CHAPTER - 5

SYNTHESIS OF 4-AMINOPYRIMIDINES FROM PYRIMIDIN-4-ONES via CHLORINATION, AZIDOLYSIS AND REDUCTION

Substituted heterocycles containing fused pyrimidines have received a considerable attention during last twenty years, as a consequence of their exciting biological properties and their role as pharmacophores. Many of these compounds have proved to be active anticancer, antipyretic and antiinflammatory, antiviral, anti HIV and antimetabolic agents.

Compounds of this class are prepared from suitable precursors in which an amino functional group is situated at a position adjacent to a functional groups like nitrile, carboxamide and carboxylates. The annelation of pyrimidine ring to a variety of existing rings has recently been reviewed by Albert et al.

It is fundamentally important for the purpose of the annelation to distinguish between \( \pi \)-deficient and \( \pi \)-excessive heterocyclic rings. Annellation onto a \( \pi \)-excessive nucleus becomes easier. Thiophene part of thienopyridine is a \( \pi \)-excessive nucleus, pyrimidine ring can be fused to the \( \pi \)-excessive thiophene ring having o-aminocarbonyl, o-aminocarboxylate and o-aminonitrile functionality of thienopyridine.


5.1.1 Introduction

A convenient route for the annelation of 4-substituted pyrimidines has been the reaction of existing heterocyclic system having o-aminocarbonyl, o-aminocarboxylate or o-aminonitrile functionality with formamide.
2,5-Dicyano-3-amino-4-phenyl-6-oxo-7H-thieno[2,3-b]pyridines (342) were reacted with formamide at 170 °C to give 4-amino-7-oxo-8-cyano-9-phenyl-7H-pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidines (343) (Scheme-140).

![Diagram of chemical reactions]

Scheme 140

4-Oxo-5,6,7,8-tetrahydro-7-benzylpyrido[4', 3': 4, 5]thieno[2,3-d]pyrimidines (345) and 4-amino-5,6,7,8-tetrahydro-7-benzylpyrido[4', 3': 4, 5]thieno[2,3-d]pyrimidines (347) were prepared from 2-amino-3-cyano/ carbethoxy-4,5,6,7-tetrahydro-6-benzylthieno[2,3-c]pyridines (344 & 346) with formamide (Scheme-141).

![Diagram of chemical reactions]

Scheme 141
When 2-cyano-3-amino-5-ethyl-6-methylthieno[2,3-b]pyridine (348) was treated with formamide 4-amino-7-methyl-8-ethylpyrido[3', 2', 4, 5]thieno[3,2-d]pyrimidine (349) was obtained (Scheme-142)

\[
\begin{align*}
\text{H}_2\text{C} & \text{N} \quad \text{H}_2\text{C} \\
\text{H}_3\text{C} & \text{N} \\
\text{S} & \text{S} \\
\text{H}_3\text{C} & \text{CN} \\
\end{align*}
\]

\[
\text{H}_2\text{C} \quad \text{HCONHN}_2 \\
\text{H}_3\text{C} \\
\text{H}_2\text{C} \\
\text{N} \\
\]

Scheme 142

5.1.2 Present work

The annelation of pyrimidine ring is most often accomplished with $\pi$-excessive rings to prepare biologically active fused pyrimidines. Therefore it was thought of interest to annelate a $\pi$-deficient pyrimidine ring onto the existing $\pi$-excessive thiophene ring.

Although, much attention has been focused on the synthesis of pyridothienopyrimidines by the reaction of fused thiophene containing o-aminocarbonyl group and formamide because they serve as a facile route for the annelation of pyrimidine rings having various biological and chemical properties.$^{239-241}$

In continuation of our research work$^{30, 89, 90}$ on the pyridothienopyrimidines, we would like to report the synthesis of 7,9-diarylpyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidin-4(3H)-ones by the reaction of 2-carbethoxy-3-amino-4,6-diarylthieno[2,3-b]pyridines with formamide.
5.1.3 Results and Discussion

2-Carbethoxy-3-amino-4,6-diarylthieno[2,3-b]pyridines (V, 33-40) were reacted with formamide, formic acid in presence of N,N-dimethylformamide (DMF) to afford 7,9-diarylpyrido[3', 2' 4, 5]thieno[3,2-d]pyrimidin-4(3H)-ones (XVII, 121-128) (Scheme-143).

\[ \text{HCONH}_2 \quad \text{HCOOH} \quad \text{DMF} \]

\[ \text{R}_1 \]

\[ \text{R}_2 \]

\[ \text{V} \]

\[ \text{R}_1 \]

\[ \text{R}_2 \]

\[ \text{NH} \]

\[ \text{COOC}_2\text{H}_5 \]

\[ \text{XVII} \]

Scheme 143

All the synthesized 7,9-diarylpyrido[3', 2' : 4, 5]thieno[3,2-d]pyrimidin-4(3H)-ones (XVII, 121-128) were yellow to greenish yellow coloured crystalline compounds, soluble only in trifluoroacetic acid and partially soluble in DMF. Majority of these compounds have melting points higher than 340 °C. Physical constants of 7,9-diarylpyrido[3', 2' 4, 5]thieno[3,2-d]pyrimidin-4(3H)-ones (XVII, 121-128) are recorded in table-31.

<table>
<thead>
<tr>
<th>Compd no.</th>
<th>R₁</th>
<th>R₂</th>
<th>Yield (%)</th>
<th>MP °C</th>
<th>Mol Formula</th>
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<tbody>
<tr>
<td>121</td>
<td>C₆H₅</td>
<td>C₆H₅</td>
<td>70</td>
<td>360</td>
<td>C₂₁H₁₃N₃OS</td>
</tr>
<tr>
<td>122</td>
<td>C₆H₅</td>
<td>4-OCH₃C₆H₄</td>
<td>53</td>
<td>360</td>
<td>C₂₂H₁₅N₃O₂S</td>
</tr>
<tr>
<td>123</td>
<td>C₆H₅</td>
<td>4-ClC₆H₄</td>
<td>65</td>
<td>290</td>
<td>C₂₁H₁₂ClN₃OS</td>
</tr>
<tr>
<td>124</td>
<td>4-OCH₃C₆H₄</td>
<td>C₆H₅</td>
<td>65</td>
<td>335-36</td>
<td>C₂₂H₁₅N₃O₂S</td>
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<tr>
<td>125</td>
<td>4-OCH₃C₆H₄</td>
<td>4-OCH₃C₆H₄</td>
<td>60</td>
<td>347-49</td>
<td>C₂₃H₁₇N₃O₃S</td>
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<tr>
<td>126</td>
<td>4-ClC₆H₄</td>
<td>C₆H₅</td>
<td>57</td>
<td>360</td>
<td>C₂₁H₁₂ClN₃OS</td>
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<tr>
<td>127</td>
<td>4-ClC₆H₄</td>
<td>4-ClC₆H₄</td>
<td>60</td>
<td>279-80</td>
<td>C₂₃H₁₁Cl₂N₃OS</td>
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<tr>
<td>128</td>
<td>2-Thienyl</td>
<td>C₆H₅</td>
<td>65</td>
<td>245-47</td>
<td>C₁₉H₁₁N₃OS₂</td>
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</table>

IR(KBr) spectral data of 7,9-diarylpyrido[3’, 2’ · 4, 5]thieno[3,2-d]pyrimidin-4(3H)-ones (XVII, 121-128) are summarized in table-32.

IR(KBr) spectra exhibited characteristic v NH and C=O absorption in the region of 3398-3390 cm⁻¹ and 1667-1678 cm⁻¹ respectively. Shift of v C=O from the region of 1740-1734 cm⁻¹ indicated the presence of cyclic ketone, the spectral data were devoid of absorptions for either amino or carbethoxy groups. Which was supported the conversion of 2-carbethoxy-3-amino-4,6-diarylthieno[2,3-b]pyridines to 7,9-diarylpyrido[3’, 2’ · 4, 5]thieno[3,2-d]pyrimidin-4(3H)-ones.
**Table - 32 :** IR(KBr) spectral data of 7,9-diarylpyrido[3', 2' 4, 5]thieno[3,2-d]pyrimidin-4(3H)-ones (XVII, 121-128)

<table>
<thead>
<tr>
<th>Compd no</th>
<th>$\nu$ NH cm$^{-1}$</th>
<th>$\nu$ CH cm$^{-1}$</th>
<th>$\nu$ C=O cm$^{-1}$</th>
<th>$\nu$ C=C, C=N cm$^{-1}$</th>
<th>$\delta$ CH cm$^{-1}$</th>
<th>$\delta$ C-O, C-N cm$^{-1}$</th>
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<tr>
<td>121</td>
<td>3394</td>
<td>3004, 2960</td>
<td>1675</td>
<td>1579, 1514</td>
<td>1443</td>
<td>1393, 1296</td>
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<tr>
<td>122</td>
<td>3390</td>
<td>2996, 2856</td>
<td>1667</td>
<td>1605, 1524</td>
<td>1425</td>
<td>1380, 1290</td>
</tr>
<tr>
<td>123</td>
<td>3396</td>
<td>3004, 2956</td>
<td>1665</td>
<td>1604, 1556</td>
<td>1440</td>
<td>1382, 1250</td>
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<tr>
<td>124</td>
<td>3398</td>
<td>3010, 2996</td>
<td>1672</td>
<td>1605, 1520</td>
<td>1428</td>
<td>1376, 1246</td>
</tr>
<tr>
<td>125</td>
<td>3392</td>
<td>3008, 2856</td>
<td>1678</td>
<td>1596, 1524</td>
<td>1440</td>
<td>1382, 1290</td>
</tr>
<tr>
<td>126</td>
<td>3396</td>
<td>3004, 2972</td>
<td>1670</td>
<td>1576, 1556</td>
<td>1446</td>
<td>1389, 1256</td>
</tr>
<tr>
<td>127</td>
<td>3398</td>
<td>3010, 2998</td>
<td>1672</td>
<td>1596, 1520</td>
<td>1424</td>
<td>1379, 1256</td>
</tr>
<tr>
<td>128</td>
<td>3390</td>
<td>3004, 2872</td>
<td>1667</td>
<td>1604, 1550</td>
<td>1440</td>
<td>1370, 1250</td>
</tr>
</tbody>
</table>

The $^1$HNMR spectral data of 7,9-diarylpyrido[3', 2' 4, 5]thieno[3,2-d]pyrimidin-4(3H)-ones$^{30}$ (XVII, 121-128) are recorded in table-33.

$^1$HNMR spectra of 7,9-diarylpyrido[3', 2' 4, 5]thieno[3,2-d]pyrimidin-4(3H0-ones (XVII, 121-128) exhibited a broad singlet in the region of $\delta$ 8 28-8 40 integrated for one hydrogen of -NH (D$_2$O exchangable) A singlet in the region of $\delta$ 8 82-8 92 integrating for one proton is due to the CH group situated at position-2 of pyrimidine ring, and a multiplet was found to resonate in the region $\delta$ 7 25-8 20 integrated for eleven aromatic protons.
Table - 33: \(^1\)HNMR spectral data of 7,9-diarylpyrido[3', 2' 4, 5]thieno[3,2-d]pyrimidin-4(3H)-ones (XVII, 121-128)

<table>
<thead>
<tr>
<th>Compd no</th>
<th>R_1</th>
<th>R_2</th>
<th>(^1)HNMR (δ ppm, DMSO d_6 + CDCl_3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>121</td>
<td>C_6H_5</td>
<td>C_6H_5</td>
<td>7.40-8.10 (m, 11H, Ar-H), 8.89 (s, 1H, Ar-H at C-2), 8.28 (s, 1H, NH)</td>
</tr>
<tr>
<td>122</td>
<td>C_6H_5</td>
<td>4-OCH_3C_6H_4</td>
<td>4.08 (s, 3H, OCH_3), 7.19-8.19 (m, 10H, Ar-H), 8.96 (s, 1H, Ar-H at C-2), 8.28 (s, 1H, NH)</td>
</tr>
<tr>
<td>123</td>
<td>C_6H_5</td>
<td>4-ClC_6H_4</td>
<td>7.42-8.20 (m, 10H, Ar-H), 8.82 (s, 1H, Ar-H at C-2), 8.29 (s, 1H, NH)</td>
</tr>
<tr>
<td>124</td>
<td>4-OCH_3C_6H_4</td>
<td>C_6H_5</td>
<td>3.99 (s, 3H, OCH_3), 7.20-8.17 (m, 10H, Ar-H), 8.94 (s, 1H, Ar-H at C-2), 8.29 (s, 1H, NH)</td>
</tr>
<tr>
<td>125</td>
<td>4-OCH_3C_6H_4</td>
<td>4-OCH_3C_6H_4</td>
<td>3.99 (s, 6H, 2OCH_3), 7.17-8.20 (m, 9H, Ar-H), 8.96 (s, 1H, Ar-H at C-2), 8.28 (s, 1H, NH)</td>
</tr>
<tr>
<td>126</td>
<td>4-ClC_6H_4</td>
<td>C_6H_5</td>
<td>7.40-8.19 (m, 10H, Ar-H), 8.99 (s, 1H, Ar-H at C-2), 8.28 (s, 1H, NH)</td>
</tr>
<tr>
<td>127</td>
<td>4-ClC_6H_4</td>
<td>4-ClC_6H_4</td>
<td>7.41-8.20 (m, 9H, Ar-H), 8.94 (s, 1H, Ar-H at C-2), 8.28 (s, 1H, NH)</td>
</tr>
<tr>
<td>128</td>
<td>2-Thienyl</td>
<td>C_6H_5</td>
<td>7.21-8.20 (m, 9H, Ar-H), 8.89 (s, 1H, Ar-H at C-2), 8.29 (s, 1H, NH)</td>
</tr>
</tbody>
</table>

5.2.1 Introduction and present work

Pyrimidines having halogen group present at 2- and 4- position seem to be more labile, it shows powerful reactivity towards nucleophilic substitution reaction with reagent such as, piperidine, piperazine, morpholines, hydrazines, azides etc forming potent bi, tri and tetracyclic heterocyclic rings.

