CHAPTER V

OXIDATION OF MIXTURES OF 1-ARYL-3-(2-PYRIDYL)THIOUREAS AND THIOUREA

Oxidation of heterylthiourea has received some attention only in recent years. Several heterobicycles have thus been prepared.\textsuperscript{70-72} Essentially the reaction is similar to the intramolecular ring closure of 1-arylthioureas to 2-aminobenzothiazoles.\textsuperscript{45-53} Thus the oxidation of 1-phenyl-3-(2-pyridyl)thiourea (1) with bromine in chloroform, acetic acid or methanol was reported\textsuperscript{72} to yield 2-phenylamino-(1,2,4)-thiadiazolo(2,3-a)pyridinium bromide (2). However attempts to prepare the free base using mild bases like sodium acetate was found to bring about an irreversible rearrangement to 2-(2'-pyridylamino)benzothiazole (3). Treatment of (2) with alkali brought about hydrolysis resulting in the formation of sulphur and 1-phenyl-3-(2-pyridyl)urea.

\[
\text{PyNH-C-NHPh} \xrightarrow{\text{Br}_2} \text{PyNH-S-C-NHPh.Br} \xrightarrow{\text{NaOAC}} \text{PyNH-S-C-NHPy}
\]

(1) \hspace{1cm} (2) \hspace{1cm} (3)

Py = 2-pyridyl

No products with a thiadiazole or benzothiazolylguanidine
skeleton arising from two molecules of thiourea have been reported to be formed from the oxidation of 1-aryl-3-(2-pyridyl)thiourea in a reaction analogous to the oxidation of arylthioureas in polar medium. The oxidation of a mixture of 1-aryl-3-(2-pyridyl)thiourea and thiourea in acidic polar medium therefore claimed our attention; a reaction which could lead to possible 1,2,4-thiadiazole derivatives incorporating one heterocyclic ring as a substituent. Moreover it was expected that the pyridyl group in 1-aryl-3-(2-pyridyl)thiourea would remain in the protonated form in solution and therefore would influence the reaction pathway and thus throw some light on the reaction mechanism. By analogy with the oxidation of 1,3-diarylthiourea and thiourea, the reaction could have the following course yielding any of the compounds (8) to (11) arising from the intermediate bis(formamidino) sulphide salt (4)

\[
\begin{align*}
\text{ArNH}_2 - &\text{C-S-C-NH}_2 \cdot x\text{HCl} \\
\text{PyN-} &\text{-C-S-C-NH}_2 \cdot x\text{HCl} \\
&\text{or PyNH-}C-N-C-NH_2 \cdot x\text{HCl} \text{ or } H_2\text{N-C-N-C-NHPy} \cdot x\text{HCl}
\end{align*}
\]

(4)

