4.1 Introduction

Synthesis of heteroaromatic amines with the last step being an intramolecular nucleophilic addition onto a nitrile group can be carried out in different ways. Thorpe-Ziegler cyclization is one of such methods, which has been of great utility for construction of amino substituted five membered heterocyclic system in recent times. The general reaction mechanism for the construction of amino substituted five membered heterocycles is depicted in scheme-75.

Where, $X,Y= C, N; Z= O, H, S;\quad EWG = CN, COR, COOR, CONR' R", NO_2$ etc

Scheme -75
Generally, Thorpe-Ziegler cyclization reactions are catalysed by base. From scheme-75 it is clear that a nitrile 140 undergoes ring closure by intramolecular addition of deprotonated -CH$_2$ group onto the -CN group followed by 1,3-H shift in the intermediate 142, in order to obtain an amino heterocycle of type 143.

- N-Substituted 2,4-diaminothiophene-3-carbonitrile (144) were converted into the 3,4-diaminothieno[2,3-b]pyrrole (146) in a single step (Scheme-76)\(^{258}\)

\[
\text{H}_2\text{N} \quad \text{CN} \quad \text{NH}\quad \text{R} \quad + \quad \text{Br} \quad \text{COOC}_2\text{H}_5 \quad \rightarrow \quad \text{H}_2\text{N} \quad \text{CN} \quad \text{N} \quad \text{COOC}_2\text{H}_5 \quad \text{R} \quad \text{COOC}_2\text{H}_5
\]

Scheme -76

4-Aminoisothiazoles (148) were formed by Thorpe-Ziegler type of cyclization of corresponding N-alkyliminonitriles\(^{259}\) (147) (Scheme-77). Application of this reaction to different N-alkyliminonitrile (147) resulted in formation of a number of new isothiazole derivatives and also heterocondensed isothiazoles by subsequent reactions.
$Y = \text{CO}_2\text{H}, \text{CO}_2\text{Et}, \text{COCH}_3, \text{CHO}; X = \text{CONH}_2, \text{CO}_2\text{Et}, \text{COC}_6\text{H}_5, \text{C}_6\text{H}_5$

Scheme -77

$\alpha$-(N-Alkoxyimino)nitriles (149) cyclized in presence of lithium hydroxide giving 4-aminoisoaxazoles (150) \(^{260}\) (Scheme-78). Stronger bases caused cleavage of 149

Gewald et al\(^{261}\) carried out synthesis of 4,5-disubstituted 3-aminothieno[2,3-b]furans (152) in moderate yields by Thorpe-Ziegler type of cyclization of 4,5-disubstituted 2-alkyl/aryloxy-3-cyanofurans (151) using sodium ethoxide as a base (Scheme-79).
2-Alkyl/aryloxy-5-methylthiophene-2-carbonitrile (153) cyclized in presence of sodium ethoxide giving 2-alkyl/aryl-3-amino-5-methylthieno[3,2-b]furans (154) exhibiting another application of Thorpe-Ziegler type of cyclization (Scheme-80).

4-Substituted 6-phenyl-3-aminofuro[2,3-b]pyridines-2-carboxylic acid ethylester (157) was prepared by O-alkylation of 4-substituted 6-phenyl-3-cyanopyridin-2(1H)-ones (155) with ethyl chloroacetate to form 4-substituted 6-phenyl-2-ethoxycarbonylmethoxypyridine-3-carbonitrile (156), which was cyclized with sodium ethoxide to give 4-substituted 6-phenyl-3-aminofuro[2,3-b]pyridine-2-carboxylic acid ethylester (157) (Scheme-81).
Dave et al.\textsuperscript{264} synthesized 2-carbethoxy-3-aminothieno[2,3-b]pyridines (160) from the reaction of 4,6-disubstituted 2-chloropyridine-3-carbonitriles (158) and ethyl thioglycolate. The intermediates, 6-disubstituted 2-carbethoxymethylmercaptopyridine-3-carbonitriles (159), were separated for the first time in order to study the Thorpe-Ziegler type of cyclizations. The intermediates (159) thus separated were cyclized in alkaline medium using sodium methoxide (Scheme-82).

\[ R = \text{CH}_3, \text{C}_6\text{H}_5 \]

**Scheme - 82**
5,6-Disubstituted 3-aminothieno[2,3-b]pyridine-2-carboxylic acid ethylester (162) were prepared by reacting 5,6-disubstituted 3-cyanopyridin-2(1H)-thiones (161) with halo alkane derivatives (Scheme-83)

\[
\begin{align*}
\text{R}_1 & = \text{C}_2\text{H}_5, \text{H} ; \text{R}_2 = \text{CH}_3, \text{CH}_3\text{CH}_2\text{CH}_2 ; \\
\text{Z} & = \text{CONH}_2, \text{COOCH}_3, \text{COOC}_2\text{H}_5, \text{COC}_6\text{H}_5, \text{C}_{15}\text{H}_{31}, \text{CN}
\end{align*}
\]

Scheme - 83

4,6-Disubstituted 3-aminothieno[2,3-b]pyridine-2-carboxylic acid ethylesters (164) were prepared by reacting 4,6-disubstituted pyridin-2(1H)-thiones-3-carbonitriles (163) with ethyl chloroacetate and sodium ethoxide (Scheme-84)

\[
\begin{align*}
\text{R}_1 & = \text{CH}_3, \text{C}_6\text{H}_5, 4-\text{BrC}_6\text{H}_4, 4-\text{OCH}_3\text{C}_6\text{H}_4, \text{thienyl}, \text{furyl}, \\
& \text{naphthyl}, \text{pyridyl}
\end{align*}
\]

Scheme - 84
Shestopalov et al\textsuperscript{267} performed the Thorpe-Ziegler type of cyclization and converted substituted 2-(o-carboran-1-yl)methylthio-3,5-dicyano-6-aminopyridines (165) under the influence of potassium hydroxide and N,N-dimethylformamide to give the corresponding 2-substituted 3,6-diamino-5-cyanothieno[2,3-b]pyridines (166) (Scheme-85)

Scheme - 85

\[ \begin{array}{c}
\text{NC} & \text{CN} \\
\text{S} & \text{N} \\
\text{N} & \text{NH}_2 \\
\hline
\text{X} & \text{DMF} \\
\end{array} \]

\[ \begin{array}{c}
\text{H}_2\text{N} & \text{CN} \\
\text{S} & \text{N} \\
\text{N} & \text{NH}_2 \\
\hline
\text{X} & \text{DMF} \\
\end{array} \]

\( X = \text{o-carboran-1-yl} \)

The 4-aryl-6-amino-3,5-dicyanopyridin-2(1H)-thiones\textsuperscript{268} (167) were used to prepare substituted 2-(alkylthio)-4-aryl-6-amino-3,5-dicyanopyridines (168) and further 2-substituted 4-aryl-5-cyano-3,6-diaminothieno[2,3-b] pyridines (169) via base catalysed reaction

\[ \begin{array}{c}
\text{NC} & \text{Ar} & \text{CN} \\
\text{S} & \text{N} & \text{X} \\
\text{N} & \text{H} \\
\hline
\text{H}_2\text{N} & \text{CN} \\
\text{S} & \text{N} \\
\text{N} & \text{NH}_2 \\
\hline
\text{Ar} & \text{Z} \\
\end{array} \]

\[ \begin{array}{c}
\text{NC} & \text{Ar} & \text{CN} \\
\text{S} & \text{N} & \text{Z} \\
\text{N} & \text{H} \\
\hline
\text{H}_2\text{N} & \text{CN} \\
\text{S} & \text{N} \\
\text{N} & \text{NH}_2 \\
\hline
\text{Ar} & \text{Z} \\
\end{array} \]

\[ \begin{array}{c}
\text{NC} & \text{Ar} & \text{NH}_2 \\
\text{S} & \text{N} & \text{Z} \\
\text{N} & \text{H} \\
\hline
\text{H}_2\text{N} & \text{CN} \\
\text{S} & \text{N} \\
\text{N} & \text{NH}_2 \\
\hline
\text{Ar} & \text{Z} \\
\end{array} \]

167 \quad 168 \quad 169

168 : \( Z = \text{BrC}_6\text{H}_4\text{CO}, \text{CN}, \text{COOCH}_3 \)

169 : \( Z = 4-\text{BrC}_6\text{H}_4, 4-\text{ClC}_6\text{H}_4, \text{CONH}_2 \)

Pyridone and pyridinethione derivatives (170) were treated with halomethyl carbonyl compounds to afford O/S-alkylated pyridines (171) which further underwent Thorpe-Ziegler
type of cyclization in the presence of sodium ethoxide to form corresponding furo- and thieno-pyridines (Scheme-86)

4.2 Present work

There are three main reasons for the study of the synthesis of furo[2,3-b]pyridines and thieno[2,3-b]pyridines

(i) There is an obvious experimental and theoretical interest in the behaviour of these systems consisting of $\pi$-excessive (thiophene and furan) and $\pi$-deficient (pyridine) rings. Particularly interesting is, how the annelation would perturb the electronic structure of each individual and how this would manifest in the reactivity of these substrates

(ii) Expectation for pharmacologically active substances has led to the synthesis of furo[2,3-b]pyridines and thieno[2,3-b]pyridines which are the isosters of wellknown quinoline and iso-quinoline, the important moieties in many biologically active substances.
To study the utility of phase transfer catalysis in Thorpe-Ziegler type of cyclizations

In this chapter various furo[2,3-b]pyridines and thieno[2,3-b]pyridines have been synthesized under phase transfer conditions. The reactions were carried out at room temperature in presence of 18-crown-6 and potassium hydroxide. Various other phase transfer catalysts were also employed viz. triethylbenzylammonium chloride (TEBA), tetrabutylammonium bromide (TBAB), tricaprylmethylammonium chloride (aliquat 336), but all these catalysts were unsuccessful in affording the products. The solvent employed for these cyclizations was acetonitrile.

