Chapter 7

Synthesis of 1,2,3-triazolo substituted analogues of the face ‘d’ pyrimido condensed 1,4-diazepines of medicinal interest.
Abstract

This chapter describe the synthesis of compound 7.106 and 7.110 using the domino reaction proceeding through the reaction of 7.098 which was subsequently converted to 7.101 – 7.110. In another set of reaction 7.104 was converted to 7.111 – 7.114 respectively. The structure of compounds were established on the basis of elemental analysis, IR, $^1$H NMR, $^{13}$C NMR and MS spectral data
7.1 General introduction

The importance of the incorporation of biologically active pharmacophores, for instance 1,4-diazepino-1,2,3-triazolo fused benzo, furano, thiopheno, pyrazolo and pyridino scaffolds have already been discussed in the previous chapters. This chapter demonstrates, the importance of the incorporation of the 1,4-diazepine 1,2,3-triazolo in a six membered ring viz; pyrimidine and its derivatives, and describes the strategy adopted to incorporate some bioactive pharmacophores like pyrazole, isoxazole, pyrimidine, benzodiazepine, benzothiazepine, benzoxazepine through the corresponding oxoketenedithioacetal derivatives of pyrimidino-1,4-diazepine nucleus.

![Pyrimidine & 1,4-pyrimidinodiazepine](image)

**Fig. 7.1: Pyrimidine & 1,4-pyrimidinodiazepine**

Pyrimidine is the foundation of nucleic acids, DNA and RNA\(^1\). In view of this the study of pyrimidines is of immense significance. Pyrimidines play a part in many biological processes since this ring system is present in several vitamins, coenzymes, nucleic acid etc. Synthetic members of these groups are also important as chemotherapeutic agents. The pyrimidine nucleus also occurs in a considerable numbers of natural products of vital importance to living organisms\(^3\).

The biological properties of pyrimidine nucleus has prompted us to focus research on the synthesis and study of biological properties of newer series of pyrimidine incorporated derivatives formed by the fusion of 1,4-diazepino-1,2,3-triazolo annulated nucleus. Fused pyrimidines (eg.: purines, pyrrolopyrimidine, pyrimidopyrimidine, pteridine) are found in a variety of natural products, agrochemical and veterinary products on account of this pyrimidine derivatives continue to attract interest due to their wide variety of interesting biological and pharmacological activities.
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7.1.1 Importance of pyrimidine

Pyrimidine is the most important member of all the diazines as this ring system occurs widely in living organism. Purines, uric acid, alloxan, barbituric acid and a mixture of anti-malarial and anti-bacterial also contain the pyrimidine ring. It is a basic nucleus in DNA and RNA, it has been found to be associated with diverse biological activities. Pyrimidine nucleus has been the subject of substantial attention by synthetic and medicinal chemist because of the presence of fused heterocyclic rings in many biological systems.

7.1.2 Biological aspects of pyrimidines

Pyrimidines are particularly interesting targets, for the synthesis of novel fused heterocycles due to their structural diversity and impotence in the development of broad range of therapeutics. Pyrimidine is an important part of alkaloids and this nucleus is found in various medicine, in the form of anti-oxidant, anti-cancer, anti-microbial, antihypertensive, anti-malarial, anti-HIV, anti-nociceptive, selective type 4-phosphodiesterase, central nervous system activities, analgesic and anti-inflammatory agent.

Pyrimidine has long and distinguish history extending from the days of its discovery, as important constituents of nucleic acid, to its current use in the chemotherapy of AIDS. Uracil (7.003), thymine (7.004) and cytosine (7.005) having pyrimidine nucleus are the three important constituents of nucleic acids. (Fig.-7.2)

![Fig. 7.2:](image)

A variety of natural products such as alkaloids also contain the pyrimidine ring system, these includes hypoxanthine which occurs in tea and thebromine is found in cocoa beans (7.006, 7.007, 7.008) (Fig.-7.3).
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There are a large number of pyrimidine based antimetabolised, 5- fluouracil (5-FU 7.009a) and 5- thiouracil (7.009b) which have pyrimidine nucleus are useful anti-neoplastic agent\textsuperscript{15-17}. Azathiopurine (7.010) mercaptopurine, (7.011) thioguanine (7.012) and tegafur\textsuperscript{18-21} (7.013) etc. are the some antineoplastic compound which have pyrimidine nucleus. (Fig.-7.4)

Pyrimidine ring is also found in vitamins like thiamine (7.014), folic acid\textsuperscript{22} (7.015) and riboflavin (7.016) barbiton, (7.017) the first barbiturate hypnotic, sedative and anti-convulsant is also a pyrimidine derivative. (Fig.-7.5)
Derivatives of barbituric acid, oxygenated pyrimidines are the most widely used in medicines, such as veronal, luminal are used as hypnotics while pentothal is used as an anesthetic.

\[
\text{Fig. 7.6:}
\]

Eversince this important observation, was made by hitching that a large number of 2,4- diaminopyrimidine and some 2-amino-4- hydroxypyrimidine are antagonist of folic acids\(^{21}\) since then, a large no. of 2,4-diaminopyrimidines have been synthesized as anti-folates. It was eventually proves that these pyrimidimnes are inhibitors of the enzymes dihydrofolate reductase (DHFR)\(^{24,25}\). Notable amongst the 2,4- diaminopyrimidine drugs are pyrimethamine (7.022), a selective inhibitor of the DHFR of malarial plasmodia; trimethoprim (7.023), an anti-bacterial drug which selectively inhibits bacterial DHFR and most importantly, the very potent but non selective DHFR inhibitors, methotrexata (7.024a) and aminopterin (7.024b), both used in cancer therapy\(^{26}\). 3',5'-Dichloromethotrexate (7.024c), has recently been introduced for anti-cancer chemotherapy\(^{27}\). (Fig.-7.7)

\[
\text{Fig. 7.7:}
\]

Gupta et al\(^{28}\), synthesize a series of nitrophenyl 4,4,6 trimethyl,1 H, 4H pyrimidine 2 thiols (NPTP) (7.025) and examine, their anti-convulsant activity in mice against maximal electro shock and metrazol (MET) induced convulsions.
El-Gaby, Adel-Hamide and Gharab, prepared some new pyrimidine-2-thiones (7.026) and examined for their in-vitro anti-cancer activity against *Ehrlich Ascites Carcinoma* cells.

2-Thiouracil (7.027a) and its alkyl analogue, thiobarbital(7.027c), are effective drugs against, hyperthyroidism and propylthiouracil(7.027b), is used as a drug for hyperthyroidism with minimum side effects (Fig. 7.8).

Risoperidone is an antipsychotic drug, which is a structural hybrid of butyrophenone and can be used as anxiolytic, anti-depressant and anti-parkinsonian drug. (Fig. 7.9). Bruno et al reported the synthesis of some new 2,5-cycloamine-5H-benzopyran (4,3-d)pyrimidines (7.029) and screened them for anti-inflammatory, analgesic, anti-pyretic and anti-platelet activities. (Fig. 7.9).

Molina et al synthesized a number of pyrido (1,2-c) pyrimidines and tested for effects on leucocyte function in vitro and anti-inflammatory activity.

![Fig. 7.8:](image)

![Fig. 7.9:](image)

![Fig. 7.10:](image)
7.1.3 Synthetic aspects of pyrimidines

On account of the interesting medicinal properties, several synthetic strategies have been developed in the literature for the synthesis of pyrimidines, of which some are given below. Pyrimidines have been prepared by a number of methods but the most important ones are those in which the ring is formed from two fragments which contribute the C-C-C and N-C-N atoms respectively, as given below:

A series of pyrido[2,3-d]pyrimidine derivatives (7.036) have been prepared by one-pot three component reactions of 4(6)-aminouracil (7.033) malononitrile (7.034) and aromatic aldehydes. (7.035) This efficient synthesis was done under microwave irradiation conditions (method A) and also using catalytic amount of diammonium hydrogen phosphate [(NH₄)₂HPO₄] (DAHP) in aqueous media (method B). (Scheme – 7.1).

![Scheme – 7.1](image)

A ZnCl₂-catalyzed three component coupling reaction allows the synthesis of various 4,5-disubstituted pyrimidine derivatives. (7.040) in a single step from functionalized enamines. (7.037), triethyl orthoformate (7.038) and ammonium acetate (7.039) (Scheme – 7.2).

![Scheme – 7.2](image)

A NaOH catalyzed rearrangement of propargylic hydroxylamines. (7.042) allows a highly stereoselective access to Cbz-protected β-enaminones (7.043). A subsequent synthesis of pyrimidines (7.044) shows the synthetic potential of this β-enaminones. (Scheme – 7.3)
A novel and efficient synthesis\textsuperscript{37} of pyrimidine. (7.049), from β-formyl enamide. (7.047) involves, samarium chloride catalysed cyclisation of β-formyl enamides using urea, (7.048) as source of ammonia under microwave irradiation (Scheme – 7.4).

A simple, high yielding synthesis of pyrimidines from ketone in the presence of HMDS and formamide is described. In this procedure, the aromatic/hetero aromatic and aliphatic ketones. (7.050), react with formamide to give pyrimidines. (7.051) under microwave irradiation in good yields\textsuperscript{38}. (Scheme – 7.5)

Reaction of malondiamide. (7.052) with an ester such as, malonic ester gives a derivative of 4,6-dihydroxypyrimidine (7.053). The reaction may also be carried out using formamide, acetamide, CS\textsubscript{2}, formate esters and carbonates (Scheme – 7.6). Malondiamidines react in a similar manner like diamides giving 4,5-dihydroxy pyrimidines on condensation withformate esters\textsuperscript{39}. 

Scheme – 7.3

Scheme – 7.4

Scheme – 7.5

Scheme – 7.6
The coupling of acid chlorides (7.054) with terminal alkynes (7.055) using one equivalent of triethyl amine under Sonogashira condition followed by subsequent addition of amines or amidinium salts to the intermediate alkynones. (7.056) allows a straight forward access to enaminones and pyrimidines. (7.057) under miles conditions (7.060). (Scheme – 7.7)

![Scheme - 7.7](image)

The condensation of N-vinyl/aryl amides (7.058) with cyanic acid derivatives, (7.059) affords the corresponding C-4 hetroatoms substituted pyrimidines (7.060). The use of cyanic bromide and thiocyanatomethane provides versatile hetrocycles poised for further derivatization (7.061). (Scheme – 7.8).

![Scheme - 7.8](image)

The reaction of β,γ-unsaturated γ-alkoxy-α-ketoesters, (7.062) with 5-aminopyrazoles. (7.063) proceeds with high regioselectivity, to yield new pyrazolo [1,5-a] pyrimidines, (7.064) bearing an ester function in the 7-position (Scheme – 7.9) (7.065). The obtained drug like compound have a great potential for medicinal chemistry as they closely resemble the structure of several marketed pharmaceuticals (7.066).

![Scheme - 7.9](image)

Synthesis of novel dihydropyrazolo[3,4-d] pyrimidine derivative bearing a phenothiazine (7.067). The (7.068) formed by the reaction of 3-methyl-1-(10H-
phenothiazin-8-yl)-1H pyrazole 5-(4H)-one, (7.066) with an appropriate aldehyde, guanidine hydrochloride and phosphorus pentoxide under reflux condition has been reported via a modified Biginelli multicomponent reaction (Scheme – 7.10)

![Scheme 7.10](image)

**Scheme – 7.10**

Synthesis of 6-substituted-4- (4-hydroxy-6-methyl-2-oxo-2Hpyran-3-yl)- 2- S-benzylthiopyrimidine (7.070), by the condensation of 3-cinnmoyl-4-hydroxy-6-methyl-2-oxo-2Hpyran (DHA Chalcone) (7.069), with dehydro acetic acid. (7.068) (DHA) in the presence of piperidine as a base has been demonstrated. (Scheme – 7.11)

![Scheme 7.11](image)

**Scheme – 7.11**

A proficient synthesis of isoxazolo(2,3-a)pyrimidines, (7.073) has been observed by the reactions of 3-amino-5-methylisoxazole, (7.071) with 4-arylidene-2-phenyl-5-isoxazolones (7.072) (Scheme – 7.12)
A one pot multicomponent synthesis of tetra substituted saturated fused pyrimidines. (7.076) has been examined\(^{46}\). The strategic utilization of the N-PMB group enabled the construction of a broad range of N-vinyl tertiary enamide starting material (Scheme – 7.13). This stands as a flexible approach to functionalized pyrimidines with the capability of manipulating ketone, acid chlorides or nitrile reaction process.