The most common route for the synthesis of this system has to be via the reaction between pyrimidin-4-ones and phosphorous oxychloride.


Wagner et al\textsuperscript{92} have synthesized 2,7,8,9-tetrasubstituted-4-chloropyrido[3', 2' 4, 5]thieno[3,2-d]pyrimidines (359) by the reaction between 2,7,8,9-tetrasubstituted pyrido[3', 2' 4, 5]thieno[3,2-d]pyrimidin-4(3H)-ones (358) and phosphorous oxychloride (Scheme-146)

2-Substituted 7-carbethoxy-8-cyano-9-phenylpyrido[3', 2' 4, 5]thieno[3,2-d]pyrimidin-4(3H)-ones (360) were reacted with phosphorous oxychloride to afford 2-substituted 4-chloro-7-carbethoxy-8-cyano-9-phenylpyrido[3', 2' 4, 5]thieno-[3,2-d]pyrimidines\textsuperscript{98} (361) (Scheme-147)
Moreover, 4-chloropyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidines has served as a facile point of departure into the desired molecule (Scheme-148).

![Scheme 147](image)

![Scheme 148](image)
The Scheme-148 summarized the synthetic conversions accomplished by the nucleophilic substitution reactions of 4-chloropyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine. Treatment of (I) with sodium methoxide in methanol yielded the 4-methoxy derivative (II), while the reaction with morpholine, thiourea and methyl hydrazine yielded 4-morpholino (III), 4-mercapto (IV) and 4-(N-methylhydrazino) (V) derivatives respectively. Reaction of I with sodium azide resulted in 4-azido derivative (VI).

Reaction of 4-chloropyrido[3', 2' : 4, 5]thieno[3,2-d]pyrimidine (I) with hydrazine hydrate afforded 4-hydrazinopyrido[3', 2' : 4, 5]thieno[3,2-d]pyrimidine (VIII), which was easily converted to the fused triazole (IX) and fused tetrazole (VII).

In present work, a new series of 4-chloro-7,9-diarylpyrido[3', 2' : 4, 5]thieno[3,2-d]pyrimidines were synthesized by the reaction between 7,9-diarylpyrido[3', 2' : 4, 5]thieno[3,2-d]pyrimidin-4(3H)-ones and phosphorous oxychloride, which were further used as intermediate in the preparation of fused tetrazoles.

5.2.2 Results and discussion

When 7,9-diarylpyrido[3', 2' : 4, 5]thieno[3,2-d]pyrimidin-4(3H)-ones (XVII, 121-128) were refluxed with phosphorous oxychloride, 4-chloro-7,9-diarylpyrido[3', 2' : 4, 5]thieno[3,2-d]pyrimidines (XVIII, 129-136) were obtained (Scheme-149).
All the synthesized 4-chloro-7,9-diarylpyrido[3', 2' 4, 5]thieno[3,2-d]pyrimidines (XVIII, 129-136) were white to off white in colour, soluble in N,N-dimethylformamide, dimethylsulfoxide and mixture of alcohol chloroform (6:4). All the compounds were obtained in 60-70 % yields.


**Table - 34:** Physical constants of 4-chloro-7,9-diarylpyrido[3', 2' 4, 5]thieno[3,2-d]pyrimidines (XVIII, 129-136)

<table>
<thead>
<tr>
<th>Compd no</th>
<th>R&lt;sub&gt;1&lt;/sub&gt;</th>
<th>R&lt;sub&gt;2&lt;/sub&gt;</th>
<th>Yield (%)</th>
<th>M.P. °C</th>
<th>Mol. formula</th>
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<tbody>
<tr>
<td>129</td>
<td>C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>68</td>
<td>198-99</td>
<td>C&lt;sub&gt;21&lt;/sub&gt;H&lt;sub&gt;12&lt;/sub&gt;C1N&lt;sub&gt;3&lt;/sub&gt;S</td>
</tr>
<tr>
<td>130</td>
<td>C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>4-OCH&lt;sub&gt;3&lt;/sub&gt;C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>62</td>
<td>212-14</td>
<td>C&lt;sub&gt;22&lt;/sub&gt;H&lt;sub&gt;14&lt;/sub&gt;C1N&lt;sub&gt;3&lt;/sub&gt;OS</td>
</tr>
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<td>131</td>
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<td>4-ClC&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>60</td>
<td>239-40</td>
<td>C&lt;sub&gt;21&lt;/sub&gt;H&lt;sub&gt;11&lt;/sub&gt;Cl&lt;sub&gt;2&lt;/sub&gt;N&lt;sub&gt;3&lt;/sub&gt;S</td>
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<td>132</td>
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<td>C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>62</td>
<td>235-37</td>
<td>C&lt;sub&gt;22&lt;/sub&gt;H&lt;sub&gt;14&lt;/sub&gt;C1N&lt;sub&gt;3&lt;/sub&gt;OS</td>
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<td>133</td>
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<td>237-39</td>
<td>C&lt;sub&gt;23&lt;/sub&gt;H&lt;sub&gt;16&lt;/sub&gt;C1N&lt;sub&gt;3&lt;/sub&gt;O&lt;sub&gt;2&lt;/sub&gt;S</td>
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<td>68</td>
<td>222-24</td>
<td>C&lt;sub&gt;21&lt;/sub&gt;H&lt;sub&gt;11&lt;/sub&gt;Cl&lt;sub&gt;2&lt;/sub&gt;N&lt;sub&gt;3&lt;/sub&gt;S</td>
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<td>66</td>
<td>245-47</td>
<td>C&lt;sub&gt;21&lt;/sub&gt;H&lt;sub&gt;10&lt;/sub&gt;Cl&lt;sub&gt;3&lt;/sub&gt;N&lt;sub&gt;3&lt;/sub&gt;S</td>
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**Table - 35:** IR(KBr) spectral data of 4-chloro-7,9-diarylpyrido[3', 2' : 4, 5]thieno[3,2-d]pyrimidines (XVIII, 129-136)

<table>
<thead>
<tr>
<th>Compd no.</th>
<th>ν CH</th>
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<td>1562, 1531</td>
<td>1427</td>
<td>1347</td>
</tr>
</tbody>
</table>

IR(KBr) Spectra of 4-chloro-7,9-diarylpyrido[3', 2' : 4, 5]thieno[3,2-d]pyrimidines showed no absorption bands in the region of 3398-3390 cm⁻¹ and 1667-1687 cm⁻¹, which indicated the absence of NH and C=O groups and completion of chlorination at position-4 of 7,9-diarylpyrido[3', 2' : 4, 5]thieno[3,2-d]pyrimidin-4(3H)-ones.


<table>
<thead>
<tr>
<th>Compd no</th>
<th>R&lt;sub&gt;1&lt;/sub&gt;</th>
<th>R&lt;sub&gt;2&lt;/sub&gt;</th>
<th>$^1$HNMR (δ ppm, DMSO d&lt;sub&gt;6&lt;/sub&gt; + CDCl&lt;sub&gt;3&lt;/sub&gt;)</th>
</tr>
</thead>
<tbody>
<tr>
<td>129</td>
<td>C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>7.25-8.21 (m, 11H, Ar-H), 8.86 (s, 1H, Ar-H at C-2)</td>
</tr>
<tr>
<td>130</td>
<td>C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>4-OCH&lt;sub&gt;3&lt;/sub&gt;C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>3.09 (s, 3H, OCH&lt;sub&gt;3&lt;/sub&gt;), 7.27-8.22 (m, 10H, Ar-H), 8.84 (s, 1H, Ar-H at C-2)</td>
</tr>
<tr>
<td>131</td>
<td>C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>4-ClC&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>7.24-8.20 (m, 10H, Ar-H), 8.87 (s, 1H, Ar-H at C-2)</td>
</tr>
<tr>
<td>132</td>
<td>4-OCH&lt;sub&gt;3&lt;/sub&gt;C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>4.00 (s, 3H, OCH&lt;sub&gt;3&lt;/sub&gt;), 7.27-8.20 (m, 10H, Ar-H), 8.86 (s, 1H, Ar-H at C-2)</td>
</tr>
<tr>
<td>133</td>
<td>4-OCH&lt;sub&gt;3&lt;/sub&gt;C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>4-OCH&lt;sub&gt;3&lt;/sub&gt;C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>4.04 (s, 6H, 2OCH&lt;sub&gt;3&lt;/sub&gt;), 7.25-8.21 (m, 9H, Ar-H), 8.84 (s, 1H, Ar-H at C-2)</td>
</tr>
<tr>
<td>134</td>
<td>4-ClC&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>7.25-8.22 (m, 10H, Ar-H), 8.87 (s, 1H, Ar-H at C-2)</td>
</tr>
<tr>
<td>135</td>
<td>4-ClC&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>4-ClC&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>7.30-8.20 (m, 9H, Ar-H), 8.86 (s, 1H, Ar-H at C-2)</td>
</tr>
<tr>
<td>136</td>
<td>2-Thienyl</td>
<td>C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>7.24-8.20 (m, 9H, Ar-H), 8.87 (s, 1H, Ar-H at C-2)</td>
</tr>
</tbody>
</table>

$^1$HNMR Spectra of 4-chloro-7,9-diphenylpyrido[3', 2' : 4, 5]thieno[3,2-d]pyrimidine shows absence of a broad singlet in the region δ 8.28-8.29 due to NH proton at position-3 of pyrimidinone ring proved the formation of 4-chloropyrimidines. Hydrogen situated at position-2 of pyrimidine ring was found to resonate at δ 8.84-8.86 in form of a singlet integrating for 1H. A multiplet was found in the region δ 7.24-8.22 resonated for aromatic protons.
\textsuperscript{1}HNMR Spectra of 4-chloro-7,9-diphenylpyrido[3', 2' 4, 5]thieno[3,2-d]pyrimidine (129) is shown in figure-8, it showed a singlet in downfield region at $\delta$ 8.6 due to one proton of CH at position-2 of pyrimidine ring and a multiplet due to aromatic protons was found to appear at $\delta$ 7.25-8.66 integrating for 12H.

MASS Spectrum of 4-chloro-7,9-diphenylpyrido[3', 2' 4, 5]thieno[3,2-d]pyrimidine (129) showed a base peak at 373. The mass fragmentation pattern is depicted in the scheme-150.

![Scheme 150](image)

5.3.1 Introduction

Condensed tetrazolopyrimidines have played an important role in the field of pharmaceutical chemistry as well as their capability to undergo reductive ring cleavage to form aminopyrimidines having valuable pharmacological properties.

Synthesis of tetrazolopyrimidines were carried out by the nucleophilic substitution reaction of 4-chloropyrimidines with nucleophiles like hydrazine hydrate, sodium azide, potassium azide and hydrazoic acid. This may also be performed by using a phase transfer catalyst. The desired tetrazolopyrimidines have been prepared here by two different routes conventional as well as under phase transfer conditions. (I) Formation of fused tetrazoles with conventional method.