(5)  (6)  (7)
RESULTS AND DISCUSSIONS

Oxidation of a mixture of 1-(2-pyridyl)-3-\(p\)-tolyl-thiourea and thiourea in acidic ethanolic medium using hydrogen peroxide gave a base with molecular formula \(C_{14}H_{13}N_5S\). Stretching vibrations of NH and C=N are evident in the i.r. spectrum of the base at 3230, 3100 and 1640 cm\(^{-1}\) respectively. The n.m.r. spectrum shows signals at \(\delta\) 2.16 due to three methyl protons of \(p\)-tolyl group, a singlet at \(\delta\) 6.16 due to two amino protons and a multiplet at \(\delta\) 7.12-7.4 due to the pyridyl two \(\beta\) and one \(\gamma\) protons and a multiplet of 4-benzenoid protons at \(\delta\) 7.6-7.84 and a doublet due to \(\alpha\) proton of the pyridyl group at \(\delta\) 8.72-9. In the case of 3-amino-4-\(p\)-tolyl-5-\(p\)-tolylidino-4,5-dihydro-1,2,4-thiadiazole\(^{117}\) and 3-\(p\)-tolylidino-4-\(p\)-tolyl-5-\(p\)-tolylidino-4,5-dihydro-1,2,4-thiadiazole\(^{11}\)
the signal due to the methyl protons of \( p \)-tolyl group at position five of the thiadiazole ring falls at \( \delta 2.3 \) and \( \delta 2.29 \) respectively. So in the above case the singlet signal at \( \delta 2.16 \) may be assigned to the methyl group of the \( p \)-tolylimino substituent at 5-position. In all the other cases examined earlier the amino protons at 3-position shows a signal between \( \delta 4 \) and \( \delta 5 \). In this case the shift observed can be attributed to the deshielding effect of the pyridyl group at position 4. So the base now formed can be formulated as 3-amino-4-(2-pyridyl)-5-\( p \)-tolylimino-4,5-dihydro-1,2,4-thiadiazole. Mass spectrum shows the molecular ion peak at m/e 283 and the major fragments are at m/e 282, 268, 242, 241, 240, 210, 209, 208, 183, 91, 78, 77, 65 and 51. The mass spectral data did not yield any conclusive evidence for the structure of the compound as it showed fragments with possible structure \( p-\text{CH}_3\text{C}_6\text{H}_4\text{NH=CNH}^- \) m/e 133, and also due to \( \text{Py-NH=CNH}^- \) m/e 120. The mass spectrum was run at elevated temperatures close to or above the m.p. due to low volatility. It is possible that the thiadiazole under electron impact underwent rearrangement yielding 3-amino-5-(2-pyridylimino)-4-\( p \)-tolyl-4,5-dihydro-1,2,4-thiadiazole and this might be the source for the fragment at m/e 133.

The usual technique of the reduction of the thiadiazole with hydrogen sulphide yielded the amidinothiourea in solution
It could be oxidised back to the thiadiazole in quantitative yield. However its decomposition with sodium bicarbonate at room temperature did not take place. In cases studied earlier, when an aryl group was present in the amidinothiourea on the nitrogen which carried the amidino group, it was found to decompose at room temperature to yield the related arylguanidine and the isothiocyanate. The fact that amidinothiourea did not decompose at room temperature in this particular case suggests that the aryl group is not present on the nitrogen which carries the amidino function. This is also supported by the fact that the reduction of the thia diazole in warm ethanolic ammoniacal hydrogen sulphide containing dimethylformamide yielded \( p \)-tolylthiourea and 2-aminopyridine. If the \( p \)-tolyl group were present on the nitrogen which carried the amidino function as in (6a), the products should have been 2-pyridylthiourea and \( p \)-tolylguanidine. The formation of \( p \)-tolylthiourea and 2-aminopyridine in the reductive decomposition suggests that the pyridyl group in the amidinothiourea is on the nitrogen which carried the amidino function as in (5a). (2-aminopyridine is probably formed by the decomposition of 2-pyridylguanidine. Methods adopted for the preparation of arylguanidines failed when applied in the case of 2-pyridylguanidine). The amidinothiourea obtained by the reduction of the thia diazole could thus be 1-amidino-
1-pyridyl-3-p-tolylthiourea (5a) and hence the thiadiazole, 3-amino-4-(2-pyridyl)-5-p-tolylimino-4,5-dihydro-1,2,4-thiadiazole (8a). The non-formation of addition products when the thiadiazole and phenyl isothiocyanate or carbon disulphide are reacted together is also indicative of the above structure for the thiadiazole.

Oxidation of binary mixtures of 1-phenyl-3-(2-pyridyl) thioura, 1-(2-pyridyl)-3-m-tolylthiourea, 1-p-methoxyphenyl 3-(2-pyridyl)thiourea and 1-p-ethoxyphenyl-3-(2-pyridyl)-thiourea with thiourea under similar conditions yielded the related thiadiazoles. Their chemical behaviour was comparable to that of p-tolyl analogue. Stretching vibrations of the NH and C=N groups are evident in the i.r. spectra of the bases obtained from different 1-aryl-3-(2-pyridyl)-thioureas and thiourea. The n.m.r. signal due to the pyridyl \( \alpha, \beta \) and \( \gamma \) protons falls in the same region as observed for 3-amino-4-(2-pyridyl)-5-p-tolylimino-4,5-dihydro-1,2,4-thiadiazole. So these bases also have the pyridyl substituent on the 4-position of the thiadiazole ring. Reduction and subsequent decomposition of the bases with ethanolic ammoniacal hydrogen sulphide afforded arylthioureas and 2-aminopyridine.