Condensation reaction of urea. (7.078) with ethyl crotonate. (7.077) in the presence of a base gives, an intermediate. (7.079) which is cyclised into dihydropyrimidine. (7.080). The compound. (7.080) is readily oxidized to the corresponding pyrimidine\(^{47}\). (7.081). (Scheme – 7.14)

Dabiri and co-workers describe the synthesis of pyrimido[4,5-d]pyrimidine-2,4,7-trione (7.084) derivatives from dimethyluracil (7.082) under microwave-assisted conditions\(^{48}\) (Scheme – 7.15).
A synthesis involves a condensation between a malonic ester (7.085) and urea (7.086) in the presence of a base to yield barbituric acid\(^5\) (7.087).\(\text{(Scheme-7.16)}\)

\[
\begin{array}{c}
\text{H}_2\text{C} \overset{\text{O}}{\text{C}} \text{O} \text{C}_2\text{H}_5 + \text{NH}_2 \overset{\text{O}}{\text{C}} \overset{\text{O}}{\text{C}} \text{O} \text{C}_2\text{H}_5 \rightarrow \text{NaOC}_2\text{H}_5
\end{array}
\]

\(\text{H}_2\text{C} \overset{\text{O}}{\text{C}} \text{O} \text{C}_2\text{H}_5\)
\(\text{(7.085)}\)
\(\text{(7.086)}\)
\(\text{(7.087)}\)

\(\text{Scheme – 7.16}\)

An interesting reaction of simple \(\alpha,\beta\)-unsaturated ketone 7.088 is its reaction with amidines 7.089 gives pyrimidines 7.091. The initial product of this reaction is probably a dihydropyrimidine 7.090 which is readily oxidized by a stream of air to the corresponding pyrimidine\(^4\) 7.091.\(\text{(Scheme-7.17)}\).

\[
\begin{array}{c}
\text{C}_6\text{H}_5 \overset{\text{O}}{\text{C}} \overset{\text{O}}{\text{C}} \text{C}_6\text{H}_5 + \overset{\text{N}}{\text{N}} \text{H}_2 \overset{\text{O}}{\text{C}} \overset{\text{O}}{\text{C}} \text{C}_6\text{H}_5 \rightarrow \text{Air, Ox} \rightarrow \overset{\text{N}}{\text{N}} \text{R} \overset{\text{O}}{\text{C}} \overset{\text{O}}{\text{C}} \text{C}_6\text{H}_5
\end{array}
\]

\(\text{C}_6\text{H}_5\)
\(\text{C}_6\text{H}_5\)
\(\text{(7.088)}\)
\(\text{(7.089)}\)
\(\text{(7.090)}\)
\(\text{(7.091)}\)

\(\text{Scheme – 7.17}\)

The sodium salt of 3, 3-dimethoxy-2-methoxycarbonylprope-1-ol (7.093) has been found to react with a variety of amidinium salts (7.092) to afford the corresponding 2-substituted pyrimidine-5-carboxylic esters\(^5\) 7.094.\(\text{(Scheme-7.18)}\).

\[
\begin{array}{c}
\overset{\text{O}}{\text{C}} \overset{\text{O}}{\text{C}} \text{Me} \overset{\text{O}}{\text{C}} \overset{\text{O}}{\text{C}} \text{Me} + \overset{\text{N}}{\text{N}} \text{H}_2 \overset{\text{O}}{\text{C}} \overset{\text{O}}{\text{C}} \text{Me} + \overset{\text{O}}{\text{C}} \overset{\text{O}}{\text{C}} \text{Me} \rightarrow \text{DMF, 100°C, 1h} \rightarrow \overset{\text{N}}{\text{N}} \text{R} \overset{\text{O}}{\text{C}} \overset{\text{O}}{\text{C}} \text{Me}
\end{array}
\]

\(\text{R} \overset{\text{N}}{\text{H}}_2\overset{\text{O}}{\text{C}} \overset{\text{O}}{\text{C}} \text{R'}\)
\(\text{(7.092)}\)
\(\text{(7.093)}\)
\(\text{(7.094)}\)

\(\text{Scheme – 7.18}\)

A novel and efficient synthesis\(^5\) of pyrimidine 7.097 from \(\beta\)-formyl enamide 7.095 involves samarium chloride catalysed cyclisation of \(\beta\)-formyl enamide 7.095 using urea 7.096 as a source of ammonia under microwave irradiation (\(\text{Scheme-7.19}\)).

\[
\begin{array}{c}
\text{R} \overset{\text{N}}{\text{HAc}} \overset{\text{O}}{\text{C}} \overset{\text{O}}{\text{C}} \text{CHO} + \text{H}_2\text{N} \overset{\text{O}}{\text{C}} \overset{\text{O}}{\text{C}} \text{NH}_2 \overset{\text{O}}{\text{C}} \overset{\text{O}}{\text{C}} \text{H}_2 \text{N} \overset{\text{O}}{\text{C}} \overset{\text{O}}{\text{C}} \text{NH}_2 \rightarrow \text{1.5eq.SmCl}_3.6\text{H}_2\text{O, MW (<300W, open vessel) heat, 140°C, 8-10min}} \rightarrow \overset{\text{N}}{\text{N}} \text{R} \overset{\text{O}}{\text{C}} \overset{\text{O}}{\text{C}} \text{R'}
\end{array}
\]

\(\text{R} \overset{\text{N}}{\text{HAc}} \overset{\text{O}}{\text{C}} \overset{\text{O}}{\text{C}} \text{CHO}\)
\(\text{(7.095)}\)
\(\text{(7.096)}\)
\(\text{(7.097)}\)

\(\text{Scheme – 7.19}\)
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7.2 Present work

Fused pyrimidines ring systems are often incorporated into drug designed for cancer and antiviral treatment\textsuperscript{52}. They have a long history extending from the days of their discovery as important constituents of nucleic acids to their current use in the chemotherapy of AIDS\textsuperscript{53}. They form an integral part of the genetic materials viz. DNA and RNA\textsuperscript{54}. Pyrimidines occupy a distinct and unique place in our life. This heterocyclic moiety has great biological and medicinal significance. A large array of pyrimidine drugs possess a variety of medicinal properties. It was mention earlier in this chapter that pyrimidines have been studied extensively because of their ready accessibility, diverse chemical reactivity and broad spectrum of biological activities such as antimicrobial, cytotoxic, anti-HIV\textsuperscript{53} (AZT and Etravirine), anti-inflammatory, anti tumor, anti convulsant, anti tubercular, antioxidant\textsuperscript{55}, antimalarial\textsuperscript{56}, antidiabetic\textsuperscript{57}, insecticidal\textsuperscript{58} etc.

This aroused our interests in these molecules and prompted us to undertake a study to seek structural modification of 6- Benzoyl-8-methyl-7-methylsulfanyl-9-oxo 8,9-dihydro-pyrimido [5,4-e][1,4]diazepine-5-carboxylic acid ethyl ester (7.104) by incorporating isoxazole, pyrazole, pyrimidine, 1,4-benzodiazepine, 1,4-benzooxazepine and 1,4-benzothiazepine on to 2,3-position as shown in (scheme-7.21).

As mentioned earlier that 1,4-pyrimidodiazepine has been exploited as versatile important synthons for the synthesis of a wide variety of heterocycles and fused heterocycles, so much so that the number of applications of these materials in the synthesis of heterocycles have grown exponentially in last few decades\textsuperscript{59,60}.

Based on the precedence in the literature, on the wide spread pharmacological activity of pyrimidine 1,4-diazepine nucleus, it was assumed that incorporation of 1,2,3-triazole bio active pharamacophore on second position of this bio active pyrimidino-1,4-diazepine nucleus, could produce interesting series of pyrimidine ring incorporated with 1,4-diazipine 1,2,3-triazole derivatives with an impressive impact on the enhanced biological activity in the resulting molecules (scheme-7.20 (a),(b)).

With this idea in mind, the present investigation was undertaken with a view to incorporate these moieties on the 2-position of 1,4- pyrimidodiazepine nucleus\textsuperscript{61}. 
Although, the chemical literature is replete with great variety of examples of the synthesis isoxazole, pyrazole, pyrimidine, 1,4-benzodiazepine, 1,4-benzoxazepine and 1,4-benzothiaiazepine, but a large number of them, if not all, are burdened with one liability or the other. It posed a very serious limitation on the use of these procedures and called attention to develop much simpler routes which use easily accessible starting materials. Clearly a refinement in the existing methodology and development of newer strategies for the synthesis was required. Consideration of reactivity, compound availability, synthetic economy and simplicity in operation has led us to favor the use of 5-amino1-pyrimidine 4-carbonitrile appended with amine, ketone derivatives etc to the synthesis of corresponding isoxazole, pyrazole, pyrimidine, 1,4-benzodiazepine, 1,4-benzoxazepine and 1,4-benzothiaiazepine incorporated heterocyclic systems and it was considered of interest in the present work to design molecules in which these moieties were present in a single molecular framework, to provide an additive effect on the overall biological efficacy in the resulting molecules.

7.3 Result and discussion

In view of the impressive biological activities shown by pyrimido1,4-diazepine nucleus and its derivatives it was thought of interest in the present work to construct a system, which carried pyrimido-1,4-diazepine as one part along with the1, 2, 3-triazole, isoxazole, pyrazole, pyrimidine, 1,4-benzodiazepine, 1,4-benzoxazepine and 1, 4-benzothiaiazepine as the other part in the same molecular framework via multicomponent one pot synthesis ‘domino reaction’. The idea behind building such a system was to incorporate the biological activities of these well established molecules in a single molecular framework. It was envisaged that the precursors which could fulfill this synthetic requirement and accessible easily, could operated through two different methodologies scheme [Scheme-7.20(a), (b)] and (Scheme-7.21). The strategy outlined in first part [scheme-7.20 (a)] was employed in the preparation of 7.100, 7.101, 7.102, 7.103, 7.104, 7.105, 7.106 and second part [scheme-7.20 (b)] in the synthesis of 7.109, 7.110 from 5-substituted pyrimido-carbonitrile (7.100).

The reaction of 7.098 with ethylchloroformate in presence of ethanol and base sodium carbonate (Na₂CO₃) allowed the formation of 7.099. Its (7.099) reaction with phenacyl bromide (mostly preferred) or phenacyl chloride gave 7.100. The compound 7.100 which is a main intermediate for further synthesis was obtained in a two step procedure through two different reaction processes [Scheme-
7.20(a), (b)] to give different 1,4-diazepine 1,2,3-triazole as final products. In the first process compound 7.100 [Scheme-7.20(a)] was reacted with carbon disulphide (CS$_2$) followed by methyl iodide (CH$_3$I) to give compound 7.101 in accordance to the procedure reported in literature on other related substrates. Compound 7.101 was utilized as a key intermediate for the preparation of compounds 7.102, 7.103, 7.104, 7.105, 7.106, 7.109, 7.110 (Scheme- 7.20), 7.111, 7.112, 7.113 (a-d), 7.114 (a-c) (Scheme- 7.21). Literature is replete with examples showing the involvement of oxoketen dithioacetals in the nucleophilic displacement reactions. This property was utilized in subsequent reaction with ethylamine or methylamine to give 7.102 and later underwent cyclization to give 7.103 in presence of solvent DMF which gave pyrimido-1,4-diazepine ring in compound 7.103 which hydrolysed later to give 7.104 respectively in one pot synthetic process. The same strategy which produced 7.102, 7.103, 7.104 was also be used separately on step wise procedure through the intermediacy of 7.101. The compounds 7.105 and 7.106 was obtained with reaction of NaN$_3$ and propargyl amine in one pot synthetic domino reaction from 7.104 in presence of Cu catalyst as final product of first reaction respectively.

In the second reaction in [Scheme- 7.20 (b)] an extra amount of NaH or NaOEt was used to allow to it undergo nucleophilic addition reaction followed by hydrolysis to give cyclized product which formed five membered aza-ring to give 7.107 and 7.108 respectively in a straight forward manner. In this scheme an innovative approach for the incorporation of a free N$_3$ group on the 3-position (by replacing NH$_2$ group) of the aza-ring via diazotization process simply with NaN$_3$ or also by using ionic solvent [bmim]Cl with NaN$_3$ was employed in for the formation of compound 7.109 which introduced 1,4-diazepine nucleus with triazole ring in the compound 7.109. This strategy was based on the nucleophilic displacement reaction of NaN$_3$ under feasible conditions. The compound 7.109 underwent insitu reaction with propargyl amine in the same reaction vessel via domino reaction in the presence of Cu catalyst to gave compound 7.110 as the final product of this second reaction containing pyrimido-1,4-diazepine 1,2,3-triazole ring in the final product. The strategies in [Scheme- 7.20 (b)] were designed, keeping in mind the fact that incorporation of the triazole on to the 1,4-diazepine nucleus was possible through reaction of N$_3$ with the propargyl amine functions when present on 3-position of five membered aza ring to give the cyclised product on 1,4-diazepine ring and at the same time form triazole ring on 1,4-diazepine nucleus. This had called upon to
formulate such strategies [Scheme- 7.20 (a), (b)] which fitted to this requirement and allowed the triazole fragment to be incorporated to 1,4-pyrimidodiazepine nucleus through the azide function present on 3-position.

In the second part of scheme- 7.21 the intermediate 7.104 of 1,4-pyrimidodiazepine compound formed during first reaction was used in the synthesis of various 1,4-pyrimidodiazepine derivatives with reaction with different reagents like hydrazine hydrate, hydroxyl amine hydrochloride, urea, thiourea, guanidine, acetamidine, o-phenylenediamine, o-aminothiophenol and o-aminophenol to give pyrazole 7.111, isoxazole 7.112, pyrimidine 7.113 (a-d), 1,4-benzodiazepine, 1,4-benzothiazepine, 1,4-benzooxazepine incorporated 7.114(a-c) derivatives from pyrimido-1,4-diazepine nucleus respectively.

The physical and spectral data summarized in tables – 7.1 and 7.2 supported the structures assigned to the compounds.

7.4 Structures of compounds whose synthesis is described in this chapter:
### 7.5 Schematic presentation of the formation of starting materials

- **Scheme - 7.20 (a), (b)**

- **Equation:**

\[
\begin{align*}
\text{N} & \quad \text{C} \quad \text{N} \\
\text{N} & \quad \text{C} \quad \text{N} \\
\text{C} & \quad \text{O} \quad \text{C} \\
\text{H} & \quad \text{C}_6 \text{H}_5 \\
\end{align*}
\]

\[
\begin{align*}
\text{N} & \quad \text{C} \quad \text{N} \\
\text{N} & \quad \text{C} \quad \text{N} \\
\text{Cl} & \quad \text{Et} \\
\text{H}_2 \quad \text{C} \quad \text{C}_6 \text{H}_5 \\
\end{align*}
\]

\[
\begin{align*}
\text{N} & \quad \text{C} \quad \text{N} \\
\text{N} & \quad \text{C} \quad \text{N} \\
\text{O} & \quad \text{Et} \\
\text{C}_6 \text{H}_5 & \quad \text{O} \\
\end{align*}
\]

\[
\begin{align*}
\text{N} & \quad \text{C} \quad \text{N} \\
\text{N} & \quad \text{C} \quad \text{N} \\
\text{H}_2 & \quad \text{C} \quad \text{C}_6 \text{H}_5 \\
\end{align*}
\]

- **Steps:**

1. **Step 1:**
   - **Reagent:** EtOOC
   - **Product:** EtOOC
   - **Condition:** H$_2$O

2. **Step 2:**
   - **Reagent:** NaN$_3$-NaN$_2$
   - **Product:** NaN$_3$-NaN$_2$

3. **Step 3:**
   - **Reagent:** NaN$_3$-NaN$_2$
   - **Product:** NaN$_3$-NaN$_2$

4. **Step 4:**
   - **Reagent:** NaN$_3$-NaN$_2$
   - **Product:** NaN$_3$-NaN$_2$

5. **Step 5:**
   - **Reagent:** NaN$_3$-NaN$_2$
   - **Product:** NaN$_3$-NaN$_2$
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### Table 7.1: Physical and analytical data of compounds 7.100 – 7.114

