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By Mohamed Abdel-Megid, K. M. Elmahdy & Aymn E. Rashad

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Keywords: *pyrimidinethiones, therapeutic applications.*

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Synthesis and Applications of Pyrimidinethiones

Mohamed Abdel-Megid [α σ], K. M. Elmahdy [α] & Aymn E. Rashad [σ ρ]

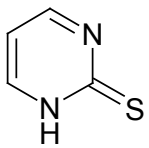
Abstract- One important class of pyrimidine is pyrimidinethione, which is also well known as mercapto or thioxopyrimidine compounds. This review deals with the synthesis and applicaions of pyrimidinethiones.

Keywords: pyrimidinethiones, therapeutic applications.

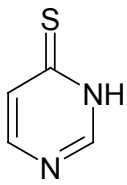
I. Introduction

Pyrimidine derivatives have been very well known in medicinal chemistry for their therapeutic applications. One possible reason for their activity is the presence of a pyrimidine base in thymine, cytosine and uracil, which are essential building blocks of nucleic acids, DNA and RNA. Pyrimidinethione derivatives have attracted substantial interest of synthetic-biochemists.[1]

Pyrimidinethiones exist in three possible structures, depending on the position of thione group. There are 2-pyrimidinethione (I), 4-pyrimidinethione (II) and 2,4-pyrimidinethione (III).



I



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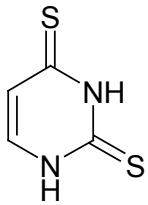
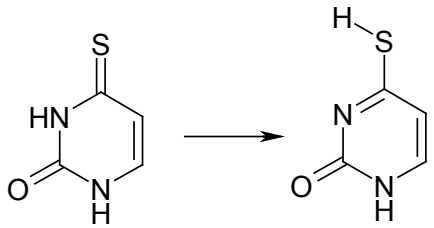
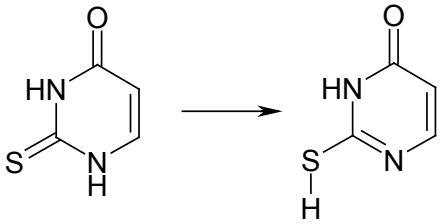


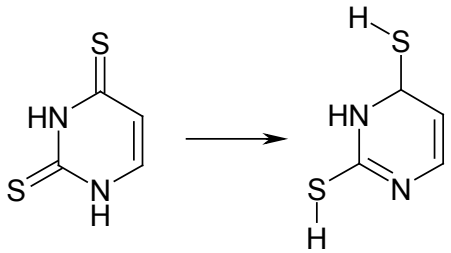
III

It was found that, upon UV irradiation of monomers of thione compounds isolated in low-temperature inert gas matrices, a proton from the N–H group was shifted to the C=S group placed in the α-position. That led to the conversion of the thione form of studied compounds into the thiol tautomer. Very recently, analogous unimolecular thione→thiol photo-tautomeric transformations were found to occur also for matrix-isolated monomers of 4-thiouracil and 2-thiouracil. For these species, the photoprocesses involving transfer of protons from the N–H groups to the thiocarbonyl (C=S) groups dominated strongly over the transfer of protons to the carbonyl (C=O) groups[2].





For 2,4-dithiouracil, the presence of two N–H and two C=S groups in a molecule opens the gate for more than one, simple pathway of the UV-induced thione→thiol phototautomeric reaction. The thiol–thione tautomers of the compound could be expected as products of a single-proton-transfer photoreaction and the dithiol tautomer can be photogenerated in a double-proton-transfer process. the dithiol tautomer of 2,4-dithio- uracil, generated by the transfer of both N–H protons to the thiocarbonyl C=S groups[2].



The crystal structure of 2,4-dithiouracil has been determined. The dimers of 2,4-dithiouracil are present in the structure. Every molecule is connected with two neighbouring molecules by means of two kinds of pair coupling hydrogen bonds. At the same time each molecule is a donor and an acceptor in four hydrogen bonds of the N–H·· ·S type[3].

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Authors σ : Faculty of science and Humanities, Shaqra University Saudi Arabia.
Author ρ : Photochemistry Department, NRC, Egypt.

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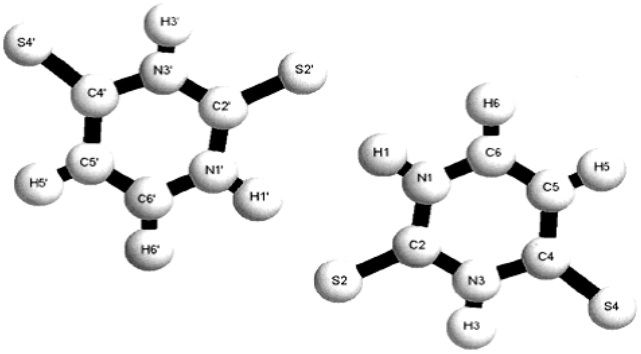
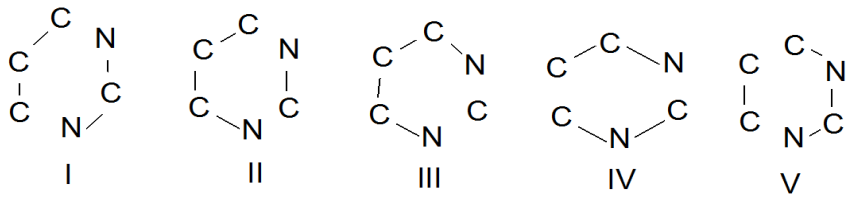


II. Synthesis of Pyrimidinethiones

Pyrimidinethiones were generally prepared by five types of ring synthesis (I, II, III, IV and V) according to the nature of the fragments which combine together to form pyrimidinethione nucleus.



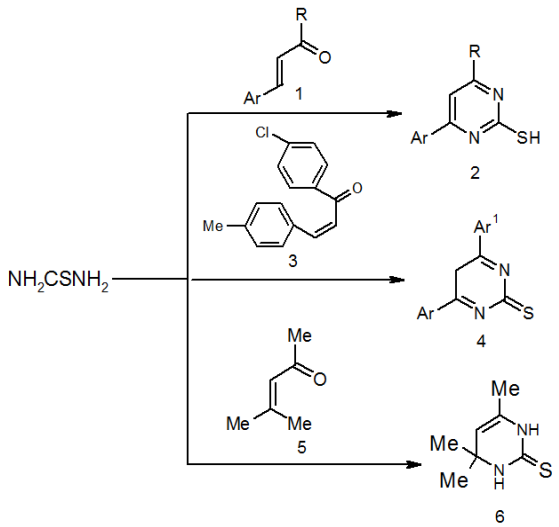
a) Synthesis from C-C-C and N-C-N fragments

i. *From thiourea and its derivatives*

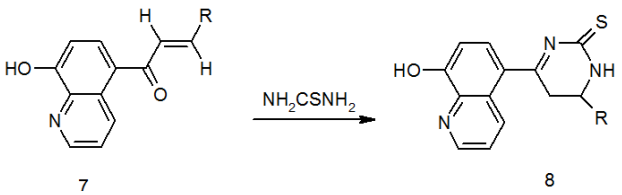
Thiourea and its derivatives considered as good synthons for the synthesis of 2-thiopyrimidine derivatives *via* their interaction with enones, 1,3-dicarbonyl-compounds, acetylenic compounds, arylidene, ethoxymethylene derivatives, acrylonitriles and enamines.

a. *With enone derivatives*

Reaction of thiourea with ethylenic ketone 1[4], benzoylethylene derivative 3[5] and mesityl oxide (5)[6]afforded pyrimidine derivatives 2, 4 and 6, respectively.



4-(8-Hydroxyquinolin-5-yl)-6-substituted-1,2,5,6-tetra-hydropyrimidine-2-thiones 8 were prepared from the reaction of compound 7 with thiourea in the presence of sodium ethoxide[7].



R = C_6H_5, 4-MeO-C_6H_4, 4-Cl-C_6H_4, 2-furyl, C_3H_7 n

On the other hand, 5-chloro-4-formyl-3-methyl-1-phenylpyrazole (9) was condensed with 10 to form an α,β-unsaturated ketonic intermediates 11, which were then cyclocondensed with thiourea to give pyrimidine-2-thione derivatives 12[8].

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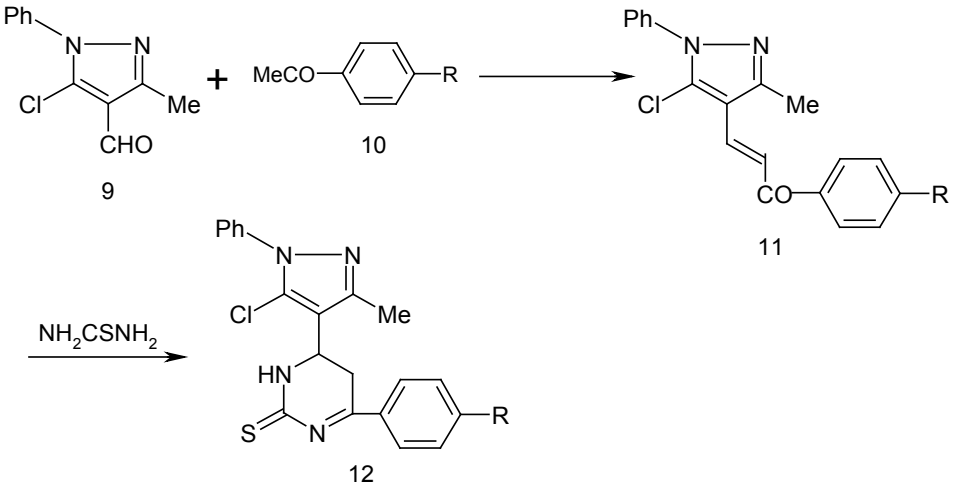
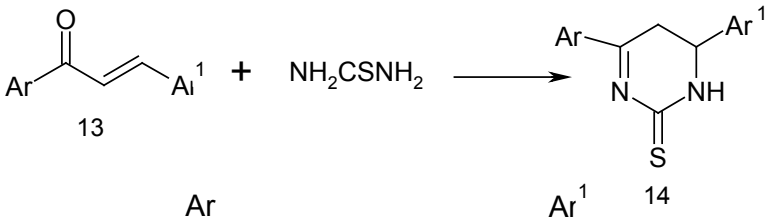
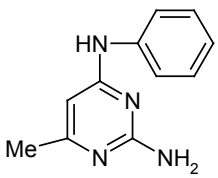


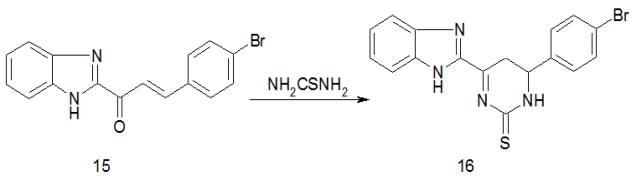
Reaction of chalcons 13 with thiourea afforded pyrimidine-2-thione derivatives 14[9-13].