4.3 Results and discussions

4.3.1 Synthesis of 4,6-disubstituted 2-carbethoxy-3-aminofuro[2,3-b]pyridines via Thorpe-Ziegler type of cyclization under phase transfer condition:

4,6-Disubstituted 3-cyanopyridin-2(1H)-ones (II) required for the synthesis of the titled compounds were prepared according to the known procedure. These 4,6-disubstituted 3-cyanopyridones (II, 15-30) were reacted with ethyl bromoacetate using N,N-dimethylformamide as a solvent and the base employed was potassium carbonate. The reactions were carried out at room temperature. The 4,6-disubstituted 2-ethoxycarbonylmethyloxy-3-cyanopyridines (VIII) thus obtained were used for the syntheses of 4,6-disubstituted 2-carbethoxy-3-aminofuro[2,3-b]pyridines (IX) (Scheme-87).

![Scheme 87](image-url)
The physical constants of 4,6-disubstituted 2-ethoxycarbonylmethyloxy-3-cyanopyridines (VIII, 91-103) are given in table-40

Table- 40 : Physical constants of 4,6-disubstituted 2-ethoxycarbonylmethyloxy-3-cyanopyridines (VIII, 91-103)

<table>
<thead>
<tr>
<th>Compd. No.</th>
<th>$R_1$</th>
<th>$R_2$</th>
<th>Yield (%)</th>
<th>M.P. °C</th>
<th>Mole Formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>91</td>
<td>C$_6$H$_5$</td>
<td>C$_6$H$_5$</td>
<td>80</td>
<td>119-20</td>
<td>C$<em>{22}$H$</em>{18}$N$_2$O$_3$</td>
</tr>
<tr>
<td>92</td>
<td>C$_6$H$_5$</td>
<td>4-CH$_3$C$_6$H$_4$</td>
<td>75</td>
<td>184-85</td>
<td>C$<em>{23}$H$</em>{20}$N$_2$O$_3$</td>
</tr>
<tr>
<td>93</td>
<td>C$_6$H$_5$</td>
<td>4-OCH$_3$C$_6$H$_4$</td>
<td>76</td>
<td>173-75</td>
<td>C$<em>{23}$H$</em>{20}$N$_2$O$_4$</td>
</tr>
<tr>
<td>94</td>
<td>C$_6$H$_5$</td>
<td>4-ClC$_6$H$_4$</td>
<td>70</td>
<td>458-60</td>
<td>C$<em>{22}$H$</em>{17}$ClN$_2$O$_3$</td>
</tr>
<tr>
<td>95</td>
<td>4-CH$_3$C$_6$H$_4$</td>
<td>C$_6$H$_5$</td>
<td>74</td>
<td>140-41</td>
<td>C$<em>{23}$H$</em>{20}$N$_2$O$_3$</td>
</tr>
<tr>
<td>96</td>
<td>4-CH$_3$C$_6$H$_4$</td>
<td>4-ClC$_6$H$_4$</td>
<td>75</td>
<td>167-68</td>
<td>C$<em>{23}$H$</em>{19}$ClN$_2$O$_3$</td>
</tr>
<tr>
<td>97</td>
<td>4-OCH$_3$C$_6$H$_4$</td>
<td>C$_6$H$_5$</td>
<td>80</td>
<td>145-46</td>
<td>C$<em>{23}$H$</em>{20}$N$_2$O$_4$</td>
</tr>
<tr>
<td>98</td>
<td>4-OCH$_3$C$_6$H$_4$</td>
<td>4-OCH$_3$C$_6$H$_4$</td>
<td>78</td>
<td>150-51</td>
<td>C$<em>{23}$H$</em>{22}$N$_2$O$_5$</td>
</tr>
<tr>
<td>99</td>
<td>4-ClC$_6$H$_4$</td>
<td>C$_6$H$_5$</td>
<td>79</td>
<td>147-49</td>
<td>C$<em>{22}$H$</em>{17}$ClN$_2$O$_3$</td>
</tr>
<tr>
<td>100</td>
<td>4-ClC$_6$H$_4$</td>
<td>4-CH$_3$C$_6$H$_4$</td>
<td>72</td>
<td>189-90</td>
<td>C$<em>{23}$H$</em>{19}$ClN$_2$O$_3$</td>
</tr>
<tr>
<td>101</td>
<td>2-Furyl</td>
<td>C$_6$H$_5$</td>
<td>80</td>
<td>129-30</td>
<td>C$<em>{20}$H$</em>{15}$N$_2$O$_4$</td>
</tr>
<tr>
<td>102</td>
<td>2-Furyl</td>
<td>4-CH$_3$C$_6$H$_4$</td>
<td>85</td>
<td>130-32</td>
<td>C$<em>{21}$H$</em>{18}$N$_2$O$_4$</td>
</tr>
<tr>
<td>103</td>
<td>2-Thienyl</td>
<td>C$_6$H$_5$</td>
<td>75</td>
<td>135-37</td>
<td>C$<em>{20}$H$</em>{18}$N$_2$O$_3$S</td>
</tr>
</tbody>
</table>

4,6-Disubstituted 2-ethoxycarbonylmethyloxy-3-cyanopyridines (VIII, 91-103) were cyclized using 18-crown-6 and potassium hydroxide complex dissolved in acetonitrile. The 4,6-disubstituted 2-carbethoxy-3-aminofuro[2,3-b]pyridines (IX, 104-116) thus formed were obtained in excellent yield (70-85 %) (Scheme-88)
The physical constants of 4,6-disubstituted 2-carbethoxy-3-aminofuro[2,3-b]pyridines (IX, 104-116) are recorded in table-41.

Table - 41: Physical constants of 4,6-disubstituted 2-carbethoxy-3-aminofuro[2,3-b]pyridines (IX, 104-116)

<table>
<thead>
<tr>
<th>Compd. No.</th>
<th>R_1</th>
<th>R_2</th>
<th>Yield (%)</th>
<th>M.P °C</th>
<th>Mole Formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>104</td>
<td>C_6H_5</td>
<td>C_6H_5</td>
<td>80</td>
<td>185-86</td>
<td>C_{22}H_{18}N_{2}O_{3}</td>
</tr>
<tr>
<td>105</td>
<td>C_6H_5</td>
<td>4-CH_3C_6H_4</td>
<td>63</td>
<td>148-49</td>
<td>C_{23}H_{20}N_{2}O_{3}</td>
</tr>
<tr>
<td>106</td>
<td>C_6H_5</td>
<td>4-OCH_3C_6H_4</td>
<td>75</td>
<td>155-56</td>
<td>C_{23}H_{20}N_{2}O_{4}</td>
</tr>
<tr>
<td>107</td>
<td>C_6H_5</td>
<td>4-ClC_6H_4</td>
<td>78</td>
<td>161-62</td>
<td>C_{22}H_{17}ClN_{2}O_{3}</td>
</tr>
<tr>
<td>108</td>
<td>4-CH_3C_6H_4</td>
<td>C_6H_5</td>
<td>60</td>
<td>164-65</td>
<td>C_{23}H_{20}N_{2}O_{3}</td>
</tr>
<tr>
<td>109</td>
<td>4-CH_3C_6H_4</td>
<td>4-ClC_6H_4</td>
<td>70</td>
<td>185-86</td>
<td>C_{23}H_{19}ClN_{2}O_{3}</td>
</tr>
<tr>
<td>110</td>
<td>4-OCH_3C_6H_4</td>
<td>C_6H_5</td>
<td>75</td>
<td>169-70</td>
<td>C_{23}H_{20}N_{2}O_{4}</td>
</tr>
<tr>
<td>111</td>
<td>4-OCH_3C_6H_4</td>
<td>4-OCH_3C_6H_4</td>
<td>80</td>
<td>152-54</td>
<td>C_{23}H_{22}N_{2}O_{5}</td>
</tr>
<tr>
<td>112</td>
<td>4-ClC_6H_4</td>
<td>C_6H_5</td>
<td>72</td>
<td>167-68</td>
<td>C_{22}H_{17}ClN_{2}O_{3}</td>
</tr>
<tr>
<td>113</td>
<td>4-ClC_6H_4</td>
<td>4-CH_3C_6H_4</td>
<td>65</td>
<td>192-93</td>
<td>C_{23}H_{19}ClN_{2}O_{3}</td>
</tr>
<tr>
<td>114</td>
<td>2-Furyl</td>
<td>C_6H_5</td>
<td>78</td>
<td>205-06</td>
<td>C_{20}H_{16}N_{2}O_{4}</td>
</tr>
<tr>
<td>115</td>
<td>2-Furyl</td>
<td>4-CH_3C_6H_4</td>
<td>70</td>
<td>180-82</td>
<td>C_{21}H_{18}N_{2}O_{4}</td>
</tr>
<tr>
<td>116</td>
<td>2-Thienyl</td>
<td>C_6H_5</td>
<td>72</td>
<td>177-78</td>
<td>C_{20}H_{16}N_{2}O_{3}S</td>
</tr>
</tbody>
</table>
All the cyclizations were carried out under solid-liquid phase transfer conditions, the mechanism for such Thorpe-Ziegler type under phase transfer condition is shown in scheme-89.

From the mechanism it seems that initially the crown ether forms a complex with potassium hydroxide as a result potassium salt solubilized in acetonitrile This complex extracts
proton from the 4,6-disubstituted 2-ethoxycarbonylmethyloxy-3-cyanopyridines (VIII) and induces the cyclization. The same procedure was attempted for the cyclization of 4,6-disubstituted 2-carbethoxy-3-aminofuro[2,3-b]pyridines (IX) using various other phase transfer catalysts like tetrabutylammonium bromide (TBAB), triethylbenzylammonium chloride (TEBA), tricaprylmethylammonium chloride (aliquat 336) and cetyltrimethylammonium chloride (CTAC), but no other system gave satisfactory results.

All these reactions were carried out at room temperature. The amount of potassium hydroxide employed was 2.5 times the theoretical molar quantity, 18-crown-6 was employed in catalytic quantities (10-15 mole %). Higher or lower quantities of 18-crown-6 were found to give a number of by-products, which was evident from the spots seen on thin layer chromatograph. The increase in temperature also resulted in formation of undesired products. At temperature less than 20 °C, the rate of reaction was very slow. Optimum temperature for such reaction was 30-35 °C. With the progress of reaction, slow precipitation of product occurred. The solid obtained was filtered and washed with water. All the products were light yellow to green in colour and their melting points were slightly higher than the 4,6-disubstituted 2-ethoxycarbonylmethyloxy-3-cyanopyridines (VIII).