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Compound</th>
<th>Mol. wt.</th>
<th>Mol. formula</th>
<th>M.P. (°C)</th>
<th>Yield (%)</th>
<th>Elemental analysis VII</th>
</tr>
</thead>
<tbody>
<tr>
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<td>C Calcd/ exp</td>
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<tr>
<td>1</td>
<td>7.100</td>
<td>399.37</td>
<td>C₁₀H₁₀N₆O₃</td>
<td>165-169</td>
<td>80.3</td>
<td>63.70/63.20</td>
</tr>
<tr>
<td>2</td>
<td>7.101</td>
<td>414.50</td>
<td>C₁₀H₁₀N₆O₃S₂</td>
<td>179-180</td>
<td>82</td>
<td>55.05/55.38</td>
</tr>
<tr>
<td>3</td>
<td>7.102</td>
<td>397.45</td>
<td>C₁₀H₁₀N₆O₃S</td>
<td>231-233</td>
<td>76</td>
<td>57.42/57.72</td>
</tr>
<tr>
<td>4</td>
<td>7.104</td>
<td>398.44</td>
<td>C₁₀H₁₀N₆O₃S</td>
<td>235-237</td>
<td>80</td>
<td>57.27/57.55</td>
</tr>
<tr>
<td>5</td>
<td>7.105</td>
<td>393.13</td>
<td>C₁₀H₁₁N₅O₄</td>
<td>205-208</td>
<td>78</td>
<td>54.96/54.48</td>
</tr>
<tr>
<td>6</td>
<td>7.106</td>
<td>430.42</td>
<td>C₁₂H₁₀N₆O₃</td>
<td>213-215</td>
<td>75</td>
<td>58.60/58.24</td>
</tr>
<tr>
<td>7</td>
<td>7.108</td>
<td>310.31</td>
<td>C₁₀H₁₁N₆O₃</td>
<td>175-177</td>
<td>79</td>
<td>61.93/61.50</td>
</tr>
<tr>
<td>8</td>
<td>7.109</td>
<td>336.30</td>
<td>C₁₀H₁₁N₆O₃</td>
<td>183-185</td>
<td>78</td>
<td>57.17/57.62</td>
</tr>
<tr>
<td>9</td>
<td>7.110</td>
<td>373.37</td>
<td>C₁₀H₁₁N₅O₃</td>
<td>195-198</td>
<td>75</td>
<td>61.12/61.44</td>
</tr>
<tr>
<td>10</td>
<td>7.111</td>
<td>364.36</td>
<td>C₁₀H₁₁N₅O₃</td>
<td>223-225</td>
<td>72</td>
<td>59.34/59.60</td>
</tr>
<tr>
<td>11</td>
<td>7.112</td>
<td>364.35</td>
<td>C₁₀H₁₁N₅O₃</td>
<td>232-235</td>
<td>80</td>
<td>62.63/62.13</td>
</tr>
<tr>
<td>12</td>
<td>7.113a</td>
<td>392.37</td>
<td>C₁₀H₁₁N₅O₄</td>
<td>243-245</td>
<td>79</td>
<td>58.16/58.50</td>
</tr>
<tr>
<td>13</td>
<td>7.113b</td>
<td>408.43</td>
<td>C₁₀H₁₁N₅O₃S</td>
<td>245-247</td>
<td>74</td>
<td>55.87/55.35</td>
</tr>
<tr>
<td>14</td>
<td>7.113c</td>
<td>391.38</td>
<td>C₁₀H₁₁N₅O₃</td>
<td>233-238</td>
<td>72</td>
<td>58.31/58.52</td>
</tr>
<tr>
<td>15</td>
<td>7.113d</td>
<td>392.41</td>
<td>C₁₀H₁₁N₅O₃</td>
<td>231-232</td>
<td>74</td>
<td>61.21/61.58</td>
</tr>
<tr>
<td>16</td>
<td>7.114a</td>
<td>440.45</td>
<td>C₁₀H₁₁N₅O₃</td>
<td>231-233</td>
<td>72</td>
<td>65.45/65.16</td>
</tr>
<tr>
<td>17</td>
<td>7.114b</td>
<td>457.50</td>
<td>C₁₀H₁₁N₅O₃S</td>
<td>234-235</td>
<td>75</td>
<td>63.01/63.36</td>
</tr>
<tr>
<td>18</td>
<td>7.114c</td>
<td>441.44</td>
<td>C₁₀H₁₁N₅O₄</td>
<td>229-233</td>
<td>70</td>
<td>65.30/63.65</td>
</tr>
</tbody>
</table>
Table 7.2: Interpretation of spectral data with the help of IR (cm⁻¹) (KBr), \(^{13}\text{C}\)-NMR, \(^{1}\text{H}\)-NMR and Mass (MS (m/z)) of compound 7.099 – 7.114

<table>
<thead>
<tr>
<th>S.No</th>
<th>Compound</th>
<th>IR(KBr) cm⁻¹</th>
<th>(^{1}\text{H}) NMR (CDCl₃(\delta) (ppm) and MS; m/z (relative abundance))</th>
<th>(^{13}\text{C}) NMR (CDCl₃(\delta) (ppm))</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7.099</td>
<td>3240(N-H str.) 3290(C-H str.) 2900,1400(-CH₂ next to C=O) 1712 (C=O) 1535(C=C str.)</td>
<td>9.29, 9.10(1H,s, CH of 4-pyrimidine) 8.0(1H,s,NH sec.amide) 1.30(3H,s,CH₃) 4.12[2H,s,CH₂,methylene]</td>
<td>Ar-C[148.6(CH),146.1(CH), 147.9(C),126.3(C) pyrimidine] 118.0(C of nitrile) 154.8 (C of 1-amide ) Al-C[13.3( CH₃), 56.90 ( CH₂)] 196.50 (C of 1-carbonyl -CO)</td>
</tr>
<tr>
<td>2</td>
<td>7.100</td>
<td>3400(C-N-H str.) 3280(N-H str.) 3000(C-H str.) 2980,1400(-CH₂ next to C=O) 1704,1720(C=O) 1630(C=N) 1535(C=C str.) 1165(C-O-C)</td>
<td>9.29, 9.10(1H,s, CH of 4-pyrimidine) 1.30(3H,s,CH₃) 4.12[2H,s,CH₂,methylene] 7.37-7.86(5H,Ar-H) 4.22(2H,CH₂ methylene)</td>
<td>MS,m/z: 322.2(M⁺70%), 305.0(28.6%), 318.1(100.0%),311.11(18.1%),312.11(2.4%), 217.14(21.4%),216.13(99%),218.14(2.4%).</td>
</tr>
<tr>
<td>3</td>
<td>7.101</td>
<td>3270(N-H str.) 3125,3320(NH,NH₂) 2990(C-H str.) 2970,1400(-CH₂ next to C=O) 1660,1710(C=O) 1625(C=N) 1540(C=C str.) 1620(C=O of α,β – unsaturated ketone) 685(C-S str.) 1165(C-O-C)</td>
<td>9.29, 9.10(1H,s, CH of 4-pyrimidine) 7.45-7.81(5H,Ar-H) 1.30, (3H,s,CH₃-carbonyl) 4.12[2H,s,CH₂,methylene(=CO)] 2.25,2.25(3H,methyl of –S=C=C)</td>
<td>MS,m/z:336.3(M⁺80%),318.1(19.5%), 396.13(25%),397.13(5.5%),414.08(100.0%), 415.09(21.5%),416.08(9.5%), 415.08(8.9%), 393.14(99%),394.14(29.9%),395.13(8.9%)</td>
</tr>
<tr>
<td>4</td>
<td>7.103</td>
<td>3270(N-H str.)</td>
<td>3125,3320(NH,NH₂)</td>
<td>2990(C-H str.)</td>
</tr>
<tr>
<td>5</td>
<td>7.104</td>
<td>3290(N-H str.)</td>
<td>3010(C-H str.)</td>
<td>2900,1400(-CH₂ next to C=O)</td>
</tr>
<tr>
<td>6</td>
<td>7.105</td>
<td>3280(N-H str.)</td>
<td>2990(C-H str.)</td>
<td>2970,1400(-CH₂ next to C=O)</td>
</tr>
<tr>
<td>7</td>
<td>7.106</td>
<td>3240(N-H str.)</td>
<td>3090(C-H str.)</td>
<td>2900,1400(-CH₂ next to C=O)</td>
</tr>
<tr>
<td>C=O)</td>
<td>2.74(3H₃, methyl of -N=C=C)</td>
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<tr>
<td>1800(C=O)</td>
<td>7.29-7.62(5H₃,m,Ar-H benzylidenimin)</td>
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<tr>
<td>1630(C=N)</td>
<td>7.4 (H,s, CH of 1,2,3-triazole)</td>
<td></td>
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</tr>
<tr>
<td>1590(C=C str.)</td>
<td>4.12(2H₃,CH₂ methylene)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>1506 (N=N)</td>
<td><strong>MS,m/z:377.3(M⁺ 27.0%),395.18(31.9%), 431.15 (26.4%),432.16(2.7%), 430.15(100.0%),144.2(40.0%)</strong></td>
<td></td>
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</tr>
<tr>
<td>1285(N-N=N- )</td>
<td>1156(C-O-C)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1156(C-O-C)</td>
<td>130.8(CH), 128.6(CH), 129.0(CH)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.109</td>
<td>187.0(C of Carbonyl -CO)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>3432,3336(NH₂)</td>
<td>162.8(C of 1-amide)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3270(N-H str.)</td>
<td>149.4(C of 1-amide)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3160(C-H str.)</td>
<td>83.0, 112(C of ethylene)</td>
<td></td>
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<tr>
<td>2980,-CH₂ next to C=O</td>
<td>164.6(C of 1-imine)</td>
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</tr>
<tr>
<td>1680(C-O )</td>
<td>143( C of 1,2,3triazole )</td>
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<tr>
<td>1625(C-N)</td>
<td>131(C of 1,2,3-triazole )</td>
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<tr>
<td>1540(C=C str.)</td>
<td>182(2H₃,CH₂ methylene)</td>
<td></td>
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<tr>
<td>1156(C-O-C)</td>
<td><strong>MS,m/z:292.4(M⁺ 70.0%),277.0(20.0%), 336.10(100.0%),337.10(18.1%), 338.10(2.5%) 159.5 (14.8%)</strong></td>
<td></td>
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<tr>
<td>8.110</td>
<td>Ar-C[158(CH),156.4(CH),pyrimidine]</td>
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<tr>
<td>3400(NH₂)</td>
<td>Ar-C[127(CH),111.0(CH),122.0 (C),132.0(C) 1-pyrrole]</td>
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<tr>
<td>3220(N-H str.)</td>
<td>Ar-C[133.2 (C), 129.5(CH), 128.6 (CH), 132.4(CH), 128.6(CH), 129.5(CH)]</td>
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<tr>
<td>3000(C-H str.)</td>
<td>Ar-C[ 57.3 (CH₃), 13.3 ( CH₃)]</td>
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<tr>
<td>2980,-CH₂ next to C=O</td>
<td>177.0(C of Carbonyl -CO)</td>
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<tr>
<td>2200(CN)</td>
<td>161.0(C of carboxyl)</td>
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<tr>
<td>1600,1800(C=O)</td>
<td>7.26(1H₃, CH of 2-pyrimidine)</td>
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<tr>
<td>1595(C=C str.)</td>
<td>9.26, 8.78(1H₃, CH of 2-pyrimidine)</td>
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<tr>
<td>1156(C-O-C)</td>
<td>7.45-7.81(5H₃,Ar-H)</td>
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<tr>
<td>1506 (N=N)</td>
<td>1.30, (3H₃,CH₂-carbonyl)</td>
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</tr>
<tr>
<td>1285(N-N=N- )</td>
<td>4.20(2H₃,CH₂ methylene)</td>
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<tr>
<td>1156(C-O-C)</td>
<td><strong>MS,m/z:321.3(M⁺ 70.0%),373.13(100.0%), 374.13(100.0%),375.14(18.1%), 376.10(2.5%) 159.5 (14.8%)</strong></td>
<td></td>
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<tr>
<td>9.111</td>
<td>Ar-C[158(CH),156.4(CH),pyrimidine]</td>
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<tr>
<td>3390(N-H str.)</td>
<td>Ar-C[118.0(CH),108.0(CH), 108.0 (C),118.0(C) 1-pyrrole]</td>
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<tr>
<td>3210 (N-H of pyrazole ring)</td>
<td>Ar-C[137.3 (C), 129.0(CH), 128.6 (CH), 130.8(CH), 128.6(CH), 129.0(CH)]</td>
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<tr>
<td>3090 (C-H str.)</td>
<td>Ar-C[ 42.50(CH₂),13.3 ( CH₃), 57.3( CH₃)]</td>
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<tr>
<td>2990,1400(-CH₂ next to C=O)</td>
<td>161.0(C of carbonyl)</td>
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</tr>
<tr>
<td>3390(N-H str.)</td>
<td>7.26(1H₃, CH of 2-pyrimidine)</td>
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</tr>
<tr>
<td>3210 (N-H of pyrazole ring)</td>
<td>9.20, 9.19(1H₃, CH of 2-pyrimidine)</td>
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<tr>
<td>3090 (C-H str.)</td>
<td>7.22-7.48(5H₃,m,Ar-H)</td>
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</tr>
<tr>
<td>2990,1400(-CH₂ next to C=O)</td>
<td>2.74(3H₃,methyl of –N=C=O)</td>
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<td></td>
</tr>
<tr>
<td>13.7(H₃,NH)</td>
<td>13.7(H₃,NH)</td>
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<td></td>
</tr>
<tr>
<td>1.30(3H₃,CH₃ of –OC(=O))</td>
<td><strong>MS,m/z:374.13(100.0%),375.14(22.2%), 376.10(52%),152.2(39.8%)</strong></td>
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</tr>
</tbody>
</table>
### Chapter 7: Synthesis of 1,2,3-triazolo substitute analogues of the pyrimidine

| 
| C=N | C=O | 4.12(2H,s,CH\_2 methylene, -OC(=O)N) |
| 1600(C=O) | 1590(C=C str.) | MS,m/z:312.3(M\(^+\)70.0%), 364.13(100.0%), 365.13(22.6%), 366.14(2.0%), 315.1(52%), 152.2(39.8%) |
| 1515(C=N) | 1156(C-O-C) | 150.3(C of 1-amide) |
| 177.0(C of carbonyl) |
| 163.7(C of 1-amide) |
| 115.8,144.20,138.20 (C of 3-pyrazole) |

