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**Studies on Heterocyclization and Biological Activity
of Mercaptopyrimidine Derivatives**

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Abstract

2-amino-6-thioxouracil (**1**) undergoes cyclo-condensation with pyruvic acid derivative **2** and ninhydrin (**6**) to furnish thiopyranopyrimidine **5** and thienopyrimidine **8**, respectively. Alkylation of aminopyrimidine **1** with benzyl chloride consumed two moles to form S- and N-alkylated product **9**. Subjecting compound **9** to aminolysis with aniline derivatives resulted in 4-aminopyrimidine **10a,b** through Dimorth rearrangement. Furthermore, the addition of cyclic enamine **10a,b** to ninhydrin and benzoyl isothiocyanate produced pyrimidine derivatives **12a,b** and **14**. Finally, the addition of enamenic carbon of **10a,b** to polarized systems **2** or **18** afforded the pyrido[2,3-d]pyrimidines **17** and **21a-d** in moderate to good yield. Condensation of aminopyrimidine derivative **9** with acetophenone leads to olefinic pyrimidine **23**, various addition-cyclization reactions of which give the corresponding bicyclic pyrimidines **25**, **27**, and **29**. Cycloaddition reaction of pyrimidine **9** to benzoyl isothiocyanate gives thiourea derivative **30**. Intramolecular cyclization of compound **9** with NaOH or Br₂ produces pyrimidine derivatives **31** or **33**, respectively. Heteroannulation of pyrimidine **9** with ninhydrin or α -carbonyl carboxylic acid **35** gives the tetracyclic pyrimidine **34** and diazepine derivative **38**, respectively. Fluorescence properties of pyrimidine derivatives have been tested. The three synthesized pyrimidines derivatives compounds **9**, **27**, **30**, are able to have a toxic effect on male albino rats as they produced both hepatotoxicity, renal damage besides their hazardous effects on the Hb and inhibition of ChE.

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Abbreviations

Ac.	Acetyl
Anal. Calcd.	Analyses Calculated
Ar	Aryl
br	Broad
Bu	Butyl
CHCl₃	Chloroform
CO₂	Carbon dioxide
Conc	Concentrated
D₂O	Deuterium oxide
DCM	Dichloromethane
DMF	Dimethyl formamide
DNA	Deoxy ribonucleic acid
Et	Ethyl
h	Hour(s)
LC₅₀	The concentration that induces 50% growth inhibition
LDA	Lithium diisopropyl amide
Me	Methyl
MHz	Mega Hertz
ML	Microliliter
ml,	Mililiter
Mp	Melting point
MW	Microwave
NMR	Nuclear magnetic resonance spectroscopy
p-	para
PBr₃	Phosphorus Tribromide
Ph	Phenyl
PPM	Parts per million (NMR)
Pr	Propyl
RNA	Ribonucleic acid
rt.	Room temperature
TBAHS	Tetrabutylammonium hydrogen sulphate
UV	Visible ultraviolet
δ	delta (NMR)