Hiedo et al have reacted 2-substituted 4-chloro-5,6,7,8-tetrahydro-quinazolines with hydrazine hydrate to give 2-substituted 4-hydrazino-5,6,7,8-tetrahydroquinazolines which on diazotization with sodium nitrite in hydrochloric acid gave 5-substituted-7,8,9,10-tetrahydrotetrazolo[1,5-c]quinazolines. 5-Substituted-7,8,9,10-tetrahydrotetrazolo[1,5-c]quinazolines were also obtained by the direct reaction of 2-substituted 4-chloro-5,6,7,8-tetrahydroquinazolines with sodium azide in alcohol (Scheme-151).

\[
\begin{align*}
\text{Cl} & \quad \text{NH}_2\text{NH}_2 \\
362 & \quad \text{NHNNH}_2 \\
\text{NaN}_3 / \text{Alcohol} & \quad \text{NaNO}_2 \\
362 & \quad \text{NaN}_3 / \text{Alcohol} \\
364 & \quad \text{HCl} \quad 0-5^\circ\text{C}
\end{align*}
\]

Scheme 151
Substituted tetrazolo[1,5-c]thieno[2,3-b]pyrimidines\(^{257}\) (366) and tetrazolo[1,5-c]furo[2,3-b]pyrimidines\(^{258}\) (369) were obtained by the reaction of 4-chloroderivatives with sodium azide (Scheme-152 &153)

![Scheme 152](image)

4-chloropyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (370) was reacted with sodium azide and 95 % ethanol to afford tetrazolo[1,5-c]pyrido[3', 2' 4, 5]thieno[3,2-d]pyrimidine\(^{28}\) (371) (Scheme-154)

![Scheme 154](image)
2-Substituted 4-chloro-7,9-dimethylpyrido[3', 2' 4, 5]thieno[3,2-d]pyrimidines\textsuperscript{255} (372) were reacted with hydrazine hydrate to give 4-hydrazino-7,9-dimethylpyrido[3', 2' 4, 5]thieno[3,2-d]pyrimidines (373), which was further treated with sodium nitrite in glycerol to give 5-Substituted 7,9-dimethyl-tetrazolo[1,5-c]pyrido[3', 2' 4, 5]thieno[3,2-d]pyrimidines (374) (Scheme-155)

\begin{center}
\includegraphics[width=0.8\textwidth]{Scheme155.png}
\end{center}

Scheme 155

Rudolph\textsuperscript{259} showed that tetrazolo[1,5-a]pyrimidines (376) was formed by reaction of hydrazoic acid with 2-chloropyridine (375) (Scheme-156)

\begin{center}
\includegraphics[width=0.3\textwidth]{Scheme156.png}
\end{center}

Scheme 156

196
2-Chloro-3,5-dinitropyridine\textsuperscript{260} (377) with two equivalents of potassium azide (KN\textsubscript{3}) in the presence of alcohol to give 6,8-dinitrotetrazolo[1,5-a]pyridine (378) (Scheme-157)

![Scheme 157](image)

Dave et al\textsuperscript{250} have synthesized 7,9-disubstituted-1,2,3,4-tetrazolo[1,5-c]-7H-pyrrolo[3,2-c]pyrimidines (380) by the reaction of 4-chloro-5,7-disubstituted-7H-pyrrolo[2,3-d]pyrimidines (379) with sodium azide and ammonium chloride in dimethylsulfoxide (Scheme-158)

![Scheme 158](image)

(II) Synthesis of tetrazolo/azido moiety by using phase transfer catalysis

Reeves et al\textsuperscript{261} have reported that cyclohexyl bromide (381) was reacted with sodium azide using tricapryllylmarlmonium chloride (Aliquat 336\textsuperscript{®}) as phase transfer catalyst to afford cyclohexyl azide (382)(Scheme-159)
2-Chloro-3-cyano-4,6-diarylpyridines (383) were reacted with sodium azide in chlorobenzene under phase transfer conditions to afford 5,7-diaryl-3-cyanotetrazolo[1,5-a]pyridines (384) (Scheme 160).

Benzyl chloride (385) was reacted with 25% aqueous sodium azide and trioctylmethylammonium chloride to afford benzyl azide (386) (Scheme 161).
5.3.2 **Present work**

The literature study related to fused tetrazoles reveals that there has been no attention attributed towards the synthesis of substituted tetrazolo[1,5-c]pyrido[3', 2' 4, 5]thieno[3,2-d]pyrimidines under phase transfer catalysis conditions.

The technique of phase transfer catalysis offers many advantages like, the reaction time can be reduced and better yield of products can be obtained.


5.3.3 **Results and discussion**

The desired 7,9-diaryltetrazolo[1,5-c]pyrido[3', 2' 4, 5]thieno[3,2-d]pyrimidines (XIX, 137-144) were synthesized by two different routes. In the first route, 4-chloro-7,9-diarylpypyrido[3', 2' 4, 5]thieno[3,2-d]pyrimidines (XVIII, 129-136) were reacted with sodium azide and ammonium chloride in dimethylsulfoxide with stirring at 80-90 °C. In this method *in situ* generation of ammonium azide facilitated the reaction (Scheme-162).

![Scheme 162](image-url)
All the compounds were white to off-white in colour and obtained in 60-67% yields. They are soluble in chloroform, methylene chloride, N,N-dimethylformamide and dimethylsulfoxide. Recovery of dimethyl sulfoxide from the reaction mixture and longer reaction times are the main problem associated with such reactions.

In the second route, 7,9-diaryltetrazolo[1,5-c]pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidines (XIX, 137-144) were obtained by the reaction of 4-chloro-7,9-diaryltetrazolo[3', 2': 4, 5]thieno[3,2-d]pyrimidines (XVIII, 129-136) with sodium azide using chlorobenzene as a solvent under liquid-liquid phase transfer condition. Tricaprylmethylammonium chloride (Aliquat 336®) was used as a phase transfer catalyst (Scheme-163).

\[
\begin{align*}
\text{XVIII} & \quad \text{NaN}_3/\text{H}_2\text{O} \\
& \quad \text{Aliquat 336} \quad \text{1-1.5 hrs} \\
\rightarrow & \quad \text{XIX}
\end{align*}
\]

Scheme 163

The mechanism for such a displacement reaction carried out under phase transfer conditions is shown in scheme-164.
The mechanism suggested that initially all sodium azide remains dissolved in aqueous phase. Here displacement reaction between tricaprylmethylammonium chloride and sodium azide occurred to form tricaprylmethylammonium azide. The tricaprylmethylammonium azide thus formed is extracted in the organic phase where it underwent displacement reaction with 4-chloro-7,9-diarylpyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidines (XVIII) to form 7,9-diaryltetrazolo[1,5-c]pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidines (XIX) and tricaprylmethylammonium chloride, which was then leads towards aqueous phase and set of reaction were repeated.

The same reaction was tried with different catalysts like tetrabutylammonium bromide (TBAB), benzyltriethylammonium chloride, tetraethylammonium bromide and cetyltrimethylammonium chloride but none of these catalysts gave satisfactory results.

The reaction period for all these reaction was between 1-1.5 hours, with the progress of reaction the organic phase became darker. The product thus obtained were white...
to off-white in colour. The products were obtained in 75-85 % yield, moreover the solvent is also recoverable.

Physical constants of 7,9-diaryltetrazolo[1,5-c]pyrido[3', 2' : 4, 5]thieno-[3,2-d]pyrimidines (XIX, 137-144) are recorded in table-37


<table>
<thead>
<tr>
<th>Compd no</th>
<th>R_1</th>
<th>R_2</th>
<th>Yield (%)</th>
<th>M.P.</th>
<th>Mol. formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>137</td>
<td>C_6H_5</td>
<td>C_6H_5</td>
<td>60</td>
<td>75</td>
<td>210-12</td>
</tr>
<tr>
<td>138</td>
<td>C_6H_5</td>
<td>4-OCH_3 C_6H_4</td>
<td>62</td>
<td>78</td>
<td>195-96</td>
</tr>
<tr>
<td>139</td>
<td>C_6H_5</td>
<td>4-ClC_6H_4</td>
<td>64</td>
<td>75</td>
<td>190-92</td>
</tr>
<tr>
<td>140</td>
<td>4-OCH_3 C_6H_4</td>
<td>C_6H_5</td>
<td>60</td>
<td>75</td>
<td>193-94</td>
</tr>
<tr>
<td>141</td>
<td>4-OCH_3 C_6H_4</td>
<td>4-OCH_3 C_6H_4</td>
<td>65</td>
<td>72</td>
<td>103-05</td>
</tr>
<tr>
<td>142</td>
<td>4-ClC_6H_4</td>
<td>C_6H_5</td>
<td>62</td>
<td>75</td>
<td>187-88</td>
</tr>
<tr>
<td>143</td>
<td>4-ClC_6H_4</td>
<td>4-ClC_6H_4</td>
<td>65</td>
<td>74</td>
<td>215-17</td>
</tr>
<tr>
<td>144</td>
<td>2-Thienyl</td>
<td>C_6H_5</td>
<td>65</td>
<td>78</td>
<td>198-99</td>
</tr>
</tbody>
</table>

a = conventional method, reaction time 3-4 hours
b = phase transfer method, reaction time 1-1.5 hours

IR(KBr) Spectral data of 7,9-diaryltetrazolo[1,5-c]pyrido[3', 2' : 4, 5]thieno[3,2-d]pyrimidine (XIX, 137-144) are summerized in table-38. IR(KBr) spectra of compounds XIX showed no absorption bands in the region around 2100 cm\(^{-1}\) for azido fuctionality excluding the possibility of azido formation and prove the formation of tetrazole ring.
Table - 38 : IR(KBr) spectral data of 7,9-diaryltetrazolo[1,5-c]pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidines (XIX, 137-144)

<table>
<thead>
<tr>
<th>Compd no.</th>
<th>v CH cm(^{-1})</th>
<th>v C=C, C=N cm(^{-1})</th>
<th>δ CH cm(^{-1})</th>
<th>δ C-N cm(^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>137</td>
<td>3010, 2998</td>
<td>1568, 1536</td>
<td>1429</td>
<td>1261</td>
</tr>
<tr>
<td>138</td>
<td>3004, 2972</td>
<td>1576, 1524</td>
<td>1425</td>
<td>1250</td>
</tr>
<tr>
<td>139</td>
<td>3010, 2956</td>
<td>1566, 1520</td>
<td>1440</td>
<td>1254</td>
</tr>
<tr>
<td>140</td>
<td>3010, 2996</td>
<td>1576, 1550</td>
<td>1436</td>
<td>1261</td>
</tr>
<tr>
<td>141</td>
<td>3004, 2976</td>
<td>1575, 1524</td>
<td>1425</td>
<td>1256</td>
</tr>
<tr>
<td>142</td>
<td>3010, 2956</td>
<td>1576, 1536</td>
<td>1424</td>
<td>1254</td>
</tr>
<tr>
<td>143</td>
<td>3010, 2972</td>
<td>1556, 1530</td>
<td>1440</td>
<td>1250</td>
</tr>
<tr>
<td>144</td>
<td>3010, 2982</td>
<td>1576, 1524</td>
<td>1424</td>
<td>1262</td>
</tr>
</tbody>
</table>


\(^1\)HNMR Spectra showed aromatic protons were resonated in the region δ 7.50-9.93 integrating for 12H. A singlet at δ 9.90-9.93 integrating for 1H of CH at position-2 of pyrimidine ring.