| 7.112 |
| 3300 (N-H str.) |
| 3010 (C-H str.) |
| 2990,1400(-CH\_2 next to C=O) |
| 1600(C=O) |
| 1580(C=C str.) |
| 1510(C=N) |
| 900(C-O-N str. Of isoxazole ring) |
| 1156(C-O-C) |
| 9.20, 9.19(1H,s, CH of 2-pyrimidine) |
| 2.74(3H\_s,methyl of -N-C=C) |
| 7.22-7.48(5H,m,Ar-H) |
| 1.30(3H\_s,CH\_3 of -OC(=O)) |
| 4.12(2H\_s,CH\_2 methylene, -OC(=O)) |
| MS,m/z:312.3(M\(^+\)70.0%), 366.12(100.0%), 367.12(2.8%), 315.1(52%), 152.2(39.8%), 148.05(25.0%), 109.41(37.5%) |
| 150.3(C of 1-amide) |
| 177.0(C of carbonyl) |
| 163.7(C of 1-amide) |
| 100.0(C of isoxazole) |
| 150.0(C of 3 isoxazole) |
| 158.9(C of isoxazole) |

| 7.113a |
| 3380(N-H str.) |
| 3000(C-H str.) |
| 2980,1400(-CH\_2 next to C=O) |
| 1670,1710(C=O) |
| 1570(C=C str.) |
| 1500(C=N) |
| 1156(C-O-C) |
| 9.20, 9.19(1H,s, CH of 2-pyrimidine) |
| 2.74(3H\_s,methyl of -N-C=C) |
| 8.0(H\_s,NH) |
| 7.30-7.60(5H,m,Ar-H,benzyldenimin) |
| 1.30(3H\_s,CH\_3 of -OC(=O)) |
| 4.12(2H\_s,CH\_2 methylene, -OC(=O)) |
| MS,m/z:312.3(M\(^+\)70.0%), 392.12(100.0%), 393.13(21.5%), 394.13(3.0%), 315.1(52%), 152.2(39.8%) |
| Ar-C[145.8(CH),146.0(CH), 141.7(C),142.3(C) pyrimidine] |
| Ar-C[131.20 (C),129.0(CH),128.60 (CH), 130.80(CH), 128.60(CH), 129(CH)] |
| Al-C[27.6(CH\_2), 31.3(CH\_3), 57.3(CH\_2)] |
| 149.4(C of 1-amide) |
| 177.0(C of carbonyl) |
| 162.8(C of 1-amide) |
| 160(C of 1-amide) |
| 164.6(C of 1-imine) |
| 80,114 (C of 3 ethylene(-NC=O)) |

| 7.113b |
| 3370(N-H str.) |
| 2990(C-H str.) |
| 2980,1400(-CH\_2 next to C=O) |
| 1680(C=O) |
| 1570(C=C str.) |
| 1510(C=N) |
| 780(C=S of pyrimidine) |
| 9.20, 9.19(1H,s, CH of 2-pyrimidine) |
| 2.74(3H\_s,CH\_3 of -N-C=C) |
| 7.30-7.60(5H,m,Ar-H,benzyldenimin) |
| 2.0(H\_s,NH of amine) |
| 1.30(3H\_s,CH\_3 of -OC(=O)) |
| 4.12(2H\_s,CH\_2 methylene, -OC(=O)N) |
| MS,m/z:312.3(M\(^+\)70.0%), 408.10(100.0%) |
| Ar-C[145.8(CH),146.0(CH), 141.7(C),142.3(C) pyrimidine] |
| Ar-C[131.20 (C),129.0(CH),128.60 (CH), 130.80(CH), 128.60(CH), 129(CH)] |
| Al-C[27.6(CH\_2), 31.3(CH\_3), 57.3(CH\_2)] |
| 149.4(C of 1-amide) |
| 177.0(C of carbonyl) |
| 162.8(C of 1-amide) |
Chapter-7: Synthesis of 1,2,3-triazolo substitute analogues of the...

<table>
<thead>
<tr>
<th>14</th>
<th>7.113c</th>
<th>3300(N-H str.)</th>
<th>3000(C-H str.)</th>
<th>2990(CH&lt;sub&gt;3&lt;/sub&gt; Str.)</th>
<th>2980,1400(-CH&lt;sub&gt;2&lt;/sub&gt; next to C=O)</th>
<th>1600(C=O)</th>
<th>1570(C=C str.)</th>
<th>1510(C=N)</th>
<th>1156(C-O-C)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>9.20, 9.19(1H,s, CH of 2-pyrimidine)</td>
<td>7.30-7.60(5H,m,Ar-H bezylidenimin)</td>
<td>2.0(H,s, NH of amine)</td>
<td>2.74(3H,s,CH&lt;sub&gt;3&lt;/sub&gt; of (-N-C=O))</td>
<td>1.30(3H,s,CH&lt;sub&gt;3&lt;/sub&gt; of (-OC(=O)))</td>
<td>4.12(2H,s,CH&lt;sub&gt;2&lt;/sub&gt; methylene, (-OC(=O))N)</td>
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<td><strong>MS,m/z</strong>:312.3(M&lt;sup&gt;+&lt;/sup&gt;70.0%),391.14(100.0%),392.14(23.9%),393.15(2.2%),315.1(52%),152.2(39.8%)</td>
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<th>15</th>
<th>7.113d</th>
<th>3380(N-H str.)</th>
<th>3270(NH&lt;sub&gt;2&lt;/sub&gt;)</th>
<th>3000(C-H str.)</th>
<th>2975,1400(-CH&lt;sub&gt;2&lt;/sub&gt; next to C=O)</th>
<th>1650(C=O)</th>
<th>1540(C=C str.)</th>
<th>1510(C=N)</th>
<th>1156(C-O-C)</th>
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<td>9.20, 9.19(1H,s, CH of 2-pyrimidine)</td>
<td>7.30-7.60(5H,m,Ar-H bezylidenimin)</td>
<td>2.74(3H,s,CH&lt;sub&gt;3&lt;/sub&gt; of (-N-C=O))</td>
<td>2.0(H,s, NH of amine)</td>
<td>1.30(3H,s,CH&lt;sub&gt;3&lt;/sub&gt; of (-OC(=O)))</td>
<td>4.12(2H,s,CH&lt;sub&gt;2&lt;/sub&gt; methylene, (-OC(=O))N)</td>
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<td><strong>MS,m/z</strong>:312.3(M&lt;sup&gt;+&lt;/sup&gt;70.0%),392.16(100.0%),393.16(24.6%),394.17(2.4%),315.1(52%),152.2(39.8%)</td>
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<th>16</th>
<th>7.114a</th>
<th>3370(N-H str.)</th>
<th>2980(C-H str.)</th>
<th>2980,1400(-CH&lt;sub&gt;2&lt;/sub&gt; next to C=O)</th>
<th>1680(C=O)</th>
<th>1585(C=N)</th>
<th>1525(C=C str.)</th>
<th>1156(C-O-C)</th>
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<td></td>
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<td>9.20, 9.19(1H,s, CH of 2-pyrimidine)</td>
<td>7.29-7.62(5H,s, Ar-H, benzylidenimin)</td>
<td>4.0(H,s, Ar-C-NH of amine)</td>
<td>1.30(3H,s,CH&lt;sub&gt;3&lt;/sub&gt; of (-OC(=O)))</td>
<td>4.12(2H,s,CH&lt;sub&gt;2&lt;/sub&gt; methylene, (-OC(=O))N)</td>
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<td><strong>MS,m/z</strong>:412.3(M&lt;sup&gt;+&lt;/sup&gt;70.0%),440.16(100.0%),312.3(M&lt;sup&gt;+&lt;/sup&gt;70.0%),391.14(100.0%),392.14(23.9%),393.15(2.2%),315.1(52%),152.2(39.8%)</td>
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| 17  | 7.114b | 3300(N-H str.)  
3010(C-H str.)  
2975, 1400(-CH₂ next to C=O)  
1600(C=O)  
1589(C=N)  
1568(C=C str.)  
710(C-S-C)  
688(C-S str.) | 9.20, 9.19(1H, s, CH of 2-pyrimidine)  
2.74(3H, s, CH₃ of -N-C=O)  
7.0-7.20(4H, m, Ar-H)  
7.29-7.62(5H, s, Ar-H, benzylidenimin)  
1.30(3H, s, CH₃ of -OC(=O))  
4.12(2H, s, CH₂ methylene, -OC(=O)N) | MS, m/z: 412.3(M⁺70.0%), 457.12(100.0%), 458.12(29.3%), 459.12(5.2%), 315.1(52%), 152.2(39.8%) | 177.0(C of carbonyl)  
162.8(C of 1-amide)  
76, 122 (C of ethylene(-NC=O))  
Ar-C[145.8(CH), 146.0(CH), 141.7(C), 142.3(CH) pyrimidine]  
Ar-C[153.9(C), 126.0(CH), 122.3(CH), 126.6(CH), 127.3(CH), 130.5(CH)]  
Ar-C[131.2(C), 129.0(CH), 128.6(CH), 130.8(CH), 128.6(CH), 129.0(CH)]  
Ar-C[129.4(CH) 13.3(CH), 57.3(CH₂)]  
149.4(C of 1-amide)  
164.6(C of 1-imine)  
177.0(C of carbonyl)  
162.8(C of 1-amide)  
88.122 (C of ethylene(-NC=O)) |
| 18  | 7.114c | 3370(N-H str.)  
2975(C-H str.)  
2990, 1400  
1680(C=O)  
1579(C=N)  
1565(C=C str.)  
1096(C-O-C)  
1156(C-O-C) | 9.20, 9.19(1H, s, CH of 2-pyrimidine)  
2.74(3H, s, CH₃ of -N-C=O)  
6.70-7.10(4H, m, Ar-H)  
7.29-7.62(5H, s, Ar-H, benzylidenimin)  
1.30(3H, s, CH₃ of -OC(=O))  
4.12(2H, s, CH₂ methylene, -OC(=O)N) | MS, m/z: 412.3(M⁺70.0%), 441.14(100.0%), 442.15(27.1%), 443.15(4.3%), 315.1(52%), 152.2(39.8%) | 177.0(C of carbonyl)  
162.8(C of 1-amide)  
77.132 (C of ethylene(-NC=O))  
Ar-C[145.8(CH), 146.0(CH), 141.7(C), 142.3(CH) pyrimidine]  
Ar-C[141.70(CH), 150.2(CH), 122.7(CH), 124.0(CH), 127.7(CH), 118.3(CH)]  
Ar-C[131.2(CH), 129.0(CH), 128.6(CH), 130.8(CH), 128.6(CH), 129.0(CH)]  
Ar-C[26.8(CH) 13.3(CH), 57.3(CH₂)]  
149.4(C of 1-amide)  
164.6(C of 1-imine)  
177.0(C of carbonyl)  
162.8(C of 1-amide)  
88.122 (C of ethylene(-NC=O)) |
7.6 Interpretation of spectral data for the elucidation of structure of compounds

Structure of all the compounds were established on the basis of elemental analyses, IR, $^1$H NMR, $^{13}$C NMR and MS spectral data. Physical data of all the compounds were found to be consistent to the structures assigned to these molecules. The physical data, microanalyses, infrared, $^1$H NMR, $^{13}$C NMR and MS spectral data of all the compounds are given in table 7.1 and 7.2 and the spectral graphs are presented at the end of this chapter.

Infrared spectra:

Infrared spectrum of 7.099 on KBr pellet exhibited peak at 3240 cm$^{-1}$ [N-H str. of pyrimidine ring] and a peak at 1712 cm$^{-1}$ for [C=O attached with pyrimidine ring] which provided a strong evidence for the formation of 7.099 from 7.098. The IR spectrum of 7.099 also exhibited bands at 2990 cm$^{-1}$ [C-H str.], 2900, 1400 cm$^{-1}$ [CH$_2$ next to C=O], 1535 cm$^{-1}$ [C=C str.].

Formation of 7.100 from 7.099 was ascertained by the appearance of additional peaks at 3500 cm$^{-1}$ [O-H str. of COOH] and twin peak at 1712 cm$^{-1}$, 1704 cm$^{-1}$ for two [C=O attached with pyrimidine ring], peak at 1535 [due to C=C str. of benzene ring], also exhibited 3000 [due to C-H str.] and peak at 1630 [due to C=N str.]. Other peaks in the IR spectrum of 7.100 were found to be present almost in the same region as of 7.099.

The formation of acid hydrazide derivative 7.101 from 7.100 was ascertained by the appearance of peak at a medium intensity band at 1620 cm$^{-1}$ [for C=C of α,β-unsaturated ketone] and by the disappearance of peak for [NH] group, along with this IR spectrum also exhibited bands at 3270 cm$^{-1}$ [N-H str.], 2990 cm$^{-1}$ [C-H str.], 2970 and 1400 cm$^{-1}$ [-CH$_2$ next to C=O], 1625 [due to C=N str.], 1535 cm$^{-1}$ [C=C str.], 680 cm$^{-1}$ [C-S str.]

The formation of 7.103 from 7.101 was ascertained by the disappearance of peak for [-NH] group of 7.100 and the appearance of peaks at 3290 cm$^{-1}$ [N-H str.], 3010 cm$^{-1}$ [C-H str.], 2900, 1400 cm$^{-1}$ [CH$_2$ next to C=O], 1680, cm$^{-1}$ 1712 cm$^{-1}$, 1704 cm$^{-1}$ for three [C=O str.], 1535 cm$^{-1}$ [C=C str.], 1340, 680 cm$^{-1}$ [C-S] in its IR spectrum. Appearance of additional peak at 1165 cm$^{-1}$ for [C-O-C str. of diazole ring] provided a strong evidence for the formation of 7.103 from 7.101.

Infrared spectrum of 7.104 on KBr pellet exhibited strong absorption bands at 1640 cm$^{-1}$ and 1685 cm$^{-1}$ for the carbonyl group of CONH and for the another CO group respectively and a medium intensity band at 1620 cm$^{-1}$ [for C=C of α,β-unsaturated ketone], along with this IR spectrum also exhibited bands at 3240 cm$^{-1}$ [N-H str.], 3000 cm$^{-1}$ [C-H str.], 2900 and 1400 cm$^{-1}$ [-CH$_2$ next to C=O], 1535 cm$^{-1}$ [C=C str.], 680 cm$^{-1}$ [C-S str.]
Appearance of additional peaks at 3210 cm\(^{-1}\) [NH of pyrazole ring], 1515 cm\(^{-1}\) [C=N], 690 cm\(^{-1}\) [C-S str.] in the IR spectrum of compound 7.111 clearly indicated the formation of pyrazole ring in 7.111. Along with this, its IR spectrum also exhibited bands at 3390 cm\(^{-1}\) [NH str.], 3090 cm\(^{-1}\) [C-H str.], 2990 and 1400 cm\(^{-1}\) [-CH\(_2\) next to C=O], 1600 cm\(^{-1}\) [C=O], 1590 cm\(^{-1}\) [C=C str.]. The formation of 7.111 from 7.104 was further supported by the disappearance of band for C=C of unsaturated ketone at 1620 cm\(^{-1}\) of 7.104 in the IR spectrum of compound 7.111. This clearly indicated the formation of pyrazole ring in 7.111 from its precursor 7.104.