Partial oxidation of the binary mixtures of thioureas did not afford any amidinothiourea. Instead, thiadiazole (8) and some unreacted thiourea were obtained. It is possible
that the amidinothiourea which was formed underwent rapid oxidation.

In these oxidations the usual reaction pathway and intermediates, viz. the bis(formamidino) disulphide, sulphide, amidinothiourea and its further oxidation to the thiadiazole do not appear to hold good because it has been reported that 1-phenyl-3-(2-pyridyl)thiourea undergoes facile oxidation in polar solution to 2-phenylamino-(1,2,4)-thiadiazolo-(2,3-a)pyridinium bromide. In order to verify whether these thiadiazolopyridinium salts are 'involved' in the reaction pathway, 2(phenylamino-(1,2,4)-thiadiazolo-(2,3-a)pyridinium bromide was prepared, mixed with thiourea in ethanol and warmed. Since no change was observed a further quantity of the oxidant was added and the mixture was kept warm on a water bath. Gradual separation of sulphur was observed. When the reaction appeared complete, i.e. when no further sulphur separation was observed, the reaction mixture was worked up. The thiadiazole (8b) was obtained in the same yield as observed in the direct oxidation. The mechanism of the oxidation is, therefore not the usual one. The formation of the thiadiazole (8) in the above experiment suggests that an amidinothiourea intermediate, possibly (5), is however formed.

Since in the oxidation of 1-phenyl-3-(2-pyridyl)-
thiourea and thiourea mixture in acid medium yielded considerable amount of 1-phenyl-3-(2-pyridyl)urea in addition to the thiadiazole, it is reasonable to assume that the thiadiazolopyridinium bromide (2) in acid medium decomposed to yield the related carbodiimide or the chloroamidine. This could react with thiourea to yield the bis(formamidino)sulphide or undergo hydrolysis and yield urea. If the bis(formamidino)sulphide salt is formed, then the migration of the unsubstituted amidino group to the nitrogen carrying the pyridyl group could only occur as the nitrogen which carries the aryl ring is the protonated one and the amidinothiourea formed would be (5). This is because the pyridyl ring will be protonated and therefore will prevent protonation of nitrogen linked to it. In fact the amidinothiourea formed is indicated to be (5) from its behaviour during reductive degradation. The thiadiazole on reduction yielded the amidinothiourea (5). This on oxidation yielded the thiadiazole back. Thus it is proved that during reduction no rearrangement has occurred. In conclusion it may be reasonably assumed that in the formation of these thiadiazoles the bis(formamidino)sulphide salt and amidinothiourea hydrochloride intermediates are involved. The non-formation of bis(formamidino)sulphide salt by the interaction of 1-aryl-3-(2-pyridyl)thiourea with cyanamide in presence of hydrochloric acid may be due to the fact that pyridyl ring gets
protonated and thus prevents the enolization of the thio-keto form to the enol form. Dehydrosulphurisation of 1-aryl-3-(2-pyridyl)thiourea to carbodiimide could not be carried out because of the insolubility of thiourea in acetone. Hence the verification of the involvement of the above suggested intermediates in the reaction could not be undertaken.

EXPERIMENTAL

Mass spectra were recorded on a CEC 21-110B mass spectrometer at 70 eV using the direct inlet system. 1-aryl-3-(2-pyridyl)thioureas were prepared by the condensation of arylisothiocyanates and 2-aminopyridine. The purity of all the thiadiazoles reported in this chapter was verified by t.l.c.