Literature survey revealed that furo[2,3-b]pyridines are prepared in multiple step synthesis using hard bases like sodium or potassium alkoxide, sodium hydride, etc., which are relatively difficult to handle, moreover, the yield of products formed are also very low.

4,6-Disubstituted 3-cyano-pyridin-2(1H)-ones (II) were first O-alkylated to give corresponding 4,6-disubstituted 2-ethoxycarbonylmethyloxy-3-cyanopyridines (VIII) compounds, which were separately cyclized to furo[2,3-b]pyridines (IX). Attempts to cyclize 4,6-disubstituted 3-cyanopyridin-2(1H)-ones (II) directly to 4,6-disubstituted 2-carbethoxy-3-aminofuro[2,3-b]pyridines (IX) without isolating 4,6-disubstituted 2-ethoxycarbonylmethyloxy-3-cyano pyridines (VIII) was successful only in preparation of 2-carbethoxy-3-amino-4-(4-chlorophenyl)-6-phenylfuro[2,3-b]pyridine (112).
In cyclization of all other compounds (IX, 104-111, 113-116), a number of unwanted byproducts (ticol) were formed.

An important achievement of this method was the cyclization of 4,6-disubstituted 2-ethoxycarbonylmethyloxy-3-cyanopyridines (VIII) containing parasubstituted substituents in position 4 and 6 of pyridine ring. When the uncyclic compound 4,6-disubstituted 2-ethoxycarbonylmethyloxy-3-cyanopyridines (VIII) were studied for the cyclization using various bases like sodium methoxide, sodium ethoxide, and sodium hydride, the 4,6-disubstituted 2-carbethoxy-3-amino[2,3-b]pyridines (IX) were obtained in poor yield (20-25%).

Attempts were also made to cyclize 4,6-disubstituted 2-ethoxycarbonylmethyloxy-3-cyanopyridines (VIII) using other phase transfer catalysts like TBAB, TEBA, aliquat 336 and CTAC. However, it was found that the rates of reaction were very slow and the desired final products 4,6-disubstituted 2-carbethoxy-3-amino[2,3-b]pyridines (IX) were not obtained as a single product (ticol).

The extraction of complex formed by 18-crown-6 and potassium hydroxide was performed in many solvent and then these solvents were employed for cyclization. The solvents tried were acetonitrile, toluene, benzene, chlorobenzene, diethylether, methanol and hexane. However, except for acetonitrile no other solvent was found to be suitable for the cyclization of 4,6-disubstituted 2-ethoxycarbonylmethyloxy-3-cyanopyridines (VIII) to 4,6-disubstituted 2-carbethoxy-3-amino[2,3-b]pyridines (IX), therefore acetonitrile was the solvent of choice for the Thorpe-Ziegler type of cyclization. The same cyclization was studied at various temperatures less than 20 °C, but they were not useful as the rates of the reactions were very slow, and the formation of by-products was quite pronounced when the temperature was more than 40 °C. The optimum temperature condition for such Thorpe-Ziegler type of reactions was 30-35 °C.
The IR(KBr) spectral data of 4,6-disubstituted 2-ethoxycarbonylmethyloxy-3-cyano-pyridines (VIII, 91-103) are recorded in table-42.

### Table -42: IR Spectral data of 4,6-disubstituted 2-ethoxycarbonylmethyloxy-3-cyano-pyridines (VIII, 91-103)

<table>
<thead>
<tr>
<th>Compd No.</th>
<th>v C-H cm⁻¹</th>
<th>v C=O cm⁻¹</th>
<th>vC=C, C=N cm⁻¹</th>
<th>δ C-H cm⁻¹</th>
<th>δ C-O, C-N cm⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>91</td>
<td>3010, 2999</td>
<td>2234</td>
<td>1748</td>
<td>1597, 1552</td>
<td>1444</td>
</tr>
<tr>
<td>92</td>
<td>3004, 2993</td>
<td>2233</td>
<td>1750</td>
<td>1595, 1520</td>
<td>1441</td>
</tr>
<tr>
<td>93</td>
<td>3008, 2950, 2840</td>
<td>2234</td>
<td>1752</td>
<td>1597, 1516</td>
<td>1442</td>
</tr>
<tr>
<td>94</td>
<td>3010, 2994</td>
<td>2232</td>
<td>1750</td>
<td>1593, 1512</td>
<td>1424</td>
</tr>
<tr>
<td>95</td>
<td>3004, 2990, 2940</td>
<td>2233</td>
<td>1758</td>
<td>1593, 1553</td>
<td>1458</td>
</tr>
<tr>
<td>96</td>
<td>3010, 2995, 2840</td>
<td>2234</td>
<td>1749</td>
<td>1597, 1520</td>
<td>1450</td>
</tr>
<tr>
<td>97</td>
<td>3010, 2997, 2880</td>
<td>2230</td>
<td>1750</td>
<td>1576, 1516</td>
<td>1448</td>
</tr>
<tr>
<td>98</td>
<td>3004, 2990, 2942</td>
<td>2232</td>
<td>1756</td>
<td>1579, 1524</td>
<td>1452</td>
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<td>99</td>
<td>3008, 2950</td>
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<td>1755</td>
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<td>1458</td>
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<td>2233</td>
<td>1748</td>
<td>1595, 1524</td>
<td>1442</td>
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<tr>
<td>102</td>
<td>3010, 2995, 2885</td>
<td>2230</td>
<td>1750</td>
<td>1598, 1520</td>
<td>1440</td>
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<tr>
<td>103</td>
<td>3010, 2956, 2854</td>
<td>2236</td>
<td>1756</td>
<td>1579, 1514</td>
<td>1426</td>
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</table>
The absence of stretching vibrations near 1665-1641 cm\(^{-1}\) due to cyclic ketone (C=O), and presence of sharp band near 1758-1748 responsible for carbonyl group (C=O) of ester functionality suggested O-alkylation of 2-pyridones, which confirmed the formation of 4,6-disubstituted 2-ethoxycarbonylmethyloxy-3-cyanopyridines (VIII, 104-116).

The IR(KBr) spectral data of 4,6-disubstituted 2-carbethoxy-3-aminofuro[2,3-b]pyridines (IX, 104-116) are summarized in table-43. The IR(KBr) spectra exhibited two stretching bands at 3500-3350 cm\(^{-1}\) and bending vibrations around 1615 cm\(^{-1}\) which proved the presence of amino (NH\(_2\)) group. The absorption due to carbonyl group (C=O) was shifted in the region between 1690-1665 cm\(^{-1}\) which was little downfield as compared to the carbonyl group of 4,6-disubstituted 2-ethoxycarbonylmethoxy-3-cyanopyridines (VIII). The absence of a sharp peak around 2233-2220 cm\(^{-1}\) responsible for cyano (C≡N) group provided strong evidence for the cyclization of 4,6-disubstituted 2-ethoxycarbonylmethoxy-3-cyanopyridines (VIII) and formation of 4,6-disubstituted 2-carbethoxy-3-aminofuro[2,3-b]pyridines (IX, 104-116).
Table 43: IR Spectral data of 4,6-disubstituted 2-carbethoxy-3-aminofuro[2,3-b]pyridines (IX, 104-116)

<table>
<thead>
<tr>
<th>Compd No</th>
<th>v N-H cm(^{-1})</th>
<th>v C-H cm(^{-1})</th>
<th>v C=O cm(^{-1})</th>
<th>v C=C, C=N cm(^{-1})</th>
<th>δ N-H cm(^{-1})</th>
<th>δ C-H cm(^{-1})</th>
<th>δ C-O, C-N cm(^{-1})</th>
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<tbody>
<tr>
<td>104</td>
<td>3501, 3386</td>
<td>3020, 2754</td>
<td>1665</td>
<td>1569, 1532</td>
<td>1617</td>
<td>1456</td>
<td>1337, 1264</td>
</tr>
<tr>
<td>105</td>
<td>3500, 3382</td>
<td>3010, 2980</td>
<td>1670</td>
<td>1560, 1530</td>
<td>1618</td>
<td>1450</td>
<td>1332, 1232</td>
</tr>
<tr>
<td>106</td>
<td>3490, 3387</td>
<td>3030, 2986</td>
<td>1662</td>
<td>1569, 1534</td>
<td>1617</td>
<td>1445</td>
<td>1335, 1260</td>
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<td>3020</td>
<td>1680</td>
<td>1586, 1550</td>
<td>1619</td>
<td>1450</td>
<td>1369, 1245</td>
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<td>108</td>
<td>3492, 3380</td>
<td>3020, 2980</td>
<td>1673</td>
<td>1586, 1549</td>
<td>1618</td>
<td>1446</td>
<td>1335, 1263</td>
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<tr>
<td>109</td>
<td>3500, 3362</td>
<td>3010, 2996</td>
<td>1667</td>
<td>1576, 1555</td>
<td>1617</td>
<td>1456</td>
<td>1330, 1263</td>
</tr>
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<td>3497, 3387</td>
<td>3044, 2986</td>
<td>1668</td>
<td>1586, 1550</td>
<td>1618</td>
<td>1450</td>
<td>1337, 1265</td>
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<tr>
<td>111</td>
<td>3490, 3380</td>
<td>3040, 2980</td>
<td>1665</td>
<td>1580, 1532</td>
<td>1618</td>
<td>1446</td>
<td>1337, 1264</td>
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<tr>
<td>112</td>
<td>3492, 3380</td>
<td>3020</td>
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<td>1586, 1530</td>
<td>1618</td>
<td>1456</td>
<td>1335, 1250</td>
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<td>3010, 2980</td>
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<td>1585, 1548</td>
<td>1620</td>
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<td>1369, 1249</td>
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<td>3490, 3382</td>
<td>3020, 2995</td>
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<td>1590, 1554</td>
<td>1618</td>
<td>1450</td>
<td>1350, 1245</td>
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<tr>
<td>115</td>
<td>3500, 3345</td>
<td>3010, 2967</td>
<td>1670</td>
<td>1576, 1550</td>
<td>1617</td>
<td>1456</td>
<td>1355, 1250</td>
</tr>
<tr>
<td>116</td>
<td>3480, 3340</td>
<td>3010, 2898</td>
<td>1665</td>
<td>1589, 1524</td>
<td>1621</td>
<td>1450</td>
<td>1334, 1260</td>
</tr>
</tbody>
</table>
The table-44 shows $^1$HNMR (CDCl$_3$) spectral data of 4,6-disubstituted 2-carbethoxy-3-aminofuro[2,3-b]pyridines (IX, 104-116). The triplet at $\delta$ 1.40-1.59 due to methyl protons and a quartet at $\delta$ 4.3-4.4 due to the methylene group integrating for three hydrogens and two hydrogens respectively were assigned to the ethyl (CH$_2$CH$_3$) protons present in ester functionality. A broad singlet due to amino protons (D$_2$O exchangable) integrating for two protons was found to be present near $\delta$ 4.91-4.93. The aromatic protons resonated in the region $\delta$ 7.00-8.30 in form of a multiplet.