The formation of compound 7.112 from 7.104 was ascertained by the appearance of two strong absorption bands at 1510 cm\(^{-1}\) [C=N] and 900 cm\(^{-1}\) [C–O–N str. of isoxazole ring]. Along with this, its IR spectrum also exhibited bands at 3300 cm\(^{-1}\) [N-H str.], 3010 cm\(^{-1}\) [C-H str.], 2990 and 1400 cm\(^{-1}\) [-CH\(_2\) next to C=O], 1600 cm\(^{-1}\) [C=O], 1580 cm\(^{-1}\) [C=C str.], 695 cm\(^{-1}\) [C-S str.]. The formation of 7.112 from 7.104 was supported by the disappearance of band for C=C of α,β-unsaturated ketone at 1620 cm\(^{-1}\) of 7.104 in the IR spectrum of compound 7.112. In this way, the formation of isoxazole ring in 7.112 from its precursor 7.104 was ascertained by IR spectrum.

The formation of compound 7.113a from 7.104 was indicated by the appearance of strong absorption bands at 1500 cm\(^{-1}\) [C=N] and 1710 cm\(^{-1}\) [C=O of pyrimidine ring]. Along with this, its IR spectrum also exhibited bands at 3380 cm\(^{-1}\) [N-H str.], 3000 cm\(^{-1}\) [C-H str.], 2980 and 1400 cm\(^{-1}\) [-CH\(_2\) next to C=O], 1670 cm\(^{-1}\) [C=O], 1570 cm\(^{-1}\) [C=C str.], 685 cm\(^{-1}\) [C-S str.]. The formation of 7.113a from 7.104 was supported by the disappearance of band for C=C of α,β-unsaturated ketone at 1620 cm\(^{-1}\) in the IR spectrum of compound 7.113a. In this way, the formation of pyrimidine ring in compound 7.113a from its precursor 7.104 was strongly corroborated by its IR spectrum. Similar spectral interpretations established the formation of 7.113b, 7.113c and 7.113d from 7.104 respectively.

Appearance of additional peaks at 1585 cm\(^{-1}\) [C=N] and 697 cm\(^{-1}\) [C-S str.] in the IR spectrum of compound 7.114a, indicated clearly the incorporation of 1,5-diazepine ring in compound 7.114a. The formation of 7.114a from 7.104 was supported by the disappearance of band for C=C of α,β-unsaturated ketone at 1620 cm\(^{-1}\) in the IR spectrum of compound 7.114a. Similar spectral interpretations substantiated the formation of 7.114b and 7.114c from 7.104.

\(^1\)H NMR spectra:

The \(^1\)H NMR spectrum of 7.099 in DMSO-d\(_6\)-CDCl\(_3\) displayed signals for the presence of eight protons, a singlet for one proton at δ 8.0 was due to a secondary amide function, two singlets at
δ 9.29 and δ 9.10 were attributed to two protons of pyrimidine ring. In addition to this, a singlet for 2H which appeared at δ4.12 was attributed to the one methylene (CH₂) and a singlet for 3H at δ1.30 was attributed to one methyl (CH₃) group.

The ¹H NMR spectrum of 7.100 has the same δ 9.29 and δ 9.10 value of two singlet peaks as above for pyrimidine ring, δ4.12 for ethylene, δ 8.0 for secondary amide and δ1.30 for methyl, also exhibited a multiplet at δ 7.37-7.86 for five protons of benzene ring and a singlet for 2H at δ4.22 was attributed to another methyl group, which provided a strong evidence for the formation of compound 7.100 from 7.099. For 7.101 with the same pyrimidine two singlet peaks at δ 9.29 and 9.10 due to 2H same as above, a multiplet at δ 7.45-7.81 was due to five protons of second benzene ring. A distinguishing feature in the spectrum of 7.101 which established its formation from 7.100 was the appearance of two singlet peaks for six protons at δ 2.25 was of a methyl functional group of –SCH₃, a singlet at δ 4.12 was for two protons of methylene (CH₂) group and a singlet which appeared at δ 1.30 was attributed to the presence of three proton of methyl group (CH₃) respectively.

The ¹H NMR spectrum of 7.103, exhibited a multiplet at δ 7.45-7.81 for five protons of benzene ring, two singlets at δ 8.90 and 8.79 were for two protons of pyrimidine ring, a singlet for three protons at δ 1.30 was of a methyl carbonyl-amide functional group, a singlet at δ 4.12 for two protons of methylene (CH₂) attached to diazeppine ring and two singlets which appeared at δ 2.25 and δ 2.74 were attributed to the presence of three protons of methyl of –S-C=O and three protons of methyl group attached with carbonyl respectively.

The ¹H NMR spectrum of 7.104 in DMSO-d₆-CDCl₃ displayed signals for the presence of 18 protons. Their assignments attributed a singlet for one proton at δ 1.30 of a methyl attached to carbonyl function, a multiplet at δ 7.45-7.81 for five protons of diazepine ring, also exhibited two singlet at δ 9.20 and 9.19 for two protons of pyrimidine ring, and a singlet at δ4.12 for two protons of methylene (CH₂) of diazepine ring. In addition to this, a upfield singlet for six protons which appeared at δ2.74 and δ2.25 was attributed to the two methyl groups attached to the sulphur atoms in the α,β-unsaturated ketone structure and amide group attached to carbonyl function. Formation of oxoketene dithioacetal 7.104 from 7.103 was confirmed by the ¹H NMR spectrum which showed the upfield singlet for six protons at δ2.74 and δ2.25 was attributed to the two methyl groups attached to the sulphur atoms in the α,β-unsaturated ketone structure and amide group attached to carbonyl function.
The $^1$H NMR spectrum of 7.105, exhibited a multiplet at δ 7.45-7.81 for five protons of benzene ring, two singlets at δ 9.20 and 9.19 for two protons of pyrimidine ring others peaks are all same for 7.105. For 7.106 two singlets at δ 9.26 and δ 8.78 was attributed for two protons of pyrimidine ring, also exhibited a multiplet at δ 7.29-7.62 for five protons of diazepine ring (benzylidenimin) has a singlet for one proton at δ 7.40 of 1,2,3triazole function, a singlet at δ 4.81 and δ 4.12 for two protons of methylene (CH$_2$) attached to diazepine ring. In addition to this, two singlet which appeared at δ 2.74 and δ 2.25 in upfield region for three protons of methyl group attached to –N-C=C and –S-C=C of ring and a singlet at δ 1.30 for one proton of a methyl carbonyl function provided a strong evidence for the formation of compound 7.105 from 7.106.

The $^1$H NMR spectrum of compound 7.109, exhibited a multiplet at δ 7.45-8.78 for five protons of benzene ring, two singlets at δ 9.26 and δ 8.78 for two protons of pyrimidine ring, a singlet at δ 1.30 for one proton of a methyl carbonyl function, a singlet at δ 4.12 for two protons of methylene (CH$_2$) attached to diazepine ring. For 7.110 exhibited two singlets at δ 9.26 and δ 8.78 for two protons of pyrimidine ring, a multiplet at δ 7.29-7.62 for five protons of diazepine ring (benzylidenimin), one singlets which appeared at δ 7.56 were attributed to the presence for one proton of (NH) of 1,2,3-triazole ring, one singlet peat at δ1.30 was attributed for methyl group and two singlet peaks at δ4.81 and δ4.20 for methylene group attached to diazepine ring respectively which provided a strong evidence for the formation of compound 7.110 from 7.109.

The $^1$H NMR spectrum of 7.111 exhibited two singlets at δ 9.20 and 9.19 for two protons of pyrimidine ring, a singlet for one proton at δ 13.7 of a secondary amide(-NH) function, a multiplet at δ 7.22-7.48 for five protons of benzene ring, a singlet at δ4.12 for two protons of methylene (CH$_2$) of diazepine ring. In addition to this, a singlet for three protons which appeared at δ2.74 was attributed to the methyl group attached to the sulphur atoms in pyrazole ring and a singlet at δ 1.30 for one proton of a methyl carbonyl function. A distinguishing feature in $^1$H NMR spectrum of 7.111 which established its formation from 7.104 was the appearence of a highly downfield broad singlet for 1H at δ13.70 attributable to NH group of pyrazole ring.

$^1$H NMR spectrum of 7.112 exhibited a singlet for one proton at δ 1.30 of a methyl group attached to carbonyl function, two singlets at δ 9.20 and 9.19 for two protons of pyrimidine ring, a multiplet at δ 7.22-7.48 for five protons of diazepine ring, a singlet at δ4.12 for two protons of methylene (CH$_2$) of diazepine ring. In addition to this, a singlet for 3H which appeared at δ2.74 was attributed to the methyl group attached to the sulphur atoms in isoxazole ring. The loss of one -SCH$_3$.
group from 7.112 provided the strong evidence for the formation of isoxazole ring in 7.112 from 7.104.

The $^1$H NMR spectrum of 7.113a in DMSO-d$_6$-CDCl$_3$ exhibited a singlet for one proton at $\delta$ 8.0 of a secondary amide(-NH) function, a multiplet at $\delta$ 7.30-7.60 for five protons of aromatic diazepine ring (benzylidenimin), a singlet for one proton at $\delta$ 1.30 of a methyl group attached to carbonyl function, two singlets at $\delta$ 9.20 and 9.19 for two protons of pyrimidine ring, a singlet at $\delta$4.12 for two protons of methylene (CH$_2$) of diazepine ring, and a singlet at $\delta$ 2.74 for three protons of methyl (CH$_3$) group attached to sulphur atom. In addition to this, a singlet for 1H which appeared at $\delta$8.0 was attributed to NH group of pyrimidine ring, which provided a strong evidence for the formation of pyrimidine ring in 7.113a from 7.104.

The $^1$H NMR spectrum of 7.113b in DMSO-d$_6$-CDCl$_3$ exhibited a singlet for one proton at $\delta$ 2.0 of a secondary amide(-NH) function, which provided a strong evidence for the formation of pyrimidine ring in 7.113b from 7.104. Rest is the similar spectral interpretations with 7.113a which established the formation of compounds 7.113b from 7.104 respectively.

The $^1$H NMR spectrum of 7.113c exhibited a singlet for one proton at $\delta$ 2.0 of a secondary amide (-NH) function, two singlets at $\delta$ 9.20 and 9.19 for two protons of pyrimidine ring, a multiplet at $\delta$ 7.30-7.60 for five protons of aromatic diazepine ring (benzylidenimin), a singlet at $\delta$4.12 for two protons of methylene (CH$_2$) of diazepine ring, a singlet at $\delta$2.74 for three protons of methyl (CH$_3$) group attached to sulphur atom. In addition to this, a singlet for three protons which appeared at $\delta$1.30 was attributed to the protons of methyl group attached to pyrimidine ring. The loss of one SCH$_3$ group from 7.113c provided a strong evidence for the formation of pyrimidine ring in 7.113c from 7.104.

Similar spectral interpretations established the formation of compounds 7.113d from 7.104 respectively, except two peaks at $\delta$1.32 and $\delta$4.44 were attributed to the three protons of methyl group of nitrogen atom and one proton of methine this clearly established a strong evidence for the formation of pyrimidine ring in 7.113d from 7.104.

The $^1$H NMR spectrum of 7.114a exhibited a singlet for one proton at $\delta$ 4.0 of a secondary amide function attached to aromatic ring,, two singlets at $\delta$ 9.20 and 9.19 for two protons of pyrimidine ring, a singlet for one proton at $\delta$ 1.30 of a methyl group attached to carbonyl function, a multiplet at $\delta$ 7.29-7.62 for five protons of aromatic diazepine ring (benzylidenimin), a singlet at $\delta$4.12 for two protons of methylene (CH$_2$) of diazepine ring. In addition to this, a singlet for three
protons which appeared at δ2.74 was attributed to the methyl group attached to the sulphur atom. A distinguishing feature in $^1$H NMR spectrum of 7.114a which established its formation from 7.104 was the appearance of broad singlet for 1H at δ4.0 which was attributed to NH group of 1,5-diazepine ring. The formation of 7.114a from 7.104 was further supported by the appearance of multiplet for 4H in the region of δ 6.50-7.0 which was attributed to four protons of benzene ring of 1,5-benzodiazepine nucleus in 7.114a.

The $^1$H NMR spectrum of 7.114b showed similar spectral interpretations established the formation of compounds 7.113b from 7.104 respectively, except the presence of multiplet for 4H in the region of δ 7.0-7.20 which were assigned to four protons of benzene ring of 1,5-benzothiazepine nucleus in 7.114b. It provided a strong evidence for the formation of thiazepine ring in 7.114b from 7.104. This clearly established the formation of 7.114b from its precursor 7.104.

The $^1$H NMR spectrum of 7.114c showed similar spectral interpretations established the formation of compounds 7.114c from 7.104 respectively, except the presence of multiplet for 4H in the region of δ 6.70-7.10 which were assigned to four protons of benzene ring of 1,5-benzoxazepine nucleus in 7.114c. It provided a strong evidence for the formation of oxazepine ring in 7.114c from 7.104. This clearly established the formation of 7.114c from its precursor 7.104.

Mass spectra:

Mass spectrum of 7.099 gave peaks at m/z 193.1(M$^+$ 70%), 175.4(25.6%), 192.06(100.0%). The molecular ion peak which appeared at m/z 193.1 (M$^+$ 70%) provided a strong evidence for its molecular weight. The base peak which appeared at m/z 192.06 (100%) substantiated further the structure assigned to this molecule.

Mass spectrum of 7.100 gave peaks at m/z 322.2(M$^+$ 70%), 311.11(18.1%), 310.11(100.0%), 312.11(2.4%), 217.14(21.4%). The molecular ion peak which appeared at m/z 322.2 (M$^+$ 70%) provided a strong evidence for its molecular weight. The base peak which appeared at m/z 310.11 (100%) substantiated further the structure assigned to this molecule.

Mass spectrum of 7.101 gave peaks at m/z 336.3(M$^+$ 80%), 318.1(19.5%), 414.08(100.0%), 416.09(9.5%), 415.09(21.5%). The molecular ion peak which appeared at m/z 336.3 (M$^+$ 80%) provided a strong evidence for its molecular weight. The base peak which appeared at m/z 414.08 (100%) substantiated further the structure assigned to this molecule.