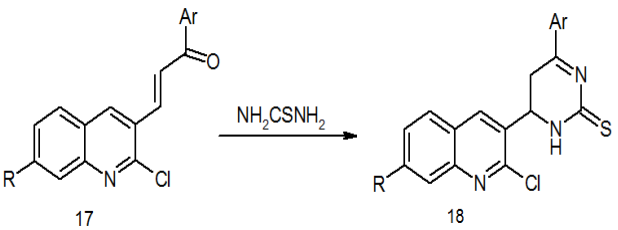
Ar	Ar^1
a, 2,4-$(Me)_2C_6H_3$	, 4-ClC_6H_4
b, 3,4-$(Me)_2C_6H_3$	, 4-ClC_6H_4
c, 2-OMe-4-MeC_6H_3	, 4-ClC_6H_4
d, C_6H_3-CH_2-C_6H_4	, C_6H_5
e, C_6H_5	
f, 2-ClC_6H_4	
g, 2-$MeOC_6H_4$	
h, 2,4-$(MeO)_2C_6H_3$	
i, 4-ClC_6H_4	
j, 3-$O_2NC_6H_4$	



4-[1-H-benzimidazol-2-yl]-6-(4-bromophenyl)-5,6-dihydropyrimidine-2(1H)thione (16) was prepared through cyclocondensation of 1-(benzimidazol-2-yl]-3-(4-bromophenyl)-2-propen-1-one (15) with thiourea[14].



Interaction of 3-(1-aryl-1-oxoprop2-2en-3-yl)-7-substituted -2-chloroquinoline (17) with thiourea in the presence of ethanolic sodium ethoxide afforded 4-aryl-6-(2-chloro-7-substituted-quinolin-3-yl)-5,6-dihydroprimidine-2(3H)thione (18)[15] .



Anisoyl vinylaryl quinazolines 19 was reacted with thiourea to give pyrimidine-2-thione derivatives 20[16,17].

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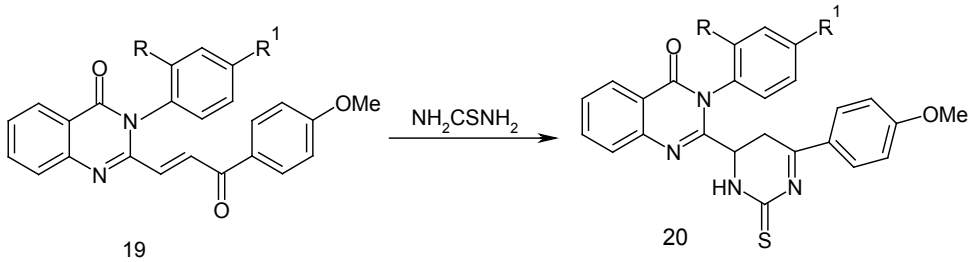
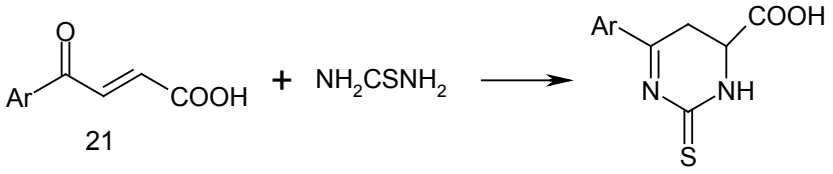


19 20

R = Me, R1 = H; R = H, R1 = NH2

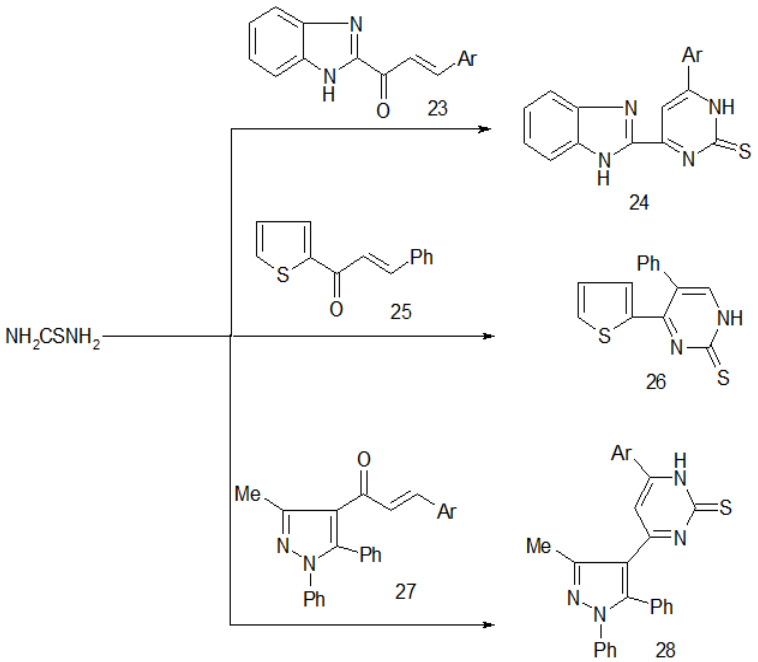
Reaction of β-aroylacrylic acids 21 with thiourea in the presence of ethanolic sodium ethoxide afforded the corresponding 6-aryl-4-carboxy-4,5-dihydropyrimidine-2(1H)-thiones 22[18].



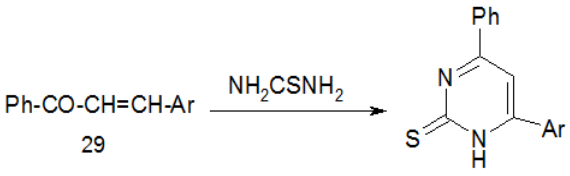
21 22

Ar = C_6H_5, 3,4-$Cl_2C_6H_3$ 2,5-C_6H_3(Me)(Cl)

Reaction of thiourea with 2-cinnamoyl benzimidazole (23), benzal-α-acetothienone (25) and 4-cinnamoyl-3-methyl-1,5-diphenylpyrazole (27) afforded pyrimidine-2-thiones 24, 26 and 28[19, 20, 21], respectively.



4,6-Disubstituted-2(1H)-pyrimidinethione 30[22] has been prepared by treatment of 4-nitrobenzylidene-acetophenone (29) with thiourea.



29 30

Ar = 4 -$O_2NC_6H_4$

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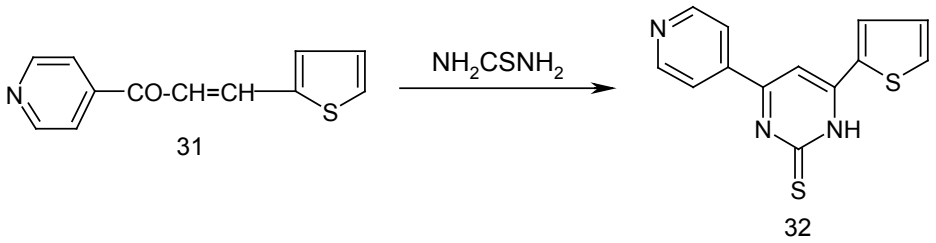
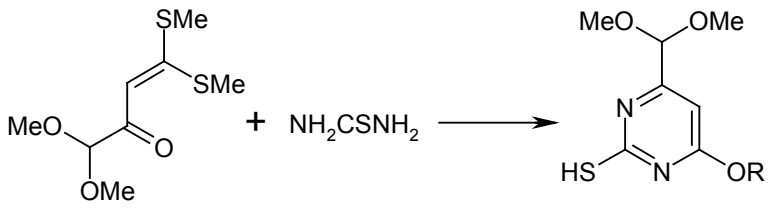
On the other hand, the chalcone 31 was reacted with thiourea to afford pyrimidinethione 32[23].



31 32

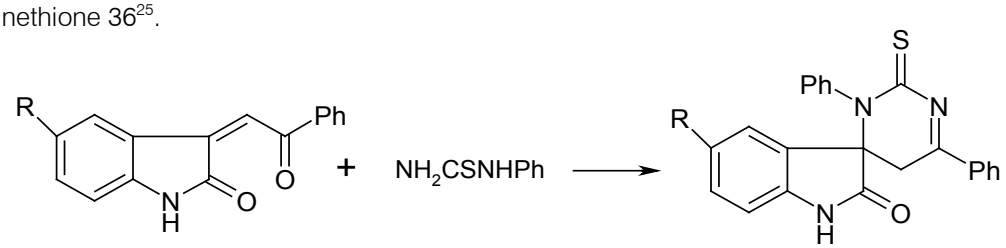
Treatment of α-oxoketene dithioacetal 33 with thiourea in the presence of sodium methoxide furnished the respective 6-alkoxy-4-[bis(methoxy)methyl]-2-mercaptopyrimidines (34) [24].



33 34

R = Me, Et

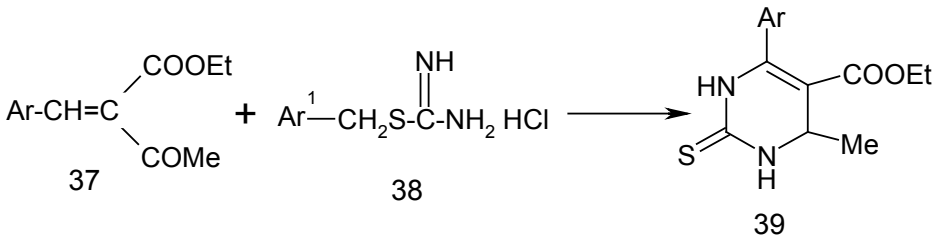
Condensation of compound 35 with phenylthiourea in ethanol under microwave irradiation yielded spiroindol pyrimidinethione 36[25].



35 36

R = Cl, Me

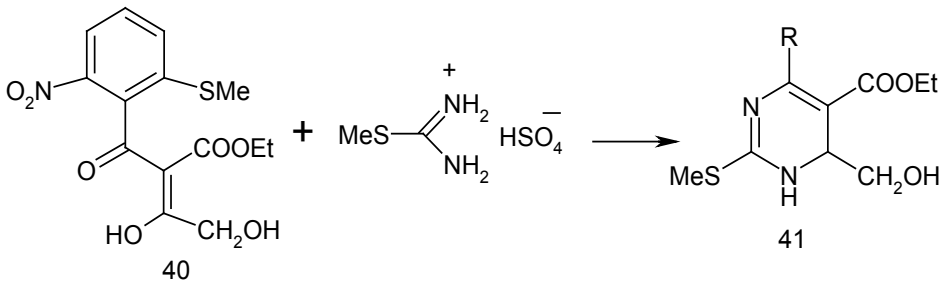
Treatment of *p*-nitrobenzylidine ethyl acetoacetate (37) with *p*-methoxybenzylthioamidine hydrochloride (38) gave pyrimidinethione 39[26].



