CHEMISTRY OF PYRIMIDINE

SYNITHESIS OF PYRIMIDINE DERIVATIVES

Pyrimidine derivatives were generally prepared by four types of ring synthesis (I, II, III and IV) according to the nature of compounds which combine together to form the pyrimidine nucleus[1].

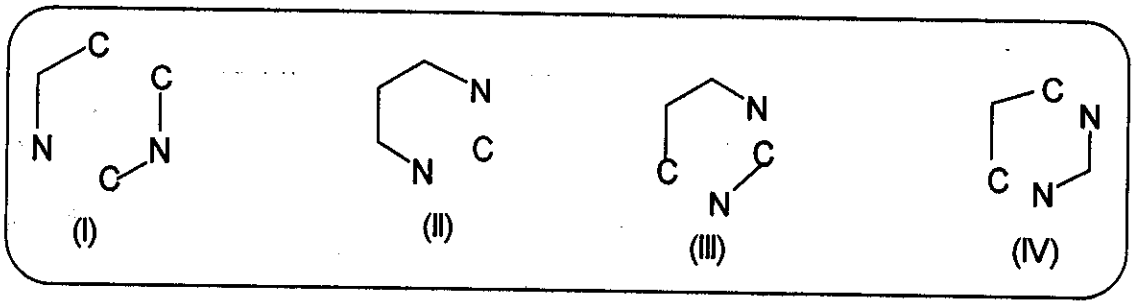
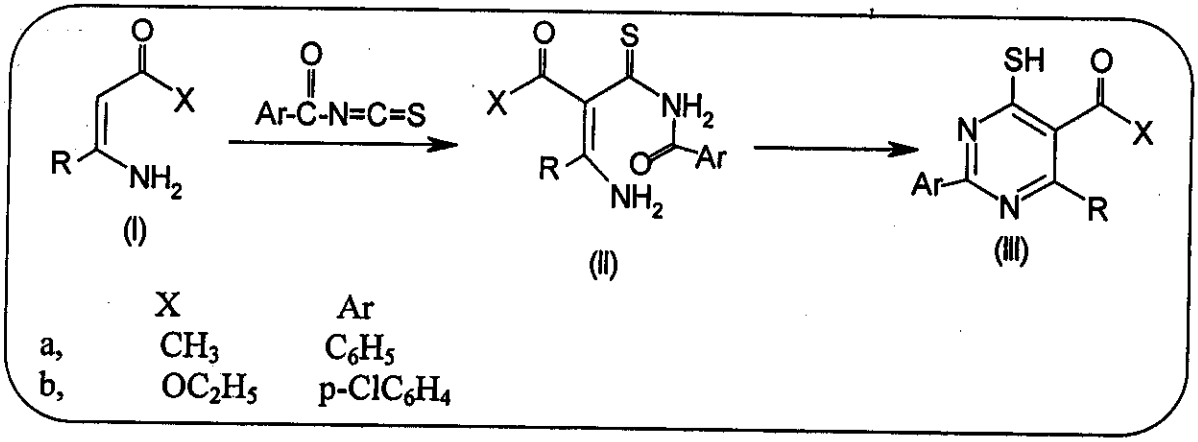


Fig (1): Some possible condensation to form the pyrimidine ring

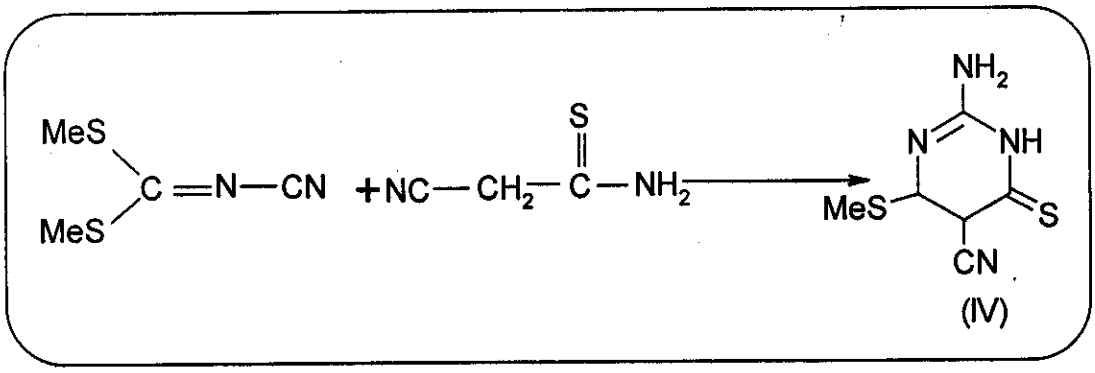
1. Type (I): synthesis of pyrimidine ring from N-C-C and C-N-C fragments:

Addition of enaminoketones or enaminoesters (I) to benzoyl isothiocyanates or alkoxycarbonyl isothiocyanates gave the intermediate (II) which cyclized in base medium to give pyrimidine thione(III) [2,3]



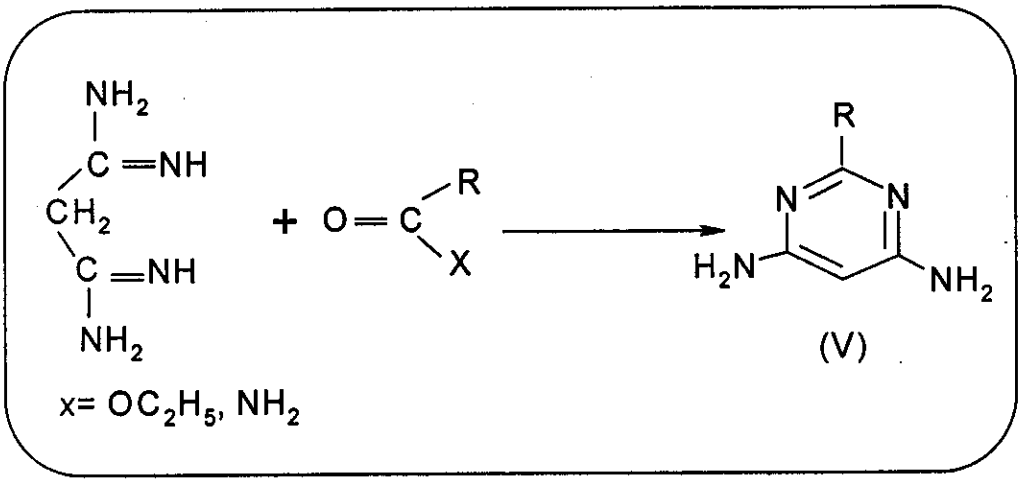
	X	Ar
a,	CH_3	C_6H_5
b,	OC_2H_5	p-ClC_6H_4

Cycloaddition of chalcon [$(MeS)_2C{:}N\text{-}CN$] with $NC\text{-}CH_2\text{-}CS\text{-}NH_2$ in ethanol containing sodium ethoxide yielded pyrimidine thione (IV) after acidification [4].

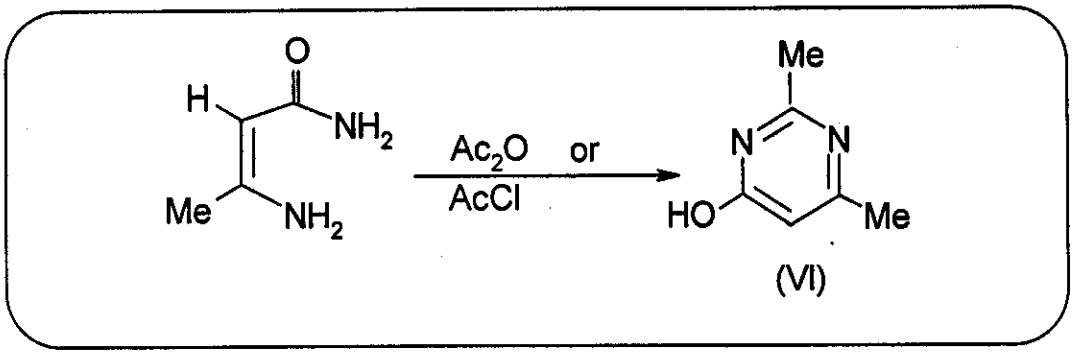


2. Type (II): Synthesis of pyrimidine ring from N-C-C-C-N and C- fragments:

Condensation of malonodiamidine and esters or amide as one carbon fragment yielded 4,6-diaminopyrimidine (V) [5].