\(^1\)HNMR Spectra of 7,9-diphenyltetrazolo[1,5-c]pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (137) was given in figure-9. The \(^1\)HNMR spectra of compound 137 exhibited a multiplet due to aromatic proton in the region δ 7.54-9.93 integrating for 12H. Proton situated at position-2 of pyrimidine ring was found to resonate at δ 9.93 integrating for 1H.
Table - 39: $^1$HNMR spectral data of 7,9-diaryltetrazolo[1,5-c]pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidines (XIX, 137-144)

<table>
<thead>
<tr>
<th>Compd no</th>
<th>R$_1$</th>
<th>R$_2$</th>
<th>$^1$HNMR (δ ppm, DMSO d$_6$ + CDC$_3$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>137</td>
<td>C$_6$H$_5$</td>
<td>C$_6$H$_5$</td>
<td>7.54-8.30 (m, 11H, Ar-H), 9.93 (s, 1H, Ar-H at C-2)</td>
</tr>
<tr>
<td>138</td>
<td>C$_6$H$_5$</td>
<td>4-OCH$_3$C$_6$H$_4$</td>
<td>3.99 (s, 3H, OCH$_3$), 7.55-8.29 (m, 10H, Ar-H), 9.92 (s, 1H, Ar-H at C-2)</td>
</tr>
<tr>
<td>139</td>
<td>C$_6$H$_5$</td>
<td>4-ClC$_6$H$_4$</td>
<td>7.59-8.29 (m, 10H, Ar-H), 9.94 (s, 1H, Ar-H at C-2)</td>
</tr>
<tr>
<td>140</td>
<td>4-OCH$_3$C$_6$H$_4$</td>
<td>C$_6$H$_5$</td>
<td>4.00 (s, 3H, OCH$_3$), 7.54-8.30 (m, 10H, Ar-H), 9.92 (s, 1H, Ar-H at C-2)</td>
</tr>
<tr>
<td>141</td>
<td>4-OCH$_3$C$_6$H$_4$</td>
<td>4-OCH$_3$C$_6$H$_4$</td>
<td>4.04 (s, 6H, 2OCH$_3$), 7.59-8.28 (m, 9H, Ar-H), 9.94 (s, 1H, Ar-H at C-2)</td>
</tr>
<tr>
<td>142</td>
<td>4-ClC$_6$H$_4$</td>
<td>C$_6$H$_5$</td>
<td>7.54-8.25 (m, 10H, Ar-H), 9.92 (s, 1H, Ar-H at C-2)</td>
</tr>
<tr>
<td>143</td>
<td>4-ClC$_6$H$_4$</td>
<td>4-ClC$_6$H$_4$</td>
<td>7.60-8.30 (m, 9H, Ar-H), 9.94 (s, 1H, Ar-H at C-2)</td>
</tr>
<tr>
<td>144</td>
<td>2-Thienyl</td>
<td>C$_6$H$_5$</td>
<td>7.59-8.19 (m, 9H, Ar-H), 8.87 (s, 1H, Ar-H at C-2)</td>
</tr>
</tbody>
</table>


5.4.1 Introduction

Reductive ring cleavage of tetrazole moiety constitutes a synthetically important process for the preparation of amines. Heterocyclic amines were found to be possess antiviral, antineoplastic, anti HIV and antimetabolic activities.
The reduction of tetrazoles/azides by lithium aluminium hydride\textsuperscript{264-266} or by catalytic hydrogenation\textsuperscript{267, 268} represents an important tool in organic chemistry for the preparation of amines. Other reagents employed are either costly, difficult to prepare or give lower yields, e.g. chloromethyl silane,\textsuperscript{269} tributyltin hydride (Bu\textsubscript{3}SnH)\textsuperscript{270} etc.

Various reagents have been employed in the literature for the reduction of tetrazolo/azido moiety leading to the formation of corresponding amino compounds.

Guttsait et al\textsuperscript{271} have reported reduction of 2-azido-3-cyano-4-trifluoromethyl-6-phenylpyridine (387) to the corresponding 2-amino-3-cyano-4-trifluoromethyl-6-phenylpyridine (388) using stannous chloride (SnCl\textsubscript{2}) as a reducing agent (Scheme-166).

\[
\begin{align*}
\text{CF}_3 & \quad \text{CN} \\
\text{Ph} & \quad \text{N}_3 \\
\text{SnCl}_2 & \\
\text{387} & \quad \text{SnCl}_2 \\
\text{CN} & \quad \text{NH}_2 \\
\text{Ph} & \quad \text{388}
\end{align*}
\]

\textbf{Scheme 166}

4-Azidonitrobenzene\textsuperscript{272} (389) was reduced with one equivalent of triphenylphosphine in the presence of water in tetrahydrofuran to give 4-aminonitrobenzene (390) (Scheme-167).

\[
\begin{align*}
\text{N}_3 & \\
\text{NO}_2 & \quad \text{PPh}_3 / \text{H}_2\text{O} \\
\text{389} & \quad \text{THF} \\
\text{NH}_2 & \\
\text{NO}_2 & \quad \text{390}
\end{align*}
\]

\textbf{Scheme 167}

7,9-Disubstituted-7H-1,2,3,4-tetrazolo[1,5-c]pyrrolo[3,2-e]pyrimidines\textsuperscript{270} (391) were reacted with powdered zinc in glacial acetic acid to afford 4-amino-5,7-disubstituted-7H-pyrrolo[2,3-d]pyrimidines (392) (Scheme-168).
Soai and co-workers\textsuperscript{273} carried out reduction of azides (393) in tetrahydrofuran-methanol using sodium borohydride to give respective amines (394) (Scheme-169).

\[
\text{RN}_3 + \text{NaBH}_4 / \text{CH}_3\text{OH} \rightarrow \text{RNH}_2
\]

\[393 \quad 394\]

\[R = \text{C}_6\text{H}_5, \text{ClC}_6\text{H}_4, \text{O}_2\text{NC}_6\text{H}_4, \text{C}_6\text{H}_3\text{NH}_2\]

**Scheme 169**

Reduction of benzyl azide (395) were carried out using sodium borohydride and nickel chloride, \textit{in situ} generation of nickel boride facilitates the reaction to form benzyl amine\textsuperscript{274} (396) (Scheme-170).

\[
\text{CH}_2\text{N}_3 + \text{NiCl}_4 \cdot 6\text{H}_2\text{O} + \text{NaBH}_4 \rightarrow \text{CH}_2\text{NH}_2
\]

\[395 \quad 396\]

**Scheme 170**

5,7-Diaryl-8-cyanotetrazolo[1,5-a]pyridines (397) were reacted with sodium borohydride using phase transfer catalyst to afford 4,6-diaryl-2-amino-3-cyanopyridines\textsuperscript{262} (398) (Scheme-171).
Scheme 171

Kabalka et al.\(^{275}\) have reported reduction of aryl azides (399) to anilines (400) by using p-substituted benzyltrimethylammonium borohydride as PTC in methanol under reflux condition (scheme-172).

\[
\begin{align*}
R_1 & \quad \text{CN} \\
R_2 & \quad \text{N} \quad \text{N} \\
\text{N} & \quad \text{N} \\
\text{N} & \quad \text{N} \\
\text{NaBH}_4 / \text{H}_2\text{O} & \quad \text{R}_{1} \quad \text{CN} \\
& \quad \text{Toluene} \\
& \quad \text{PTC} \\
& \quad \text{RN}_3 \quad \text{NaBH}_4 / \text{H}_2\text{O} \quad \text{Toluene} \quad \text{PTC} \quad \text{RNH}_2
\end{align*}
\]

**Scheme 172**


The reaction was also carried out for the first time, using phase transfer catalyst. The detailed survey of literature suggested that different 4-aminopyridothenopyrimidines were prepared by the reaction of appropriate ring having o-aminonitrile and formamide,\(^{98,118,210-32}\) but no attention has been given to the reduction of tetrazole ring.
5.4.3 Results and discussion

4-Amino-7,9-diarylpyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidines (XX, 145-152) were synthesized by the reductive ring cleavage of 7,9-diaryltetrazolo[1,5-c]pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidines (XIX, 137-144), using zinc in acetic acid as the reducing agent under boiling condition (scheme-173)

![Scheme 173](image)

All synthesized 4-amino-7,9-diarylpyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidines were yellow to greenish yellow in colour having high melting points and soluble in ethanol, N,N-dimethylformamide and acetic acid. They are obtained in 60-65% yield. All the reactions took 6-8 hrs. for completion.

In second route, 7,9-diaryltetrazolo[1,5-c]pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidines (XIX, 137-144) were reduced using sodium borohydride as reducing agent. The reactions were carried out in two phase system, employing tricaprylmethylammonium chloride (Aliquat 336®) as phase transfer catalyst to afford 4-amino-7,9-diarylpyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidines (XX, 145-152) (Scheme-174)
The reactions were performed under liquid-liquid phase transfer condition. The solvent employed was toluene. The ratio of toluene and water was 3:1 (v/v).

It seems that initially tricaprylmethylammonium chloride underwent exchange reaction with sodium borohydride to form tricaprylmethylammonium borohydride. This salt was then extracted in organic phase, where it reduced the 7,9-diaryltetrazolo[1,5-c]pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidines (XIX, 137-144) to form corresponding 4-amino-7,9-diarylpyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidines (XX, 145-152).

Reduction of same 7,9-diaryltetrazolo[1,5-c]pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidines were carried out in toluene in the presence of 18-crown-6 as PTC were little longer and some side reactions also seemed to occur, which were evident from different spots visualized on tlc (benzene/ethanol- 8:2).

The other catalysts tried for the reaction were tetrabutylammonium bromide (TBAB), triethylbenzylammonium chloride (TEBA), tetaethylammonium chloride (TEAC) and benzyltributylammonium bromide (BTBAC) out of all the catalysts studied, tricaprylmethylammonium chloride (Aliquat 336®) was the only catalyst found to give satisfactory results and so it was the catalyst of choice.

All these reactions took 1.0-1.5 hours for completion. Sodium borohydride was finely powdered and added portion wise. The reaction was performed at room temperature. All the products were yellow to greenish yellow in colour. Melting point of compounds were found to be similar as prepared by using conventional methodology.


<table>
<thead>
<tr>
<th>Compd No.</th>
<th>R₁</th>
<th>R₂</th>
<th>Yield (%)</th>
<th>M.P. °C</th>
<th>Mol. formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>145</td>
<td>C₆H₅</td>
<td>C₆H₅</td>
<td>60 75</td>
<td>255-57</td>
<td>C₁₂H₁₄N₄S</td>
</tr>
<tr>
<td>146</td>
<td>C₆H₅</td>
<td>4-OCH₃C₆H₄</td>
<td>62 80</td>
<td>281-82</td>
<td>C₁₂H₁₄N₄OS</td>
</tr>
<tr>
<td>147</td>
<td>C₆H₅</td>
<td>4-ClC₆H₄</td>
<td>60 75</td>
<td>267-69</td>
<td>C₁₂H₁₄ClN₄S</td>
</tr>
<tr>
<td>148</td>
<td>4-OCH₃C₆H₄</td>
<td>C₆H₅</td>
<td>63 78</td>
<td>259-60</td>
<td>C₁₂H₁₄N₄OS</td>
</tr>
<tr>
<td>149</td>
<td>4-OCH₃C₆H₄</td>
<td>4-OCH₃C₆H₄</td>
<td>64 76</td>
<td>279-80</td>
<td>C₁₂H₁₄N₄O₂S</td>
</tr>
<tr>
<td>150</td>
<td>4-ClC₆H₄</td>
<td>C₆H₅</td>
<td>60 75</td>
<td>272-73</td>
<td>C₁₂H₁₄ClN₄S</td>
</tr>
<tr>
<td>151</td>
<td>4-ClC₆H₄</td>
<td>4-ClC₆H₄</td>
<td>60 75</td>
<td>239-40</td>
<td>C₁₂H₁₂Cl₂N₄S</td>
</tr>
<tr>
<td>152</td>
<td>2-Thienyl</td>
<td>C₆H₅</td>
<td>65 80</td>
<td>230-32</td>
<td>C₁₉H₁₂N₄S₂</td>
</tr>
</tbody>
</table>

a = conventional method, reaction time 6-8 hours
b = phase transfer method, reaction time 1-1.5 hours

IR(KBr) Spectral data of 4-amino-7,9-diarylpyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidines (XX, 145-152) are recorded in table-41.

IR(KBr) Spectra of 4-amino-7,9-diarylpyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidines (XX, 145-152) showed absorption bands in the region 3455- 3295 cm⁻¹ and bending absorption at 1633 cm⁻¹ suggested the presence of amino (-NH₂) group.
Table - 41: IR(KBr) spectral data of 4-amino-7,9-diarylpyrido[3', 2' 4, 5]thieno[3,2-d]pyrimidines (XX, 145-152)

<table>
<thead>
<tr>
<th>Compd no</th>
<th>(\nu) NH cm(^{-1})</th>
<th>(\nu) CH cm(^{-1})</th>
<th>(\nu) C=C, C=N cm(^{-1})</th>
<th>(\delta) NH cm(^{-1})</th>
<th>(\delta) CH cm(^{-1})</th>
<th>(\delta) C-N cm(^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>145</td>
<td>3455, 3295</td>
<td>3010, 2919, 2849</td>
<td>1564, 1539</td>
<td>1633</td>
<td>1442</td>
<td>1260</td>
</tr>
<tr>
<td>146</td>
<td>3456, 3272</td>
<td>3004, 2996, 2872</td>
<td>1576, 1540</td>
<td>1632</td>
<td>1440</td>
<td>1276</td>
</tr>
<tr>
<td>147</td>
<td>3450, 3270</td>
<td>3010, 2998, 2852</td>
<td>1578, 1524</td>
<td>1633</td>
<td>1445</td>
<td>1250</td>
</tr>
<tr>
<td>148</td>
<td>3455, 3272</td>
<td>3008, 2972, 2882</td>
<td>1576, 1539</td>
<td>1633</td>
<td>1424</td>
<td>1256</td>
</tr>
<tr>
<td>149</td>
<td>3450, 3292</td>
<td>3010, 2996, 2889</td>
<td>1586, 1540</td>
<td>1632</td>
<td>1440</td>
<td>1250</td>
</tr>
<tr>
<td>150</td>
<td>3455, 3270</td>
<td>3004, 2897, 2842</td>
<td>1570, 1524</td>
<td>1634</td>
<td>1440</td>
<td>1242</td>
</tr>
<tr>
<td>151</td>
<td>3456, 3272</td>
<td>3010, 2972, 2849</td>
<td>1587, 1530</td>
<td>1632</td>
<td>1442</td>
<td>1246</td>
</tr>
<tr>
<td>152</td>
<td>3450, 3295</td>
<td>3010, 2996, 2852</td>
<td>1589, 1540</td>
<td>1633</td>
<td>1424</td>
<td>1250</td>
</tr>
</tbody>
</table>