I. OXIDATION OF MIXTURES OF 1-ARYL-3-(2-PYRIDYL)THIOUREAS AND THIOUREA: FORMATION OF 3-AMINO-5-ARYLIMINO-4-(2-PYRIDYL)-4,5-DIHYDRO-1,2,4-THIADIAZOLES

(a) 3-Amino-4-(2-pyridyl)-5-<p>-tolylimino-4,5-dihydro-1,2,4-thiadiazole (8a)

1-(2-Pyridyl)-3-<p>-tolylthiourea (4.8g, 0.02 mol) and thiourea (1.5g, 0.02 mol) were suspended in ethanol (150 ml) containing concentrated hydrochloric acid (4.6 ml, 32%, 0.04 mol) and oxidised with hydrogen peroxide (4.6 ml,
30%, 0.04 mol). The reaction mixture was warmed on a water bath for 1 hr. The precipitated sulphur was filtered off, the filtrate neutralised with sodium bicarbonate and diluted with water (300 ml). The precipitate formed was filtered, washed with water and dried. The product (2.5g, 44%) was crystallised from dimethylformamide - ethanol mixture as colourless shining plates, m.p. 275°. (Found: C,59.2; H,4.4; N,24.6; S,11.1. C\textsubscript{14}H\textsubscript{13}N\textsubscript{5}S requires C,59.4; H,4.6; N,24.7; S,11.3%). $\nu_{\text{max}}$(KBr): 3230s, 3100s (NH\textsubscript{2}); 1640s (C=N); 1550s, 1505s, 1450s, (C=C aryl); 820m (1,4 disub. aryl); 785m, 725m (pyridyl), 845s cm\textsuperscript{-1}. N.m.r. (DMSO-d\textsubscript{6}): $\delta$ 2.16, s, 3 methyl H of C5-NCH\textsubscript{3}C\textsubscript{6}H\textsubscript{4}; 6.16, s, 2 amino H; 7.12-7.4, m, 2 β pyridyl H and one γ pyridyl H; 7.6-7.84, m, 4 benzenoid H; 8.72-9, d, α pyridyl H. Mass spectrum, Fig.1.

When a solution of the base in acidic ethanol was treated with aqueous picric acid, a picrate was obtained which when crystallised from ethanol, gave shining yellow needles, m.p. 262°. (Found: N,21.2; S,6.0. C\textsubscript{14}H\textsubscript{13}N\textsubscript{5}S. C\textsubscript{6}H\textsubscript{3}N\textsubscript{3}O\textsubscript{7} requires N,21.9; S,6.3%).

(b) 3-Amino-5-phenylimino-4-(2-pyridyl)-4,5-dihydro-1,2,4-thiadiazole (8b)

1-Phenyl-3-(2-pyridyl)thiourea (23 g, 0.01 mol) and thiourea (0.8g, 0.01 mol) were suspended in ethanol (50 ml)
containing strong hydrochloric acid (2.3 ml, 32%, 0.02 mol). Hydrogen peroxide (2.3 ml, 30%, 0.02 mol) was added gradually with stirring. With the addition of the oxidant, the thioureas were found to go into solution and sulphur began to separate. The reaction mixture was warmed on a water bath till no further separation of sulphur was observed (1/2 hour).

Sulphur which got precipitated was removed by filtration. The reaction mixture was basified with sodium bicarbonate solution and diluted to 150 ml. The precipitate was collected and was subsequently extracted with dilute hydrochloric acid (150 ml) and the acidic extract basified. The white powder formed was collected (1.9g) and dried. T.l.c. analysis showed the presence of two components. These were separated by fractional crystallisation from ethanol. 3-Amino-5-phenylimino-4(3'-pyridyl)-4,5-dihydro-1,2,4-thiadiazole being less soluble in ethanol separated out first (0.7g, 27%). From the ethanolic filtrate, 1-phenyl-3-(2-pyridyl)urea was isolated, m.p. and m.m.p. 186°. This was the major product. The base was further purified by chromatography on a column of alumina using benzene as the eluent. Traces of 1-phenyl-3-(2-pyridyl)urea present emerged as the first fraction. Repeated crystallisation of the second fraction from ethanol yielded the base as shining needles, m.p. 228°. (Found: C, 57.8; H, 4.2; N, 25.8; S, 11.6.
C_{13}H_{11}N_5S requires C, 58.0; H, 4.1; N, 26.0; S, 11.9%.