37 38 39

Ar = 4- $O_2NC_6H_4$; Ar^1 = 4- $MeOC_6H_4$

Reaction of ethyl 4-(acetyloxy)-2-[2-(methylthio)-3-nitrophenyl methylene-3-oxobutanoate (40) and 2-methyl-2-thio pseudourea sulphate in the presence of sodium acetate afforded ethyl (hydroxymethyl) pyrimidine carboxylate derivative 41[27,28].



40 41

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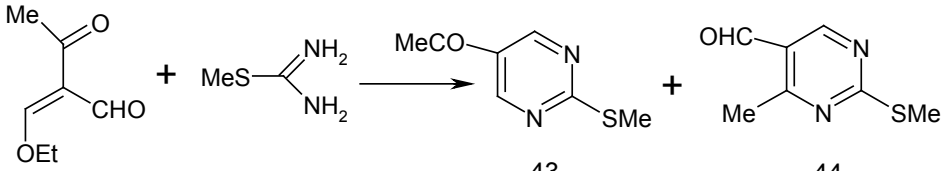
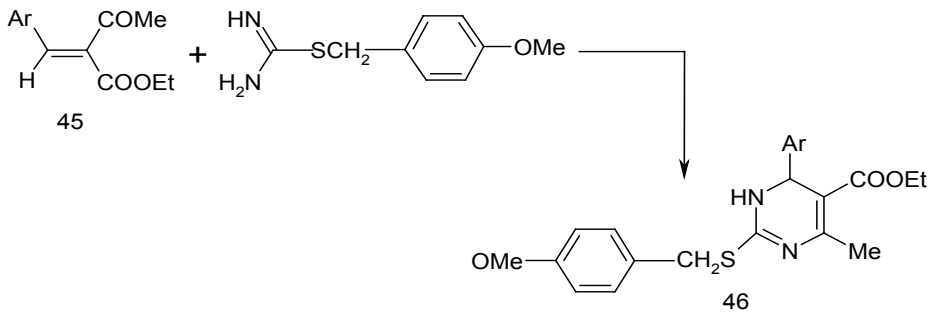
Condensation of 4-ethoxy-3-formyl-3-buten-2-one (42) with methyl thiourea afforded a mixture of 5-acetyl-2-methylthiopyrimidine (43) and 5-formyl-4-methyl-2-methylthiopyrimidine (44)[29,30].



42 43 44

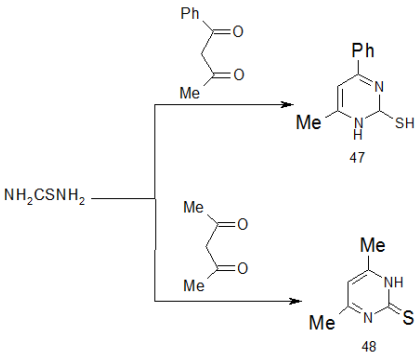
Treatment of α-acetylcinnamic esters 45 with S-(p-methoxybenzyl) thiourea in the presence of sodium hydroxide yielded 4-methyl-5-pyrimidine carboxylic acid esters 46[31].



45 46

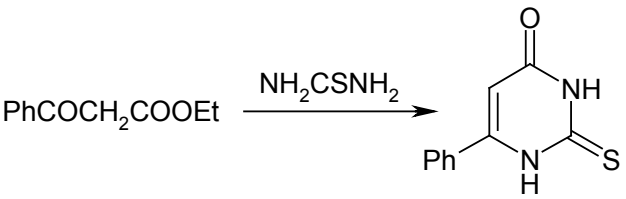
b. *With Dicarbonyl Compounds*

Reaction of thiourea with benzoylacetone[32] and acetylacetone[33,34,35] gave pyrimidine derivatives 47 and 48, respectively.



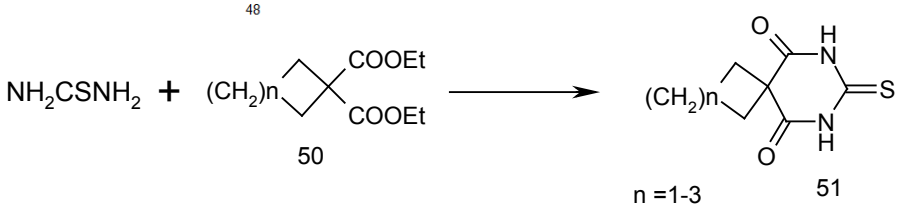
47 48

Reaction of ethyl benzoylacetate and thiourea in ethanolic sodium acetate afforded pyrimidinethione 49[36].



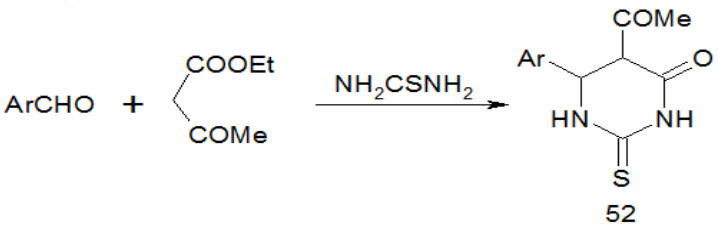
49

Interaction of thiourea with 1,1-cycloalkane-dicarboxylic acid diethyl esters (50) gave spiropyrimidinethione 51[37].



50 n =1-3 51

Ternary condensation of aromatic aldehyde, ethyl acetoacetate and thiourea produced tetrahydropyrimidine-2-thiones 52[38].



52

Ar = 4 -F-C_6H_4; 2,4 -F_2-C_6H_3

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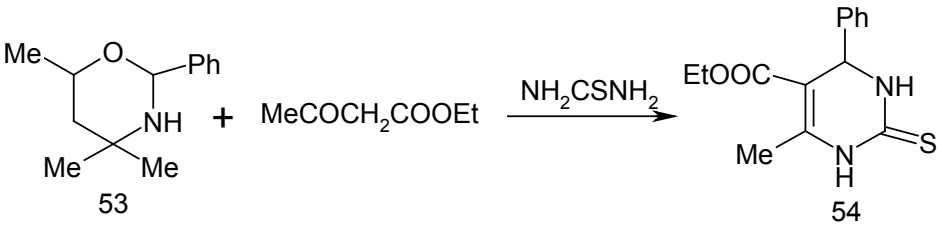
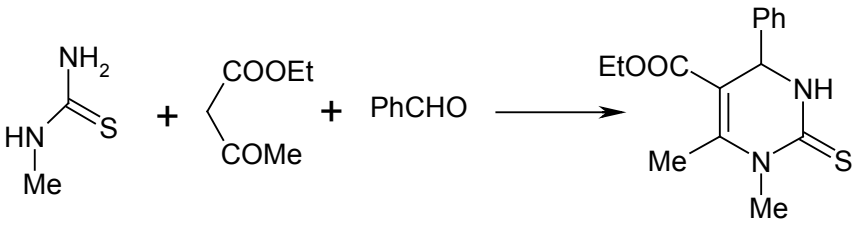
Reaction of oxazinane 53 with a mixture of ethyl acetoacetate and thiourea in the presence of anhydrous acetonitrile and trifluoroacetic acid furnished ethyl 6-methyl-4-phenyl-1,2,3,4-tetrahydropyrimidine-2-thione-5-carboxylate 54[39].



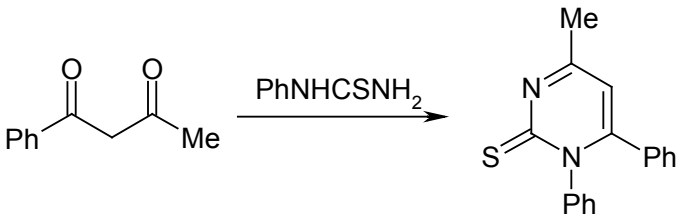
53 54

1,6-Dimethyl-4-phenyl-2-thioxo-3,4-dihydropyrimidine-5-carboxylic acid ethyl ester (55) was synthesized by condensation of ethyl acetoacetate, benzaldehyde and N-methylthiourea[40].



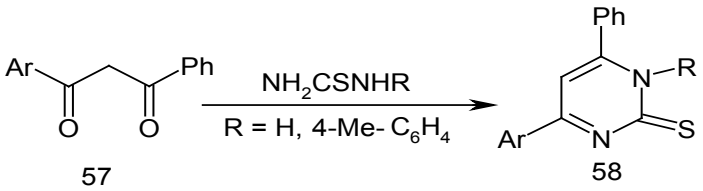
55

Further, 1-phenyl-1,3-butanedione was reacted with *N*-phenylthiourea in the presence of hydrochloric acid to produce 1,6-diphenyl-4-methyl-2-pyrimidinethione (56)[41].

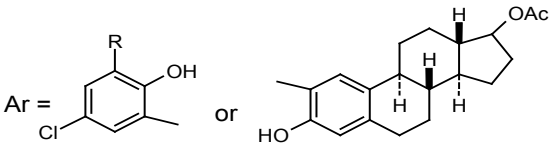


56

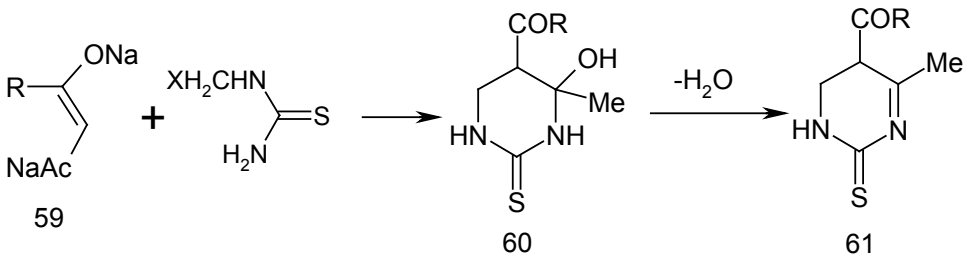
Diaroylmethane derivatives 78 were treated with thiourea to give pyrimidine-2-thione derivatives 79[18,42].



57 58



Heterocyclization of thiourea derivative with the enolate of 1,3-dicarbonyl derivative 59 yielded hydroxyhexahydropyrimidines 60 which underwent dehydration to afford tetrahydropyrimidines 61[43].