Mass spectrum of 7.103 gave peaks at m/z 378.3(M$^+$ 30%), 397.12(100.0%), 398.12(28.0%), 141.0(23%), 399.12(4.9%). The molecular ion peak which appeared at m/z 378.3 (M$^+$
30%) provided a strong evidence for its molecular weight. The base peak which appeared at m/z 397.12 (100%) substantiated further the structure assigned to this molecule.

Mass spectrum of 7.104 gave peaks at m/z 378.3 (M\(^+\)70.0%), 399.11 (21.6%), 398.10(100%), 398.11(24.3%), 400.10(4.5%). The molecular ion peak which appeared at m/z 388.3 (M\(^+\)70%) provided a strong evidence for its molecular weight. The base peak which appeared at m/z 398.10(100%) substantiated further the structure assigned to this molecule.

Mass spectrum of 7.105 gave peaks at m/z 388.3 (M\(^+\)70.0%), 351.4(29.9%), 393.12(100%),394.13(23.0%), 395.13(2.0%). The molecular ion peak which appeared at m/z 388.3 (M\(^+\)70%) provided a strong evidence for its molecular weight. The base peak which appeared at m/z 393.12 (100%) substantiated further the structure assigned to this molecule.

Mass spectrum of 7.106 gave peaks at m/z 377.3 (M\(^+\)27.0%), 395.18(31.9%), 430.13(100%),394.13(23.0%), 395.13(2.0%). The molecular ion peak which appeared at m/z 377.3 (M\(^+\)27%) provided a strong evidence for its molecular weight. The base peak which appeared at m/z 430.13 (100%) substantiated further the structure assigned to this molecule.

Mass spectrum of 7.109 gave peaks at m/z 292.4 (M\(^+\)70.0%), 277.0(20.0%), 336.10 (100%), 337.10(18.1%), 338.10(2.5%). The molecular ion peak which appeared at m/z 292.4 (M\(^+\)70%) provided a strong evidence for its molecular weight. The base peak which appeared at m/z 336.10 (100%) substantiated further the structure assigned to this molecule.

Mass spectrum of 7.110 gave peaks at m/z 312.3 (M\(^+\)70.0%), 315.1(52%), 373.13(100%),374.13(24.0%), 375.14(2.2%). The molecular ion peak which appeared at m/z 312.3 (M\(^+\)70%) provided a strong evidence for its molecular weight. The base peak which appeared at m/z 373.13 (100%) substantiated further the structure assigned to this molecule.

Mass spectrum of compound 7.104 gave peaks at m/z 378.3 (M\(^+\)70.0%), 399.11 (21.6%), 398.10(100%), 398.11(24.3%), 400.10(4.5%). The molecular ion peak which appeared at m/z 388.3 (M\(^+\)70%) provided a strong evidence for its molecular weight. The base peak which appeared at m/z 398.10(100%) substantiated further the structure assigned to this molecule.

Mass spectrum of compound 7.111 gave peaks at m/z 312.3 (M\(^+\)80.0%), 315.10 (52%), 364.13(100%), 365.13(22.6%), 366.14(2.0%) gave peaks at m/z. The molecular ion peak which appeared at m/z 312.3 (M\(^+\)80%) provided a strong evidence for its molecular weight. The base peak which appeared at m/z 364.13(100%), substantiated further the structure assigned to this molecule.
Mass spectrum of compound 7.112 gave peaks at m/z 312.30 (M^+70%), 365.11 (100.0%), 366.12 (20.4%), 179.47 (34.8%), 148.05 (25.0%), 109.41 (37.5%), 152.20 (39.8%). The molecular ion peak which appeared at m/z 312.30 (M^+70%) provided a strong evidence for its molecular weight. The base peak which appeared at m/z 365.11 (100%) substantiated further the structure assigned to this molecule.

Mass spectrum of compound 7.113a gave peaks at m/z 312.30 (M^+70.0%), 392.12 (100.0%), 393.13 (21.5%), 394.13 (3.0%), 315.1 (52%), 152.2 (39.8%). 7.113b gave peaks at m/z 312.30 (M^+70.0%), 315.10 (52%), 408.10 (100%), 409.10 (24.3%), 410.10 (5.7%), 152.2 (39.8%). 7.113c gave peaks at m/z 312.30 (M^+70.0%), 391.14 (100%), 392.14 (23.9%), 393.15 (2.2%), 315.1 (52%), 152.2 (39.8%). 7.113d gave peaks at m/z 312.30 (M^+70.0%), 392.16 (100%), 393.16 (24.6%), 394.17 (2.4%), 315.1 (52%), 152.2 (39.8%). The molecular ion peak which appeared at m/z 312.3 (M^+70%) provided a strong evidence for its molecular weight. The base peak which appeared at m/z 392.12 (100%), 408.10 (100%), 391.14 (100%), 392.16 (100%) was attributed for 7.113a, 7.113b, 7.113c, 7.113d substantiated further the structure assigned to this molecule.

Mass spectrum of compound 7.114a gave peaks at m/z 412.30 (M^+70.0%), 440.16 (100.0%), 441.16 (29.0%), 442.16 (3.5%), 315.1 (52%), 152.2 (39.8%). 7.114b gave peaks at m/z 412.30 (M^+70.0%), 315.10 (52%), 457.12 (100%), 458.12 (29.3%), 459.12 (5.2%), 152.2 (39.8%). 7.114c gave peaks at m/z 412.30 (M^+70.0%), 441.14 (100%), 442.15 (27.1%), 443.15 (4.3%), 315.1 (52%), 152.2 (39.8%). The molecular ion peak which appeared at m/z 312.3 (M^+70%) provided a strong evidence for its molecular weight. The base peak which appeared at m/z 440.16 (100%), 457.12 (100%), 441.14 (100%) was attributed for 7.114a, 7.114b, 7.114c substantiated further the structure assigned to this molecule.

In a likewise manner the molecular weights of the compounds were ascertained on the basis of mass spectrum.

\(^{13}\text{C} \text{NMR spectra:}\)

\(^{13}\text{C} \text{NMR spectrum of 7.099 in CDCl}_3\) displayed signals for the presence of 18 carbons, peaks at \(\delta 148.60, \delta 146.10, \delta 147.90, \delta 126.30\) for four carbons of pyrimidine ring, peaks at \(\delta 196.50\) for one carbon of (C=O) attached to pyrimidine ring, peaks at \(\delta 118.0, \delta 154.80\) were attributed for the remaining one carbon for nitrile and one carbon for amide attached with pyrimidine ring, peaks at
δ 13.3, δ 56.90 were due to one carbon of methyl (CH$_3$) and one carbon methylene (CH$_2$) attached to pyrimidine ring.

$^{13}$C NMR spectrum of 7.100 in CDCl$_3$ displayed signals for the presence of 18 carbons, peaks at δ 148.60, δ 146.10, δ 147.90, δ 126.30 for four carbons of pyrimidine ring, peaks at δ 196.50 for one carbon of (C=O) attached to pyrimidine ring, peaks at δ 118.0, δ 153.30 were attributed for the remaining one carbon for nitrile and one carbon for amide attached with pyrimidine ring. The formation of 7.100 was confirmed by the appearance of additional peaks at δ137.40, δ 128.60, δ 128.40, δ 132.90, δ 128.40, δ 128.60 for six carbons of benzene ring and peaks at δ 13.3, δ 59.70 and δ 57.20 were due to one carbons of methyl (CH$_3$) and two carbon methylene (CH$_2$) attached to pyrimidine ring.

The formation of 7.101 was confirmed by the appearance of additional peaks at δ136.70, δ 129.70, δ 129.0, δ 134.30, δ 129.0, δ 129.70 for six carbons of benzene ring and peaks at δ 13.3, and δ 57.30 were due to one carbons of methyl (CH$_3$) and one carbon methylene (CH$_2$) attached to pyrimidine ring, peaks at δ 107.30, δ 142.50 were due to two carbons of ethylene (CH$_2$) in diazepine ring, peaks at δ 148.60, δ 146.10, δ 147.90, δ 126.30 for four carbons of pyrimidine ring, peaks at δ 187.0 for one carbon of carbonyl(C=O) attached to pyrimidine ring, peaks at δ 118.0, δ 149.40 were attributed for the remaining one carbon for nitrile and one carbon for amide attached with pyrimidine ring. In addition to this, peak at δ 142.50 for carbon of ethylene which contained two (SMe) groups confirmed the formation of 7.101 from 7.100. Formation of oxoketene dithioacetal 7.101 from 7.100 was further confirmed by their $^{13}$C NMR spectra which showed the same peak for two carbons at δ 13.2 and δ 13.2 for the two methyl carbons attached to the sulphur atoms.

With the same pyrimidine and benzene ring δ value The formation of 7.103 was confirmed by the appearance of additional peaks at δ 29.2, δ 11.7, δ 13.3 and δ 57.30 were due to three carbons of methyl (CH$_3$) and one carbon methylene (CH$_2$) attached to pyrimidine ring, peaks at δ 96.80, δ 144.50 were due to two carbons of ethylene (CH$_2$) in diazepine ring, peaks at δ 187.0 for one carbon of (C=O) attached to diazepine ring, peaks at δ 118.0, δ 149.40, δ 164.0 were attributed for the remaining one carbon for nitrile one carbon for amide and one carbon of imine attached with pyrimidine ring.

The formation of 7.104 was confirmed by the appearance of additional peaks at δ136.70, δ 129.70, δ 129.0, δ 134.30, δ 129.0, δ 129.70 for six carbons of benzene ring and peaks at δ 13.3, δ 29.4, δ 11.7 and δ 57.30 were due to three carbons of methyl (CH$_3$) and one carbon methylene (CH$_2$)
attached to pyrimidine ring, peaks at δ 99.0, δ 131.50 were due to two carbons of ethylene (CH\textsubscript{2}) in
diazepine ring, peaks at δ 145.80, δ 146.0, δ 141.70, δ 142.30 for four carbons of pyrimidine ring,
peaks at δ 187.0 for one carbon of (C=O) attached to diazepine ring, peaks at δ 149.40, δ 162.80
were attributed for the remaining two carbon for amide attached with pyrimidine ring.

The formation of azide derivative 7.105 from 7.104 was ascertained by the appearance of
peak at δ 164.80 for carbon of CON- group and appearance of peak at δ 117.0, δ 113.0 were due to
two carbons of ethylene (CH\textsubscript{2}) in diazepine ring.

A distinguishing feature in the spectrum of 7.106 which established its formation from 7.105
was the appearance of two peaks, at δ143.0 for carbon of 1,2,3-triazole(C-N) ring, at δ 131.0 for
another carbon of 1,2,3-triazole ring respectively. Similar spectral interpretations established the
formation of 7.106 from 7.105 except the appearance of additional peaks at δ 83.0, δ 112.0 were due
to two carbons of ethylene (CH\textsubscript{2}) in diazepine ring and at δ 164.6 was attributed for one carbon for
imine group.

The formation of 7.109 was confirmed by the appearance of additional peaks at δ 127.0, δ
111.0, δ 122.0, δ 132.0 for four carbons of pyrrole ring, peaks at δ133.20, δ 129.50, δ 128.60, δ
134.40, δ 128.60, δ 129.50 for six carbons of benzene ring and peaks at δ 13.3 and δ 57.30 were due
to one carbons of methyl (CH\textsubscript{3}) and one carbon methylene (CH\textsubscript{2}) attached to pyrimidine ring, peaks
at δ 158.0, δ 156.4 for two carbons of pyrimidine ring, peaks at δ 177.0 for one carbon of carbonyl
(C=O) attached to pyrrole ring, peaks at δ 161.0 were attributed for the remaining one carbon for
carboxyl group attached with pyrrole ring.

A distinguishing feature in the spectrum of 7.110 which established its formation from 7.109
was the appearance of two peaks at δ143.0 for one carbon of 1,2,3-triazole(C-N) ring, at δ 131.0 for
another carbon of 1,2,3-triazole ring respectively. The formation of 7.110 was confirmed by the
appearance of additional peaks at δ118.0, δ 108.0, δ 108.0, δ 118.0 for four carbons of pyrrole ring,
peaks at δ137.30, δ 129.0, δ 128.60, δ 130.80, δ 128.60, δ 129.0 for six carbons of benzene ring and
peaks at δ 13.3, δ 42.50 and δ 57.30 were due to one carbons of methyl (CH\textsubscript{3}) and two carbon
methylene (CH\textsubscript{2}) attached to diazepine ring, peaks at δ 158.0, δ 156.4 for two carbons of pyrimidine
ring, peaks at δ 177.0 for one carbon of (C=O) attached to pyrrole ring, peaks at δ 161.0 were
attributed for the remaining one carbon for carboxyl group attached with pyrrole ring, at δ 164.6 was
attributed for one carbon for imine group.
$^{13}$C NMR spectrum of 7.111 in CDCl$_3$ displayed signals for the presence of 19 carbons. The signals at $\delta$ 145.80, $\delta$ 146.0, $\delta$ 141.7, $\delta$ 142.30 were for four carbons of pyrimidine ring, peaks at $\delta$136.50, $\delta$ 127.0, $\delta$ 129.0, $\delta$ 128.50, $\delta$ 129.0, $\delta$ 127.0 for six carbons of benzene ring, at $\delta$ 13.3, $\delta$ 34.80 and $\delta$ 57.20 were due to two carbons of methyl (CH$_3$) and one carbon methylene (CH$_2$), peaks at $\delta$ 150.3 and $\delta$ 163.7 for carbon of amide, at $\delta$ 177.0 for carbon of carbonyl in diazepine ring, at $\delta$115.8, $\delta$ 144.20, $\delta$ 138.20 for the remaining three carbons of pyrazole ring which attached the -SMe in pyrazole ring.

A distinguishing feature in the spectrum of 7.112 which established its formation from 7.104 was the appearance of three peaks at $\delta$100.50, $\delta$150.50, $\delta$158.90, for carbon which attached the SMe in isoxazole ring with diazepine ring.

