Part I

Oxidimetric Determination of Thiourea

and its Organic Derivatives.
INTRODUCTION

Thiourea possesses several industrial, medicinal and analytical applications; and consequently its estimation has received considerable attention. The various methods used for the determination of thiourea are based either on its tendency to react with metals to undergo desulphurisation or complex formation or its quantitative oxidation to different products by various oxidants in acidic and alkaline solutions.

The earliest method regarding the determination of thiourea seems to be that of Velhard\textsuperscript{55} who titrated its hot ammoniacal solution with standard silver nitrate using an external end-point method.

\[ 2\text{AgNO}_3 + 2\text{NH}_4\text{OH} + \text{CS(NH}_2)_2 = \text{Ag}_2\text{S} + 2\text{NH}_4\text{NO}_3 + \text{H}_2\text{O} \]

Cuthill and Atkins\textsuperscript{17}, finding no precise location of the end-point by this method, developed a modified procedure by treating thiourea with an excess of strongly ammoniacal silver nitrate solution and titrating its unreacted excess, after acidification of the solution with nitric acid and removal of the precipitated silver sulphide against standard thiocyanate using ferric alum as an indicator. Williams\textsuperscript{59} determined thiourea in presence of thiocyanate by boiling its solution with sodium hydroxide and sodium argentocyanide,
2NaAg(CN)₂ + CS(NH₂)₂ + 2NaOH = CNH₂⁺ + Ag₂S + 4NaCN + 2H₂O

removing silver sulphide by filtration and determining sodium cyanide in the filtrate by Liebig titration with silver nitrate. Landa and Soukenik 36 proposed a method for determining thiourea by precipitating it with ammoniacal silver nitrate in presence of potassium cyanide, igniting the precipitate and weighing the silver formed. Nakanishi and Kobayashi 39 used coulometric method with a constant current for the argentometric titration of thiourea.

Korinskii 35 estimated thiourea by treating it with cadmium acetate and determining the cadmium sulphide formed iodometrically. The method was found to be suitable in the presence of cyanamide derivatives, sulphides and thiocyanates. Gupta 24 desulphurised the liquid containing thiourea with alkaline solution of lead acetate containing sodium hydroxide in excess in an atmosphere of hydrogen at 40 to 60°C for thirty minutes. Lead sulphide formed was converted to lead sulphate through lead chloride; and lead sulphate was determined gravimetrically. The method was successful in the presence of thiocyanate, chloride and aniline salts. Rulfs and Mackela 47 determined thiourea by digesting it with lead nitrate in Carius tube, dissolving the lead sulphate formed in acetate buffer and titrating the resulting solution of lead ions with standard dichromate amperometrically.
Gutiérrez developed a method for the estimation of thiourea based on its tendency to form a complex with alkaline mercuric iodide. The complex so formed was heated under reflux with potassium iodide when sulphur separated as mercuric sulphide. The sulphide was oxidised with a known excess of standard bromine solution and its unreacted excess was determined iodometrically or the free bromine was eliminated by treatment with mercurous chloride and the hydrobromic acid formed was titrated with standard sodium hydroxide using a mixture of bromoresol green and methyl red as indicator. Brada titrated thiourea with copper sulphate at 30°C using bismuth nitrate as an indicator. Based on the property of thiourea to form a complex with mercury, Kies and Wessel developed a 'dead-stop end-point' method with two mercury electrodes for the estimation of thiourea. Kies and Wessel also developed a coulometric method for the estimation of thiourea. Kies et al. further extended this method for the determination of some derivatives of thiourea. Wronski found that thiourea can be titrated with compounds like HDAHgOH or HOOCArHgOH in presence of sodium nitroprusside, diphenylcarbazone, diphenyl thiocarbzone, monohydroxymercuriphenolphthalein or thiofluorescein as indicators. Wronski also titrated thiourea and some of its derivatives in aqueous or alcoholic solution with tris (acetoxymercuri) aniline solution in presence of perchloric acid using p-diethylaminobenzylidinerhodanine as an indicator.
Maly found that when thiourea is oxidised with permanganate in neutral solutions, urea is formed and nearly all the sulphur is oxidised to sulphuric acid.

\[ \text{CS(NH}_2\text{)}_2 + 4(\text{O}) \rightarrow \text{CO(NH}_2\text{)}_2 + \text{SO}_3 \]

He, however, noticed that the amount of oxygen consumed was less than that required by the above equation. Schmidt stated that thiourea was quantitatively oxidised to urea by permanganate in neutral medium. Werner studied the reaction and observed that although 98.7 per cent of sulphur is oxidised to sulphuric acid, only 44 per cent of urea is obtained; and in addition to urea, ammonia, carbon dioxide and a substance C \(_3\)H\(_7\)N\(_8\) are also formed.