The $^1$HNMR (CDCl$_3$) spectrum of 2-carbethoxy-3-amino-4-(4-methylphenyl)-6-phenylfuro[2,3-b]pyridine (108) is shown in figure-12. It exhibited a triplet in the region $\delta$ 1.40-1.45 ($J$=6.9) and a quartet between $\delta$ 4.38-4.45 ($J$=7.1) integrating for three hydrogens and two hydrogens respectively, due to ethyl (CH$_2$CH$_3$) protons of ester group at position-2 of furan ring. A singlet at $\delta$ 2.47 integrating for 3 protons was suggestive of the presence of methyl (CH$_3$) group. Amino protons (D$_2$O exchangable) were found to be present at $\delta$ 4.93 integrating for two hydrogens giving a broad singlet. A multiplet giving an integration of ten hydrogens due to aromatic protons was found in the region of $\delta$ 7.26-8.16.
Table- 44: $^1$HNMR Spectral data of 4,6-disubstituted 2-carbethoxy-3-aminofuro[2,3-b]-pyridines (IX, 104-116).

<table>
<thead>
<tr>
<th>Compd. No.</th>
<th>R$_1$</th>
<th>R$_2$</th>
<th>$^1$HNMR (CDCl$_3$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>104</td>
<td>C$_6$H$_5$</td>
<td>C$_6$H$_5$</td>
<td>1.4-1.45(t, J=7.2, 3H, CH$_3$), 4.38-4.45(q, J=6.9, 2H, CH$_2$), 4.93(s, 2H, CH$_2$), 7.26-8.16 (m, 11H, Ar-H)</td>
</tr>
<tr>
<td>105</td>
<td>C$_6$H$_5$</td>
<td>4-CH$_3$C$_6$H$_4$</td>
<td>1.41-1.46(t, J=7.2, 3H, CH$_3$), 2.48(s, 3H, CH$_3$), 4.27-4.42(q, J=6.9, 2H, CH$_2$), 4.92 (s, 2H, NH$_2$), 7.18-8.00(m, 10H, Ar-H)</td>
</tr>
<tr>
<td>106</td>
<td>C$_6$H$_5$</td>
<td>4-OCH$_3$C$_6$H$_4$</td>
<td>1.40-1.45(t, J=7.2, 3H, CH$_3$), 4.0(s, 3H, OCH$_3$), 4.39-4.40(q, J=6.9, 2H, CH$_2$), 4.93 (s, 2H, NH$_2$), 7.16-8.16(m, 10H, Ar-H)</td>
</tr>
<tr>
<td>107</td>
<td>C$_6$H$_5$</td>
<td>4-ClC$_6$H$_4$</td>
<td>1.40-1.45(t, J=7.2, 3H, CH$_3$), 4.29-4.49(q, J=6.9, 2H, CH$_2$), 4.92(s, 2H, NH$_2$), 7.45-8.12(m, 10H, Ar-H)</td>
</tr>
<tr>
<td>108</td>
<td>4-CH$_3$C$_6$H$_4$</td>
<td>C$_6$H$_5$</td>
<td>1.40-1.45(t, J=7.2, 3H, CH$_3$), 2.47(s, 3H, CH$_3$), 4.38-4.45(q, J=6.9, 2H, CH$_2$), 4.93 (s, 2H, NH$_2$), 7.26-8.16(m, 9H, Ar-H)</td>
</tr>
<tr>
<td>109</td>
<td>4-CH$_3$C$_6$H$_4$</td>
<td>4-ClC$_6$H$_4$</td>
<td>1.41-1.47(t, J=7.2, 3H, CH$_3$), 2.48(s, 3H, CH$_3$), 4.39-4.46(q, J=6.9, 2H, CH$_2$), 4.93 (s, 2H, NH$_2$), 7.13-8.19(m, 9H, Ar-H)</td>
</tr>
<tr>
<td>110</td>
<td>4-OCH$_3$C$_6$H$_4$</td>
<td>C$_6$H$_5$</td>
<td>1.4-1.45(t, J=7.2, 3H, CH$_3$), 4.0(s, 3H, OCH$_3$), 4.40-4.49(q, J=6.9, 2H, CH$_2$), 4.92 (s, 2H, NH$_2$), 7.27-8.24 (m, 10H, Ar-H)</td>
</tr>
<tr>
<td>111</td>
<td>4-OCH₃C₆H₄</td>
<td>4-OCH₃C₆H₄</td>
<td>1.4-1.45(t, J=7.2, 3H, CH₃), 4.12(s, 6H, 2OCH₃), 4.38-4.45(q, J=6.9, 2H, CH₂), 4.93(s, 2H, NH₂), 7.26-8.16(m, 9H, Ar-H)</td>
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<tr>
<td>112</td>
<td>4-ClC₆H₄</td>
<td>C₆H₅</td>
<td>1.4-1.45(t, J=7.2, 3H, CH₃), 4.40-4.49(q, J=6.9, 2H, CH₂), 4.93(s, 2H, NH₂), 7.21-8.24(m, 10H, Ar-H)</td>
</tr>
<tr>
<td>113</td>
<td>4-ClC₆H₄</td>
<td>4-CH₃C₆H₄</td>
<td>1.42-1.47(t, J=7.2, 3H, CH₃), 2.48(s, 3H, CH₃), 4.38-4.44(q, J=6.9, 2H, CH₂), 4.92(s, 2H, NH₂), 7.19-8.01(m, 9H, Ar-H)</td>
</tr>
<tr>
<td>114</td>
<td>2-Furyl</td>
<td>C₆H₅</td>
<td>1.4-1.47(t, J=7.2, 3H, CH₃), 4.30-4.40(q, J=6.9, 2H, CH₂), 4.93(s, 2H, NH₂), 7.00-8.25(m, 9H, Ar-H)</td>
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<tr>
<td>115</td>
<td>2-Furyl</td>
<td>4-CH₃C₆H₄</td>
<td>1.4-1.47(t, J=7.2, 3H, CH₃), 2.47(s, 2H, CH₂), 4.31-4.48(q, J=6.9, 2H, CH₂), 4.93(s, 2H, NH₂), 7.00-8.21(m, 9H, Ar-H)</td>
</tr>
<tr>
<td>116</td>
<td>2-Thienyl</td>
<td>C₆H₅</td>
<td>1.42-1.47(t, J=7.2, 3H, CH₃), 4.40-4.47(q, J=6.9, 2H, CH₂), 4.93(s, 2H, NH₂), 7.21-8.20(m, 9H, Ar-H)</td>
</tr>
</tbody>
</table>

Mass fragmentation pattern of compound 106 is depicted in scheme-90. It exhibited a molecular ion peak at m/e = 388 and base peak at m/e = 372.
Scheme - 90
4.3.2 Synthesis of 4,6-disubstituted 2-carbethoxy-3-aminothieno[2,3-b]pyridines (XI, 117-123):

4,6-Disubstituted 2-chloro-3-cyanopyridines (V, 56-70) were taken as starting material for the synthesis of 4,6-disubstituted 2-carbethoxy-3-aminothieno[2,3-b]pyridines (XI) via Thorpe-Ziegler type of cyclization.

4,6-Disubstituted 2-chloro-3-cyanopyridines (V) were treated with ethyl thioglycolate in acetonitrile. A complex of 18-crown-6 and potassium hydroxide was added to acetonitrile to effect the cyclization. A single cyclization was afforded, producing the corresponding 4,6-disubstituted 2-carbethoxy-3-aminothieno[2,3-b]pyridines (XI, 117-123) (Scheme-91)

![Scheme - 91](image)

The mechanism for such a Thorpe-Ziegler cyclization is similar to the one given in scheme-89 for the preparation of furo[2,3-b]pyridines (IX)

In these reactions, the intermediates 4,6-disubstituted 2-carbethoxymethylmercapto-3-cyanopyridines (X) obtained by reaction of 4,6-disubstituted 2-chloro-3-cyanopyridines (V)
and ethyl thioglycolate could also be separated. These 4,6-disubstituted 2-carbethoxymethylmercapto-3-cyanopyridines (X) could then be cyclized to the corresponding 4,6-disubstituted 2-carbethoxy-3-aminothieno[2,3-b]pyridines maintaining the same conditions employed single step cyclization of 4,6-disubstituted 2-chloro-3-cyanopyridines (V) to the corresponding 4,6-disubstituted 2-carbethoxy-3-aminothieno[2,3-b]pyridines (XI, 117-123).

Almost all reactions took about 2.5-3.0 hours for completion and the products 4,6-disubstituted 2-carbethoxy-3-aminothieno[2,3-b]pyridines were obtained in excellent yields (70-80%). Single step cyclizations were preferred over the two steps cyclizations, without the isolation of the intermediates 4,6-disubstituted 2-carbethoxymethylmercapto-3-cyanopyridines (X) as single step cyclization afforded better yield of final products.

The 4,6-disubstituted 2-carbethoxy-3-aminothieno[2,3-b]pyridines (XI, 117-123) obtained were pale to dark yellow in colour and their melting points were little less than those of corresponding 4,6-disubstituted 2-chloro-3-cyanopyridines (V). The physical constants of 4,6-disubstituted 2-carbethoxy-3-aminothieno[2,3-b]pyridines (XI, 117-123) are recorded in table-45.