The formation of 7.113a from 7.104 was confirmed by the appearance of additional peak at $\delta$ 177.0 for carbon of carbonyl (C=O) of pyrimidine ring. The signals at $\delta$ 145.80, $\delta$ 146.0, $\delta$ 141.7, $\delta$ 142.30 were for four carbons of pyrimidine ring, peaks at $\delta$131.20, $\delta$ 129.0, $\delta$ 128.60, $\delta$ 130.80, $\delta$ 128.60, $\delta$ 129.0 for six carbons of benzene ring, at $\delta$ 27.6, $\delta$ 13.30 and $\delta$ 57.20 were due to two carbons of methyl (CH$_3$) and one carbon methylene (CH$_2$), peaks at $\delta$ 149.4, $\delta$ 160.0 and $\delta$ 162.8 for carbon of amide, peaks at $\delta$ 164.6 for carbon of 1-amine attached to in diazepine ring, peaks at $\delta$ 80.0, $\delta$ 114.0 were due to two carbons of ethylene (CH$_2$) in diazepine ring.

The formation of 7.113b from 7.104 was confirmed by the appearance of additional peak at $\delta$ 182.0 for carbon of thioamide (C=S) of pyrimidine ring and peaks at $\delta$ 78.0, $\delta$ 127.0 were due to two carbons of ethylene (CH$_2$) in diazepine ring.

A distinguishing feature in the spectrum of 7.113c which established its formation from 7.104 was the appearance of two additional peaks, at $\delta$163.0 $\delta$ 164.60 for carbon which contained imine group in pyrimidine ring, peaks at $\delta$ 78.0 $\delta$ 127.0 for carbon of ethylene of diazepine ring. Similar spectral interpretations established the formation of 7.113d from 7.104 except four additional peaks at $\delta$ 84.0, $\delta$ 148.4, $\delta$ 76.0, $\delta$ 116.0, for carbon of ethylene of diazepine ring. respectively.

A distinguishing feature in the spectrum of 7.114a which established its formation from 7.104 was the appearance of additional peaks at $\delta$ 139.8, 140.2, 122.8, 119.8, 127.8, 116.4 for six carbons of second benzene ring and peak at $\delta$ 76.0 and $\delta$ 122.0 for two carbon of ethylene (CH$_2$) flanked between benzene and sulphur.
The formation of 7.114b was confirmed by the presence of additional peaks at δ 153.9, 126.0, 122.3, 126.6, 127.3, 130.5 for six carbons of second benzene ring and peak at δ 88.0 and δ 122.0 for two carbon of ethylene (CH₂) flanked between benzene and sulphur.

The formation of 7.114c was confirmed by the presence of additional peaks at δ 141.70, 150.20, 122.7, 124.0, 127.7, 118.3 for six carbons of second benzene ring and peak at δ 77.0 and δ 132.0 for two carbon of ethylene (CH₂) flanked between benzene and sulphur.

7.7 Experimental section
1) The purity of the compounds was checked by TLC on silica gel (G) plates.
2) Melting points were determined in open glass capillaries and are uncorrected.
3) ¹H- NMR and ¹³C NMR spectra were recorded on model Avance II 400 (BRUKER) using DMSO-d₆ and CDCl₃ as solvent and TMS as an internal reference. Chemical shifts are expressed in δ ppm.
4) IR spectra were recorded on KBr (BRUKER) FTIR-8400 S.
5) Mass spectra were recorded on a 3000 LC/MS system.
6) Before analysis all samples were dried for one hour under reduced pressure.
7) Physical and spectral data for all compounds are given in table 7.1 and 7.2.

7.8 Synthetic procedures
Preparation of (4-Cyano-pyrimidine-5-y1)-carbamic acid ethyl ester (7.099):
To 5-amino-pyrimidine-4-carbonitrile (7.098) (0.14g, 0.02 mol) was mixed sodium carbonate (0.21g, 0.02mol) and to this dropwise ethyl chloro formate (2.0ml, 0.02 mol) in ethanol (5.0 ml) was added and the mixture was stirred continuously for 4 hrs at low temperature in ice bath. Cold reaction mixture was kept on continuous stirring to 150-200ml ice cold water. The solid which settled was filtered, washed with cold water, recrystallized from rectified spirit and water. The progress of the reaction was monitored by TLC. The reaction mixture was cooled to 2°C and a concentrated aqueous solution of Na₂CO₃ was added to make it alkaline. The product was extracted with ethyl acetate (3x10 ml). The violet coloured extract was dried over anhydrous Na₂SO₄ and concentrated in vacuum. The violet coloured residue was purified by column chromatography on silica gel with CHCl₃ as an eluent to give 7.099, 0.71g, yield (89%), m.p.159-160°C.

Preparation of (4-Cyano-pyrimidine-5-y1)-(2-oxo-2-phenyl-ethyl)-carbamic acid ethyl ester
(7.100):

A solution of (4-cyano-pyrimidine-5-yl)-carbamic acid ethyl ester (7.099) (0.86g, 0.01 mole) in DMF(4.0 ml) and ethanol (10.0ml) was stirred in cold bath. Sodium hydroxide (NAH) (0.7g, 0.01 mol) was added during stirring in ice cold bath at the same time. After 15 min. of continuous stirring phenacyl bromide (0.4g, 0.01mol) was added portionwise and solution was stirred overnight at room temperature. The solid which settled was filtered, washed with cold water, extracted with ethyl acetate organic layer was washed with brine solution and concentrated to yield a light brown solid. The progress of the reaction was monitored by TLC. The solid was covered with ether (20.0ml) evaporated on steam bath and filtered while hot to remove suspended starting material and impurities. After distillation of most of the solvent, water was added, the neutral impurities were removed by ether extraction. Further evaporation to 3ml on cooling gave dark violet crystals which were collected and recrystallized by methyl cyanide (MeCN) to give 7.100, 0.740g, yield (80.3%), m.p.165-169°C.

Preparation of (1-Benzoyl-2,2-bis methylsulfanyl-vinyl) - (4-cyano-pyrimidine-5-yl) - carbamic acid ethyl ester (7.101):

To a solution of (4-Cyano-pyrimidine-5-yl)-(2-oxo-2-phenyl-ethyl)-carbamic acid ethyl ester (7.100) (0.64g, 0.02 mol) in dry ethanol (20 ml), a mixture of carbon disulfide (0.64 ml, 0.04mol) and thus a cooled suspension of potassium tertiary butoxide (1.6g, 0.04mol) was added in dry benzene and DMF (10:6 ml ratio) at 0°C. The reaction mixture was allowed to stand at room temperature for 4 hrs. Methyl Iodide (2.82ml,0.02mol) was gradually added with stirring and external cooling (exothermic reaction) and the reaction mixture was allowed to stand for 4 hrs at room temperature with occasional shaking and then refluxed on a water bath for 4-6 hrs. After the completion of reaction (monitored by TLC), the aqueous portion was extracted with benzene and the combined extract were washed with water, pH was adjusted to neutral point with 5% aqueous HCl and filtered, dried over anhydrous sodium sulphate and the solvent was removed by distillation. The product thus obtained was purified by crystallization in ethyl acetate to give brown coloured solid mass which was also purified later by silica column and TLC (eluent: petroleum ether/EtOAc) (v:v = 8:2) to give the product 7.101, 1.1g. yield 82%, m.p. 179-180°C.
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Preparation of (1-Benzoyl-2-methylamino-2-methylsulfanyl-vinyl)- (4-cyano-pyrimidine-5-yl) carbamic acid ethyl ester (7.102), 6-Benzoyl-9-imino-8-methyl-7-methylsulfanyl-8,9-dihydro-pyrimido [5,4-e] [1,4] diazepine-5-carboxylic acid ethyl ester (7.103) and 6- Benzoyl-8-methyl-7-methylsulfanyl-9-oxo 8,9-dihydro-pyrimido [5,4-e][1,4]diazepine-5-carboxylic acid ethyl ester (7.104):

To 7.101 was added methyl amine and was subjected to protonolysis or hydrolysis. In a stepwise preparation a solution of compound 7.101 (0.5g,0.02mol) was taken with methyl amine (2ml,0.04ml) in DMF and to this a cooled suspension of potassium tertiary butoxide was added with continuous stirring in 1 hr to give 7.106 (yield:76%; m.p. 231-233 °C) and this was on refluxed for 3-4 hrs. for further cyclization to form compound 7.103 (yield:78%; m.p. 232-235 °C). The progress of reaction was monitored by TLC. The mixture was poured into ice water, pH was adjusted to neutral point by the addition of 5% HCl sol, and the mixture was dried through rotatory evaporator. The desired solid product 7.104 was obtained and purified by silica column and TLC (eluent: petroleum ether/EtOAc) (v:v = 8:2) (0.88g, yield: 80%; m.p. 235-237°C).

Preparation of 7-Azido-6-Benzoyl-8-methyl-9-oxo-8,9-dihydro-pyrimido[5,4-e][1,4]diazepine-5-carboxylic acid ethyl ester (7.105) and 1’,2’,3’-Triazolo-[b,e,]-[1,4]diazepino- pyrimido[b,d][1,4]diazepino-1-methyl-9-one -7'-phenyl-4-carboxylic acid ethyl ester (7.106):

To a stirred solution of 5.079 (1.3g, 0.02mol) in tertiary butanol and water (1:1mix, 5ml), copper sulfate (CuSO₄·5H₂O) (0.66g,0.02mol) and sodium ascorbate (2.8g, 0.02mol) were added to this reaction mixture. After 15 min. sodium azide (1.4g, 0.02mol) was added to the above mixture and the reaction mixture was stirred for 8h to give 7.105. The mixture was diluted with water and ethylacetate was added to it, the organic layer was separated and the aqueous layer was extracted with ethylacetate (20.0 ml). The combined organic layer were dried over anhydrous sodium sulfate and evaporated under reduced pressure to afford 7.105, which was precipitated using n-hexane –EtOAc affording pure 1,3-triazole containing product 7.105 as a light brown coloured viscous mass ( 0.96g, yield: 78%; m.p. 205-208°C).

To this was added propargyl amine (0.87g, 0.02mol) and kept on continuous stirring for 4-5 hrs to give product 7.106. The progress of the reaction was monitored by TLC. The mixture was poured into ice water and later ethylacetate was added to it. The organic layer was separated
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and the aqueous layer was extracted with ethylacetate (20.0 ml). The combined organic layer were dried over anhydrous sodium sulfate and evaporated under reduced pressure to afford 7.106. 1’,2’,3’-Triazolo-[b,e]-[1,4]diazepino-[b,d][1,4]diazepino-1-methyl-9-one - 7’-phenyl-4-carboxylic acid ethyl ester (7.106) as a thick brown colored viscous mass, which was dried through rotatory evaporator. The desired solid product 7.106 was obtained and purified by silica column and TLC (eluent: petroleum ether/EtOAc) (v:v = 8:2) (0.76g, yield: 75%; m.p. 213-215°C).

Preparation of 7-Amino-6-benzoyl-pyrrolo [3,2-d]pyrimidine-5-carboxylic acid ethyl ester (7.108):

A stirred solution of (4-cyano-pyrimidine-5-yl)-(2-oxo-2-phenyl-ethyl)-carbamic acid ethyl ester (7.100) (1.02g, 0.02mol) in DMF (2.5ml, 0.02mol) and kept on stirring for 15 min., sodium hydride (2.2g, 0.02mol) was portion wise added with continuous stirring and the solution was kept on stirring at room temperature for 3 hrs for cyclisation to give 7.108. The solid which settled was filtered, washed with cold water, extracted with ethyl acetate. Organic layer was washed with brine solution and concentrated to yield a light brown solid. The progress of the reaction was monitored by TLC. The solid covered with ether (4.0ml) was evaporated on steam bath and filtered while hot to remove suspended starting material and impurities. After distillation of most of the solvent, water was added, the neutral impurities were removed by ether extraction. The obtained solid mass was dried over anhydrous sodium sulfate and evaporated under reduced pressure and purified by silica column and TLC (eluent: petroleum ether/EtOAc) (v:v = 8:2) (0.86g, yield: 79%; m.p. 175-177°C).

Preparation of 4-Azido-6-benzoyl-pyrrolo [3,2-d]pyrimidine-5-carboxylic acid ethyl ester (7.109):

To a solution of compound 7.108 (0.96g, 0.02mol) was added a mixture of NaNO₂ solution in H₂O + HCl (1.30gm :1.37ml) (1:1) with continuous stirring at room temperature for 1 hr. After this a solution of NaN₃ was added and kept it for further stirring for two hrs at room temperature.

The solid which settled was filtered, washed with cold water, extracted with ethyl acetate. Organic layer was taken in ether and washed with brine solution and concentrated to yield a brown solid. The progress of the reaction was monitored by TLC. The solid covered with ether
(20.0ml) was evaporated on steam bath and filtered while hot to remove suspended materials and impurities. After distillation of most of the solvent, water was added, the neutral impurities were removed by ether extraction. Further evaporation to 3ml gave on cooling gave brown colored solid crystals which are collected and recrystallized by rectified spirit to give 7.109, 0.80g, yield (78%), m.p.183-185°C.

In an alternate method ionic liqid [bmim]Cl was used. In this method first [bmim]Cl (0.15g, 0.02mol) was stirred with NaNO₂ solution for half an hr to give [bmim]NO₂, to this solution itself NaN₃ solution was added with continuous stirring for 1 hr to give [bmim]N₃. To [bmim]N₃ solution, a solution of reactant 7.108 was added and kept on continuous stirring for 3hrs to give 7.109 as a brown colored solid which settled was filtered, washed with cold water, extracted with ethyl acetate organic layer was washed with brine solution and concentrated to yield a brown solid. The progress of the reaction was monitored by TLC. The solid covered with ether (20.0ml) was evaporated on steam bath and filtered while hot to remove suspended starting material and impurities. After distillation of most of the solvent, water was added, the neutral impurities were removed by ether extraction. Further evaporation to 3ml and cooling gave brown colored solid crystals which were collected and recrystallized by rectified spirit to give 7.109, 0.98g, yield (79%), m.p.183-185°C.

Preparation of 1,2',3'-Triazolo-[1,4]diazepine pyrimido – d -e- pyrrole-[b,c]-6-carboxylic acid ethyl ester (7.110):

To a stirred solution of 7.109 (1.3g, 0.02mol) was stirred in tertiary butanol and water (1:1mix, 5ml), CuSO₄.5H₂O (0.66g,0.02mol) and sodium ascorbate (2.8g, 0.02mol) were added to the reaction mixture and was further stirred for 15 min., then propargyl amine (0.87gm, 0.02mol) was added and was stirred for 4hr to give 7.110. The mixture was diluted with water and ethylacetate was added to it. The organic layer was separated and the aqueous layer was extracted with ethylacetate (20.0 ml). The combined organic layer were dried over anhydrous sodium sulfate and evaporated under reduced pressure to afford 7.110, which was precipitated using n-hexane –EtOAc affording pure 1,3-triazole containing product 7.110 as a light brown coloured viscous mass (0.96g, yield: 79%; m.p. 179-180°C).