Cuthill and Atkins developed an indirect method for the estimation of thiourea with ceric sulphate or potassium dichromate in sulphuric acid medium by adding an excess of these reagents to the thiourea solution, boiling the solution under reflux condenser for thirty minutes and titrating the excess of the reagents with standard ferrous ammonium sulphate. They represented the reactions of thiourea with these reagents as:

\[ 3\text{Ce(\text{SO}_4\text{)}_2} + \text{H}_2\text{O} \rightarrow \text{Ce}_2(\text{SO}_4\text{)}_3 + \text{H}_2\text{SO}_4 + 0 \]
\[ \text{CS(NH}_2\text{)}_2 + 4(\text{O}) + \text{H}_2\text{O} \rightarrow \text{CO(NH}_2\text{)}_2 + \text{H}_2\text{SO}_4 \]
\[ 4\text{K}_2\text{Cr}_2\text{O}_7 + 16\text{H}_2\text{SO}_4 \rightarrow 4\text{K}_2\text{SO}_4 + 4\text{Cr}_2(\text{SO}_4\text{)}_3 + 16\text{H}_2\text{O} + 12(\text{O}) \]
\[ 3\text{CS(NH}_2\text{)}_2 + 12(\text{O}) \rightarrow 3\text{CO(NH}_2\text{)}_2 + 3\text{SO}_3 \]
Kimoto\textsuperscript{33} also proposed an indirect method for the estimation of thiourea with ceric sulphate.

Szabels\textsuperscript{ed}y and Mad\textsuperscript{i}\textsuperscript{s}\textsuperscript{53} determined thiourea by titrating it with standard potassium bromate in hydrochloric acid medium at 40 to 50\(^\circ\)C in presence of potassium bromide and a little of gold chloride.

\[ 3\text{(NH}_2\text{)}_2 + 4\text{HBrO}_3 + 3\text{H}_2\text{O} = 3\text{CO(NH}_2\text{)}_2 + 3\text{H}_2\text{SO}_4 + 4\text{HBr} \]

The end-point was marked by the appearance of yellow colour which persisted for 5 to 10 seconds only. Zeiner and Varga\textsuperscript{63} found that bromatometric determination of thiourea is influenced by the presence of excess of bromide; the greater the amount of bromide present the lower is the percentage of compound found. Mahr\textsuperscript{37} titrated thiourea with standard bromate-bromide solution in sulphuric acid medium at 35\(^\circ\)C in presence of potassium iodide and a little of starch. The end-point was marked by the appearance of blue colour when thiourea was oxidised to formamidine disulphide \((\text{NH}_2(\text{NH}_3\text{C})\text{)}_2\).

Banerjee\textsuperscript{5} determined thiourea in presence of varied amounts of mercuric chloride by using Mahr's method in a modified form. Rao and Neelakantan\textsuperscript{44} found the Mahr's method to be erratic and developed a method replacing potassium bromate by potassium permanganate and using lower concentration of sulphuric acid and double the amount of potassium iodide.
Estimate thiourea by oxidising it with bromine

$$\text{CSNH}_2 + 4 \text{Br}_2 + 6\text{H}_2\text{O} \rightarrow \text{SC}_4\text{O}_6 + 8\text{Br}^- + \text{CNNH}_2 + 10\text{H}^+$$

and titrating the acid formed with sodium hydroxide. Berka and Zyka determined thiourea with N-bromosuccinimide in sodium bicarbonate medium.

Afanas'ev titrated thiourea with chloramine-T in hot dilute sulphuric acid using methyl red or indigo carmine as an indicator. Singh et al. carried out a potentiometric titration of thiourea with chloramine-T in sulphuric acid at 80°C when thiourea was oxidised to carbon dioxide, sulphur trioxide and nitrogen.

$$7\text{CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{N(Na)}\text{Cl} + 6\text{H}_2\text{O} + 8\text{C(NH}_2)_2$$

$$= 7\text{CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{NH}_2 + 7\text{NaCl} + \text{N}_2 + \text{CO}_2 + \text{H}_2\text{SO}_4$$