**Table - 45**: Physical constants of 4,6-disubstituted 2-carbethoxy-3-aminothieno[2,3-b]pyridines (XI, 117-123)

<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>Mole. Formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>117</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>94</td>
<td>171-72</td>
<td>C&lt;sub&gt;22&lt;/sub&gt;H&lt;sub&gt;18&lt;/sub&gt;N&lt;sub&gt;2&lt;/sub&gt;O&lt;sub&gt;2&lt;/sub&gt;S</td>
</tr>
<tr>
<td>118</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>90</td>
<td>183-84</td>
<td>C&lt;sub&gt;23&lt;/sub&gt;H&lt;sub&gt;20&lt;/sub&gt;N&lt;sub&gt;2&lt;/sub&gt;O&lt;sub&gt;3&lt;/sub&gt;S</td>
</tr>
<tr>
<td>119</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>89</td>
<td>186-87</td>
<td>C&lt;sub&gt;22&lt;/sub&gt;H&lt;sub&gt;17&lt;/sub&gt;C1N&lt;sub&gt;2&lt;/sub&gt;O&lt;sub&gt;2&lt;/sub&gt;S</td>
</tr>
<tr>
<td>120</td>
<td>4-CH&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>87</td>
<td>173-75</td>
<td>C&lt;sub&gt;23&lt;/sub&gt;H&lt;sub&gt;20&lt;/sub&gt;N&lt;sub&gt;2&lt;/sub&gt;O&lt;sub&gt;2&lt;/sub&gt;S</td>
</tr>
<tr>
<td>121</td>
<td>4-CH&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-ClC&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>90</td>
<td>206-08</td>
<td>C&lt;sub&gt;23&lt;/sub&gt;H&lt;sub&gt;19&lt;/sub&gt;C1N&lt;sub&gt;2&lt;/sub&gt;O&lt;sub&gt;2&lt;/sub&gt;S</td>
</tr>
<tr>
<td>122</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>90</td>
<td>188-89</td>
<td>C&lt;sub&gt;23&lt;/sub&gt;H&lt;sub&gt;20&lt;/sub&gt;N&lt;sub&gt;2&lt;/sub&gt;O&lt;sub&gt;3&lt;/sub&gt;S</td>
</tr>
<tr>
<td>123</td>
<td>4-ClC&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>4-CH&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>89</td>
<td>190-91</td>
<td>C&lt;sub&gt;23&lt;/sub&gt;H&lt;sub&gt;19&lt;/sub&gt;C1N&lt;sub&gt;2&lt;/sub&gt;O&lt;sub&gt;2&lt;/sub&gt;S</td>
</tr>
</tbody>
</table>
All these Thorpe-Ziegler type of cyclizations between 4,6-disubstituted 2-chloro-3-cyanopyridines (V) and ethyl thioglycolate were carried out under solid-liquid phase transfer conditions. Attempts to carry out these reaction under liquid-liquid phase transfer conditions was unsuccessful, as the desired products were not formed. The reason for this may be attributed to the formation of hydrolysis products.

The amount of potassium hydroxide employed was three times the theoretically required molar quantity. 18-Crown-6 was used in catalytic quantity (10-20 mole %). The ideal temperature for this reaction between 4,6-disubstituted 2-chloro-3-cyanopyridines (V) and ethyl thioglycolate was 30-35 °C. With the progress of reaction the yellow products were separated, which were filtered, washed with water, dried and crystallized from suitable solvents.

From the literature, it is known that 4,6-disubstituted 2-carbethoxy-3-aminothieno[2,3-b]pyridines (XI, 117-123) are normally prepared using bases like sodium ethoxide or sodium methoxide. The yields obtained under such conditions are moderate. The reactions are carried out at room temperature.

In this process the reaction between 4,6-disubstituted 2-chloro-3-cyanopyridines (V) and ethyl thioglycolate using KOH/18-crown-6 complex under phase transfer condition was also attempted employing various other phase transfer catalysts like tetraethylammonium bromide (TBAB), triethylbenzylammonium chloride (TEBA) and tributylethylammonium bromide (TBEA). All these phase transfer catalysts failed to afford products in desired yield. Solvents like toluene, chloroform, methylene chloride and chlorobenzene were tried but they were not useful, as the extraction of the complex formed by 18-crown-6 and KOH was excellent in acetonitrile, which once again proved to be a better solvent for such base catalyzed Thorpe-Ziegler type of cyclization.
The IR(KBr) spectral data of thieno[2,3-b]pyridines (XI, 117-123) are recorded in table-46. The IR(KBr) spectra of 4,6-disubstituted 2-carbethoxy-3-aminothieno[2,3-b]pyridines (XI, 117-123) exhibited two stretching bands in the region 3400-3305 cm\(^{-1}\) and a bending vibration around 1610 cm\(^{-1}\) proving the presence of amino (NH\(_2\)) functionality. The absence of a sharp peak around 2210 cm\(^{-1}\) responsible for cyano (-C≡N) group provided the strong evidence for the cyclization of 4,6-disubstituted 2-chloro-3-cyanopyridines (V) and formation of 4,6-disubstituted 2-carbethoxy-3-aminothieno[2,3-b]pyridines (XI, 117-123).

Table -46 : IR Spectral data of 4,6-disubstituted 2-carbethoxy-3-aminothieno[2,3-b]pyridines (XI, 117-123)

<table>
<thead>
<tr>
<th>Compd. No.</th>
<th>vN-H cm(^{-1})</th>
<th>vC-H cm(^{-1})</th>
<th>vC=O cm(^{-1})</th>
<th>v C= C, C≡N cm(^{-1})</th>
<th>δ N-H cm(^{-1})</th>
<th>δ C-H cm(^{-1})</th>
<th>δ C-O, C-N cm(^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>117</td>
<td>3485, 3355</td>
<td>3010, 2980</td>
<td>1680</td>
<td>1600, 1535</td>
<td>1600</td>
<td>1424</td>
<td>1332, 1260</td>
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<td>118</td>
<td>3500, 3490</td>
<td>2996, 2940</td>
<td>1670</td>
<td>1590, 1545</td>
<td>1618</td>
<td>1450</td>
<td>1290, 1224</td>
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<tr>
<td>119</td>
<td>3490, 3360</td>
<td>3010, 2980</td>
<td>1675</td>
<td>1575, 1515</td>
<td>1610</td>
<td>1435</td>
<td>1330, 1224</td>
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<td>120</td>
<td>3475, 3350</td>
<td>3004, 2958</td>
<td>1680</td>
<td>1590, 1510</td>
<td>1610</td>
<td>1495</td>
<td>1305, 1224</td>
</tr>
<tr>
<td>121</td>
<td>3480, 3359</td>
<td>3010, 2875</td>
<td>1675</td>
<td>1579, 1524</td>
<td>1610</td>
<td>1424</td>
<td>1365, 1240</td>
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<tr>
<td>122</td>
<td>3480, 3355</td>
<td>3010, 2968</td>
<td>1680</td>
<td>1589, 1535</td>
<td>1618</td>
<td>1446</td>
<td>1295, 1225</td>
</tr>
<tr>
<td>123</td>
<td>3498, 3387</td>
<td>3008, 2958</td>
<td>1680</td>
<td>1587, 1526</td>
<td>1614</td>
<td>1440</td>
<td>1378, 1256</td>
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</table>
The $^1$HNMR spectral data of 4,6-disubstituted 2-carbethoxy-3-aminothieno[2,3-b]pyridines (XI, 117-123) are recorded in table-47. A triplet at $\delta$ 1.42-1.49 due to methyl protons and a quartet at $\delta$ 4.25-4.38 due to the methylene protons respectively were assigned to the ethyl (CH$_2$CH$_3$) functionality present in the form of ester. A broad singlet due to amino protons (D$_2$O exchangeable) integrating for two protons was found to be present near $\delta$ 5.70-5.72. The aromatic protons resonated in the region $\delta$ 7.72-8.20 in form of multiplet.

The $^1$HNMR (CDCl$_3$) spectrum of 2-carbethoxy-3-amino-4-(4-methylphenyl)-6-phenylthieno[2,3-b]pyridines (120) is shown in figure-13. It exhibited a triplet at $\delta$ 1.35-1.40 and a quartet at $\delta$ 4.29-4.36 integrating for three hydrogens and two hydrogens respectively, due to methyl protons and the ethyl (CH$_2$CH$_3$) protons of ester group. A singlet at $\delta$ 2.47 for protons was suggestive of methyl (CH$_3$) group. Amino protons (D$_2$O exchangeable) were found to be present at $\delta$ 5.71 integrating for two hydrogen giving a broad singlet. A multiplet integrating of ten protons due to the aromatic protons resonated in the region $\delta$ 7.25-8.11.

The IR and $^1$HNMR spectral data of 4,6-disubstituted 2-carbethoxy-3-aminofuro[2,3-b]pyridines (IX, 104-116) and 4,6-disubstituted 2-carbethoxy-3-aminothieno[2,3-b]pyridines (XI, 117-123) provided excellent information for establishing the structures of these compounds.
Table - 47: $^1$HNMR Spectral data of 4,6-disubstituted 2-carbethoxy-3-amino thieno[2,3-b]pyridines (XI, 117-123).