\(^1\)HNMR Spectral data of 4-amino-7,9-diarylpyrido[3', 2' 4, 5]thieno[3,2-d]pyrimidines (XX, 145-152) are recorded in table-42. The \(^1\)HNMR spectra of compounds (XX, 145-152) exhibited a multiplet for aromatic protons in the region \(\delta\) 7.26-8.52 including a singlet integrating for one hydrogen due to CH at position-2 of pyrimidine ring. A singlet was found to resonate in the region \(\delta\) 5-6 integrated for two hydrogens.
Figure-11
Table - 42: \(^1\)HNMR Spectral data of 4-amino-7,9-diarylpyrido[3', 2', 4, 5]thieno[3,2-d]pyrimidines (XX, 145-152)

<table>
<thead>
<tr>
<th>Compd no.</th>
<th>(R_1)</th>
<th>(R_2)</th>
<th>(^1)HNMR (δ ppm, DMSO d(_6) + CDCl(_3))</th>
</tr>
</thead>
<tbody>
<tr>
<td>145</td>
<td>C(_6)H(_5)</td>
<td>C(_6)H(_5)</td>
<td>6.45 (s, 2H, NH(_2)), 7.46-8.19 (m, 11H, Ar-H), 8.37 (s, 1H, Ar-H at C-2)</td>
</tr>
<tr>
<td>146</td>
<td>C(_6)H(_5)</td>
<td>4-OCH(_3)C(_6)H(_4)</td>
<td>3.99 (s, 3H, OCH(_3)), 6.49 (s, 2H, NH(_2)), 7.50-8.18 (m, 10H, Ar-H), 8.39 (s, 1H, Ar-H at C-2)</td>
</tr>
<tr>
<td>147</td>
<td>C(_6)H(_5)</td>
<td>4-ClC(_6)H(_4)</td>
<td>5.18 (s, 2H, NH(_2)), 7.26-8.15 (m, 10H, Ar-H), 8.52 (s, 1H, Ar-H at C-2)</td>
</tr>
<tr>
<td>148</td>
<td>4-OCH(_3)C(_6)H(_4)</td>
<td>C(_6)H(_5)</td>
<td>4.00 (s, 3H, OCH(_3)), 6.45 (s, 2H, NH(_2)), 7.49-8.19 (m, 10H, Ar-H), 8.38 (s, 1H, Ar-H at C-2)</td>
</tr>
<tr>
<td>149</td>
<td>4-OCH(_3)C(_6)H(_4)</td>
<td>4-OCH(_3)C(_6)H(_4)</td>
<td>4.02 (s, 6H, 2OCH(_3)), 6.26 (s, 2H, NH(_2)), 7.51-8.19 (m, 9H, Ar-H), 8.48 (s, 1H, Ar-H at C-2)</td>
</tr>
<tr>
<td>150</td>
<td>4-ClC(_6)H(_4)</td>
<td>C(_6)H(_5)</td>
<td>5.20 (s, 2H, NH(_2)), 7.28-8.13 (m, 10H, Ar-H), 8.49 (s, 1H, Ar-H at C-2)</td>
</tr>
<tr>
<td>151</td>
<td>4-ClC(_6)H(_4)</td>
<td>4-ClC(_6)H(_4)</td>
<td>5.25 (s, 2H, NH(_2)), 7.27-8.19 (m, 9H, Ar-H), 8.52 (s, 1H, Ar-H at C-2)</td>
</tr>
<tr>
<td>152</td>
<td>2-Thienyl</td>
<td>C(_6)H(_5)</td>
<td>6.42 (s, 2H, NH(_2)), 7.46-8.13 (m, 9H, Ar-H), 8.40 (s, 1H, Ar-H at C-2)</td>
</tr>
</tbody>
</table>

\(^1\)HNMR (DMSO d\(_6\)) Spectra of 4-amino-7,9-diphenylpyrido[3', 2', 4, 5]thieno[3,2-d]pyrimidine (137) (figure-10) exhibited aromatic region at δ 7.46-8.37 integrating for 11H in form of multiplet. Proton at C-2 of pyrimidine was found to resonate at...
\[ \delta 8.37 \text{ in form of a singlet integrating for one hydrogen. The protons for amino functionality were resonated at } \delta 6.45 \text{ integrating for two protons.} \]

\[ ^1\text{HNMR (DMSO } d_6) \text{ Spectra of } 4\text{-amino-7-(4-chlorophenyl)}-9\text{-phenylpyrido}[3', 2' 4, 5]\text{thieno}[3,2-d]\text{pyrimidine (137) (figure-11), it shows a multiplet due to aromatic proton at } \delta 7.26-8.52 \text{ integrating for 10H. Proton at C-2 of pyrimidine was found to resonate at } \delta 8.52 \text{ in form of a singlet integrating for 1H. The protons for amino functionality were resonated at } \delta 5.18 \text{ integrating for two hydrogens.} \]

### 5.5 Experimental

Melting points were uncorrected and determined on Toshniwal melting point apparatus in open capillary tubes. Carbon, hydrogen and nitrogen of all compounds were estimated gravimetrically using Column Model-33 carbon, hydrogen and nitrogen analyser, performed at Ahmedabad Textile Industrial Research Association (ATIRA), Ahmedabad.

IR(KBr) Spectra of compounds XVII, XVIII, XIX and XX are recorded on Buck-500 spectrophotometer and spectrum one FT IR spectrophotometer. Samples were run in form of pellets which were prepared by smearing 2 mg compound in 150 mg KBr powder and results were recorded in cm\(^{-1}\).

\[ ^1\text{HNMR Spectra of } 4\text{-chloro-7,9-diarylpyrido}[3', 2' : 4, 5]\text{thieno}[3,2-d]\text{pyrimidines (XVIII), 7,9-diaryltetrazolo[1,5-c]pyrido}[3', 2' : 4, 5]\text{thieno}[3,2-d]\text{pyrimidines (XIX), 4-amino-7,9-diarylpyrido}[3', 2' : 4, 5]\text{thieno}[3,2-d]\text{pyrimidines (XX) were recorded on Varian Model-400 spectrometer using TMS as an internal standard. The values are given in } \delta \text{ ppm.} \]

The purity of compounds XVII, XVIII, XIX and XX was checked routinely by TLC (1-mm thickness) using silica gel-G and spots were visualized by exposing the dry plates in iodine vapours.

2-Carbethoxy-3-amino-4,6-diphenylthieno[2,3-b]pyridine (33, 0.01 mole, 3.74 g) was refluxed with formamide (15 ml), formic acid (2 ml) in N,N-dimethylformamide (5 ml) for 17 hrs. After completion of the reaction, the solvent was removed in vacuo. Solid separated was filtered, washed with alcohol, dried and recrystallized with N,N-dimethylformamide.

Yield: 70%  
mp: 360°C  
Analysis: C$_{21}$H$_{13}$N$_3$OS  
Calcd: C 70.97 H 3.68 N 11.28 %  
Found: C 71.20 H 3.99 N 11.01 %  
IR(KBr) cm$^{-1}$: 3394 (NH), 3004, 2960 (CH), 1675 (C=O), 1579, 1514 (C=C, C=N)  
$^1$HNMR δ ppm: 7.40-8.10 (m, 11H, Ar-H), 8.89 (s, 1H, Ar-H at C-2), 8.28 (s, 1H, NH)

7-(4-Methoxyphenyl)-9-phenylpyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidin-4(3H)-one (122):

A mixture of 2-carbethoxy-3-amino-4-phenyl-6-(4-methoxyphenyl)thieno[2,3-b]pyridine (34, 0.01 mole, 4.04 g), formamide (15 ml), formic acid (2 ml) in N,N-dimethylformamide (5 ml) was refluxed for 15 hrs. After completion of the reaction, the work-up was carried out according to the procedure described for 121 to get the titled product.

Yield: 53%  
mp: 360°C  
Analysis: C$_{22}$H$_{15}$N$_3$O$_2$S  
Calcd: C 68.56 H 3.92 N 10.90 %  
Found: C 68.20 H 3.70 N 11.22 %  
IR(KBr) cm$^{-1}$: 3390 (NH), 2996, 2856 (CH), 1667 (C=O), 1605, 1524 (C=C, C=N)  
$^1$HNMR δ ppm: 4.08 (s, 3H, OCH$_3$), 7.19-8.19 (m, 10H, Ar-H), 8.96 (s, 1H, Ar-H at C-2), 8.28 (s, 1H, NH)

7-(4-Chlorophenyl)-9-phenylpyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidin-4(3H)-one (123):

A mixture of formamide (15 ml), 2-Carbethoxy-3-amino-4-phenyl-6-(4-chlorophenyl)thieno[2,3-b]pyridine (35, 0.01 mole, 4.08 g) and formic acid (2 ml) in N,N-
dimethylformamide (5 ml) was refluxed for 15 hrs. After completion of the reaction, the work-up was carried out according to the procedure described for 121 to get the titled product.

Yield : 65 %  
mp 290-91 °C

Analysis :  
C_{21}H_{12}ClN_{3}OS (389.82)

Calcd :  
C 64.69  H 3.10  N 10.77 %

Found :  
C 64.92  H 3.34  N 11.95 %

IR(KBr) cm\(^{-1}\) : 3396 (NH), 3004, 2956 (CH), 1665 (C=O), 1604, 1556 (C=C, C=N)

\(^1\)HNMR \(\delta\) ppm : 7.42-8.20 (m, 10H, Ar-H), 8.82 (s, 1H, Ar-H at C-2), 8.29 (s, 1H, NH)

7-Phenyl-9-(4-methoxyphenyl)pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidin-4(3H)-one (124)

A mixture of 2-carbethoxy-3-amino-4-(4-methoxyphenyl)-6-phenylthieno[2,3-b]pyridine (36, 0.01 mole, 4.04 g), formamide (15 ml), formic acid (2 ml) in N,N-dimethylformamide (5 ml) was refluxed for 17 hrs. After completion of the reaction, the work-up was carried out according to the procedure described for 121 to get the titled product.

Yield : 65 %  
mp 335-36 °C

Analysis :  
C_{22}H_{15}N_{3}O_{2}S (385.35)

Calcd :  
C 68.56  H 3.92  N 10.90 %

Found :  
C 68.20  H 3.69  N 10.73 %

IR(KBr) cm\(^{-1}\) : 3398 (NH), 3010, 2996 (CH), 1672 (C=O), 1605, 1520 (C=C, C=N)

\(^1\)HNMR \(\delta\) ppm : 3.99 (s, 3H, OCH\(_3\)), 7.20-8.17 (m, 10H, Ar-H), 8.94 (s, 1H, Ar-H at C-2), 8.29 (s, 1H, NH)

7,9-Di(4-methoxyphenyl)pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidin-4(3H)-one (125)

2-Carbethoxy-3-amino-4,6-di(4-methoxyphenyl)thieno[2,3-b]pyridine (37, 0.01 mole, 4.04 g), formamide (15 ml) and formic acid (2 ml) in N,N-dimethylformamide (5 ml) was refluxed for 16 hrs. On completion of the reaction, the work-up was carried out as the procedure described for 121 to get the titled product.