$\nu_{\text{max}}$(KBr) 3200m, 3080s (NH); 1635s (C=N); 1570s, 1540s, 1490s, 1440s (C=C aryl); 775s, 730m (pyridyl); 670s (Ph), 1270s 820s, 730s cm$^{-1}$. N.m.r. (DMSO-$d_6$): $\delta$ 6.39, s, 2 amino H; 7.2-7.32, m, 2$\beta$ pyridyl H and one $\gamma$ pyridyl H; 7.79-8.1, m, 5 benzenoid H; 8.88, d, $\alpha$ pyridyl H. Mass spectrum, Fig. 2. Picrate: needles from ethanol, m.p. 260°. (Found: N, 22.9; S, 6.1. C_{13}H_{11}N_5S. C_{6}H_{3}N_{2}O_{7} requires N, 22.5; S, 6.4%).

(c) 3-Amino-4-(2-pyridyl)-5-m-tolylimino-4,5-dihydro-1,2,4-thiadiazole (8c)

The oxidation of a mixture of 1-(2-pyridyl)-3-m-tolylthiourea (4.8g, 0.02 mol) and thiourea (1.5g, 0.02 mol) afforded (8c), (2g, 35%), which gave needles when crystallised from ethanol, m.p. 231°. (Found: C, 59.1; H, 4.9; N, 24.5; S, 11.2. C_{14}H_{13}N_5S requires C, 59.4; H, 4.6; N, 24.7; S, 11.3%). $\nu_{\text{max}}$(KBr) 3300s, 3250m, 3150s (NH); 1660s (C=N); 1580s, 1520s, 1460s, 1440s (C=C aryl): 800s (pyridyl); 700s, (1,3 disub.aryl), 880s cm$^{-1}$. N.m.r. (DMSO-d$_6$): $\delta$ 2.56, s, 3 methyl H of C$_5$NCH$_3$C$_6$H$_4$; 6.32, s, 2 amino H; 7.2-7.4, m, 2$\beta$ pyridyl H and one $\gamma$ pyridyl H; 7.48-7.88, m, 4 benzenoid H; 8.72-9, d, $\alpha$ pyridyl H. Mass spectrum, (Fig. 3). Picrate, needles from ethanol, m.p. 248°. (Found: N, 21.4; S, 6.1. C_{14}H_{13}N_5S. C_{6}H_{3}N_{2}O_{7} requires N, 21.9; S, 6.3%).
(d) 3-Amino-5-β-methoxyphenylimino-4-(2-pyridyl)-4,5-dihydro-1,2,4-thiadiazole (8d)

1-β-Methoxyphenyl-3-(2-pyridyl)thiourea (2.6g, 0.01 mol) and thiourea (0.8g, 0.01 mol) were oxidised and worked up. The product (8d) obtained (1.5g, 50%) on crystallisation from dimethyl formamide-ethanol mixture gave colourless shining plates, m.p. 275°. (Found: C, 55.8; H, 4.5; N, 23.2; S, 10.9; C_{14}H_{13}N_{5}OS requires C, 56.2; H, 4.3; N, 23.4 and S, 10.7%). \(\nu_{\text{max}}(\text{KBr})\) 3300s, 3150s (NH); 1670s (C=N); 1590s, 1570s, 1520s, 1480s (C=C aryl); 780s, 898s, 730m (pyridyl); 840s cm\(^{-1}\). N.m.r. (DMSO d\(_6\)): \(\delta 4.08, s, 3\) methyl H of -OCH\(_3\); 6.36, s, 2 amino H; 7.2-7.4, m, 2 \(\beta\) pyridyl H and one \(\gamma\) pyridyl H; 7.44-8.2, m, 4 benzenoid H; 8.76-8.96, d, \(\alpha\) pyridyl H. Mass spectrum, Fig.4. Picrate, needles from ethanol, m.p. 254°. (Found: N, 20.8; S, 5.9. C_{14}H_{13}N_{5}OS. C_{6}H_{3}N_{3}O_{7} requires N, 21.2; S, 6.1%).