Berka and Zyka found that the direct potentiometric titration of thiourea with chloramine-T in presence of potassium bromide in acidic medium is possible. Grover and Mehrotra reported that thiourea is oxidised to urea and sulphate by hypobromite and to sulphate, carbonate and nitrogen by hypobromite in alkaline solutions. Claeyss et al. determined thiourea by oxidising it with an excess of sodium hypobromite in alkaline medium and determining the unreacted excess of the reagent iodometrically. Berka and Zyka titrated thiourea potentiometrically with potassium metaperiodate in
hydrochloric acid medium. Bapat and Sharma developed direct and indirect procedures for the estimation of thiourea with alkaline potassium ferricyanide with osmium tetroxide as a catalyst.

\[
\begin{align*}
\text{H}_2\text{N} = \text{C} + 3\text{OH}^- &= 3e^- \\
\text{H}_2\text{N} = \text{C} + 3\text{H}_2\text{O} + \text{H}_2\text{SO}_4
\end{align*}
\]

\[
\left[\text{Fe(CN)}_6\right]^{3-} + e^- \rightarrow \left[\text{Fe(CN)}_6\right]^{4-}
\]

In the direct method, potassium ferricyanide was titrated with dilute thiourea solution with amperometric 'dead-stop end-point' indication. The reverse method of operation was not found to be possible. In the indirect method, either the excess of ferricyanide was titrated with standard arsenious oxide amperometrically or the potassium ferrocyanide formed equivalent to thiourea was titrated with ceric sulphate in acidic medium with ferroin as an indicator. Bapat and Tatawadi performed a colorimetric titration for the estimation of thiourea with alkaline potassium ferricyanide in presence of osmium tetroxide as catalyst. Joshi also reported a method for the estimation of thiourea with alkaline ferricyanide; the accuracy of the method, however, depended on the order of mixing the reagents.

Joshi determined thiourea by treating it with an excess of selenium acid in hydrochloric acid medium, heating the mixture under reflux for 30 to 30 minutes and determining
the unreacted excess of the reagent iodometrically. He represented the oxidation of thiourea as

\[ 5\text{H}_2\text{SeO}_3 = 5\text{Se} + 5\text{H}_2\text{O} + 5\text{O}_2 \]

\[ \text{Co(NH}_2\text{)}_2 + 2\text{O}_2 + \text{H}_2\text{O} = \text{Co(NH}_2\text{)}_2 + \text{H}_2\text{SO}_4 \]

\[ 3\text{Co(NH}_2\text{)}_2 + 3\text{O}_2 = 2\text{NH}_2\text{C(NH}_2\text{)}_2\cdot\text{SO}_3\text{H} \]

formamidine sulphonie acid

Werner developed another indirect method representing the oxidation of thiourea to formamidine disulphide in sulphuric acid medium by selenious acid.

\[ 4\text{Co(NH}_2\text{)}_2 + \text{H}_2\text{SeO}_3 + \text{H}_2\text{SO}_4 = 2\left[\text{HN = C}\left<\begin{array}{c}\text{NH}_2 \\ \text{S}\end{array}\right>\right]_2 \text{H}_2\text{SO}_4 + \text{Se} + 3\text{H}_2\text{O} \]

The excess of selenious acid was determined iodometrically or by direct titration with standard sodium hydroxide. Bapat and Sharma determined thiourea by adding an excess of potassium iodate and determining the unreacted excess of the reagent by titration with arsenious oxide in presence of saturated mercuric chloride solution using 'dead-stop end-point' with 0.1 V applied potential. Deshmukh and Bapat found that the oxidation of thiourea with potassium iodate by using iodine monochloride end-point is not quantitative. Recently Bagbanly and Guseinov developed a method based on the reaction

\[ \text{Co(NH}_2\text{)}_2 + 2\text{KIO}_3 + 2\text{HCl} = \text{Co(NH}_2\text{)}_2 + \text{K}_2\text{SO}_4 + 2\text{ICI} + \text{H}_2\text{O} \]
To a solution of thiourea in 3 N hydrochloric acid heated at 60°C, 10 ml. of benzene (thiophene free) was added and 1/3rd of the expected volume of potassium iodate was run in. The contents were mixed to liberate iodine which was titrated dropwise with iodate until the benzene layer became colourless.