To this solution of 7.109 before workup propargyl amine (0.87g, 0.02mol) was added and kept on continuous stirring for 4-5 hrs to give product 7.110. The progress of the reaction was monitored by TLC. The mixture was poured into ice water and later ethylacetate was added to it,
the organic layer was separated and the aqueous layer was extracted with ethylacetate (2*10 ml). The combined organic layer were dried over anhydrous sodium sulfate and evaporated under reduced pressure to afford, 1,2',3'-Triazolo-[1,4]diazepine pyrimido – d -e- pyrrole-[b,c]-6-carboxylic acid ethyl ester (7.110) as a thick brown colored viscous mass, which was dried through rotatoy evaporator. The desired solid product 7.110 was obtained and purified by silica column and TLC (eluent: petroleum ether/EtOAc) (v:v = 8:2) (0.81g, yield: 75%; m.p. 195-198°C).

**Preparation of 10-methyl-9-oxo-3-phenyl-9,10-dihydro-1H-1,2,4,6,9,10-hexaaza-benzo[f]azulene-4- carboxylic acid ethyl ester (7.111):**

Hydrazine hydrate (1.0ml, 0.04mol) was added to a solution of sodium methoxide (1.12g, 0.06mol) in absolute methanol(15ml) and was stirred for 10 min. To this mixture, 6- benzoyl-8-methyl-7-methylsulfanyl-9-oxo 8,9-dihydro-pyrimido [5,4-e][1,4]diazepine-5-carboxylic acid ethyl ester (7.104) (1.54g, 0.04mol)was added after which the solvent was evaporated under reduced pressure. The mixture was then poured on crushed ice. The solid mass was separated by filtration, washed with di ethyl ether, dried and recrystallized from ethanol. The desired solid product 7.111 was obtained and purified by silica column and TLC (eluent: petroleum ether/EtOAc) (v:v = 8:2) (0.76g, yield: 72%; m.p. 223-225°C).

**Preparation of 10-Methyl-9-oxo-3-phenyl-9,10-dihydro-1-oxa-4,6,8,10-tetraaaza-benzo[f]azulene-4- carboxylic acid ethyl ester (7.112):**

Hydroxylamine hydrochloride (1.78g, 0.04mol) was added to a solution of sodium methoxide (2.12g, 0.04mol) in absolute methanol (15ml) and was stirred for 10 min., to this mixture, 6-benzoyl-8-methyl-7-methylsulfanyl-9-oxo 8,9-dihydro-pyrimido [5,4-e][1,4]diazepine-5-carboxylic acid ethyl ester (7.104) (1.54g, 0.04mol) was added and the mixture was evaporated under reduced pressure. The mixture was then poured on crushed ice. The solid mass was separated by filtration, washed with diethyl ether, dried and recrystallized from ethanol. The desired solid product 7.112 was obtained and purified by silica column and TLC (eluent: petroleum ether/EtOAc) (v:v = 8:2) (0.86g, yield: 80%; m.p. 232-235°C).

**Preparation of 10-Methyl-10,11-dioxo-6-phenyl-8,9,10,11-tetrahydro-1,3,5,7,9,10-hexaaza-dibenzo[a,d]cycloheptane-5-carboxylic acid ethyl ester (7.113 a):**
To a mixture of urea (1.52g, 0.02mol), sodium ethoxide (0.14g, 0.002mol) in ethanol (20-25ml) was added 6- Benzoyl-8-methyl-7-methylsulfanyl-9-oxo 8,9-dihydro-pyrimido [5,4-e][1,4]diazepine-5-carboxylic acid ethyl ester (7.104) (1.27g, 0.02mol) and refluxed for 10-14 h. The solvent was removed by distillation and the residue was treated with glacial acetic acid (3-5ml) just enough to dissolve sodium salt of the pyrimidine and refluxed for 15 min. The reaction mixture was then poured on crushed ice and precipitate obtained was purified by recrystallization with ethanol. The desired solid product 7.113 a was obtained and purified by silica column and TLC (eluent: petroleum ether/EtOAc) (v:v = 8:2) (0.72g, yield: 79%; m.p. 243-245 °C).

Preparation of 10-Methyl-11-oxo-6-phenyl-8-thioxo-8,9,10,11-tetrahydro-1, 3, 5, 7, 9, 10-hexaaza-dibenzo[a,d]cycloheptane-5-carboxylic acid ethyl ester (7.113 b):

To a mixture of thiourea (1.52g, 0.02mol), sodium ethoxide (0.14g, 0.002mol) in ethanol (20-25ml) was added to compound 6- benzoyl-8-methyl-7-methylsulfanyl-9-oxo 8,9-dihydro-pyrimido [5,4-e][1,4]diazepine-5-carboxylic acid ethyl ester (7.104) (1.27g, 0.02mol) and refluxed for 10-14 hrs. The solvent was removed by distillation and the residue was treated with glacial acetic acid (3-5ml) just enough to dissolve sodium salt of the pyrimidine and refluxed for 15 min. The reaction mixture was then poured on crushed ice and precipitate obtained was purified by recrystallization with ethanol. The desired solid product 7.113 b was obtained and purified by silica column and TLC (eluent: petroleum ether/EtOAc) (v:v = 8:2) (0.70g, yield: 74%; m.p. 245-247 °C).

Preparation of 8-Imino-10-methyl-11-oxo-6-phenyl-8,9,10,11-tetrahydro-1, 3, 5, 7, 9, 10-hexaaza-benzo[a,d]cycloheptane-5-carboxylic acid ethyl ester (7.113 c):

To a solution of compound 6- benzoyl-8-methyl-7-methylsulfanyl-9-oxo 8,9-dihydro-pyrimido [5,4-e][1,4]diazepine-5-carboxylic acid ethyl ester (7.104) (1.01g, 0.0033mol) in ethanol (25ml) was added guanidine nitrate (30.0g, 0.167mol) and sodium acetate (27.0g, 0.334mol). The mixture was heated under reflux for 48 h. It was then filtered, and the organic layer was dried over anhydrous MgSO₄ and was evaporated to give 7.113 c. The desired solid product 7.113 c was obtained and purified by silica column and TLC (eluent: petroleum ether/EtOAc) (v:v = 8:2) (0.76g, yield: 72%; m.p. 237-238 °C).
Preparation of 10-Methyl-8-methylene-11-oxo-6-phenyl-8,9,10,11-tetrahydro-1,3,5,7,9,10-hexaaza-dibenzo[a,d]cycloheptene-5-carboxylic acid ethyl ester (7.113 d):

To a solution of compound, 6- benzoyl-8-methyl-7-methylsulfanyl-9-oxo 8,9-dihydro-pyrimido [5,4-e][1,4]diazepine-5-carboxylic acid ethyl ester (7.104) (1.23g, 0.00417mol) in ethanol (25ml) was added acetamidine hydrochloride (1.54g,0.005mol) and sodium acetate (27.0g, 0.334mol). The mixture was heated under reflux for 48 h. It was then filtered, and the organic layer was dried over anhydrous MgSO$_4$ and was evaporated to give 7.113 d. The desired solid product 7.113 d was obtained and purified by silica column and TLC (eluent: petroleum ether/EtOAc) (v:v = 8:2) (0.71g, yield: 74%; m.p. 231-232 °C).

Preparation of 13-methyl-14-oxo-6-phenyl-13,14dihydro-12H-1, 3, 5, 7, 12, 13-hexaaza-dibenzo [b,h]heptalene-5-carboxylic acid ethyl ester (7.114 a):

A mixture of o-phenylene diamine (1.08g,0.01mol), 6-benzoyl-8-methyl-7-methylsulfanyl-9-oxo 8,9-dihydro-pyrimido [5,4-e][1,4]diazepine-5-carboxylic acid ethyl ester (7.104) (0.625g, 0.01mol) in ethanol (25-30ml) was refluxed for 4-5h. The solvent was distilled under reduced pressure and the residue was quenched in crushed ice. It was extracted with chloroform, washed with water and dried over anhydrous sodium sulphate to give 7.114 a. The desired solid product 7.114 a was obtained and purified by silica column and TLC (eluent: petroleum ether/EtOAc) (v:v = 8:2) (0.76g, yield: 72%; m.p. 231-233 °C).

Preparation of 13-methyl-14-oxo-6-phenyl-13,14dihydro-12-thia-1, 3, 5, 7, 13-pentaaza-dibenzo[b,h]heptalene-5-carboxylic acid ethyl ester (7.114 b):

A mixture of o-aminothiophenol (1.25g,0.01mol), 6-benzoyl-8-methyl-7-methylsulfanyl-9-oxo 8,9-dihydro-pyrimido [5,4-e][1,4]diazepine-5-carboxylic acid ethyl ester (7.104) (0.625g,0.01mol) in ethanol (25-30ml) was refluxed for 3-4h. The solvent was distilled under reduced pressure and the residue was quenched in crushed ice. It was extracted with chloroform, washed with water and dried over anhydrous sodium sulphate to give 7.114 b. The desired solid product 7.114 was obtained and purified by silica column and TLC (eluent: petroleum ether/EtOAc) (v:v = 8:2) (0.76g, yield: 75%; m.p. 234-235 °C).

Preparation of 13-methyl-14-oxo-6-phenyl-13,14dihydro-12-oxa-1, 3, 5, 7, 13-pentaaza-dibenzo[b,h]heptalene-5-carboxylic acid ethyl ester (7.114 c):
A mixture of o-aminophenol (1.09g,0.01mol), 6- benzoyl-8-methyl-7-methylsulfanyl-9-oxo 8,9-dihydro-pyrimido [5,4-e][1,4]diazepine-5-carboxylic acid ethyl ester (7.104) (1.16g,0.012mol) in ethanol (25-30ml) was refluxed for 5h. The solvent was distilled under reduced pressure and the residue was quenched in crushed ice. It was extracted with chloroform, washed with water and dried over anhydrous sodium sulphate to give 7.114 c. The desired solid product 5.089 c was obtained and purified by silica column and TLC (eluent: petroleum ether/EtOAc) (v:v = 8:2) (0.76g, yield: 70%; m.p. 229-233 °C).

7.9  Mechanism of formation of compounds

7.9.1  Mechanism of formation of compound 7.099 from 7.098:

7.9.2  Mechanism of formation of compound 7.100 from 7.099

7.9.3  Mechanism of formation of compound 7.101 from 7.100
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7.9.4 Mechanism of formation of compound 7.102, 7.103, 7.104 from 7.101

7.9.5 Mechanism of formation of compound 7.105, 7.106 from 7.104

7.9.6 Mechanism of formation of compound 7.107, 7.108, 7.109, 7.110 from 7.100
7.9.7 Mechanism of formation of compound 7.111 and 7.112 from 7.104

7.9.8 Mechanism of formation of compound 7.113 (a-d) from 7.104
7.9.9 Mechanism of formation of compound 7.114 (a-c) from 7.104

IR spectrum (4-Cyano-pyrimidine-5-yl)-(2-oxo-2-phenyl-ethyl)-carbamic acid ethyl ester (7.101)
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Chart 7.02: IR spectrum (4-Cyano-pyrimidine-5-yl)-(2-oxo-2-phenyl-ethyl)-carbamic acid ethyl ester (7.103)

Chart 7.03: IR spectrum 1’,2’,3’-Triazolo-[b,e,][1,4]diazepin-pyrimido [b,d] [1,4]diazepino-1-methyl-9-one -7’-phenyl-4-carboxylic acid ethyl ester (7.106)
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Chart 7.04: IR spectrum 1,2',3'-Triazolo-[1,4]diazepine pyrimido – d-e- pyrrole-[b,c]-6-carboxylic acid ethyl ester (7.110)

Chart 7.05: IR spectrum (4-Cyano-pyrimidine-5-yl)-(2-oxo-2-phenyl-ethyl)-carbamic acid ethyl ester (7.112)
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Chart 7.06:
Mass spectrum (4-Cyano-pyrimidine-5-yl)-(2-oxo-2-phenyl-ethyl)-carbamic acid ethyl ester (7.100)

Chart 7.07:
Mass spectrum of 6- Benzoyl-8-methyl-7-methylsulfanyl-9-oxo 8,9-dihydro-pyrimido [5,4-e][1,4]diazepine-5-carboxylic acid ethyl ester (7.104)
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Chart 7.08:
Mass spectrum of 1’,2’,3’-Triazolo-[b,e]-[1,4]diazepin- pyrimido [b,d] [1,4]diazepino-1-methyl-9-one -7’-phenyl-4-carboxylic acid ethyl ester (7.106)

Chart 7.09
Mass spectrum of 1,2’,3’-Triazolo-[1,4]diazepine pyrimido – d -e- pyrrole-[b,c]-6-carboxylic acid ethyl ester (7.110)
7.10: $^1$HNMR spectrum of 1',2',3'-Triazolo-[b,e]-[1,4]diazepin- pyrimido [b,d]
[1,4]diazepino-1-methyl-9-one -7'-phenyl-4-carboxylic acid ethyl ester (7.106)

7.11: $^1$HNMR spectrum of 1,2',3'-Triazolo-[1,4]diazepine pyrimido – d -e- pyrrole-[b,c]-6-
carboxylic acid ethyl ester (7.110)
Chapter 7: Synthesis of 1,2,3-triazolo substitute analogues of the...

7.12: $^{13}$C nmr spectrum of 6-Benzoyl-8-methyl-7-methylsulfanyl-9-oxo 8,9-dihydropyrimido [5,4-e][1,4]diazepine-5-carboxylic acid ethyl ester (7.104)

7.13: $^{13}$C nmr spectrum of 1',2',3'-Triazolo-[b,e]-[1,4]diazepin- pyrimido [b,d] [1,4]diazepino-1-methyl-9-one -7'-phenyl-4-carboxylic acid ethyl ester (7.106)
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Chart 7.14: $^1$H nmr spectrum of 1,2',3'-Triazolo-[1,4]diazepine pyrimido – d -e- pyrrole-[b,c]-6-carboxylic acid ethyl ester (7.110)

Chart 7.15: $^1$H nmr spectrum of 10-methyl-9-oxo-3-phenyl-9,10-dihydro-1H-1,2,4,6,9,10-hexaaza-benzo[f] azulene-4-carboxylic acid ethyl ester (7.111)
Chart 7.16: $^{13}$C nmr spectrum of 10-Methyl-9-oxo-3-phenyl-9,10-dihydro-1-oxa-4,6,8,10-tetraaza-benzo[f] azulene-4-carboxylic acid ethyl ester (7.112)