Yield : 60 %  
mp 347-50 °C
Analysis . C_{23}H_{17}N_{3}O_{3}S (415.36)
Calcd : C 66.50 H 4.12 N 10.11 %
Found : C 66.76 H 3.80 N 9.89 %
IR(KBr) cm^{-1} . 3392 (NH), 3008, 2856 (CH), 1678 (C=O), 1596, 1524 (C=C, C=N)
^1HNMR δ ppm : 3.99 (s, 6H, 20CH₃), 7.17-8.20 (m, 9H, Ar-H), 8.96 (s, 1H, Ar-H
at C-2), 8.28 (s, 1H, NH)
7-Phenyl-9-(4-chlorophenyl)pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidin-4(3H)-one (126)

A mixture of 2-carbethoxy-3-amino-4-(4-methoxyphenyl)-6-phenylthieno[2,3-b]pyridine (38, 0.01 mole, 4.08 g), formamide (15 ml), formic acid (2 ml) in N,N-dimethylformamide (5 ml) was refluxed for 15 hrs. After completion of the reaction, the work-up was carried out according to the procedure described for 121 to get the titled product.
Yield  57 % mp : 360 °C
Analysis . C_{21}H_{12}ClN_{3}O_{3}S (389 82)
Calcd : C 64.69 H 3.10 N 10.77 %
Found : C 64.38 H 3.35 N 10.56 %
IR(KBr) cm^{-1} . 3396 (NH), 3004, 2972 (CH), 1670 (C=O), 1576, 1556 (C=C, C=N)
^1HNMR δ ppm : 7.40-8.19 (m, 10H, Ar-H), 8.99 (s, 1H, Ar-H at C-2), 8.28 (s, 1H, NH)
7-(4-Chlorophenyl)-9-(4-chlorophenyl)pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidin-4(3H)-one (127):

A mixture of formamide (15 ml), 2-carbethoxy-3-amino-4-(4-chlorophenyl)-6-(4-chlorophenyl)thieno-[2,3-b]pyridine (39, 0.01 mole, 4.43 g) and formic acid (2 ml) in N,N-dimethylformamide (5 ml) was refluxed for 12 hrs. After completion of the reaction, the titled product was obtained after the work-up according to the procedure described for 121.
Yield  60 % mp  279-80 °C
Analysis . C_{21}H_{11}Cl_{2}N_{3}OS (424.32)
Calcd : C 59.43 H 2.61 N 9.90 %
Found \( \text{C} \ 59.70 \text{ H} \ 2.86 \text{ N} \ 10.16 \% \)

IR(KBr) cm\(^{-1}\) 3398 (NH), 3010, 2998 (CH), 1672 (C=O), 1596, 1520 (C=C, C=H)

\(^1\)HNMR \( \delta \text{ppm} \) 7 41-8 20 (m, 9H, Ar-H), 8.94 (s, 1H, Ar-H at C-2), 8.28 (s, 1H, NH)


A mixture of 2-Carbethoxy-3-amino-4-(2-thienyl)-6-phenylthieno[2,3-b]pyridine (40, 0.01 mole, 3.80 g), formamide (15 ml), formic acid (2 ml) in N,N-dimethylformamide (5 ml) was refluxed for 12 hrs. After completion of the reaction, the work-up was carried out as the procedure described for 121 to get the titled product.

Yield \( 65 \% \)

Analysis \( \text{C}_{39} \text{H}_{11} \text{N}_{3} \text{OS}_{2} \) (361.3)

Calcd \( \text{C} \ 63.15 \text{ H} \ 3.06 \text{ N} \ 11.63 \% \)

Found \( \text{C} \ 63.38 \text{ H} \ 3.29 \text{ N} \ 11.28 \% \)

IR(KBr) cm\(^{-1}\) 3390 (NH), 3004, 2872 (CH), 1667 (C=O), 1604, 1550 (C=C, C=N)

\(^1\)HNMR \( \delta \text{ppm} \) 7 21-8 20 (m, 9H, Ar-H), 8.89 (s, 1H, Ar-H at C-2), 8.29 (s, 1H, NH)


7,9-Diphenylpyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidin-4(3H)-ones (121, 0.01 mole, 3.55 g) was refluxed with phosphorous oxychloride (15 ml) for 6 hrs. Completion of reaction was cheked by tlc. After completion of reaction the reaction mixture was poured on to the crushed ice. Solid separated was filtered, dried and recrystallized with a mixture of alcohol/ chloroform (6:4).

Yield \( 68 \% \)

mp \( 198-99 \degree \text{C} \)

Analysis \( \text{C}_{21} \text{H}_{12} \text{ClN}_{3} \text{OS} \) (373.82)

Calcd \( \text{C} \ 67.46 \text{ H} \ 3.23 \text{ N} \ 11.24 \% \)

Found \( \text{C} \ 67.69 \text{ H} \ 2.99 \text{ N} \ 10.95 \% \)

IR(KBr) cm\(^{-1}\) 3010, 2992 (CH), 1600, 1550 (C=C, C=N)

\(^1\)HNMR \( \delta \text{ppm} \) 7 25-8.21 (m, 11H, Ar-H), 8.86 (s, 1H, Ar-H at C-2)

A mixture of 7-(4-methoxyphenyl)-9-phenylpyrido[3', 2' · 4, 5]thieno[3,2-d]pyrimidin-4(3H)-ones (122, 0.01 mole, 3.85 g) and phosphorous oxychloride (15 ml) was refluxed for 4 hrs. After completion of reaction work-up was carried out according to the procedure described for 129 to get the titled product.

Yield : 62 %

mp : 212-14 °C

Analysis

Cacld

C 65.42 H 3.49 N 10.40 %

Found

C 65.70 H 3.29 N 10.67 %

IR(KBr) cm⁻¹

3010, 2996 (CH), 1596, 1524 (C=C, ON)

¹H NMR δ ppm : 3.99 (s, 3H, OCH₃), 7.27-8.22 (m, 10H, Ar-H), 8.84 (s, 1H, Ar-H at C-2)

4-Chloro-7-(4-chlorophenyl)-9-phenylpyrido[3', 2' · 4, 5]thieno[3,2-d]pyrimidine (131)

7-(4-Chlorophenyl)-9-phenylpyrido[3', 2' · 4, 5]thieno[3,2-d]pyrimidin-4(3H)-ones (123, 0.01 mole, 3.89 g) and phosphorous oxychloride (15 ml) was refluxed for 4 hrs. On completion of reaction the titled product was obtained after the work-up according to the procedure described for 129.

Yield : 60 %

mp : 239-40 °C

Analysis

Cacld

C 61.91 H 2.72 N 10.31 %

Found

C 62.20 H 2.99 N 10.09 %

IR(KBr) cm⁻¹

3051, 3004 (CH), 1576, 1546 (C=C, C=N)

¹H NMR δ ppm : 7.24-8.20 (m, 10H, Ar-H), 8.87 (s, 1H, Ar-H at C-2)

4-Chloro-7-phenyl-9-(4-methoxyphenyl)pyrido[3', 2' · 4, 5]thieno[3,2-d]pyrimidine (132)

A mixture of 7-phenyl-9-(4-methoxyphenyl)pyrido[3', 2' · 4, 5]thieno[3,2-d]pyrimidin-4(3H)-ones (124, 0.01 mole, 3.85 g) and phosphorous oxychloride (15 ml) was refluxed for 4 hrs. After completion of reaction work-up was carried out according to the procedure described for 129 to get the titled product.

Yield : 62 %

mp : 235-37 °C
Analysis  :  C_{22}H_{14}ClN_{3}OS   (403.84)
Cacld  :  C 65.42   H 3.49   N 10.40  %
Found  :  C 65.68   H 3.68   N 10.28  %
IR(KBr) cm^{-1}  3004, 2992 (CH), 1579, 1550 (C=C, C=N)
$^1$HNMR δppm  4.00 (s, 3H, OCH₃), 7.27-8.20 (m, 10H, Ar-H), 8.86 (s, 1H, Ar-H at C-2)

4-Chloro-7,9-di(4-methoxyphenyl)pyrido[3',2':4,5]thieno[3,2-d]pyrimidine (133)

A mixture of 7,9-di(4-methoxyphenyl)pyrido[3',2':4,5]thieno[3,2-d]pyrimidin-4(3H)-ones (125, 0.01 mole, 4.15 g) and phosphorous oxychloride (15 ml) was refluxed for 4 hrs. After completion of reaction work-up was carried out according to the procedure described for 129 to get the titled product.

Yield   :  64 %
mp   :  237-39 °C

Analysis  :  C_{2_1}H_{16}Cl_{2}N_{3}O_{2}S   (433.85)
Cacld  :  C 63.66   H 3.72   N 9.68  %
Found  :  C 63.98   H 3.51   N 9.98  %
IR(KBr) cm^{-1}  3010, 2952 (CH), 1594, 1546 (C=C, C=N)
$^1$HNMR δppm  4.04 (s, 6H, 2OCH₃), 7.25-8.21 (m, 9H, Ar-H), 8.84 (s, 1H, Ar-H at C-2)

4-Chloro-7-phenyl-9-(4-chlorophenyl)pyrido[3',2':4,5]thieno[3,2-d]pyrimidine (134)

7-Phenyl-9-(4-chlorophenyl)pyrido[3',2':4,5]thieno[3,2-d]pyrimidin-4(3H)-ones (126, 0.01 mole, 3.89 g) and phosphorous oxychloride (15 ml) was refluxed for 4 hrs. On completion of reaction, work-up was carried out according to the procedure described for 129 to get the titled product.

Yield   :  68 %
mp   :  222-24 °C

Analysis  :  C_{2_1}H_{11}ClN_{3}S   (407.32)
Cacld  :  C 61.91   H 2.72   N 10.31  %
Found  :  C 61.72   H 2.99   N 10.03  %
IR(KBr) cm^{-1}  3040, 2998 (CH), 1596, 1524 (C=C, C=N)
$^1$HNMR δppm  7.25-8.22 (m, 10H, Ar-H), 8.87 (s, 1H, Ar-H at C-2)
4-Chloro-7,9-di(4-chlorophenyl)pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (135)

7,9-Di(4-chlorophenyl)pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidin-4(3H)-ones (127, 0.01 mole, 4.24 g) and phosphorous oxychloride (15 ml) was refluxed for 4 hrs. On completion of reaction the titled product was obtaine after the work-up according to the procedure described for 129.

Yield 66 %  
mp 245-47 °C

Analysis  :  C_{21}H_{16}Cl_3N_3S  (441.82)
Cacld    C 57.08  H 2.27  N 9.51 %
Found    :  C 57.32  H 2.50  N 9.76 %

IR(KBr) cm\(^{-1}\)  : 3051, 3004 (CH), 1576, 1525 (C=C, C=N)

\(^1\)HNMR δppm : 7.30-8.20 (m, 9H, Ar-H), 8.86 (s, 1H, Ar-H at C-2)

4-Chloro-7-phenyl-9-(2-thienyl)pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (136)

7-Phenyl-9-(2-thienyl)pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidin-4(3H)-ones (128, 0.01 mole, 3.61 g) and phosphorous oxychloride (15 ml) was refluxed for 4 hrs. On completion of reaction the titled product was obtaine after the work-up according to the procedure described for 129.

Yield 65 %  
mp 208-09 °C

Analysis  :  C_{19}H_{10}ClN_3S_2  (379.7)
Cacld    C 60.09  H 2.65  N 11.06 %
Found    :  C 59.82  H 2.38  N 11.35 %

IR(KBr) cm\(^{-1}\)  : 3010, 2972 (CH), 1562, 1531 (C=C, C=N)

\(^1\)HNMR δppm : 7.24-8.20 (m, 9H, Ar-H), 8.87 (s, 1H, Ar-H at C-2)


Method-A

To a well stirred solution of ammonium chloride (0.011 mole, 0.59 g) and sodium azide (0.011 mole, 0.072 g) in dimethylsulfoxide (25 ml) was added 4-chloro-7,9-
diphenylpyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (129, 0.01 mole, 3.73 g). The reaction mixture was stirred at 80-90 °C for 3hrs. The mixture was cooled, poured onto the crushed ice, solid separated was filtered, wased with water, dried and recrystallized with a mixture of alcohol/ chloroform (8:2).

Yield 60 %  
mp : 210-12 °C

Analysis  
C21H12N6S (380.34)  
Calcd : C 66.31  H 3.17  N 22.10 %  
Found : C 66.02  H 3.32  N 21.90 %

IR(KBr) cm⁻¹ : 3010, 2998 (CH), 1586, 1536 (C=C, C=N)

¹HNMR δ ppm : 7.51-8.30 (m, 11H, Ar-H), 9.93 (s, 1H, Ar-H at C-2)

Method-B

To a mixture of 4-chloro-7,9-pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (129, 0.005 mole, 1.86 g) and tricaprylmethylammonium chloride (aliquat 336®) (0.0005 mole, 0.202 g) in chlorobenzene (15 ml) was added a solution of sodium azide (0.006 mole, 0.390 g) in water (5 ml). The mixture was stirred at 50°C for 15 hrs. on completion of the reaction two phase were separated. The aqueous phase was given one wash of chlorobenzene (15 ml). The combined organic layers were washed with water (2 × 15 ml) and dried over magnesium sulfate and the solvent was removed in vacuo. To the residue obtained after distillation was added methanol (10 ml) and cooled to 5 °C. The solid separated was filtered, dried and recrystallized with a mixture of alcohol/ chloroform (8:2).

yield : 75 %


Method-A

To a well stirred solution of sodium azide (0.011 mole, 0.072 g) and ammonium chloride (0.011 mole, 0.59 g) in dimethylsulfoxide (25 ml) was added 4-chloro-7-(4-methoxyphenyl)-9-phenylpyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (130, 0.01 mole, 4.0
g). The reaction mixture was stirred at 80-90 °C for 3.5 hrs. On completion of the reaction work-up was carried out as described for 137 to get the titled product.