Preisler and Berger found the oxidation-reduction potential of thiourea-formamidine disulphide system:

\[ 2 \text{H}_2\text{N}-\text{C}-\text{S}\text{H} \xrightarrow{+} \text{H}_3\text{N}-\text{C}-\text{S}-\text{S}-\text{C}\text{NH}_3 + 2\text{H}^+ + 2\text{e} \]

to be +0.420 volts in 0.05 to 1.00 N hydrochloric acid. Reynolds and Werner developed a method for the estimation of thiourea by oxidising it quantitatively to formamidine disulphide by iodine in aqueous solution. Werner found that this method gives low results if the concentration of thiourea exceeds 0.02 g. per 100 ml. of the titration mixture. Gilfillan, however, in an attempt to analyse a mixture of thiourea and ammonium thiocyanate reported that this method did not give accurate results if more than 5 mg. of thiourea per 100 ml. of the reaction mixture is titrated. Guthill and Atkins estimated thiourea by oxidising it quantitatively to urea and sulphate in alkaline medium with iodine.

\[ 2\text{NaOH} + \text{I}_2 = \text{NaIO} + \text{NaI} + \text{H}_2\text{O} \]

\[ 4\text{NaIO} + \text{CS(NH}_2)_2 \rightarrow \text{CO(NH}_2)_2 + 4\text{NaI} + 3\text{O}_3 \]
The unreacted excess of the reagent, after acidification of the solution, was determined by titration with standard sodium thiosulphate. The results, however, varied with the order of mixing the reagents, concentration of alkali and duration of the reaction. Skramovsky adopted a similar procedure but noted the appearance of turbidity due to the formation of sulphur in solution.

\[ \text{NH}_2\text{CSNH}_2 + \text{I}_2 + \text{H}_2\text{O} = \text{NH}_2\text{CONH}_2 + \text{S} + 2\text{HI} \]

Protopopescu and Nedioglu suggested that accurate results in the iodometric determination of thiourea could be obtained, provided the determination was carried out at a low thiourea concentration in the absence of excess of potassium iodide and other alkali halides. Joshi presented a modified procedure for the estimation of thiourea and tetramethyl thiourea, by treating them with an excess of iodine in alkaline medium and determining the unreacted excess of iodine by titration with standard arsineous oxide using borax and boric acid as buffer. Gupta estimated thiourea with standard iodine in presence of sodium bicarbonate buffer and extended the use of this method to the determination of N-methyl derivatives of thiourea. Wojahn titrated thiourea and a few of its derivatives with standard iodine and silver nitrate solutions. Ghalak and Rusicka titrated thiourea at pH 4 to 7 with iodine monochloride with a potentiometric indication, the thiourea was oxidised to formamidine disulphide.
Bayer and Posgay determined thiourea and allyl thiourea by titrating their acetic acid solutions with 0.1 N perchloric acid (in anhydrous glacial acetic acid) in presence of mercuric acetate using gentian violet as an indicator. Alicino used acetic acid solutions of crystal violet or quinaldine red as indicators in the above titration. Kodama et al. developed a gravimetric method for determining a mixture of thiourea and ammonium thiocyanate by precipitating thiourea with xanthylol in methyl alcohol and weighing the xanthylol-thiourea formed. The filtrate, containing thiocyanate, was titrated against standard silver nitrate using ferric alum as an indicator.

The various oxidimetric methods proposed for the determination of thiourea are based either on its oxidation to urea and sulphate, or to sulphate, carbonate and nitrogen or to formamidine disulphide under various conditions. Oxidation of thiourea to sulphate and cyanamide; and to urea, sulphate and formamidine sulphonic acid is also reported. No systematic study regarding the oxidimetric determination of thiourea has been made so far. In this investigation potassium iodate, iodine halides (monochloride, trichloride and monobromide), potassium dichromate, diethylene tetra-ammonium sulphatocerate (DTS), potassium bromate, chloramine-T and potassium ferricyanide have been used as oxidants for the direct visual and potentiometric determination of thiourea.
in sulphuric acid medium. Thiourea has also been determined indirectly by using sodium vanadate and DTS as oxidants in acid medium.

As no visual or potentiometric methods with these oxidants seem to have been developed for the determination of organic derivatives of thiourea, this study has, therefore, been extended to their determinations. Thiourea, methyl thiourea, ethyl thiourea, iso-propyl thiourea, n-butyl thiourea, iso-butyl thiourea, n-amyl thiourea, o-tolyl thiourea, p-tolyl thiourea, o-methoxy phenyl thiourea, p-methoxy phenyl thiourea, o-ethoxy phenyl thiourea, p-ethoxy phenyl thiourea, p-carbethoxy phenyl thiourea and phenyl thiourea have been estimated. Thioureas are oxidised to their corresponding disulphides with a single-electron change by these oxidants.

\[
\begin{align*}
2 \text{RHN} & \rightarrow \text{C-SH} \\
\text{HN} & \rightarrow \text{C-S-S-C} \text{NHR} + 2\text{H}^+ + 2\text{e}^{-}
\end{align*}
\]

\( (R = \text{hydrogen atom, alkyl or aryl group}) \)

The procedural details, observations and results obtained with the various oxidants are discussed in various chapters of the thesis.