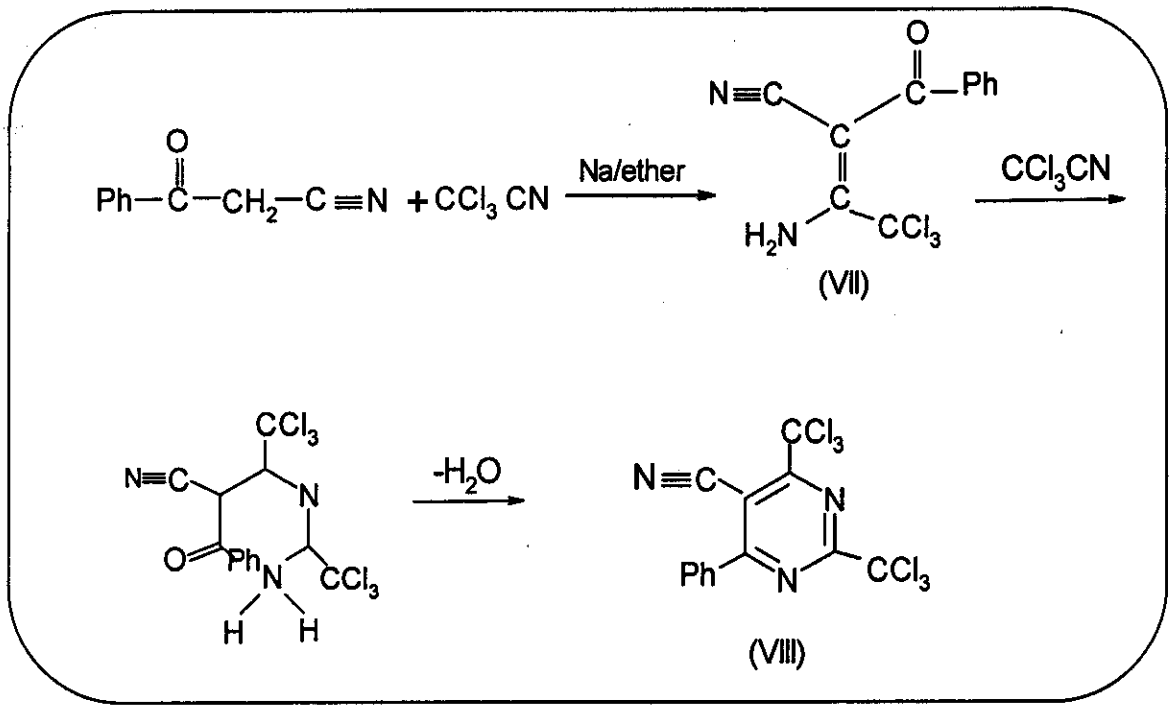
Reaction of β-aminocrotonamide with acetylating reagents (acetic anhydride or acetylchloride) gave β-acetamido-croton-amide which on treatment with base, cyclized to gave 2,6-dimethyl-4-hydroxypyrimidine(VI) [6].



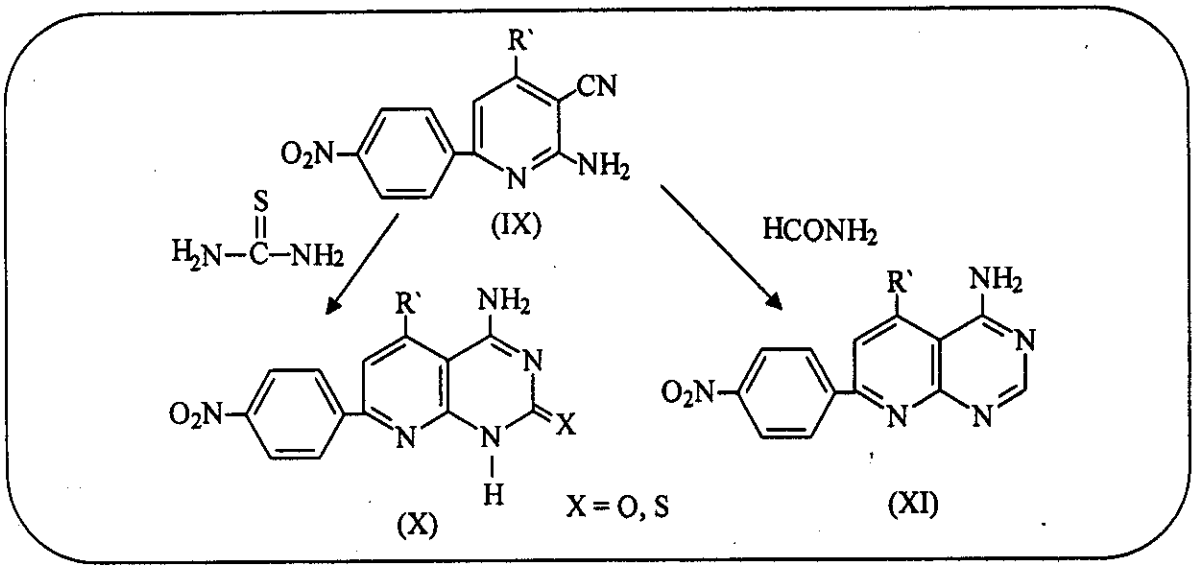
(VI)