Yield 62 %  
mp 195-96 °C

Analysis C₂₂H₁₄N₆O₅ (410.36)
Calcd C 64.38 H 3.43 N 20.48 %
Found C 64.09 H 3.15 N 20.71 %

IR(KBr) cm⁻¹ 3004, 2972 (CH), 1576, 1524 (C=C, ON)

¹HNMR δppm: 3.99 (s, 3H, OCH₃), 7.55-8.29 (m, 10H, Ar-H), 9.92 (s, 1H, Ar-H at C-2)

Method-B

To a mixture of 4-chloro-7-(4-methoxyphenyl)-9-phenylpyrido[3′, 2′ 4, 5]thieno[3,2-d]pyrimidine (130, 0.005 mole, 2.01 g) and triacaprylmethylammonium chloride (aliquat 336®) (0.0005 mole, 0.202 g) in chlorobenzene (15 ml) was added a solution of sodium azide (0.006 mole, 0.390 g) in water (5 ml). The reaction mixture was stirred for 1 hr at 50 °C. On completion of the reaction work-up was carried out according to the procedure described for 137 to get the titled product.

Yield 78 %

7-(4-Chlorophenyl)-9-phenyltetrazolo[1,5-c]pyrido[3′, 2′ 4, 5]thieno[3,2-d]pyrimidine (139)

Method-A

4-Chloro-7-(4-chlorophenyl)-9-phenylpyrido[3′, 2′ 4, 5]thieno[3,2-d]pyrimidine (131, 0.01 mole, 4.0 g) was added to a well stirred solution of ammonium chloride (0.011 mole, 0.59 g) and sodium azide (0.011 mole, 0.072 g) in dimethylsulfoxide (25 ml). The reaction mixture was stirred at 80-90 °C for 4.5 hrs. On completion of the reaction work-up was carried out as described for 137 to get the titled product.

Yield 64 %  
mp 190-92 °C

Analysis C₂₁H₁₃ClN₅S (414.84)
Calcd C 60.79 H 2.67 N 20.26 %
Found C 70.00 H 2.39 N 19.98 %
IR(KBr) cm\(^{-1}\): 3010, 2956 (CH), 1586, 1520 (C=C, C=N)

\(^{1}\)HNMR ppm: 7.59-8.29 (m, 10H, Ar-H), 9.94 (s, 1H, Ar-H at C-2)

Method-B:

To a mixture of tricaprylmethylammonium chloride (aliquat 336\(^{\circ}\)) (0.0005 mole, 0.202 g) and 4-chloro-7-(4-chlorophenyl)-9-phenylpyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (131, 0.005 mole, 2.03 g) in chlorobenzene (15 ml) was added a solution of sodium azide (0.006 mole, 0.390 g) in water (5 ml). The reaction mixture was stirred for 1.5 hrs at 50 °C. On completion of the reaction work-up was carried out according to the procedure described for 137 to get the titled product.

Yield: 75 %

7-Phenyl-9-(4-methoxyphenyl)tetrazolo[1,5-c]pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (140)

Method-A:

To a well stirred solution of ammonium chloride (0.011 mole, 0.59 g) and sodium azide (0.011 mole, 0.072 g) in dimethylsulfoxide (25 ml) was added 4-chloro-7-phenyl-9-(4-methoxyphenyl)pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (132, 0.01 mole, 4.0 g). The reaction mixture was stirred at 80-90 °C for 3 hrs. On completion of the reaction work-up was carried out as described for 137 to get the titled product.

Yield: 60 %

mp: 193-94 °C

Analysis: C\(_{22}\)H\(_{14}\)N\(_6\)O\(_5\) (410.36)

Calcd: C 64.38 H 3.43 N 20.48 %

Found: C 64.59 H 3.20 N 20.21 %

IR(KBr) cm\(^{-1}\): 3010, 2996 (CH), 1576, 1550 (C=C, C=N)

\(^{1}\)HNMR ppm: 4.00 (s, 3H, OCH\(_3\)), 7.54-8.30 (m, 10H, Ar-H), 9.92 (s, 1H, Ar-H at C-2)

Method-B:

To a mixture of 4-chloro-7-phenyl-9-(4-methoxyphenyl)pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (132, 0.005 mole, 2.01 g) and tricaprylmethylammonium chloride (aliquat 336\(^{\circ}\)) (0.0005 mole, 0.202 g) in chlorobenzene (15 ml) was added a solution of
sodium azide (0.006 mole, 0.390 g) in water (5 ml). The reaction mixture was stirred for 1 hr. at 50 °C. On completion of the reaction work-up was carried out according to the procedure described for 137 to get the titled product.

Yield 75 %

7,9-Di(4-methoxyphenyl)tetrazolo[1,5-c]pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (141)

Method-A

To a well stirred solution of sodium azide (0.011 mole, 0.072 g) and ammonium chloride (0.011 mole, 0.59 g) in dimethylsulfoxide (25 ml) was added 4-chloro-7,9 pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (133, 0.01 mole, 4.3 g). The reaction mixture was stirred at 80-90 °C for 3.5 hrs. On completion of the reaction work-up was carried out as described for 137 to get the titled product.

Yield 65 % mp 203-05 °C

Analysis C_{23}H_{16}N_{6}O_{2}S (440.41)
Calcd
C 62.72
H 3.66
N 19.08 %

Found
C 62.45
H 3.38
N 19.30 %

IR(KBr) cm⁻¹ 3004, 2976 (CH), 1575, 1524 (C=C, C=N)

¹HNMR δ ppm 4.04 (6H, 2OCH₃), 7.59-8.28 (9H, Ar-H), 9.94 (1H, Ar-H at C-2)

Method-B

To a mixture of 4-chloro-7,9-di(4-methoxyphenyl)pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (133, 0.005 mole, 0.202 g) and tricaprylmethylammonium chloride (aliquat 336°) (0.0005 mole, 0.202 g) in chlorobenzene (15 ml) was added a solution of sodium azide (0.006 mole, 0.390 g) in water (5 ml). The reaction mixture was stirred for 1 hr. at 50 °C. On completion of the reaction work-up was carried out according to the procedure described for 137 to get the titled product.

Yield 72 %

7-Phenyl-9-(4-chlorophenyl)tetrazolo[1,5-c]pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (142)

Method-A
To a well stirred solution of ammonium chloride (0.011 mole, 0.59 g) and sodium azide (0.011 mole, 0.072 g) in dimethylsulfoxide (25 ml) was added 4-chloro-7-phenyl-9-(4-chlorophenyl)pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (134, 0.01 mole, 4.0 g). The reaction mixture was stirred at 80-90 °C for 4 hrs. On completion of the reaction work-up was carried out as described for 137 to get the titled product.

Yield: 62 %
Analysis
Calcd: C 60.79  H 2.67  N 20.26 %
Found: C 60.50  H 2.89  N 20.49 %
IR(KBr) cm\(^{-1}\): 3010, 2956 (CH), 1576, 1536 (C=C, C=N)

Method-B.

To a mixture of 4-chloro-7-phenyl-9-(4-chlorophenyl)pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (134, 0.005 mole, 2.03 g) and tricaprylmethylammonium chloride (aliquat 336\(^{®}\)) (0.0005 mole, 0.202 g) in chlorobenzene (15 ml) was added a solution of sodium azide (0.006 mole, 0.390 g) in water (5 ml). The reaction mixture was stirred for 1.5 hrs. at 50 °C. On completion of the reaction work-up was carried out according to the procedure described for 137 to get the titled product.

Yield: 75 %

7,9-Di(4-chlorophenyl)tetrazolo[1,5-c]pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (143)

Method-A.

To a well stirred solution of ammonium chloride (0.011 mole, 0.59 g) and sodium azide (0.011 mole, 0.072 g) in dimethylsulfoxide (25 ml) was added 4-chloro-7,9-di(4-chlorophenyl)pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (135, 0.01 mole, 4.4 g). The reaction mixture was stirred at 80-90 °C for 5 hrs. On completion of the reaction work-up was carried out as described for 137 to get the titled product.

Yield: 65 %
Analysis: C\(_{21}\)H\(_{10}\)Cl\(_2\)N\(_6\)S (448.33)
Calcd : C 56.25 H 2.24 N 18.74 %
Found : C 55.92 H 2.49 N 18.50 %
IR(KBr) cm⁻¹ 3010, 2972 (CH), 1586, 1530 (C=C, O N)
¹HNMR δ ppm 7 60-8.30 (m, 9H, Ar-H), 9.94 (s, 1H, Ar-H at C-2)

Method-B.

To a mixture of 4-chloro-7,9-di(4-chlorophenyl)pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (135, 0.005 mole, 2.2 g) and tricaprylmethylammonium chloride (aliquat 336®) (0.0005 mole, 0.202 g) in chlorobenzene (15 ml) was added a solution of sodium azide (0.006 mole, 0.390 g) in water (5 ml). The reaction mixture was stirred for 1.25 hrs at 50 °C. On completion of the reaction work-up was carried out according to the procedure described for 137 to get the titled product.
Yield 74 %


Method-A.

To a well stirred solution of sodium azide (0.011 mole, 0.072 g) and ammonium chloride (0.011 mole, 0.59 g) in dimethylsulfoxide (25 ml) was added 4-chloro-7-phenyl-9-(2-thienyl)pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (136, 0.01 mole, 3.7 g). The reaction mixture was stirred at 80-90 °C for 4 hrs. On completion of the reaction work-up was carried out as described for 137 to get the titled product.
Yield 65 %

mp : 198-99 °C

Analysis : C₁₉H₁₉N₆S₂ (386.31)
Calcd : C 59.06 H 2.60 N 21.75 %
Found : C 56.32 H 2.31 N 21.42 %
IR(KBr) cm⁻¹ : 3010, 2982 (CH), 1576, 1524 (C=C, C=N)
¹HNMR δ ppm : 7 59-8 19 (m, 9H, Ar-H), 9.93 (s, 1H, Ar-H at C-2)

Method-B.

To a mixture of 4-chloro-7-phenyl-9-(2-thienyl)pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (136, 0.005 mole, 1.89 g) and tricaprylmethylammonium chloride (aliquat
(0.0005 mole, 0.202 g) in chlorobenzene (15 ml) was added a solution of sodium azide (0.006 mole, 0.390 g) in water (5 ml). On completion of the reaction work-up was carried out according to the procedure described for 137 to get the titled product.

Yield . 78 %


Method-A:

To a mixture of 7,9-diphenyltetrazolo[1,5-c]pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (137, 0.005 mole, 1.9 g) in acetic acid (30 ml) was heated at 70 °C with stirring. To this was added powdered zinc (0.025 mole, 1.62 g) portionwise, in such a manner that the frothing was properly controlled. The reaction mixture was then refluxed with stirring for 6 hrs. Completion of reaction was determined with the help of tlc. After completion of reaction the mixture was poured onto the crushed ice. The PH was adjusted to neutral by using ammonia solution (30 % v/v). The solid separated was filtered, dried and crystallized with alcohol.

Yield 60 %

mp : 255-57 °C

Analysis : C21H14N4S (354.35)

Caled : C 71.17 H 3.97 N 15.81 %

Found : C 71.42 H 4.25 N 16.20 %

IR(KBr) cm⁻¹ 3455, 3295 (NH), 3010, 2919, 2849 (CH), 1564, 1539 (C=C, C=N), 1633

¹HNMR δppm : 6.45 (s, 2H, NH₂), 7.46-8.19 (m, 11H, Ar-H), 8.37 (s, 1H, Ar-H at C-2)

Method-B

A mixture of 7,9-diphenyltetrazolo[1,5-a]pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (137, 0.005 mole, 1.9 g) and tricaprylmethylammonium chloride (aliquat 336 ®) (0.0005 mole, 0.202 g) was added with toluene (15 ml) and water (5 ml). The content were taken in a flat bottom flask and stirred over a magnetic stirrer at 60 °C. Powdered
sodium borohydride (0.008 mole, 0.304 g) was added portionwise in such a manner that
the frothing was properly controlled. The content were stirred for 1 hour and the end of
reaction was determined with the help of tlc. On completion of reaction two phase were
separated. The organic phase was given two washings of water (15 × 2 ml). Then the or­
ganic phase was dried over magnesium sulfate and subjected to vaccum distillation. The
content of the flask were added with alcohol (5 ml) and cooled to 0-5 °C. The solid was
separated dried and crystallized from alcohol.