<table>
<thead>
<tr>
<th>Compd No.</th>
<th>R$_1$</th>
<th>R$_2$</th>
<th>$^1$HNMR (CDCl$_3$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>117</td>
<td>C$_6$H$_5$</td>
<td>C$_6$H$_5$</td>
<td>1.35-1.39(t, J=7.2, 3H, CH$_3$), 4.30-4.35(q, J=7.0, 2H,CH$_2$), 5.71(s, 2H, NH$_2$), 7.30-8 10 (m, 11H, Ar-H)</td>
</tr>
<tr>
<td>118</td>
<td>C$_6$H$_5$</td>
<td>4-OCH$_3$C$_6$H$_4$</td>
<td>1.36-1.39(t, J=7 2, 3H, CH$_3$), 3 98(s, 3H, OCH$_3$), 4.30-4 35(q, J=7 0, 2H,CH$_2$), 5 71 (s, 2H, NH$_2$), 7.25-8.11 (m, 10H, Ar-H)</td>
</tr>
<tr>
<td>119</td>
<td>C$_6$H$_5$</td>
<td>4-ClC$_6$H$_4$</td>
<td>1.36-1.39(t, J=7.2, 3H, CH$_3$), 4.30-4.36(q, J=7.0, 2H,CH$_2$), 5.72 (s, 2H, NH$_2$), 7.28-8.02 (m, 10H, Ar-H)</td>
</tr>
<tr>
<td>120</td>
<td>4-CH$_3$C$_6$H$_4$</td>
<td>C$_6$H$_5$</td>
<td>1.35-1.40(t, J=7.2, 3H, CH$_3$), 2.47(s, 3H, CH$_3$), 4.30-4.36(q, J=7.0, 2H,CH$_2$), 5.71(s, 2H, NH$_2$), 7.29-8 11 (m, 10H, Ar-H)</td>
</tr>
<tr>
<td>121</td>
<td>4-CH$_3$C$_6$H$_4$</td>
<td>4-ClC$_6$H$_4$</td>
<td>1.35-1.39(t, J=7.2, 3H, CH$_3$), 2.49(s, 3H, CH$_3$), 4.30-4.39(q, J=7.0, 2H,CH$_2$), 5.72 (s, 2H, NH$_2$), 7.30-7.91 (m, 9H, Ar-H)</td>
</tr>
<tr>
<td>122</td>
<td>4-OCH$_3$C$_6$H$_4$</td>
<td>C$_6$H$_5$</td>
<td>1.36-1.39(t, J=7 2, 3H, CH$_3$), 3.98(s, 3H, OCH$_3$), 4.30-4.35(q, J=7 0, 2H,CH$_2$), 5.71 (s, 2H, NH$_2$), 7.25-8.11 (m, 10H, Ar-H)</td>
</tr>
<tr>
<td>123</td>
<td>4-ClC$_6$H$_4$</td>
<td>4-CH$_3$C$_6$H$_4$</td>
<td>1.35-1.40(t, J=7 2, 3H, CH$_3$), 2.47(s, 3H, CH$_3$), 4.30-4.36(q, J=7 0, 2H,CH$_2$), 5.72 (s, 2H, NH$_2$), 7.38-8 03 (m, 9H, Ar-H)</td>
</tr>
</tbody>
</table>

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4.4 Experimental

Melting points are 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. The elemental analysis was performed at Ahmedabad Textile Industrial Research Association (ATIRA), Ahmedabad.

IR(KBr)spectra of compounds VIII, IX and XI were recorded on Buck-500 spectrophotometer. Samples were run in form of pellets, which were prepared by smearing 2 mg compound in 150 mg KBr powder.

$^1$HNMR of 4,6-disubstituted 2-carbethoxy-3-aminofuro[2,3-b]pyridine (IX, 104-116) and 4,6-disubstituted 2-carbethoxy-3-aminothieno[2,3-b]pyridine (XI, 117-123) were recorded on Varian Model-400 spectrometer using TMS as an internal standard. The values are given in $\delta$ ppm.

The purity of compounds VIII, IX and XI was checked routinely by TLC (1-mm thickness) silica gel-G and spots were visualized by exposing the dry plates in iodine vapours. General method for the synthesis of 4,6-disubstituted 2-ethoxycarbonylmethoxy-3-cyano pyridines$^{262}$ (VIII, 91 to 103):

To a stirred solution of 4,6-disubstituted 3-cyanopyridin-2(1H)-ones (II, 16-30) (0.005 mole) and potassium carbonate (0.01 mole, 1.38 g) in N,N-dimethylformamide (15 ml) was added dropwise ethyl bromoacetate (0.006 mole, 1.0 g). The reaction mixture was stirred for 1 hour and completion of reaction was checked by tlc (benzene/ethanol 8:2). The reaction mixture was poured into the ice cold water to get white precipitates of the products. These precipitates were filtered, dried and recrystallized from methanol (Table - 40).
Synthesis of 4,6-disubstituted 2-carbethoxy-3-aminofuro[2,3-b]pyridines (IX, 104-116):

2-Carbethoxy-3-amino-4,6-diphenylfuro[2,3-b]pyridine (104):

To a stirred solution of powdered potassium hydroxide (0.0125 mole, 0.7 g) and 18-crown-6 (0.0005 mole, 0.139 g) in acetonitrile (15 ml) was added portionwise, 2-ethoxycarbonylmethoxy-3-cyano-4,6-diphenylpyridine (91, 0.005 mole, 1.79 g). The reaction was stirred for 1 hour at 40 °C temperature, which was then poured onto the crushed ice and the pH of this aqueous mixture was adjusted to eight by glacial acetic acid. The solid thus obtained was filtered, washed with water and dried. The crude 104 was crystallized from methanol.

Yield : 80 %
mp : 185-87 °C

Analysis : C_{22}H_{18}N_{2}O_{3} (385.39)

Calcd. : C 73.72 H 5.06 N 7.81 %
Found : C 73.59 H 5.20 N 7.68 %

IR(KBr) cm^{-1} : 3501, 3386 (NH), 3020, 2754 (CH), 1665 (C=O), 1569, 1532 (OC, C=N)

^{1}H NMR (d ppm): 1.40-1.45 (t, J=7.2, 3H, CH₃), 4.38-4.45 (q, J=6.9, 2H, CH₂)

4.93 (s, 2H, NH₂), 7.26-8.16 (m, 11H, Ar-H)

2-Carbethoxy-3-amino-4-phenyl-6-(4-methylphenyl)furo[2,3-b]pyridine (105):

To a stirred solution of powdered potassium hydroxide (0.0125 mole, 0.7 g) and 18-crown-6 (0.0005 mole, 0.132 g) in acetonitrile (15 ml) was added portionwise, 2-ethoxycarbonylmethoxy-3-cyano-4-phenyl-6-(4-methylphenyl)pyridine (92, 0.005 mole, 1.86 g). The reaction was stirred for 1 hour at 40 °C temperature. After completion of the reaction (tltc), work-up was done as per the procedure described for 104 to get the titled product.

Yield : 63 %
mp : 148-49 °C

Analysis : C_{23}H_{20}N_{2}O_{3} (372.42)
Calcd. : C 74.17 H 5.41 N 7.52 %

Found : C 74.37 H 5.26 N 7.32 %

IR(KBr) cm\(^{-1}\) : 3500, 3386 (NH), 3010, 2980 (CH), 1665 (C=O),
1569, 1532 (C=C, C=N)

\(^1\)H NMR (\(\delta\) ppm). 1.41-1.46 (t, \(J=7.2\), 3H, CH\(_3\)), 2.48 (s, 3H, CH\(_3\)), 4.29-4.42 (q,
\(J=6.9\), 2H, CH\(_2\)), 4.38 (s, 2H, NH\(_2\)), 7.18-8.00 (m, 10H, Ar-H)

2-Carbethoxy-3-amino-4-phenyl-6-(4-methoxyphenyl)furo[2,3-b]pyridine (106):

2-Ethoxycarbonylmethyloxy-3-cyano-4-phenyl-6-(4-methoxyphenyl)pyridine (93, 0.005 mole, 1.94 g) was added to a stirred solution of powdered potassium hydroxide (0.0125 mole, 0.7 g) and 18-crown-6 (0.0005 mole, 0.139 g) in acetonitrile (15 ml). The reaction was stirred for 1 hour at 45 °C temperature. After completion of the reaction, the desired product was obtained after work-up according to the procedure described for 104.

Yield : 75 %

mp : 155-56 °C

Analysis : C\(_{23}\)H\(_{20}\)N\(_2\)O\(_4\) (388.42)

Calcd. : C 71.12 H 5.19 N 7.21 %

Found : C 71.32 H 4.99 N 7.01 %

IR(KBr) cm\(^{-1}\) : 3490, 3389 (NH), 3030, 2986 (CH), 1662 (C=O),
1569, 1534 (C=C, C=N)

\(^1\)H NMR (\(\delta\) ppm): 1.42-1.47 (t, \(J=7.2\), 3H, CH\(_3\)), 4.00 (s, 3H, OCH\(_3\)), 4.39-4.40 (q,
\(J=6.9\), 2H, CH\(_2\)), 4.98 (s, 2H, NH\(_2\)), 7.16-8.10 (m, 10H, Ar-H)

2-Carbethoxy-3-amino-4-phenyl-6-(4-chlorophenyl)furo[2,3-b]pyridine (107):

To a stirred solution of powdered potassium hydroxide (0.0125 mole, 0.7 g) and 18-crown-6 (0.0005 mole, 0.139 g) in acetonitrile (15 ml) was added portionwise, 2-ethoxycarbonylmethyloxy-3-cyano-4-phenyl-6-(4-chlorophenyl)pyridine (94, 0.005 mole, 1.9 g).
The reaction was stirred for 1 hour at 40 °C temperature. After completion of the reaction, work-up was done according to the procedure described for 104.

Yield 78 %  
mp 161-62 °C

Analysis  
C_{22}H_{17}ClN_{2}O_{3} (392.88)

Calcd.  C 67.25  H 4.36  N 7.12 %

Found  C 67.50  H 4.16  N 6.98 %

IR(KBr) cm⁻¹  3501, 3402 (NH), 3020 (CH), 1680 (C=O)

1 HNMR(δ ppm)  1.40-1.46 (t, J=7.2, 3H, CH₃), 4.29-4.49 (q, J=6.9, 2H, CH₂), 4.95 (s, 2H, NH₂), 7.45-8.12 (m, 10H, Ar-H)

2-Ethoxycarbonylmethoxy-3-cyano-4-(4-methylphenyl)-6-phenylpyridine (108):  

2-Ethoxycarbonylmethoxy-3-cyano-4-(4-methylphenyl)-6-phenylpyridine (95, 0.005 mole, 1.86 g) was added portionwise to a stirred solution of powdered potassium hydroxide (0.0125 mole, 0.7 g) and 18-crown-6 (0.0005 mole, 0.132 g) in acetonitrile (15 ml). The reaction was stirred for 1 hour at 40 °C temperature. After completion of the reaction (tlc), work-up was done as per the procedure described for 104 to get the titled product.

