SUMMARY

CHAPTER I: One step synthesis of 1,3-diaryl-5-(1',3'-diaryl-6'-hydroxy-4'-oxo-1',2',3',4'-tetrahydro-2'-thioxo-5'-pyrimidinyl)-1,2,3,4-tetrahydro-2-thioxo-4H-[1]benzopyran[2,3-d]-pyrimidin-4-one.

Pyrimidine and its derivatives have been extensively investigated by organic chemists due to their close association with life processes. Association of significant biological and physiological activities with these compounds led to the synthesis of a number of their derivatives. A brief account of their uses, biological activities and methods of preparation has been given. An efficient one pot synthesis of benzopyranopyrimidines has been developed. It involves the reaction of different 1,3-diarylthiobarbituric acids with salicylaldehyde in methanol and a few drops of conc. HCl.

Thus, as a test case, the reaction of 1,3-di(4-methylphenyl)-2-thiobarbituric acid with salicylaldehyde in the ratio of 2:1 in methanol and HCl at reflux temperature resulted in the formation of a solid product in good yield. Its 'H-NMR spectrum showed a singlet at 4.5 for the hydroxyllic proton and a 1H singlet at 5.4 assigned to H-5.

The spectral data and elemental analysis confirmed the structure of the product as 1,3-di(4-methylphenyl)-5-(1',3'-di(4-methylphenyl)-6'-hydroxy-4'-oxo-1',2',3',4'-tetrahydro-2'-thioxo-5'-pyrimidinyl)-1,2,3,4-tetrahydro-2-thioxo-4H-[1]benzopyran[2,3-d]-pyrimidin-4-one (44a). Similar condensation with other 1,3-diarylthiobarbituric acids
viz. 1,3-di (2-methylphenyl)-, 1,3-di (4-chlorophenyl)-, 1,3-di (2-methoxyphenyl)-, 3-dihydro-2-thioxo-2H, 5H-pyrimidine-4, 6-diones gave the corresponding benzopyranopyrimidines (44b-f) and their structures were formulated on the basis of spectral data and elemental analysis. A mechanism for the reaction has also been proposed.

\[ (44a-f) \]

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<thead>
<tr>
<th>R</th>
<th>(44a-f)</th>
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<tbody>
<tr>
<td>a</td>
<td>4-CH₃</td>
<td>d</td>
</tr>
<tr>
<td>b</td>
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<td>e</td>
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<td>c</td>
<td>3-CH₃</td>
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**CHAPTER II: Synthesis of 1,3-diaryl-3, 3-dihydro-5-(2-substituted thiazol-4-yI)-2-thioxo-2H, 5H-pyrimidine-4, 6-diones**

The biological and therapeutic properties of thiazole and its derivatives has been well established. This prompted the investigation of new routes for the synthesis of these derivatives. Some general methods for the synthesis of thiazoles and their physiological properties have been discussed. In order to establish structure-activity relationship some new derivatives possessing pyrimidine moiety have been synthesised. A facile method for the synthesis of 1, 3-diaryl-3-
dihydro-5-(2-mercaptothiazol-4-yl)-2-thioxo-2H, 5H-pyrimidine 4,6-diones (61a-f) and 1,3-diaryl-1, 3-dihydro-5-(2-methylthiazol-4-yl)-2-thioxo-2H, 5H-pyrimidine-4, 6-diones (62a-f) has been worked out. The method involves the reaction of 1-phenyl, 3-aryl-2-thio barbituric acids with chloroacetyl chloride to give intermediate chloroacetyl derivative. This on further condensation with ammonium dithiocarbamate or thioacetamide gave the desired 2-mercapto or 2-methyl thiazole derivative respectively.

As a typical case, 1-phenyl, 3(2-methylphenyl) thiobarbituric acid was treated with equimolar quantities of chloroacetyl chloride to give 5-chloroacetyl-1 - phenyl, 3(2-methyl)-2-thiobarbituric acid. This on further condensation with ammonium dithiocarbamate in absolute ethanol afforded a solid product in good yield. The product gave a negative DNP test and its $^1$H-NMR spectral data showed a singlet for a D$_2$O exchangeable proton at $\delta$ 5.4 which was assigned to the $-\text{SH}$ group of the thiazole ring besides other expected signals. Further the mercaptothiazole was converted into its S-methyl derivative. Based on the spectral data and elemental analysis the compound was characterised as 1-phenyl-3-(2-methylphenyl)-1, 3-dihydro-5-(2-mercaptothiazol-4-yl)-2-thioxo-2H, 5H-pyrimidine-4, 6-dione (61a).

Similarly the compounds (61b-f) were synthesised by the reaction of appropriate chloroacetyl thiobarbituric acid derivative with ammonium dithiocarbamate.

The syntheses of 1,3-diaryl-1, 3-dihydro-5-(2-methylthiazol-4-yl)-2-thioxo-2H, 5H-pyrimidine-4, 6-diones (62a-f) were achieved in a similar manner by the condensation of corresponding 5-chloroacetyl-thiobarbituric acids with thioacetamide in absolute ethanol. All the
compounds synthesised were characterised by their spectral data and elemental analysis.