3. Type(III): Synthesis of Pyrimidine ring from C-C-C-N and C-N fragments:

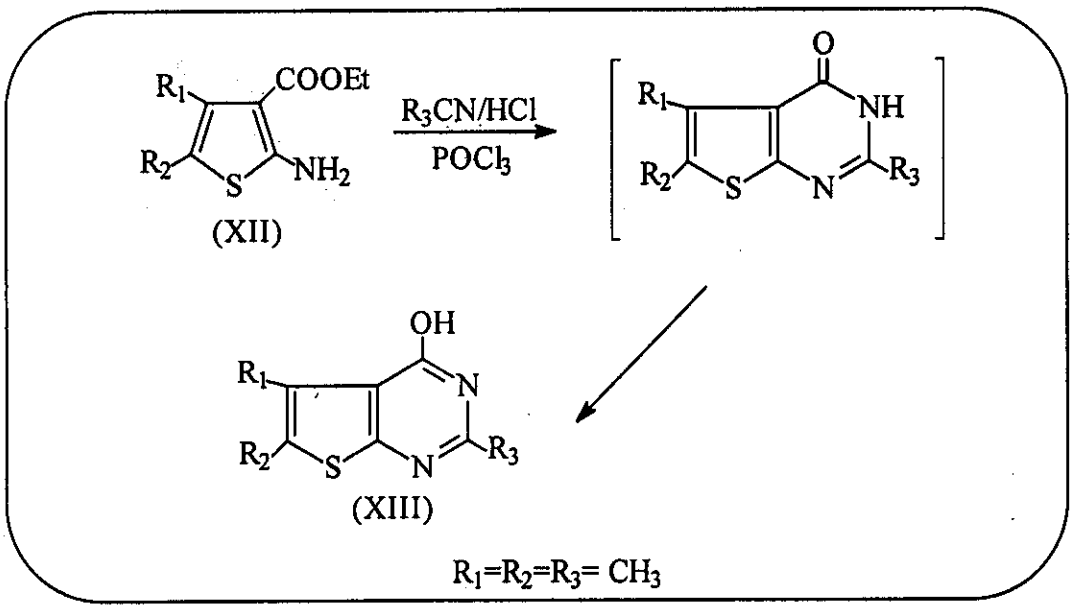
Reaction of benzoylacetonitrile with trichloroacetonitrile gave acrylonitrile derivatives (VII) which reacted with another molecule of trichloroacetonitrile to afforded 2,4-bis-trichloromethyl-5-cyano-6-phenylpyrimidine (VIII) [7].



Condensation of 2-amino-3-cyano-4,6-disubstituted pyridine (IX) (R = 4-ClC_6H_4, 4-$MeOC_6H_4$) with thiourea and formamide gave pyrido-(2,3-d) pyrimidine derivatives [8] (X), and (XI) respectively.



Reaction of 2-amino-3-carbethoxy-4,5-disubstituted thiophenes (XII) with nitriles gave the intermediates 2-subestetuted 4-hydroxy thieno [2,3-d] pyrimidines, subsequent heating under reflux in phosphours oxychloride gave thienopyrimidine (XIII) [9].



4. Type (IV): Synthesis of pyrimidine ring from C-C-C and N-C-N fragments;

It is included the condensation of an amidines, urea, thiourea, guanidine and their derivatives with β-diketones or chalcon Acetylacetone condense with thiourea in acid medium and/or