(e) 3-Amino-5-β-ethoxyphenylimino-4-(2-pyridyl)-4,5-dihydro-1,2,4-thiadiazole (8e)

1-β-Ethoxyphenyl-3-(2-pyridyl)thiourea (2.7g, 0.01 mol) and thiourea (0.8g, 0.01 mol) were suspended in ethanol (150 ml) containing hydrochloric acid (2.3 ml, 32%, 0.02 mol) and oxidised with hydrogen peroxide (2.3 ml, 30%, 0.02 mol) as described earlier. The product (1g, 32%) obtained was
crystallised from boiling ethanol, m.p. 191°. (Found: C, 57.1; H, 5.0; N, 22.5; S, 9.9. \( \text{C}_{15}\text{H}_{15}\text{N}_5\text{O}_5 \) requires C, 57.5; H, 4.8; N, 22.4; S, 10.2%). \( \nu_{\text{max}}(\text{KBr}) \): 3450s, 3150s (NH); 1660s (C=N); 1580s, 1540s, 1460s, 1420s (C=C aryl); 805s, 795s, 725m (pyridyl); 830m (1,4 disub.aryl); 860m cm\(^{-1}\).

N.m.r. (DMSO d\(_6\)): \( \delta 1.48, \text{t, 3 methyl H; 4.16}-4.48, \text{quartet, 2 methylene H; 6.32, s, 2 amino H; 7.2-8.24, m, 4 benzenoid H, 2 \beta \text{ pyridyl H and one } \gamma \text{ pyridyl H; 8.64-9, d, one } \alpha \text{ pyridyl H. Mass spectrum, Fig.5. Picrate, needles from ethanol, 215°. (Found: N, 20.1; S, 5.6; } \text{C}_{15}\text{H}_{15}\text{N}_5\text{O}_5 \text{ requires N, 20.7; S, 5.9%).}

II. REDUCTION OF 3-AMINO-5-ARYLIMINO-4-(2-PYRIDYL)-4,5-DIHYDRO-1,2,4-THIADIAZOLES

The details of a typical reduction procedure are given below:

a) With hydrogen sulphide in acid:

A slow stream of hydrogen sulphide was passed through a solution of 3-amino-4-(2-pyridyl)-5-p-tolylimino-4,5-dihydro-1,2,4-thiadiazole (2g) in dilute hydrochloric acid till the separation of sulphur was complete. The precipitate sulphur was removed by filtration and the resulting pale yellow solution was divided into three portions.

To one portion sodium bicarbonate was added and
warmed. No smell of isothiocyanate could be detected.

Another portion was steam distilled when oily drops were found in the distillate. It was extracted with ether and treated with concentrated ammonia. The colourless crystals which separated on cooling was identified as 1-\(\text{p}\)-tolylthiourea, m.p. and m.m.p. 188°. To the residual solution in the flask picric acid was added. The picrate formed was collected and crystallised from ethanol, when shining needles of 2-aminopyridine picrate was obtained, m.p. and m.m.p. 222°.

The other portion of the solution obtained after reduction was oxidised with hydrogen peroxide (0.5 ml, 30%) After keeping for a while, the solution was basified with sodium bicarbonate and the precipitate was collected and crystallised from dimethylformamide-ethanol mixture to yield (8a), m.p. and m.m.p. 275°.

b) Reduction with ammoniacal hydrogen sulphide

The base (8a, 3g) was added to a solution of ammoniacal hydrogen sulphide in warm dimethylformamide-ethanol mixture whereupon part of it went into solution. Hydrogen sulphide was passed through the solution for one hour with occasional warming. The unreacted compound was filtered off, the filtrate evaporated to dryness and the residue extracted with dilute hydrochloric acid. To this acid
solution, picric acid was added and the picrate formed was crystallised from alcohol, m.p. 221°. It did not show any depression in melting point when mixed with an authentic sample of 2-aminopyridine picrate.