59 60 61

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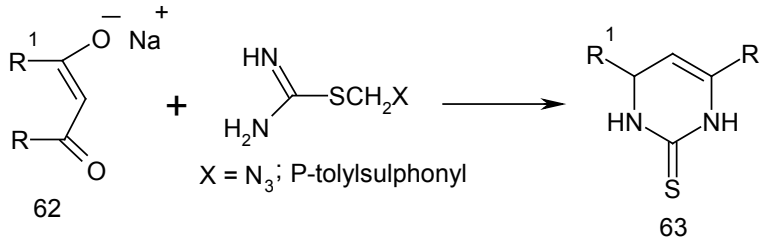
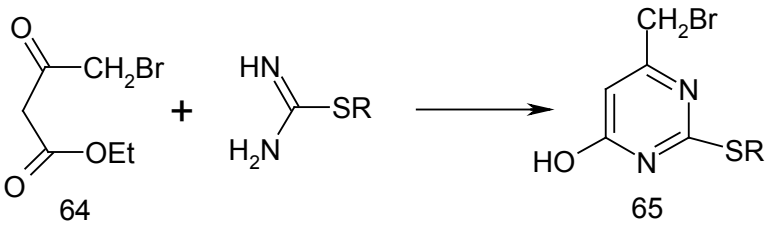
Reaction of 1,3-dicarbonyl compound 62 with (azidomethyl) thiourea or [(*p*-tolylsulphonyl)methyl] thiourea gave pyrimidine derivative 63[44].



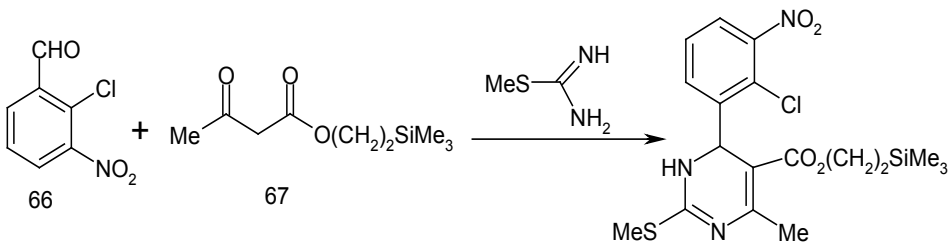
62 63

Condensation of ethyl γ-bromoacetoacetate 64 with S-methyl or S-benzyl isothiourea gave pyrimidine derivatives 65[45].



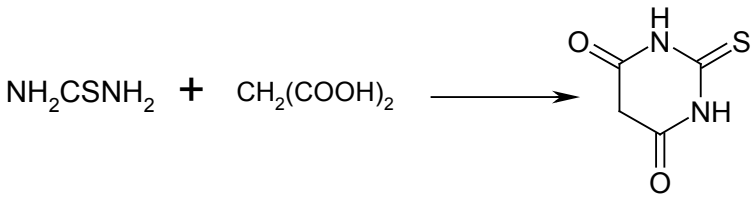
64 65

Condensation of 2-chloro-3-nitrobenzaldehyde 66 with acetoacetate derivative 67 and methyl thiourea yielded 3,4-dihydropyrimidine carboxylate 68[46].



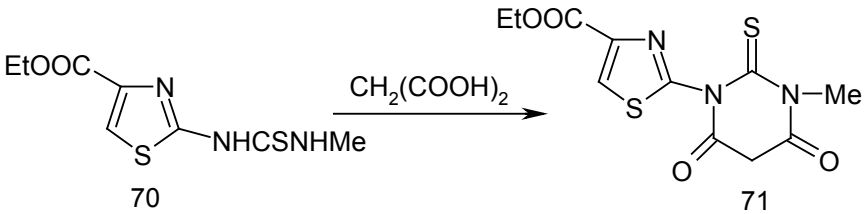
66 67 68

Dioxopyrimidinethione 69[47-49] was obtained by the reaction of thiourea with malonic acid.



69

Treatment of thioazolyl thiourea derivative 70 with malonic acid, in the presence of acetyl chloride, gave pyrimidine derivative 71[50].



70 71

c. *With Acetylenic Compounds*

Cyclocondensation of acetylene derivative 72 with thiourea produce pyrimidinethione 73[51].

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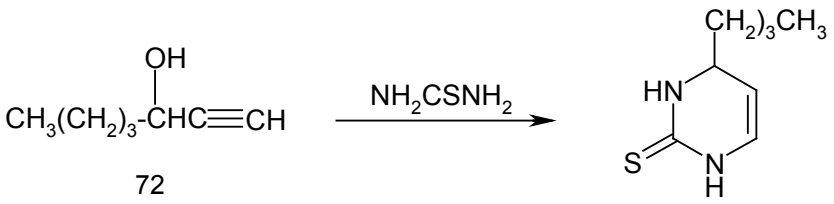
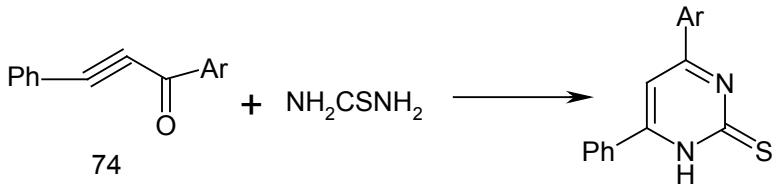


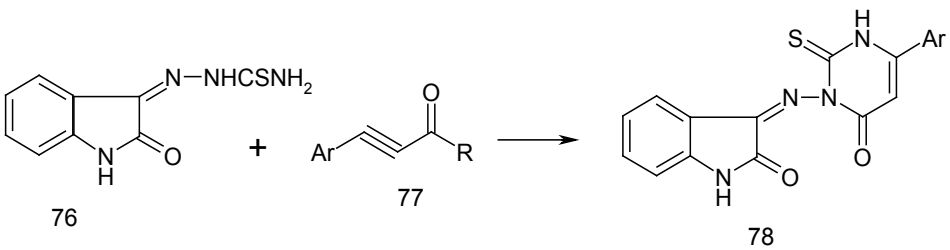
72 73

Reaction of aroylphenylacetylenes 74 with thiourea in the presence of ethanolic sodium ethoxide afforded 4-aryl-6-phenylpyrimidine-2(1H)thiones 75[52].



74 75

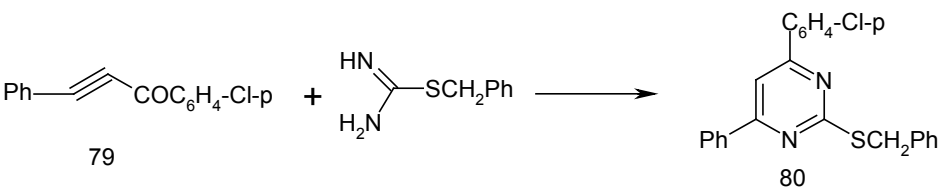
Treatment of isatin-3-thiosemicarbazone (76) with acetylenic ester 77 in the presence of ethanolic sodium ethoxide yielded 3-[2-oxo-2H,3H-benzo(b) pyrrolidine-3-iminyl]-4-oxo-2-thioxo-1,2,4-trihydropyrimidine (78)[53, 54].



76 77 78

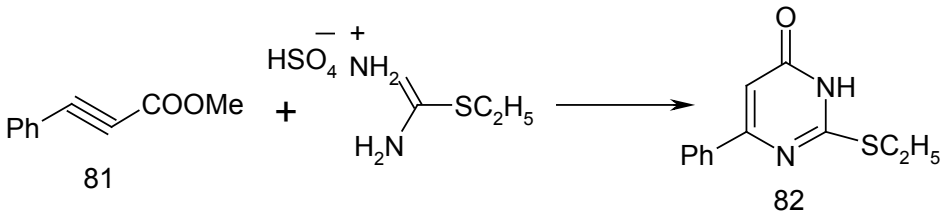
R = OMe, OEt ; Ar = 4-Cl- C_6H_4 , 4-MeO- C_6H_4

S-benzylisothiourea hydrochloride was reacted with p-chlorobenzoylphenylacetylene (79) to give 2-benzylthio-4-(*p*- chlorophenyl)-6-phenylPyrimidine(80)[4].



79 80

When S-ethylisothiourea sulphate was allowed to react with methyl propiolate 81, in the presence of sodium acetate, gave 1,6-dihydro-2-ethylthio-4-phenyl- pyrimidin-6-one (82)[55].



81 82

d. *With Arylidenes*

4-Amino-6-aryl-5-cyanopyrimidine-2(3H)-thiones 84[56,57] were obtained by the reaction of β-arylidene malononitrile 83 with thiourea in the presence of anhydrous potassium carbonate.

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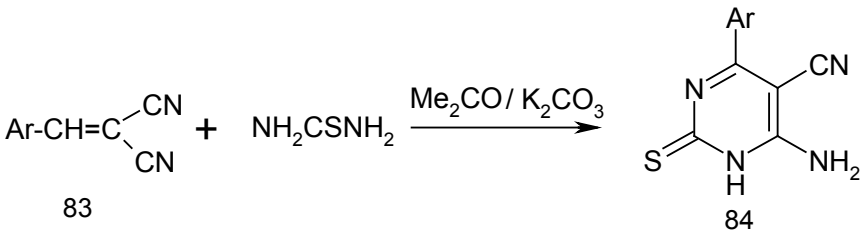
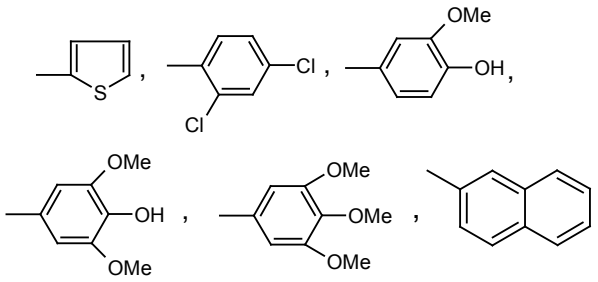
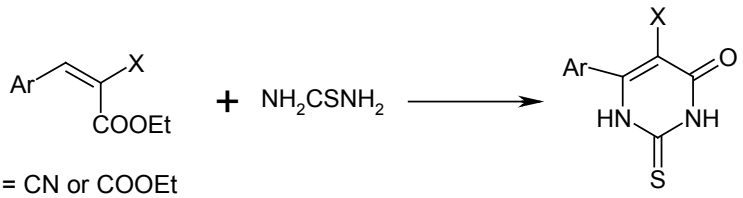


83 84

Ar =



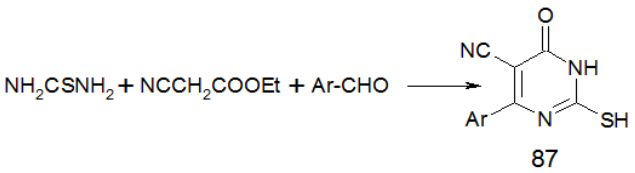
4-Oxo-2-thioxopyrimidine derivatives 86 were obtained by the reaction of arylidines 85[58,59] with thiourea.