Yield 60 %  
mp 164-65 °C

Analysis  
C_{23}H_{20}N_{2}O_{3} (372.42)

Calcd.  C 74.17  H 5.41  N 7.52 %

Found  C 74.37  H 5.20  N 7.29 %

IR(KBr) cm⁻¹  3492, 3380 (NH), 3020, 2980 (CH), 1673 (C=O), 1586, 1549 (C=C, C=N)

1 HNMR(δ ppm)  1.42-1.48 (t, J=7.2, 3H, CH₃), 2.48 (s, 3H, CH₃), 4.32-4.45 (q, J=6.9, 2H, CH₂), 4.92 (s, 2H, NH₂), 7.40-8.05 (m, 10H, Ar-H)
2-Carbethoxy-3-amino-4-(4-methylphenyl)-6-(4-chlorophenyl)furo[2,3-b]pyridine (109):

To a stirred solution of powdered potassium hydroxide (0.0125 mole, 0.7 g) and 18-crown-6 (0.0005 mole, 0.132 g) in acetonitrile (15 ml) was added portionwise, 2-ethoxycarbonylmethyloxy-3-cyano-4-(4-methylphenyl)-6-(4-chlorophenyl)pyridine (96, 0.005 mole, 2.03 g). The reaction was stirred for 1 hour at 45 °C temperature. After completion of the reaction (tlc), work-up was done as per the procedure described for 104 to get the titled product. Yield 70 % mp: 185-86 °C

Analysis
Calcd. C 67.88 H 4.70 N 6.88 %
Found C 67.59 H 4.62 N 7.05 %
IR(KBr) cm⁻¹ 3500, 3362 (NH), 3010, 2996 (CH), 1667 (C=O), 1576, 1555 (C=C, C=N)

¹HNMR(δ ppm): 1.40-1.45(t, J=7.2, 3H, CH₃), 2.48(s, 3H, CH₃), 4.39-4.46(q, J=6.9, 2H, CH₂), 4.95(s, 2H, NH₂), 7.13-8.19(m, 9H, Ar-H)

2-Carbethoxy-3-amino-4-(4-methoxyphenyl)-6-phenylfuro[2,3-b]pyridine (110):

2-Ethoxycarbonylmethyloxy-3-cyano-4-(4-methoxyphenyl)-6-phenylpyridine (97, 0.005 mole, 1.94 g) was added to a stirred solution of powdered potassium hydroxide (0.0125 mole, 0.7 g) and 18-crown-6 (0.0005 mole, 0.139 g) in acetonitrile (15 ml). The reaction was stirred for 1 hour at 45 °C temperature. After completion of the reaction, the desired product was obtained after work-up according to procedure described for 104.

Yield 75 % mp: 169-70 °C

Analysis
Calcd. C 71.12 H 5.19 N 7.21 %
Found C 71.02 H 5.01 N 7.08 %
IR(KBr) cm⁻¹ 3497, 3387 (NH), 3044, 2986 (CH), 1668 (C=O), 1586, 1550 (C=C, C=N)
2-Carbethoxy-3-amino-4-(4-methoxyphenyl)-6-(4-methoxyphenyl)furo[2,3-b]pyridine (111):

2-Ethoxycarbonylmethyloxy-3-cyano-4-(4-methoxyphenyl)-6-(4-methoxy-phenyl)pyridine (98, 0.005 mole, 2.03 g) was added to a stirred solution of powdered potassium hydroxide (0.0125 mole, 0.7 g) and 18-crown-6 (0.0005 mole, 0.139 g) in acetonitrile (15 ml). The reaction was stirred for 1 hour at 45 °C temperature. After completion of the reaction, the titled product was obtained after work-up according to the procedure described for 104.

Yield : 75 %

mp : 152-54 °C

Analysis : C_{24}H_{20}N_{2}O_{3} (406.43)

Calcd : C 67.96  H 5.45  N 6.89 %

Found : C 67.86  H 5.32  N 7.00 %

IR(KBr) cm\(^{-1}\) : 3498, 3382 (NH), 3020, 2986, 2856 (CH), 1667 (C=O), 1587, 1535 (C=C, C=N)

\(^1\)HNMR(δ ppm): 1.41-1.46(t, J=7.2, 3H, CH\(_3\)), 4.00(s, 3H, OCH\(_3\)), 4.40-4.49(q, J=6.9,2H, CH\(_2\)), 4.94(s, 2H, NH\(_2\)), 7.27-8.24(m, 10H, Ar-H)

2-Carbethoxy-3-amino-4-(4-chlorophenyl)-6-phenylfuro[2,3-b]pyridine (112):

To a stirred solution of powdered potassium hydroxide (0.0125 mole, 0.7 g) and 18-crown-6 (0.0005 mole, 0.132 g) in acetonitrile (15 ml) was added portionwise, 2-ethoxycarbonylmethyloxy-3-cyano-4-(4-chlorophenyl)-6-phenylpyridine (99, 0.005 mole, 1.96 g). The reaction was stirred for 1 hour at 40 °C temperature. After completion of the reaction, work-up was done according to the procedure described for 104.

Yield : 72 %

mp : 167-68 °C

Analysis : C_{22}H_{17}ClN_{2}O_{3} (392.88)
Calcd. : C 67.25 H 4.36 N 7.12 %
Found : C 67.05 H 4.37 N 6.90 %
IR(KBr) cm\(^{-1}\) : 3492, 3380 (NH), 3020 (CH), 1690 (C=O)

1586, 1530 (C=C, C=N)

\(^{1}\)HNMR(\(\delta\) ppm) : 1.40-1.45(t, J=7.2, 3H, CH\(_3\)), 4.40-4.49(q, J=6.9, 2H, CH\(_2\)),
4.93(s, 2H, NH\(_2\)), 7.21-8.24(m, 10H, Ar-H)

2-Carbethoxy-3-amino-4-(4-chlorophenyl)-6-(4-methylphenyl)furazane (113):

To a stirred solution of powdered potassium hydroxide (0.0125 mole, 0.7 g) and 18-crown-6 (0.0005 mole, 0.132 g) in acetonitrile (15 ml) was added portionwise, 2-ethoxycarbonylmethyloxy-3-cyano-4-(4-chlorophenyl)-6-(4-methylphenyl)pyridine (100, 0.005 mole, 2.03 g). The reaction was stirred for 1 hour at 40 °C temperature. After completion of the reaction (tlc), work-up was done as per the procedure described for 104 to get the titled product.

Yield : 65 %
mp : 193-95 °C

Analysis : C\(_{23}\)H\(_{19}\)ClN\(_2\)O\(_3\) (406.91)

Calcd. : C 67.88 H 4.70 N 6.88 %
Found : C 67.98 H 4.66 N 6.70 %
IR(KBr) cm\(^{-1}\) : 3501, 3362 (NH), 3010, 2996 (CH), 1667 (C=O),

1576, 1555 (C=C, C=N)

\(^{1}\)HNMR(\(\delta\) ppm) : 1.41-1.45(t, J=7.2, 3H, CH\(_3\)), 2.48(s, 3H, CH\(_3\)), 4.38-4.44(q, J=6.9, 2H, CH\(_2\)),
4.95(s, 2H, NH\(_2\)), 7.19-8.01(m, 9H, Ar-H)

2-Carbethoxy-3-amino-4-(4-chlorophenyl)-6-(4-chlorophenyl)furazane (114):

To a stirred solution of powdered potassium hydroxide (0.0125 mole, 0.7 g) and 18-crown-6 (0.0005 mole, 0.132 g) in acetonitrile (15 ml) was added portionwise, 2-ethoxycarbonylmethyloxy-3-cyano-4-(4-chlorophenyl)-6-(4-chlorophenyl)pyridine (101, 0.005 mole, 1.96 g). The reaction was stirred for 1 hour at 40 °C temperature. After completion of the re-
action, work-up was done according to the procedure described for 104

**Yield** 70 %  
**mp:** 205-06 °C

**Analysis**  
**Calcd.** C 61.97 H 378 N 6.56 %  
**Found:** C 61.70 H 382 N 6.32 %

**IR(KBr) cm⁻¹:**  
3490, 3382 (NH), 3020, 2995 (CH), 1662 (C=O)  
1590, 1554 (C=C, C=N)

**¹H NMR (δ ppm):**  
1.42-1.45 (t, J=7.2, 3H, CH₃), 4.30-4.40 (q, J=6.9, 2H, CH₂),  
4.95 (s, 2H, NH₂), 7.00-8.20 (m, 10H, Ar-H)

**2-Carbethoxy-3-amino-4-(2-furyl)-6-phenylfuro[2,3-b]pyridine (115):**

To a stirred solution of powdered potassium hydroxide (0.0125 mole, 0.7 g) and 18-crown-6 (0.0005 mole, 0.132 g) in acetonitrile (15 ml) was added portionwise, 2-ethoxy-carbonylmethoxy-3-cyano-4-(2-furyl)-6-phenylpyridine (102, 0.005 mole, 1.74 g). The reaction was stirred for 1 hour at 40 °C temperature. After completion of the reaction, work-up was done according to the procedure described for 104

**Yield** 78 %  
**mp:** 180-82 °C

**Analysis**  
**Calcd.** C 68.95 H 4.63 N 8.04 %  
**Found:** C 68.85 H 4.50 N 8.24 %

**IR(KBr) cm⁻¹:**  
3500, 3401 (NH), 3020, 2985 (CH), 1670 (C=O)  
1576, 1550 (C=C, C=N)

**¹H NMR (δ ppm):**  
1.42-1.45 (t, J=7.2, 3H, CH₃), 4.39-4.45 (q, J=6.9, 2H, CH₂),  
4.95 (s, 2H, NH₂), 7.21-8.20 (m, 10H, Ar-H)

**2-Carbethoxy-3-amino-4-(2-thienyl)-6-phenylfuro[2,3-b]pyridine (116):**

To a stirred solution of powdered potassium hydroxide (0.0125 mole, 0.7 g) and 18-crown-6 (0.0005 mole, 0.132 g) in acetonitrile (15 ml) was added portionwise, 2-ethoxy-
carbonylmethyloxy-3-cyano-4-(2-thienyl)-6-phenylpyridine (103, 0.005 mole, 1.82 g). The reaction was stirred for 1 hour at 40 °C temperature. After completion of the reaction, work-up was done according to the procedure described for 104.