![Chemical structures](image)

(61a-f) (62a-f)

R
a 2-CH₃
b 3-CH₃
c 4-CH₃
d 3-Cl
e 4-Cl
f 4-Br

CHAPTER III: Synthesis of 5-hydroxy-1, 3-diaryl-1,2,3,4,5-pentahydro-10-methyl-4-oxo-2-thioxopyridimido (4, 5-b) quinoline

A number of pyrimidines associated with pyridine and quinoline are well known for their importance in biological field. Some methods to synthesis pyrimidoquinolines have been illustrated. Keeping in view
the physiological and biological importance of such compounds it was considered of interest to synthesise pyrimidoquinolinethiones by a convenient route. 1,3-diaryl-1,3-dihydro-6-chloro-5-formyl-2-thioxo-2H,5H-pyrimidine-4,6-diones (26a-f) were synthesised and further condensed with N-methyl aniline to give 5-hydroxy-1,3-diaryl-1,2,3,4,5-pentahydro-10-methyl-4-oxo-2-thioxopyrimido(4,5-b)quinolines (28a-f). In the H-NMR spectrum a 1H singlet at δ 5.4 was assigned to the 5-H. Other signals were observed at expected values. Presence of the hydroxy group was confirmed by I.R spectra and derivatisation with Ac$_2$O/Py. On the basis of spectral data and elemental analysis, the structures of the title compounds were established.

![Structural formula](image)

(28a-f)

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>a</td>
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<tr>
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<tr>
<td>d</td>
<td>2-OCH$_3$</td>
</tr>
<tr>
<td>e</td>
<td>3-CH$_3$</td>
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<tr>
<td>f</td>
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</table>
CHAPTER IV : Synthesis of 5-aryldenethiobarbituric acids, 5-(pyrimidinyl) methylidene-2-thiobarbituric acids and 1,3-diaryl pyranodipyrimidines as possible redox coenzyme model

A brief account of the importance of redox coenzymes and their mode of action has been given. The importance of 5-ylidene barbituric acids, which incorporate the necessary functionality i.e. >C=O< flanked by electron withdrawing groups comparable to the redox coenzymes, has been discussed along with methods of their preparation and their biological activities. Synthesis of compounds 1, 3-diaryl-5-arylidene-2-thiobarbituric acids (22a-f), 5-(pyrimidinyl) methylidene-2-thiobarbituric acid (25a-f) and 1, 3-diaryl pyranodipyrimidines (27a-f) described in PART-A, PART-B and PART-C respectively, has been undertaken in view of their structural similarities with redox coenzymes.

PART-A: The method involves the condensation of different 1,3-diaryl-2-thiobarbituric acids with nitrobenzaldehyde. The reaction of 1,3-di(2-methylphenyl)-2-thiobarbituric acid with 0-nitrobenzaldehyde gave a white solid, characterised by its 'H-NMR, mass spectral data and elemental analysis as 1,3-di(2-methylphenyl)-5-(2-nitrobenzylidene)-2-thiobarbituric acid (22a). Similarly compounds (22b-f) were synthesised and characterised by spectral and elemental analysis.

PART B: This series involves the condensation of 1,3-diaryl-2-thiobarbituric acids with 5-chloro-1, 3-di(4-bromophenyl)-5-formyl-2-thiouracil to give a solid characterised as 5-[6'-chloro-1', 3'-di(4'-bromophenyl)-2''-thiouracil-5'-yl] methyl idene-1, 3-diaryl-2-thiobarbituric acid (25a-f) by their 'H-NMR, I.R. and elemental analysis.
PART C: The condensation of unsubstituted 2-thiobarbituric acid with different 6-chloro-1, 3-diaryl-5-formyl-2-thiouracil gave 7, 9-diarylpyrano(2,3-d:6,5-d) dipyrimidine-2(1H), 8 (10H) dithioxo,4 (3H), 6(7H) dione (27a-f). The I.R. spectra showed NH absorption at 3400 cm\(^{-1}\). In the H-NMR spectrum the 5-H was discernible at values ranging from \(\delta 8.9\) to \(\delta 9.1\) besides other expected signals. On the basis of spectral data and elemental analysis the structures were characterised as above.

\[
\begin{array}{cccc}
R_1 & R_2 \\
\hline
2-CH_3 & 2-NO_2 \\
H & 2-NO_2 \\
2-OCH_3 & 2-NO_2 \\
4-CH_3 & 2-NO_2 \\
4-Cl & 4-NO_2 \\
4-CH_3 & 4-NO_2 \\
\end{array}
\]

(22a-f)
(25a-f)

R
a 4-Br
b 2-OCH₃
c 4-Cl
d 2-CH₃
e 4-CH₃
f H

(27a-f)

R
a 4-Br
b H
c 2-CH₃
d 3-CH₃
e 4-CH₃
f 4-Cl