X = CN or COOEt

85 86

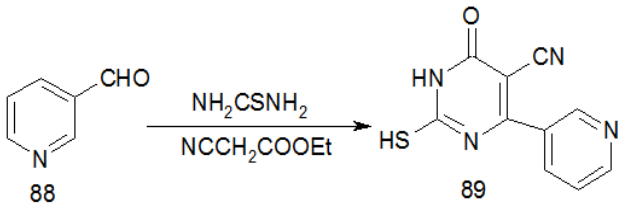
2-Mercapto-4-aryl-5-cyanopyrimidin-6(1H) ones (87)[60,61] were obtained by reaction of ethyl cyanoacetate, thiourea with aromatic aldehydes in ethanolic sodium ethoxide.



87

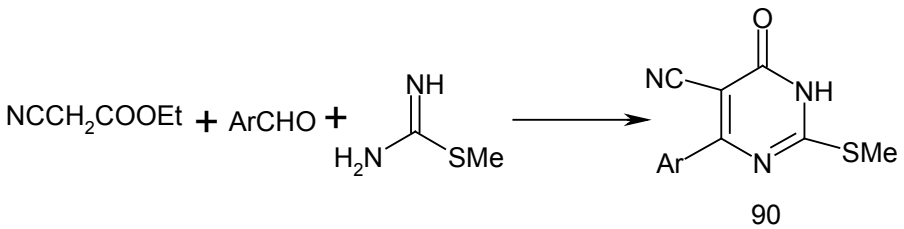
Ar = 2, 4-$Cl_2C_6H_3$, 4-$(Me)_2N$-C_6H_4

5-Cyano-2-mercapto-6(1H)pyrimidinone derivative 89[62] was obtained by reaction of 3-pyridine carboxyaldehyde (88), thiourea and ethyl cyanoacatate.



88 89

Reaction of ethyl cyanoacetate with aromatic aldehyde and methyl thiourea gave the corresponding 4-aryl-5-cyano-2-methylthio-6-oxopyrimidine derivative 90[63].



90

e. *With Ethoxymethylene Compounds*

Reaction of ethoxymethylene derivatives 91 with thiourea derivatives gave pyrimidine derivatives 92, 93, 94, 95 and 96 respectively[64].

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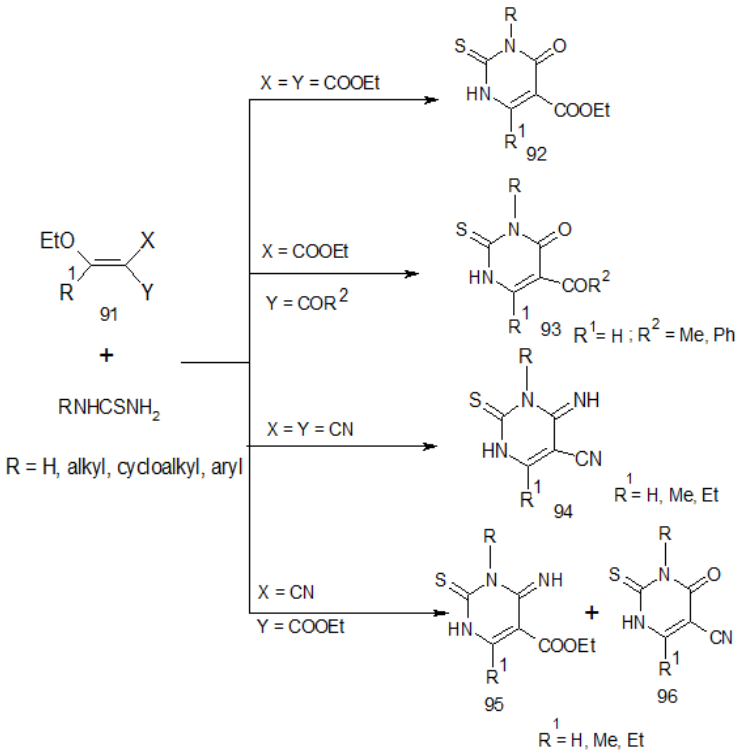
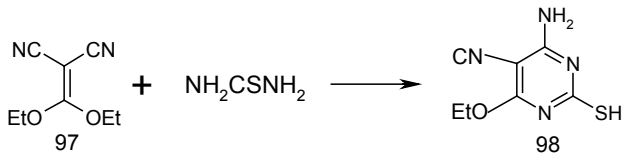
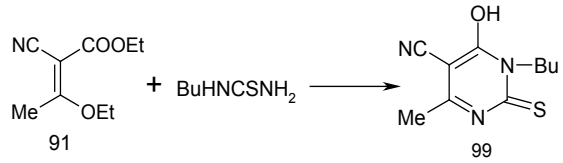


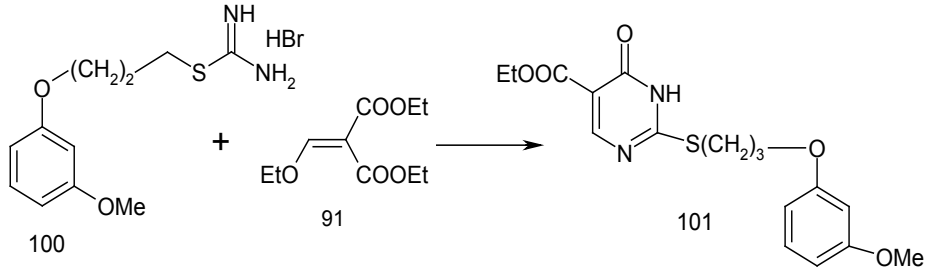
Reaction of diethoxymethylenemalononitrile (97) with thiourea afforded pyrimidine derivative 98[65,66].



Butyl-5-cyano-6-hydroxy-4-methyl-2-thiopyrimidine (99)[67] was synthesized by the reaction of ethyl α-ethoxyethylidinecyanoacetate (91) with *N*-butyl-thiourea.

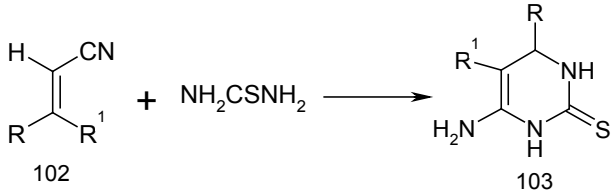


Treatment of S-[3-(methoxyphenoxy)propyl] isothiourea hydrobromide (100) with ethoxymethylidinemalonate (91) gave pyrimidine derivatives 101[68].

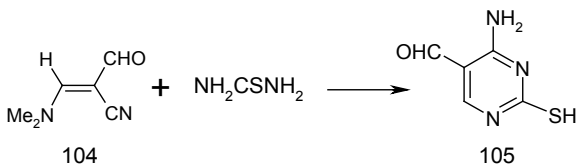


f. *With Acrylonitrile Derivatives*

Reaction of cyanoolefine 102 with thiourea gave the aminopyrimidine derivatives 103[69-71].



Interaction of acrylonitrile derivative 104 with thiourea yielded thiopyrimidine 105[72].



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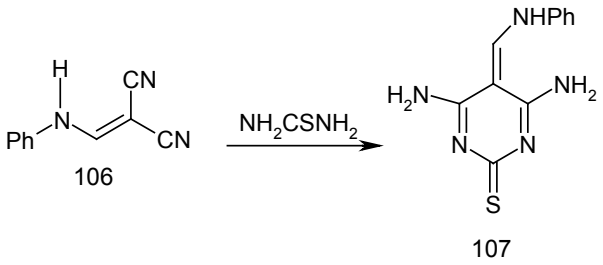
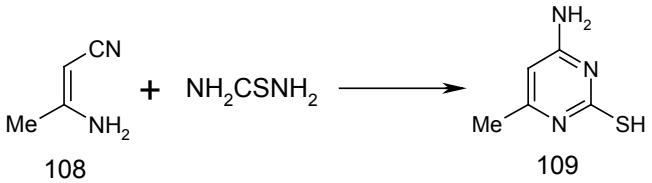
Pyrimidine-2-thione derivatives 107 was prepared via interaction between β-enaminonitrile 106 with thiourea[73,74].

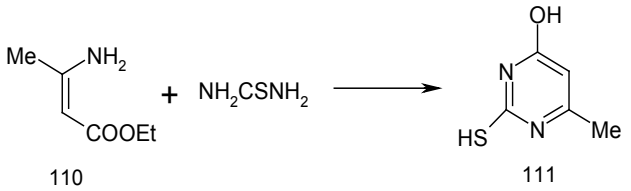


g. *With Enamine derivatives*

Reaction of 2-amino-1-cyanopropene (108) with thiourea gave thiopyrimidine 109[65].

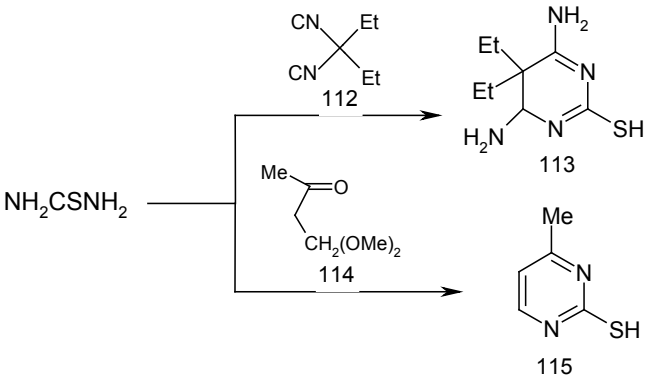


Also, interaction of 3-aminocrotonate (110) with thiourea gave thioxo-pyrimidine 111[75].

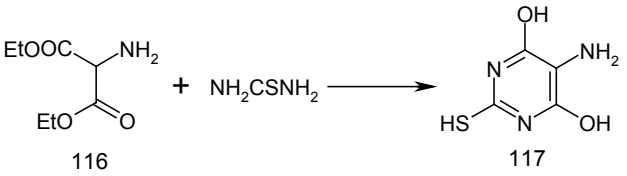


h. *With Different Compounds*

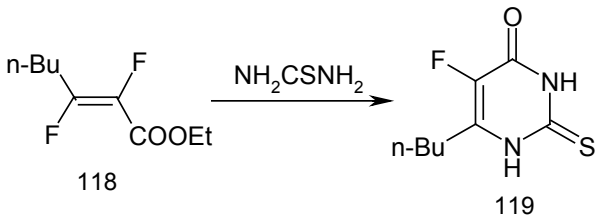
Reaction of thiourea with diethylmalononitrile (112)[69]and ketone derivative 114 afforded pyrimidine derivative 113 and 115 respectively.



