(107**and **108)** were evaluated for inhibition against the human hepatocellular carcinoma BEL-7402 cancer cell line and several compounds showed potent inhibition with an IC_{50} value less than 0.10 µM [78].



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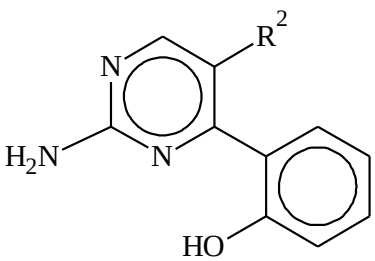
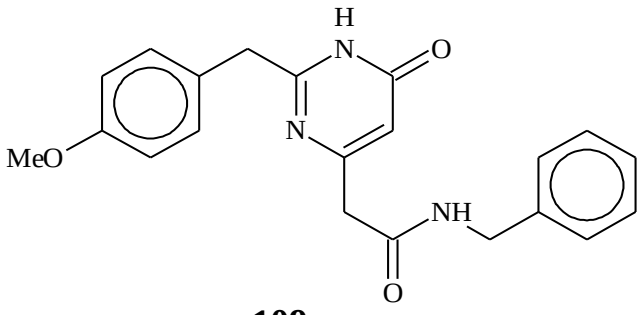


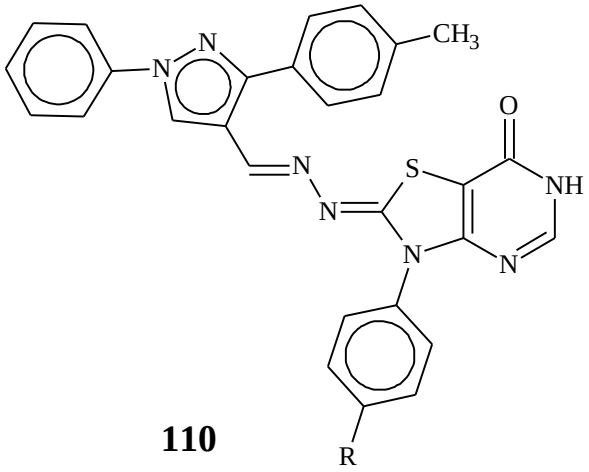
108

N-Benzyl-2-[2-(4-methoxybenzyl)-6-oxo-1,6-dihydropyrimidin-4-yl]-acetamide **(109)** can be used as inhibitor of human hydroxysteroid dehydrogenase (HSD) [79].



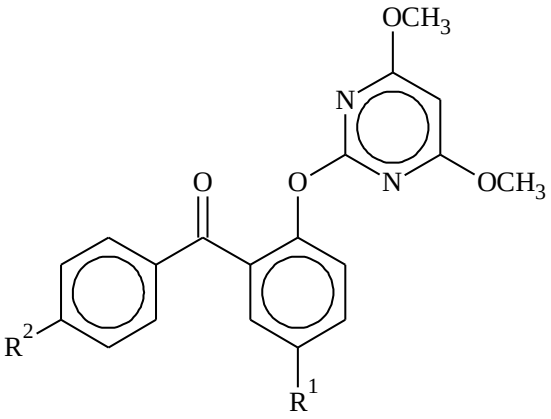
109

Pharmacological studies of some substituted 1*H*-pyrazolylthiazolo[4,5-d]-pyrimidines **(110)** showed that they possess anti-inflammatory and antimicrobial activities [80].



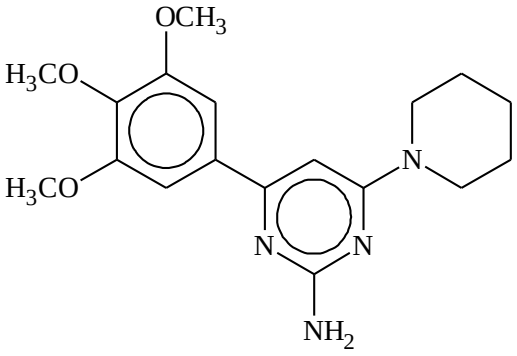
110

2-(2-Aroylaroxy)-4,6-dimethoxypyrimidines **(111)** were screened for their anti-inflammatory activity and have shown superior anti-inflammatory activity in the range 21.5-48.6 % . Compounds with chloro and fluoro groups at para position in benzoyl and phenoxy moieties of benzophenone elicited maximum inhibition (48.6 %) [81].



111

A new series of 2,4,6-trisubstituted pyrimidine derivatives **(112, 113, 114** and **115)** showed an excellent activity against leishmania [82].



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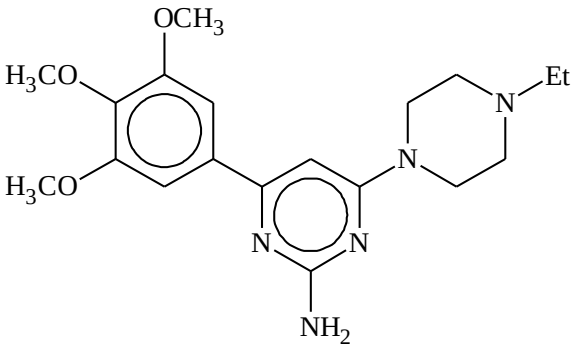
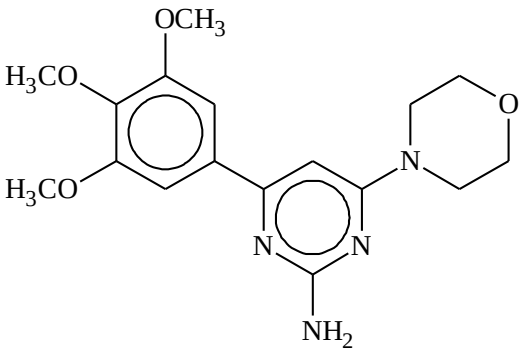


113



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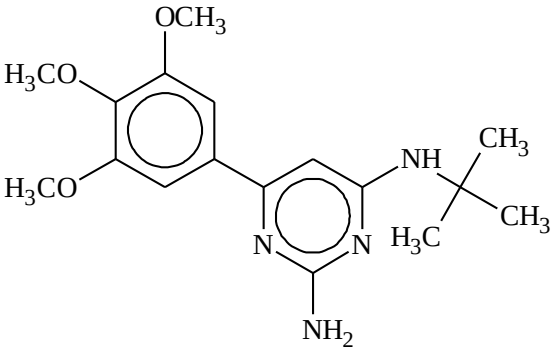

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