Yield . 72 % mp . 175-76 °C
Analysis : C_{20}H_{16}N_{2}O_{3}S (364 36)
Calcd : C 65.92 H 4.42 N 7.64 %
Found : C 65.08 H 4.22 N 7.75 %
IR(KBr) cm⁻¹ : 3504, 3382 (NH), 3010, 2995 (CH), 1669 (C=O), 1589, 1532 (C=C, C≡N)

¹HNMR(δ ppm): 1.42-1.45(t, J=7 2, 3H, CH₃), 4.40-4.47(q, J=6.9, 2H, CH₂), 4.95(s, 2H, NH₂), 7.21-8.20(m, 10H, Ar-H)

Synthesis of 4,6-disubstituted 2-carbethoxy-3-aminothieno[2,3-b]pyridines (XI, 117-123):

2-Carbethoxy-3-amino-4,6-diphenylthieno[2,3-b]pyridine (117):

Ethyl thioglycolate (0.006 mole, 0.72 g) was added dropwise to a stirred mixture of powdered potassium hydroxide (0.015 mole, 0.84 g) and 18-crown-6 (0.001 mole, 0.264 g) in acetonitrile (15 ml). 2-Chloro-3-cyano-4,6-diphenylpyridine (57, 0.005 mole, 1.45 g) was added portionwise to this reaction mixture with stirring. The reaction was continued for 2.5 hours under stirring and its completion was checked with tlc (hexane/ethyl acetate, 8:2). The reaction mixture was then poured onto the crushed ice. The pH of the resulting solution was adjusted to seven with glacial acetic acid. The yellow solid thus obtained was filtered, dried and crystallized from glacial acetic acid.

Yield . 83 % mp . 171-72 °C
Analysis : C_{22}H_{18}N_{2}O_{2}S (374.39)
Calcd : C 70.57 H 4.84 N 7.48 %
Found : C 70.43 H 4.79 N 7.32 %
IR(KBr) cm⁻¹: 3485, 3355 (NH), 3010, 2980 (CH), 1680 (C=O), 1600, 1535 (C=C, C=N)

¹HNMR(δ ppm): 1.35-1.39(t, J=7.2, 3H, CH₃), 4.30-4.35(q, J=7.0, 2H, CH₂), 5.71(s, 2H, NH₂), 7.30-8.10(m, 10H, Ar-H)

2-Carbethoxy-3-amino-4-phenyl-6-(4-methoxyphenyl)thieno[2,3-b]pyridine (118):

To a stirred solution of powdered potassium hydroxide (0.015 mole, 0.84 g) and 18-crown-6 (0.001 mole, 0.264 g) in acetonitrile (15 ml) was added dropwise ethyl thioglycolate (0.006 mole, 0.72 g). 2-Chloro-3-cyano-4-phenyl-6-(4-methoxyphenyl)pyridine (59, 0.005 mole, 1.60 g) was added portionwise under stirring to this reaction mixture. The reaction was further stirred for 2.5 hours. After completion of the reaction, the titled product was obtained after the work-up according to the procedure described for 117.

Yield: 80 % mp 183-84 °C

Analysis: C₂₂H₂₉N₂O₃S (404.42)
Calcd.: C 68.30  H 4.98  N 6.92 %
Found: C 68.40  H 4.80  N 7.06 %

IR(KBr) cm⁻¹: 3500, 3490 (NH), 2996, 2940 (CH), 1670 (C=O), 1590, 1545 (C=C, C=N)

¹HNMR(δ ppm): 1.36-1.39(t, J=7.2, 3H, CH₃), 3.98(s, 3H, OCH₃), 4.30-4.35(q, J=7.0, 2H, CH₂), 5.71(s, 2H, NH₂), 7.25-8.11(m, 10H, Ar-H)

2-Carbethoxy-3-amino-4-phenyl-6-(4-chlorophenyl)thieno[2,3-b]pyridine (119):

Ethyl thioglycolate (0.006 mole, 0.72 g) was added dropwise to a stirred mixture of powdered potassium hydroxide (0.015 mole, 0.84 g) and 18-crown-6 (0.001 mole, 0.264 g) in acetonitrile (15 ml). 2-Chloro-3-cyano-4-phenyl-6-(4-chlorophenyl)pyridine (60, 0.005 mole, 1.62 g) was added portionwise to this reaction mixture. The reaction was further stirred for 2.5 hours. After completion of the reaction, work-up was carried out according to the procedure.
dure described for 117 to get the titled product.

Yield : 82 %  
mp : 186-87 °C

Analysis :  
Calcd.  
C 62.78 H 4.06 N 6.65 %

Found  
C 62.89 H 3.99 N 6.80 %

IR(KBr) cm⁻¹ : 3490, 3360 (NH), 3010, 2980 (CH), 1675 (C=O), 1575, 1515 (C=C, C=N)

¹HNMR(δ ppm): 1.36-1.39(t, J=7.2, 3H, CH₃), 4.30-4.36(q, J=7.0, 2H, CH₂), 5.72(s, 2H, NH₂), 7.42-8.02(m, 10H, Ar-H)

2-Carbethoxv-3-amino-4-(4-methylphenyl)-6-phenylthieno[2,3-b]pyridine (120):

To a stirred solution of powdered potassium hydroxide (0.015 mole, 0.84 g) and 18-crown-6 (0.001 mole, 0.264 g) in acetonitrile (15 ml) was added dropwise ethyl thioglycolate (0.006 mole, 0.72 g). To this was added 2-chloro-3-cyano-4-(4-methylphenyl)-6-phenylpyridine (61, 0.005 mole, 1.52 g) portionwise under stirring. The reaction was stirred for 2.5 hours. After completion of the reaction, the titled product was obtained after the work-up according to the procedure described for 117.

Yield : 85 %  
mp : 172-75 °C

Analysis :  
Calcd.  
C 71.12 H 5.19 N 7.21 %

Found  
C 71.32 H 5.01 N 7.02 %

IR(KBr) cm⁻¹ : 3475, 3350 (NH), 3004, 2958 (CH), 1680 (C=O), 1590, 1510 (C=C, C=N)

¹HNMR(δ ppm): 1.35-1.40(t, J=7.2, 3H, CH₃), 2.47(s, 3H, CH₃), 4.30-4.36(q, J=7.0, 2H, CH₂), 5.71(s, 2H, NH₂), 7.29-8.11(m, 10H, Ar-H)
2-Carbethoxy-3-amino-4-(4-methylphenyl)-6-(4-chlorophenyl)thieno[2,3-b]pyridine (121)

Ethyl thioglycolate (0.006 mole, 0.72 g) was added dropwise to a stirred solution of powdered potassium hydroxide (0.015 mole, 0.84 g) and 18-crown-6 (0.001 mole, 0.264 g) in acetonitrile (15 ml). 2-Chloro-3-cyano-4-(4-methylphenyl)-6-(4-chlorophenyl)pyridine (62, 0.005 mole, 1.69 g) was added portionwise with stirring to this reaction mixture and the reaction was stirred for another 2.5 hours. After completion of the reaction, work-up was carried out according to the procedure described for 117 to get the titled product. Yield: 80 %, mp: 206-08 °C

Analysis: C_{23}H_{19}ClN_{2}O_{3}S (422.91)
Calcd. C 65.32 H 4.52 N 6.62%
Found C 65.40 H 4.72 N 6.80%

IR(KBr) cm\(^{-1}\): 3480, 3359 (NH), 3010, 2875 (CH), 1675 (C=O), 1579, 1524 (C=C, C=N)

\(^{1}\)HNMR(δ ppm): 1.35-1.39 (t, J=7.2, 3H, CH₃), 2.49 (s, 3H, CH₃), 4.30-4.39 (q, J=7.0, 2H, CH₂), 5.72 (s, 2H, NH₂), 7.30-7.91 (m, 9H, Ar-H)

2-Carbethoxy-3-amino-4-(4-methoxyphenyl)-6-phenylthieno[2,3-b]pyridine (122):

To a stirred solution of powdered potassium hydroxide (0.015 mole, 0.84 g) and 18-crown-6 (0.001 mole, 0.264 g) in acetonitrile (15 ml) was added dropwise ethyl thioglycolate (0.006 mole, 0.72 g). 2-Chloro-3-cyano-4-(4-methoxyphenyl)-6-phenylpyridine (63, 0.005 mole, 1.60 g) was added portionwise with stirring to this reaction mixture. The reaction was continued for 2.5 hours. After completion of the reaction, the titled product was obtained after the work-up according to the procedure described for 117.

Yield: 85 %, mp: 188-89 °C

Analysis: C_{23}H_{20}N_{2}O_{3}S (404.42)
Calcd.          C 63.30  H 4.98  N 6.92 %
Found           C 63.38  H 4.78  N 7.04 %
IR(KBr) cm⁻¹ : 3480, 3355 (NH), 3010, 2968 (CH), 1680 (C=O),
1589, 1535 (C=C, C=N)
¹HNMR(δ ppm): 1 36-1.39(t, J=7.2, 3H, CH₃), 3 98(s, 3H, OCH₃), 4 30-4.35
(q, J=7.0, 2H, CH₂), 5.71(s, 2H, NH₂), 7.25-8 11(m, 10H, Ar-H)
2-Carbethoxy-3-amino-4-(4-chlorophenyl)-6-(4-methylphenyl)thieno[2,3-b]pyridine (123).

To a stirred solution of powdered potassium hydroxide (0.015 mole, 0.84 g) and 18-
crown-6 (0.001 mole, 0.264 g) in acetonitrile (15 ml) was added dropwise ethyl thioglycolate
(0.006 mole, 0.72 g). 2-Chloro-3-cyano-4-(4-chlorophenyl)-6-(4-methylphenyl)pyridine (67,
0.005 mole, 1.70 g) was added in portions with stirring. The reaction was stirred for 2.5
hours. After completion of the reaction, the titled product was obtained after the work-up
according to the procedure described for 115.
Yield          82 %
mp            190-91 °C
Analysis       C₂₃H₁₉ClN₂O₂S (422.91)
Calcd          C 65.32  H 4.52  N 6.62 %
Found          C 65.20  H 4.39  N 6.84 %
IR(KBr) cm⁻¹ : 3498, 3387 (NH), 3008, 2958 (CH), 1680 (C=O),
1587, 1526 (C=C, C=N)
¹HNMR(δ ppm): 1 35-1.40(t, J=7.2, 3H, CH₃), 2.47(s, 3H, CH₃), 4 30-4.35
(q, J=7.0, 2H, CH₂), 5.72(s, 2H, NH₂), 7.38-8 03(m, 9H, Ar-H)