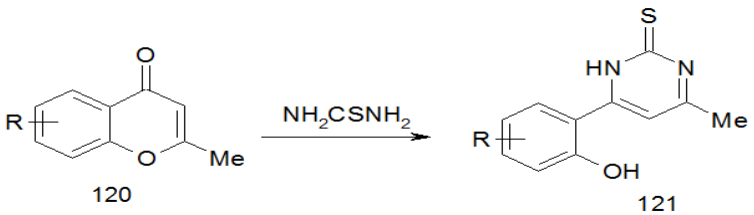
The condensation of thiourea with diethyl 2-aminomalonate 116 afforded 5-amino-2-mercapto-pyrimidine-4,6-diol (117)[76].



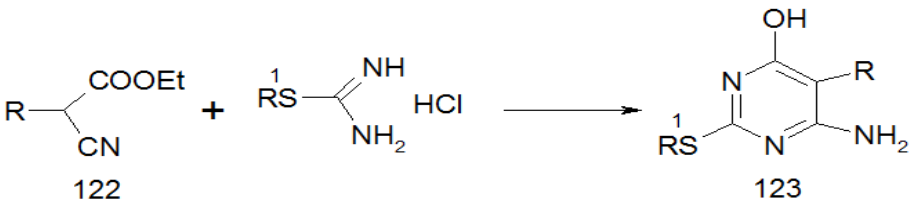
Reaction of ethyl 3-*n*-butyl-*trans*-2,3-difluoro-2-acrylate (118) with thiourea afforded the corresponding 6-*n*-butyl-5-fluoro-2-thiouracil (119)[77].



Condensation of 2-methylchromones 120 with thiourea afforded 4-methyl-6-substituted-phenyl-(1H) pyrimidinethiones 121[78].



Reaction of ethyl cyanoacetate derivatives 122 with S-alkyl thiourea derivatives yielded pyrimidine derivatives 123[79].



a, R = NHCOMe; b, R = $NHNH_2Ph$

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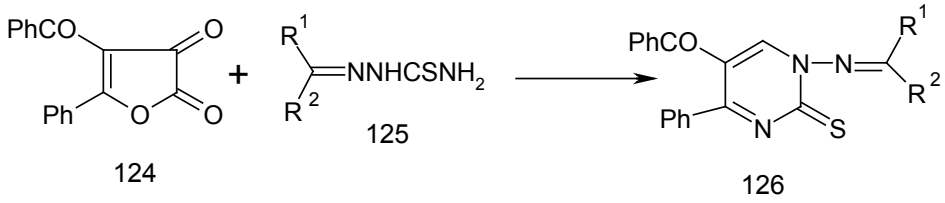
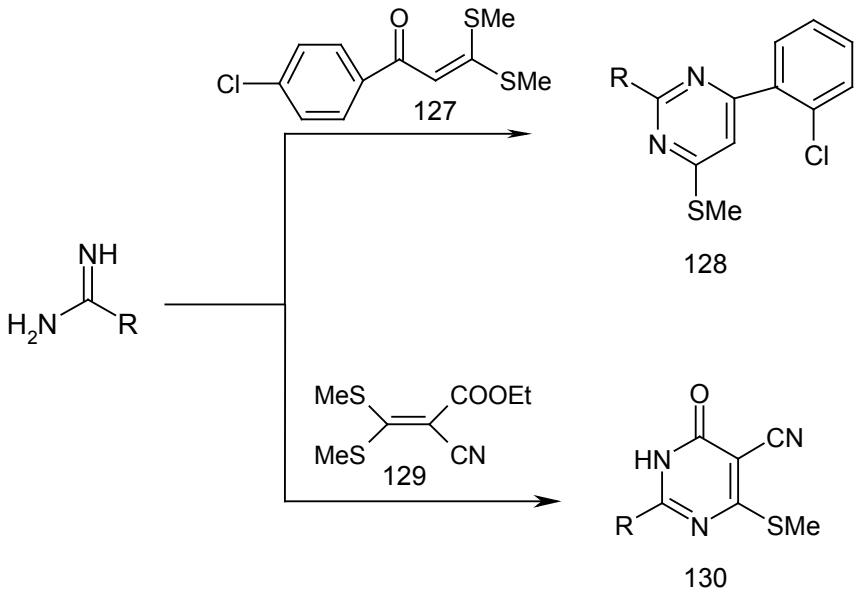
Furan-2,3-dione 124 and thiosemicarbazones 125 combined with loss of carbon dioxide and water to yield 1-methyleneaminopyrimidine-2-thione derivative 126[80].

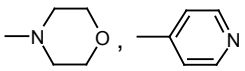


124 125 126

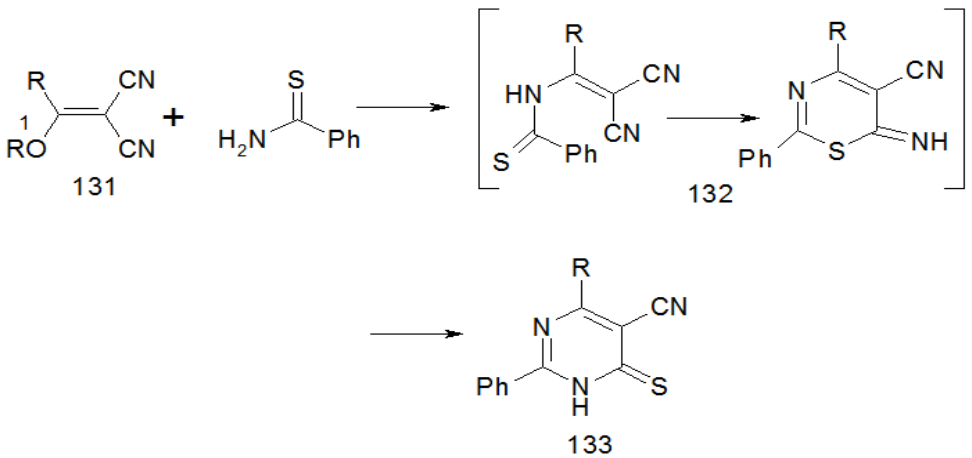
ii. *From Guanidine Derivatives*

Guanidine derivatives are considered as basic unit for the preparation of 4-thiopyrimidines. Thus, reaction of guanidine derivatives with benzoylethylene derivative 127 and acrylate derivative 129 afforded pyrimidine derivatives 128 and 130[81,82] respectively.



R = CF_3, C_6H_5 , 

Treatment of 3-alkoxy-3-aryl(or alkyl)-2-cyanoacrylonitriles (131) with thiobenzamide and sodium isopropoxide in 2-propanol yielded 6-thioxo-3,4-dihydropyrimidine derivatives 133 through the formation of 3-aryl(or alkyl)-2-cyano-3-thiobenzamide cyanoacrylonitriles (132)[83].



131 132 133

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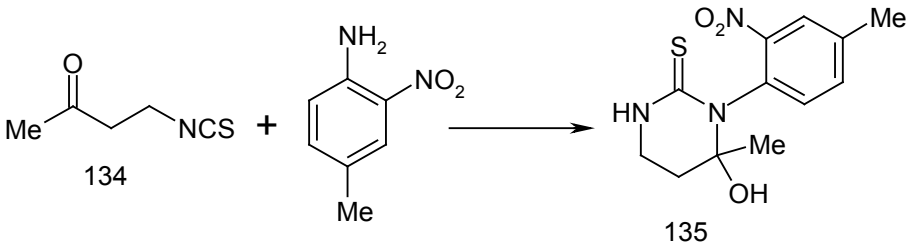
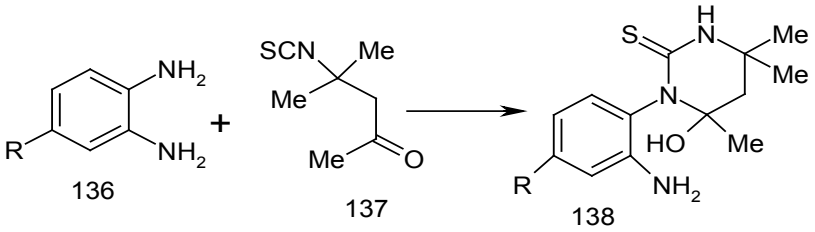
iii. *From Isothiocyanate Derivatives*

Isothiocyanate derivatives are used for the synthesis of 2- and 4-pyrimidinethiones. Thus, 1-(2-nitro-4-methylphenyl)-6-hydroxy-6-methyl-1,4,5,6-tetrahydropyrimidine-2(3H)thione (135)[84] was prepared by the reaction of 4-isothiocyanatobutan-2-one (134) with 4-methyl-2-nitroaniline.

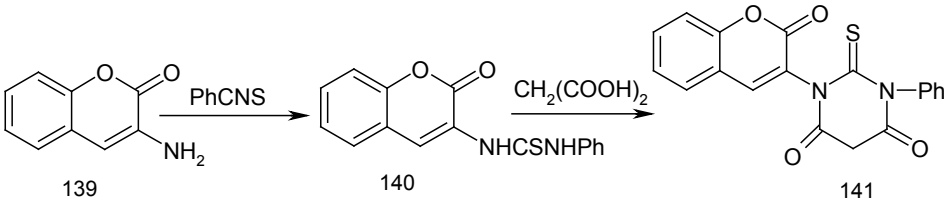


Phenylenediamines 136 was allowed to react with 4-isothiocyanato-4-methyl-2-pentanone (137) at room temperature to give aryltetrahydropyrimidine-2-thiones 138[85].

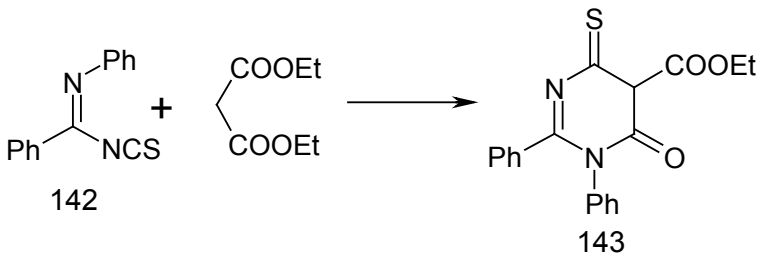


R = H, Me, OMe

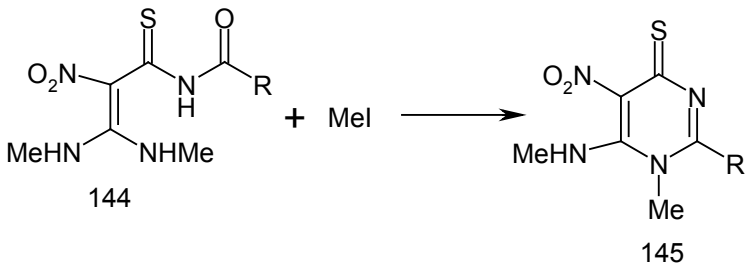
Treatment of 3-aminocoumarin (139) with phenyl isothiocyanate in ethanol afforded coumarinylphenylthiourea 140 which underwent cyclocondensation with malonic acid in acetyl chloride to give coumarnylphenylthiobarbituric acid 141[86].