Yield : 75 %

4-Amino-7-(4-methoxyphenyl)-9-phenylpyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (146) :
Method-A :

Powdered zinc (0.025 mole, 1.62 g) was added portionwise to a mixture of 7-(4-
0.005 mole, 2.0 g) in acetic acid (30 ml) which was heated at 70 °C with stirring. Zinc was
added in such a manner that the frothing was properly controlled. The reaction mixture was
then refluxed with stirring for 5 hrs. After completion of reaction work-up was carried out
as the procedure described for 145 to get the titled product.

Yield : 62 %

mp : 281-82 °C

Analysis : \( \text{C}_{22}\text{H}_{16}\text{N}_{4}\text{O} \) (384.40)

Calcd : C 68.73  H 4.19  N 14.57 %

Found : C 68.99  H 4.45  N 14.80 %

IR(KBr) cm\(^{-1}\) : 3456, 3272 (NH), 3004, 2996, 2872 (CH), 1576, 1540 (C=C, C=N),
1632 (NH)

\(^1\)HNMR \( \delta \) ppm : 3.99 (s, 3H, OCH\(_3\)), 6.45 (s, 2H, NH\(_2\)), 7.46-8.19 (m, 11H, Ar-H), 8.37
(s, 1H, Ar-H at C-2)

Method-B :

A mixture of 7-(4-methoxyphenyl)-9-phenyltetrazolo[1,5-a]pyrido[3’, 2’: 4, 5]thieno[3,2-d]pyrimidine (138, 0.005 mole, 2.0 g) and tricaprylmethylammonium chloride
(aliquat 336\(^\circledast\)) (0.0005 mole, 0.202 g) was added with toluene (15 ml) and water (5 ml).
The content were taken in a flat bottom flask and stirred over a magnetic stirrer at 60 °C. Powdered sodium borohydride (0.008 mole, 0.304 g) was added portionwise in such a manner that the frothing was properly controlled. The content were stirred for 1.5 hour. On completion of the reaction, the titled product was obtained after work-up according to the procedure described for 145.

Yield: 80 %

4-Amino-7-(4-chlorophenyl)-9-phenylpyrido[3′, 2′ 4, 5]thieno[3,2-d]pyrimidine (147)

Method-A

To a mixture of 7-(4-chlorophenyl)-9-phenyltetrazolo[1,5-c]pyrido[3′, 2′ 4, 5]thieno[3,2-d]pyrimidine (139, 0.005 mole, 2.0 g) in acetic acid (30 ml) was heated at 70 °C with stirring. To this was added powdered zinc (0.025 mole, 1.62 g) portionwise, in such a manner that the frothing was properly controlled. The reaction mixture was then refluxed with stirring for 6.5 hrs. After completion of reaction, work-up was carried out as the procedure described for 145 to get the titled product.

Yield: 60 %

mp 267-69 °C

Analysis

C_{21}H_{13}ClN_{4}S (388.85)

Calcd: C 64.86 H 3.36 N 14.41%

Found: C 65.02 H 3.55 N 14.70%

IR(KBr) cm⁻¹: 3450, 3270 (NH), 3010, 2998, 2852 (CH), 1578, 1524 (C=C, C=N), 1633 (NH)

^1HNMR δppm: 5.18 (s, 2H, NH₂), 7.26-8.15 (m, 10H, Ar-H), 8.52 (s, 1H, Ar-H at C-2)

Method-B

A mixture of tricaprylmethylammonium chloride (aliquat 336®) (0.0005 mole, 0.202 g) and 7-(4-chlorophenyl)-9-phenyltetrazolo[1,5-a]pyrido[3′, 2′ 4, 5]thieno[3,2-d]pyrimidine (139, 0.005 mole, 2.0 g) was added with toluene (15 ml) and water (5 ml). The content were taken in a flat bottom flask and stirred over a magnetic stirrer at 60 °C. Powdered sodium borohydride (0.008 mole, 0.304 g) was added portionwise. The content
were stirred for 1 hour. On completion of the reaction the titled product was obtained after work-up according to the procedure described for 145

Yield : 75 %


Method-A:

To a mixture of acetic acid (30 ml) and 7-(4-methoxyphenyl)-9-phenyltetrazolo[1,5-c]pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (140, 0.005 mole, 2.0 g) was heated at 70 °C with stirring. To this was added powdered zinc (0.025 mole, 1.62 g) portionwise, in such a manner that the frothing was properly controlled. The reaction mixture was then refluxed with stirring for 6.5 hrs. After completion of reaction work-up was carried out as the procedure described for 145 to get the titled product.

Yield : 63 %

mp : 259-60 °C

Analysis

Calcd : C 68.73 H 4.19 N 14.57 %

Found : C 68.49 H 3.80 N 14.85 %

IR(KBr) cm⁻¹ : 3455, 3272 (NH), 3008, 2972, 2882 (CH), 1576, 1539 (C=C, C=N), 1633 (NH)

¹HNMR δppm : 4.00 (s, 3H, OCH₃), 6.45 (s, 2H, NH₂), 7.49-8.19 (m, 10H, Ar-H), 8.38 (s, 1H, Ar-H at C-2)

Method-B:

A mixture of 7-(4-methoxyphenyl)-9-phenyltetrazolo[1,5-a]pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (140, 0.005 mole, 2.0 g) and tricaprylmethylammonium chloride (aliquat 336®) (0.0005 mole, 0.202 g) was added with toluene (15 ml) and water (5 ml). The content were taken in a flat bottom flask and stirred over a magnetic stirrer at 60 °C. Powdered sodium borohydride (0.008 mole, 0.304 g) was added portionwise. The content were stirred for 1 hour. On completion of the reaction work-up was carried out according to the procedure described for 145 to get the titled product.

Yield : 78 %

Method-A:

To a mixture of 7,9-di(4-methoxyphenyl)tetrazolo[1,5-a]pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (141, 0.005 mole, 2.2 g) in acetic acid (30 ml) was heated at 70 °C with stirring. To this was added powdered zinc (0.025 mole, 1.62 g) portionwise, in such a manner that the frothing was properly controlled. The reaction mixture was then refluxed with stirring for 6.5 hrs. After completion of reaction work-up was carried out as the procedure described for 145 to get the titled product.

Yield: 64 %
mp: 279-80 °C

Analysis:
C_{28}H_{18}N_{4}O_{3}S (414.43)
Calcd: C 66.65 H 4.38 N 13.52 %
Found: C 66.90 H 4.65 N 13.80 %

IR(KBr) cm⁻¹: 3450, 3292 (NH), 3010, 2996, 2889 (CH), 1586, 1540 (C=O, C=N), 1632 (NH)

¹HNMR δppm:
4.02 (s, 6H, 20€H₃), 6.26 (s, 2H, NH₂), 7.51-8 19 (m, 9H, Ar-H), 8 48 (s, 1H, Ar-H at C-2)

Method-B:

A mixture of 7,9-di(4-methoxyphenyl)tetrazolo[1,5-a]pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (141, 0.005 mole, 2.2 g) and tricaprylmethylammonium chloride (aliquat 336) (0.0005 mole, 0.202 g) was added with toluene (15 ml) and water (5 ml). The content were taken in a flat bottom flask and stirred over a magnetic stirrer at 60 °C. Powdered sodium borohydride (0.008 mole, 0.304 g) was added portionwise in such a manner that the frothing was properly controlled. The content were stirred for 1 hour. On completion of the reaction the titled product was obtained after work-up according to the procedure described for 145.

Yield: 76 %

4-Amino-7-phenyl-9-(4-chlorophenyl)pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (150):

Method-A.
To a mixture of 7-phenyl-9-(4-chlorophenyl)tetrazolo[1,5-c]pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (142, 0.005 mole, 2.0 g) in acetic acid (30 ml) was heated at 70 °C with stirring. To this was added powdered zinc (0.025 mole, 1.62 g) portionwise, in such a manner that the frothing was properly controlled. The reaction mixture was then refluxed with stirring for 6.5 hrs. After completion of reaction work-up was carried out as the procedure described for 145 to get the titled product.

Yield 60 %

Analysis
Calcd
C 64.86  H 3.36  N 14.41 %
Found
C 64.62  H 3.05  N 14.15 %

IR(KBr) cm⁻¹
3455, 3270 (NH), 3004, 2997, 2842 (CH), 1570, 1524 (C=C, C=N)
1634 (NH)

¹HNMR δ ppm  5 20 (s, 2H, NH₂), 7.28-8.13 (m, 10H, Ar-H), 8.49 (s, 1H, Ar-H at C-2)
Method-B

A mixture of 7-phenyl-9-(chlorophenyl)tetrazolo[1,5-a]pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (142, 0.005 mole, 2.0 g) and tricaprylmethylammonium chloride (aliquat 336®) (0.0005 mole, 0.202 g) was added with toluene (15 ml) and water (5 ml). The content were taken in a flat bottom flask and stirred over a magnetic stirrer at 60 °C. Powdered sodium borohydride (0.008 mole, 0.304 g) was added portionwise in such a manner that the frothing was properly controlled. The content were stirred for 1 hour. On completion of the reaction the titled product was obtained after work-up according to the procedure described for 145.

Yield 75 %


A mixture of acetic acid (30 ml) and 7,9-di(4-chlorophenyl)tetrazolo[1,5-c]pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (143, 0.005 mole, 2.2 g) was heated at 70 °C with stirring. To this was added powdered zinc (0.025 mole, 1.62 g) portionwise, in such a
manner that the frothing was properly controlled. The reaction mixture was then refluxed with stirring for 6.5 hrs. After completion of reaction work-up was carried out as the procedure described for 145 to get the titled product.

Yield 60 %

mp 239-40 °C

Analysis : C_{21}H_{12}Cl_{2}N_{4}S (422.34)

Calcd : C 59.71 H 2.86 N 13.26 %

Found : C 59.99 H 3.15 N 14.49 %

IR(KBr) cm^{-1} . 3456, 3272 (NH), 3010, 2972, 2849 (CH), 1587, 1530 (C=C, C=N) 1632 (NH)

^1HNMR δppm 5 25 (s, 2H, NH₂), 7.27-8.19 (m, 9H, Ar-H), 8.52 (s, 1H, Ar-H at C-2)

Method-B

A mixture of 7,9-di(4-chlorophenyl)tetrazolo[1,5-a]pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (143, 0.005 mole, 2.2 g) and tricaprylmethylammonium chloride (aliquat 336®) (0.0005 mole, 0.202 g) was added with toluene (15 ml) and water (5 ml). The content were taken in a flat bottom flask and stirred over a magnetic stirrer at 60 °C. Powdered sodium borohydride (0.008 mole, 0.304 g) was added portionwise in such a manner that the frothing was properly controlled. The content were stirred for 1.5 hour. On completion of the reaction the titled product was obtained after work-up according to the procedure described for 145.

Yield 75 %

4-Amino-7-phenyl-9-(2-thienyl)pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (152)

Method-A

To a mixture of 7-phenyl-9-(2-thienyl)tetrazolo[1,5-c]pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (144, 0.005 mole, 1.9 g) in acetic acid (30 ml) was heated at 70 °C with stirring, was added powdered zinc (0.025 mole, 1.62 g) portionwise, in such a manner that the frothing was properly controlled. The reaction mixture was then refluxed with stirring for 4.5 hrs. After completion of reaction work-up was carried out as the procedure described for 145 to get the titled product.
Yield . 65 % mp . 230-32 °C

Analysis : \( \text{C}_19\text{H}_{12}\text{N}_4\text{S}_2 \) (360.32)

Calcd : C 63.2 H 3.35 N 15.50 %

Found : C 63.02 H 3.65 N 15.76 %

IR(KBr) cm\(^{-1}\) : 3450, 3295 (NH), 3010, 2996, 2852 (CH), 1589, 1540 (C=C, C=N) 1633 (NH)

\(^1\)HNMR ppm : 6.42 (s, 2H, NH\(_2\)), 7.46-8.13 (m, 10H, Ar-H), 8.40 (s, 1H, Ar-H at C-2)

Method-B .

A mixture of 7-phenyl-9-(2-thienyl)tetrazolo[1,5-a]pyrido[3', 2': 4, 5]thieno[3,2-d]pyrimidine (144, 0.005 mole, 1.9 g) and tricaprylmethylammonium chloride (aliquat 336\(^\circ\)) (0.0005 mole, 0.202 g) was added with toluene (15 ml) and water (5 ml). The content were taken in a flat bottom flask and stirred over a magnetic stirrer at 60 °C. Powdered sodium borohydride (0.008 mole, 0.304 g) was added portionwise in such a manner that the frothing was properly controlled. The content were stirred for 1 hour. On completion of the reaction the titled product was obtained after work-up according to the procedure described for 145.

Yield . 80 %