The residue left after acid extraction was washed well with water and crystallised from ethanol, m.p. 188°. It was identified as 1-\(\text{p}\)-tolylthiourea by m.m.p. determination. The other thiadiazoles also showed analogous behaviour on reduction.

III. PARTIAL OXIDATION OF MIXTURES OF THIOUREAS

1-(2-Pyridyl)-3-\(\text{p}\)-tolylthiourea (2.3 g, 0.01 mol) and thiourea (0.76 g, 0.01 mol) were suspended in ethanol containing concentrated hydrochloric acid (2.3 ml, 32%, 0.02 mol) and oxidised with hydrogen peroxide (1.1 ml, 30%, 0.01 mol). The reaction mixture was warmed on a water-bath for half an hour. The precipitated sulphur was removed by filtration and the filtrate was concentrated on a water-bath. Then it was diluted with water and the residue collected. The residue when crystallised from ethanol yielded unreacted 1-(2-pyridyl)-3-\(\text{p}\)-tolylthiourea, m.p. and m.m.p. 185°.

To a portion of the filtrate obtained after removal of thiourea, hydrogen peroxide was added and warmed on a water-bath. After some time it was basified with sodium
bicarbonate and the precipitate formed was collected and crystallised from dimethylformamide-ethanol mixture, m.p. 275°. It did not show any depression in melting point when mixed with an authentic sample of 3-amino-4-(2-pyridyl)-5-p-tolylimino-4,5-dihydro-1,2,4-thiadiazole.

The rest of the filtrate was basified with sodium bicarbonate and the precipitate formed was collected and crystallised from dimethylformamide-ethanol mixture, m.p. 275°. It was found to be identical with 3-amino-4-(2-pyridyl)-5-p-tolylimino-4,5-dihydro-1,2,4-thiadiazole.

The partial oxidation of mixtures of other 1-aryl-3-(2-pyridyl)thioureas and thiourea also showed similar results.

IV. INTERACTION OF 1-ARYL-3-(2-PYRIDYL)THIOUREA WITH CYANAMIDE

In an experiment, 1-phenyl-3-(2-pyridyl)thiourea (4.6g, 0.02 mol) and cyanamide (1.5g, 0.02 mol) were mixed in acetone and dry hydrogen chloride gas was passed through it. No solid material separated out from the acetone solution. Hence acetone was evaporated and the viscous residue diluted with water. The white solid mass which separated was collected (3g) and crystallised from ethanol. It was found to be the unreacted 1-phenyl-3-(2-pyridyl)-thiourea, m.p. and m.m.p. 174°. The filtrate on oxidation
and basification did not yield any thia diazole. Similar results were obtained with other thioureas as well.

V. OXIDATION OF 1-PHENYL-3-(2-PYRIDYL)THIOUREA WITH BROMINE IN ETHANOL

1-Phenyl-3-(2-pyridyl)thiourea (2.3g, 0.01 mol) in ethanol was treated with bromine till a pale yellow colour persisted. The solid which separated was collected and crystallised from ethanol-hydrobromic acid mixture, m.p. 176-178°.

The thia diazolopyridinium salt so formed was mixed with thiourea (0.7g, 0.01 mol) in ethanol and warmed on a water bath for 30 min. The solution was then treated with bromine and warmed for another 30 minutes. The separated sulphur was filtered and the filtrate basified with sodium bicarbonate. The precipitate formed was collected, washed with water and crystallised from ethanol to constant melting point, m.p. 228°. It did not show any depression in melting point when mixed with an authentic sample of 3-amino-5-phenylimino-4-(2-pyridyl)-4,5-dihydro-1,2,4-thia diazole. The ethanolic filtrate on concentration afforded 1-phenyl-3-(2-pyridyl)urea.