When isothiocyanate derivative 142 was allowed to react with diethyl malonate gave pyrimidinethione 143[87].



2-Aryl-1-methyl-5-nitro-6-methylaminopyrimidine-4-thiones (145)[88] were synthesized by the reaction of nitrokenaminal acylisocyanate C-adducts 144 with methyl iodide.



R = C_6H_5 ; 4-ClC_6H_4 ; 4-MeO-C_6H_3-CH=CH- ; C_6H_4-CH=CH-

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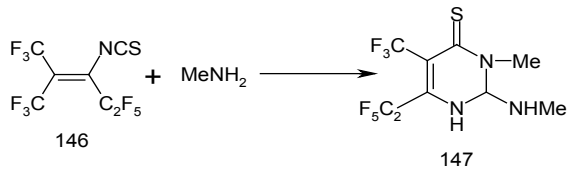
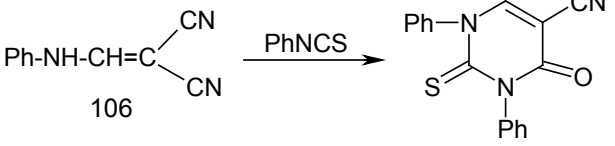
Treatment of perfluoro-2-methylpent-2-en-3-yl isothiocyanate (146) with methylamine afforded 3-methyl-2-methyl-amino-6-pentafluroethyl-5-trifluorome-thyl-3H-pyrimidine-4-thione (147)89.



146 147

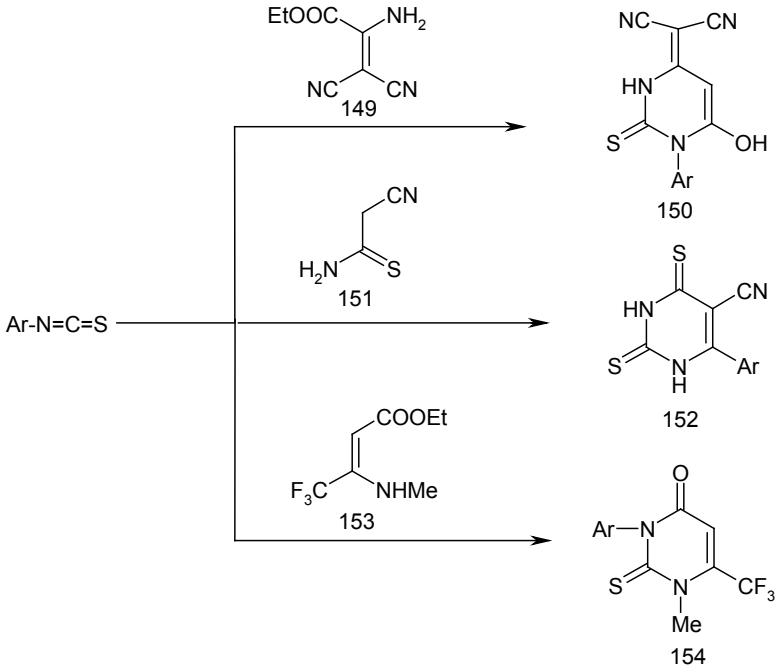
b) Synthesis from C-C-C-N and C-N fragments

Pyrimidinethiones synthesized by this manner may be contain thioxo group at 2 or 4 position. Thus, treatment of β-enaminonitrile 106 with phenyl isothiocyanate in ethanol containing sodium hydroxide furnished 5-cyano-1,3-diphenyl-4-oxo-pyrimidine-2-thione (148)[90].

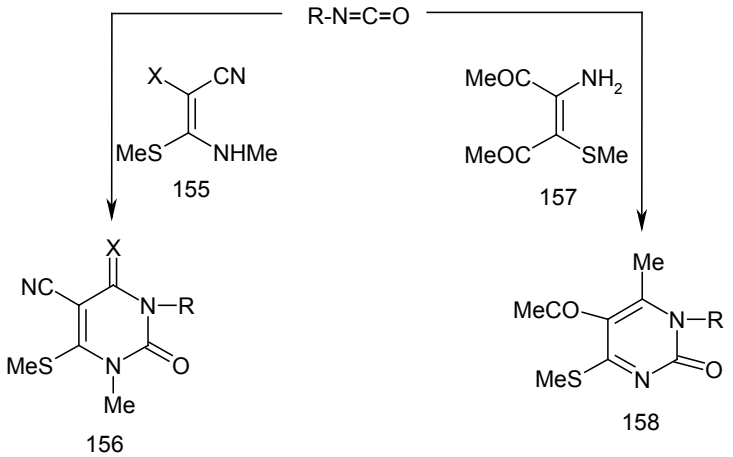


106 148

On the other hand, phenylisothiocyante derivatives was reacted with ethyl enaminonitrile 149[91], cyanothioacetamide 151[92] and methylamino acrylate 153 to give pyrimidinethio- ne derivatives 150, 152 and 154, respectively.



Reaction of isocyanate derivative with ketene S,N-acetals 155[93] and amino ethylene derivative 157[94] yielded pyrimidine derivatives 156 and 158, respectively.



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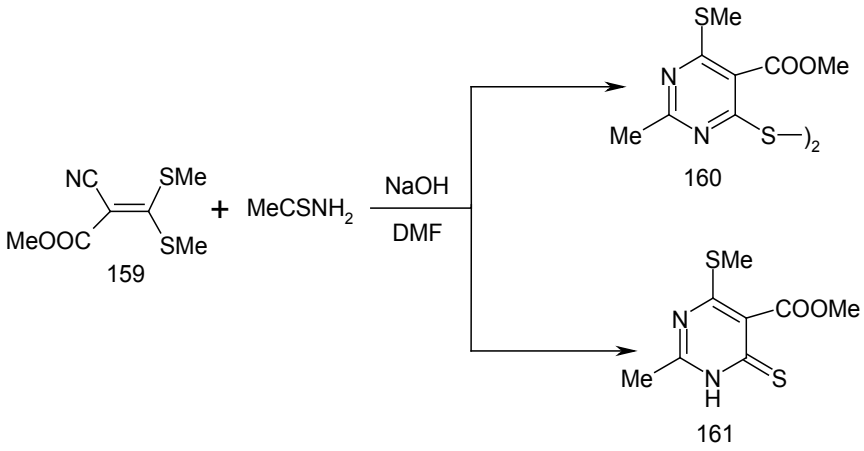
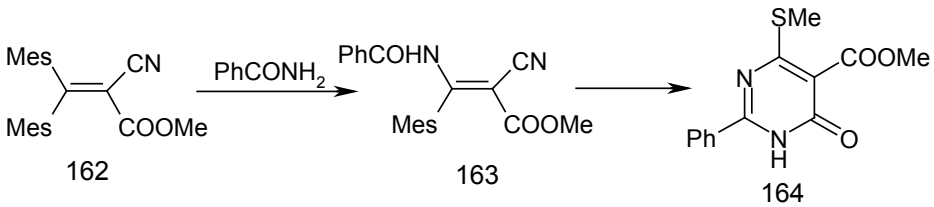
Treatment of methyl-2-cyano-3,3-bis[methylthio]propenate (159) and thioacetamide in NaOH/DMF afforded bis [5-(methoxycarbonyl)-2-methyl-6-methylthio-4-pyrimidine] disulphide (160) and 5-(methoxycarbonyl))-2-methyl-4-(methyllthio)-1(H)-pyri-midinethione 161[95].

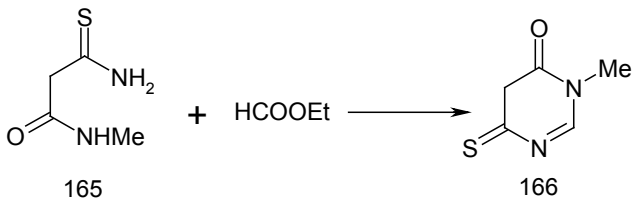


Reaction of methyl 2-cyano-3,3-bis(methylthio) acrylate (162) with benzamide in the presence of sodium hydride gave methyl 3-benzoylamino-2-cyano-3-(methylthio)acrylate (163), which readily converted to methyl 3,4-dihydro-6-(methylthio)-4-oxo-2-phenyl-pyrimidine-5-carboxylate (164)[96].

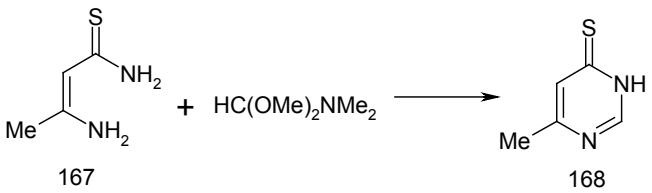


c) *Synthesis from N-C-C-C-N and C-fragments*

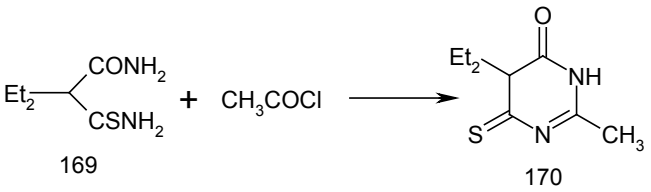
3-Amino-N-methyl-3-thioxopropanamide (165) allowed to react with ethyl formate to yield 3-methyl-6-thioxo-5,6-dihydropyrimidin-4-one (166)[97].



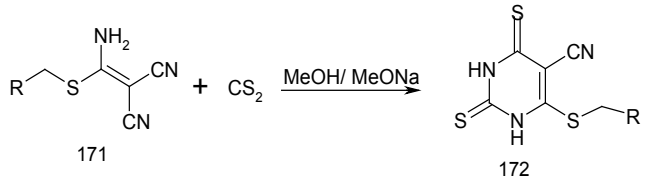
Cyclization of β-aminothiocrotamide (167) with dimethyl formamide dimethyl acetal afforded 6-methyl-4(3H)-pyrimidinethione (168)[98].



Treatment of 2-ethyl-2-thiocarbomylbutyramide (169) with acetyl chloride yielded pyrimidinethione 170[99].



Cyclocondensation of enaminonitrile 171 with carbon disulfide gave pyrimidinethione derivatives 172[100].



d) Synthesis from C-C-N and C-N-C fragments:

Reaction of acetylacetone with ammonia gave α,β-unsaturated aminoketone 173. When an equimolarcular amounts of 173 and aroylisothiocyanate were heated in dioxan afforded 4-mercapto-6-methyl-2-aryl-5-acetylpyrimidines 174[101-104].

