Zagazig University
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Studies on Heterocyclization and Biological Activity of Mercaptopyrimidine Derivatives

BY

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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 **10**a,b through Dimorth rearrangement. Furthermore, the addition of cyclic enamine **10**a,b to ninhydrin and benzoyl isothiocyanate produced pyrimidine derivatives **12**a,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 **21**a-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 Br_2 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
$CHCl_3$	Chloroform
CO_2	Carbon dioxide
Conc	Concentrated
D_2O	Deuterium oxide
DCM	Dichloromethane
DMF	Dimethyl formamide
DNA	Deoxy ribonucleic acid
Et	Ethyl
h	Hour(s)
LC_{50}	The concentration that induces 50% growth inhibition
LDA	Lithium diisopropyl amide
Me	Methyl
MH_Z	Mega Hertz
ML	Microliliter
ml,	Milililiter
Mp	Melting point
MW	Microwave
NMR	Nuclear magnetic resonance spectroscopy
p-	para
PBr_3	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)