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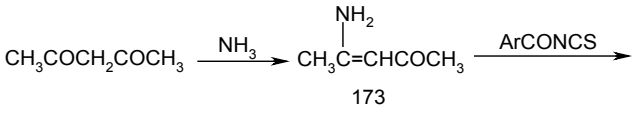
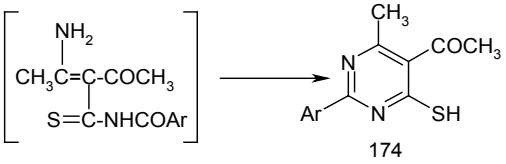
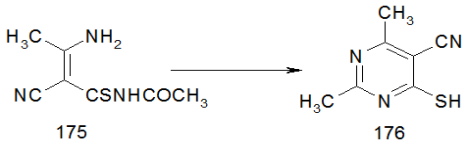


173



174

The adduct of β-aminocrotononitrile and acetylisothiocyanate 175 underwent base catalyzed cyclization to yield pyrimidine derivative 176[105,106].



175 176

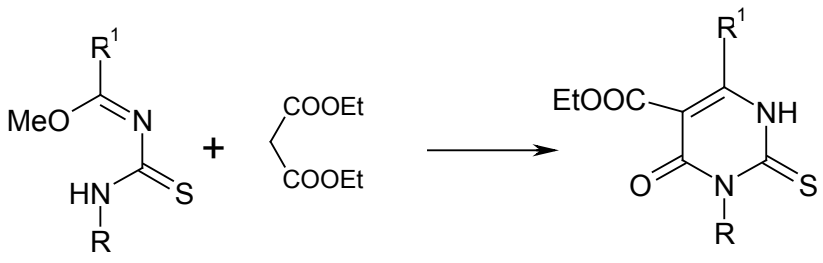
Reaction of 177 with thiocyanate derivatives in acetone gave pyrimidinethiones 178[107].

177 178

R = Ph, Me

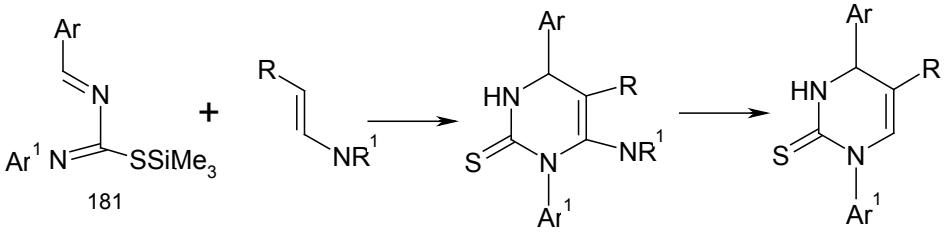
e) Synthesis from N-C-N-C and C-C fragments

Ethyl pyrimidine-5-carboxylate 180 was prepared by the reaction of 179 with diethyl malonate in the presence of ethanolic sodium ethoxide[108].



179 180

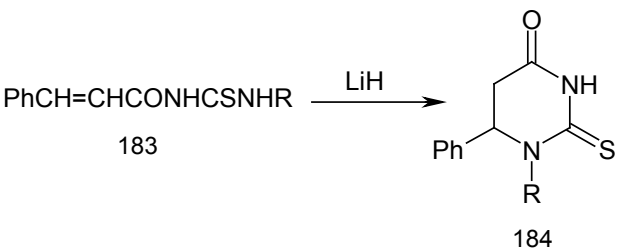
Reversed polarization in 2-trimethylsilylthio-1,3-diene 181 allows percyclic reaction with acyclic enamines to give pyrimidinethione 182[109].



181 182

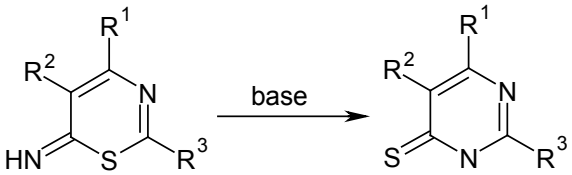
f) Miscellaneous Methods

cyclization of n-(4-substitutedphenyl)-n\-3-phenylprop enoylthiourea (183) with lithium hydride yielded thiouracil 184[110].



183 184

6-imino-6*H*-1,3-thiazines 185 underwent Dimroth rearrangement when treated with a base to form thioxopyrimidines 186[111].



185 186

III. Applications of Pyrimidinethiones

One important class of pyrimidine is 2-thiopyrimidine (2-TP) and its derivatives, which are also well known as 2-mercaptopyrimidine compounds. In 2-TP ring sulfur atom serves as an interesting replacement for the existing oxygen atom bonded to C-2 in uridine base. Studies evaluated primary activity of 2-TP

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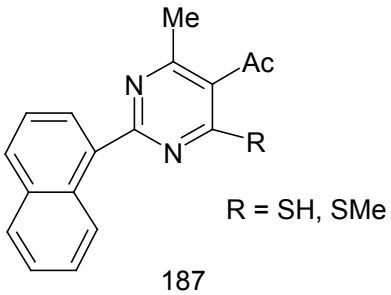
derivatives against Mycobacterium tuberculosis (Mtb). 2-TPs also serve as important precursors for asymmetric synthesis of allylic sulfides/sulfonates.

Recently, international applications revealed that, 2-TP derivatives possess potent activity against inflammation and immune disorders. Thus, search for novel, potent and selective 2-TP derivatives is desirable in order to substitute drugs having major side effects such as peptic-ulcer formation and gastro-intestinal damage. Various mono-, di-, tri- and tetra-cyclic, di/tetrahydro-2-TP derivatives have been synthesized and evaluated for anti-inflammatory and analgesic activity (both in *vivo* and in *vitro*)[1].

The widespread use of thiols as drugs, cosmetics, corrosion inhibitors, agents in photographic and vulcanization processes and chemical analysis of varied metal ions as well as different bio-oriented compounds[112].

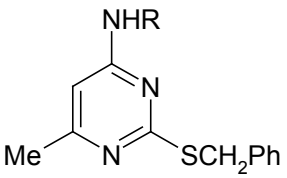
Pyrimidine derivatives 187 exhibited bactericidal activity in vitro against *Salmonella spp*., *St. albus*, and *B. subtilis*[113].



R = SH, SMe

187

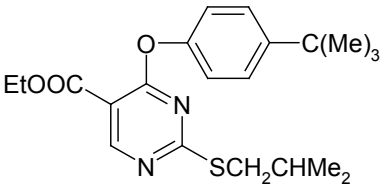
2-Benzylthio-4-substitutedamino-6-methylpyrimidines 188 were screened against selected bacteria which showed a moderate activity against *Bacillus subtilis* and *Neisseria*[114].



R = C_6H_5, 4 -Me-C_6H_5, 4 -Br-C_6H_4

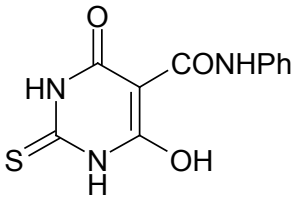
188

Phenoxypyrimidinecarboxylate 189 is a better herbicide against *Podosphaera lucotricha* on apples[115].



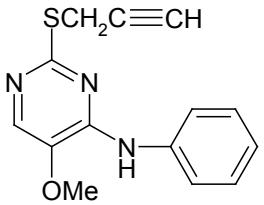
189

Pyrimidinecarboxanilide 190 is effective neoplasm inhibitors in vivo tests in mice[116].



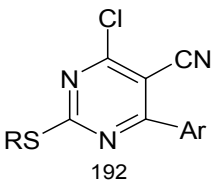
190

4-Anilinopyrimidine 191 at 60 ppm gave complete control of *Pseudo- cercosporella herbotrichoides* on wheat[117].



191

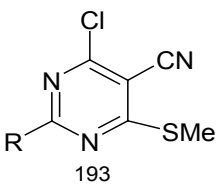
4-Chloropyrimidines 192 and 193 were submitted for preliminary evaluation of their in vitro activity against *M. tuberculosis*, human isolates of *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *S. faecalis*, *Staphylococcus aureus*, *E. coli* and antimycotic activity against *Candida albicans*, *Cryptococcus neoformans*, *Sporothrix schenckii*, *Aspergillus fumigatus* and *T. mentagrophytes*[118].



192

R = Me, Et, n-Pr, 4-Cl-$C_6H_4CH_2$

Ar = 2-thienyl, 2-furyl, 2,4- $F_2C_6H_3$, 3- FC_6H_4



193

R = SMe, S-$CH_2C_6H_5$

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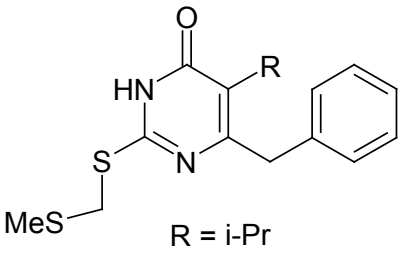
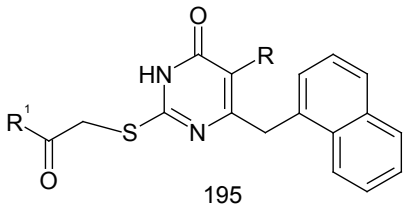
5-Isopropyl-2-[(methylthiomethyl)thio]-6-(benzyl) -pyrimidin-4-(1H)-one (194) elicited potent anti-HIV activity with an IC_{50} value less than 1 nM for inhibition of HIV replication[119].



194

6-(1-Naphthylmethyl) pyrimidin-4(3H)-ones 195 were evaluated for cytotoxicity and anti-HIV activity in MT-4 cells using the MTT method, which exhibited extremely potent inhibitory activity against HIV replication[120].



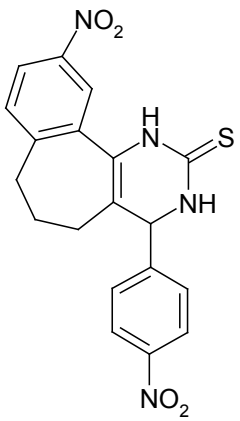
195

R = Me, Et, i-Pr

R^1 = Me, MeO, OEt, C_6H_5, 4- Cl- C_6H_4 ,

4- F- C_6H_4 , 4- Me- C_6H_4 , 4- MeO- C_6H_4

Antitumor activity screening for 10-nitro-4-(p-nitrophenyl)-1,3,4,5,6,7-hexahydro-2H-benzo[6,7] cyclo-hepta[1,2-d]-pyrimidine-2-thione (196) utilizing 59 different human tumor cell lines, representing leukemia, melanoma, and cancers of the lung, colon, brain, ovary, breast, prostate as well as kidney, was carried out. From the in vitro observed data it has been noticed that, compound 196 seem to be active against all the tested cell lines[121].



196

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