A PHOTOMETRIC TITRATION METHOD FOR THE DETERMINATION OF THIOUREA FUNCTION AND ITS APPLICATION TO THE ANALYSIS OF SOME THIOUREA-BASED COMMERCIAL PRODUCTS.

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ABSTRACT

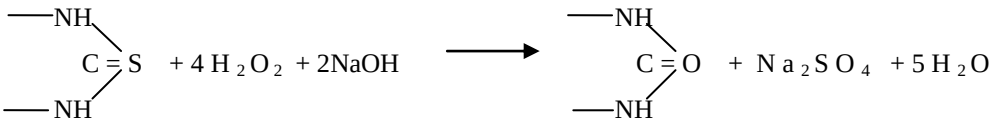
Organic compounds containing thiourea function find many industrial, agricultural, pharmaceutical and analytical applications. Consequently, convenient, reliable, rugged and cost-effective methods for ensuring the quality of commercial products based on it are highly desirable. The case with which hydrogen peroxide in the presence of an excess of sodium hydroxide oxdatively desulphurise the thiocarbonyl sulphur of thiourea into sodium sulphate and residual alkali is instantaneously transformed into bright yellow sodium benzyl trithiocarbonate (through reaction with carbon disulphide and benzyl mercaptan) showing maximum absorbance at 430mm, has been made the basis of a photometric titration method The method consists in adding a known excess of sodium hydroxide and hydrogen peroxide to thiourea solution in aqueous test-butanol (2:8v/v) followed by the addition of sodium sulphite and carbon disulphide and titrating the resulting solution photometrically at 430mm against standard benzyl mercaptan. The absorbance increases till it attains maximum value corresponding to the quantitatively transformation of sodium hydroxide into yellow sodium trithio-carbonate and thereafter, it attains almost constant values. The end-point is formed from extrapolation of two linear segments. The methods has been applied with success to the analysis of commercial formulations of thiophanate methyl (fungicide) and thiopentone sodium (drug) with recoveries in the range 99%-99.6% of the nominal content with relative standard durations in the range 0.4-0.6%.

Keywords: Benzyl mercaptan, Carbon disulphite, Spectro Photometer, Tes-Butanol

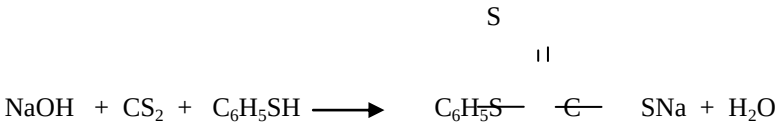
I. INTRODUCTION

Organic compounds containing thiourea function find many industrial, agricultural, pharmaceutical and analytical applications. Consequently, the development of convenient, reliable, rugged and cost-effective methods for their analysis particularly for ensuring the quality of technical and commercial products based on them are highly desirable. We have described a simple photometric titration method[1] for the determination of alkali based on the smooth and quantitative transformation of the latter in aqueous *tert.*-butanol into bright yellow sodium benzyl trithiocarbonate through reaction with carbon disulphide and benzyl mercaptan. The excellent performance of the method prompted us to explore further the avenues of its practical applications in other analytical investigations. In this endeavor, the usefulness of the method has now been extended by its application to the indirect determination of thioureas and some commercial products based on them. This has been done in the following manner:

i) In aqueous *tert.*-butanol and in the presence of sodium hydroxide, hydrogen peroxide oxidatively desulphurise the thiocarbonyl sulphur of thiourea into sodium sulphate.



ii) In the same medium, the residual alkali is measured by adding carbon disulphide and titrating the resulting solution photometrically at 430 nm against standard benzyl mercaptan. The titration is based on the smooth and quantitative transformation of sodium hydroxide into bright yellow sodium benzyl trithiocarbonate, showing λ_{max} at 430 nm.



iii) Excess hydrogen peroxide can be removed as sodium sulphate through reaction

with sodium sulphite. Ureas and sodium sulphate formed and excess carbon disulphide and sodium sulphite do not interfere in the above determination.

The method consists in adding a known excess of sodium hydroxide and hydrogen peroxide to thiourea solution in aqueous *tert.*-butanol followed by the addition of sodium sulphite and carbon disulphide and titrating the resulting solution photometrically at 430 nm against standard benzyl mercaptan. The absorbance increases till it attains a maximum value corresponding to the quantitative transformation of sodium hydroxide into above trithiocarbonate and thereafter, it attains almost constant values. The end-point it found from extrapolation of linear segments. The thioureas are not directly involved in these titrations but are stiochiometrically related to the amount of residual sodium hydroxide as trithiocarbonate. The method has been applied to the analysis of thiophanate-methyl fungicide and thiopentone sodium drug based on thioureas.

III. MATERIALS AND METHOD

Tert. Butanol AR (Extrapure) was used as such for preparing its 80% solution (by mixing solvent and water in the ratio 4:1 v/v). Benzyl mercaptan (Merck) was distilled before use. Its standard solution was prepared by dissolving a little more than the calculated amount of the compound in 80% tert. Butanol and standardizing the solution by the reported method[2]. Carbon disulphide AR (Merck) was used a received. The standard solution of sodium hydroxide and hydrogen peroxide was prepared in 80% *tert.*-butanol. Phenyl, tolyl, 0-methoxy-, o-ethoxy-, phenyl thioureas and o-phenylene-bis-thiourea were prepared and their purity was checked by the reported methods[3, 4]. The analytical standards of thiopanate-methyl (EPA, USA) and thiopentone sodium (Rhone-Poulene) were used and their purity was checked by reported methods[5, 6] Bausch and Lomb (Spectronic-20D) Spectrophotometric was used for absorbance measurements.

IV. PROCEDURES

4.1 Determination of sodium hydroxide

Aliquots of solutions in 80% *tert*.-butanol of sodium hydroxide were taken and diluted to 5 ml with the same solvent. Each solution was mixed with a drop (~100 µl) of carbon disulphide and the resulting solution titrated with standard (0.001M) benzyl mercaptan photometrically at 430 nm at room temperature (~23^{o}). Dilution corrections were applied and titration curves were plotted in the usual way. An inverted L-shaped titration curve was obtained and end-point was found by extrapolation of linear segments.

4.2 Determination of thiourea derivatives/and pure fungicide/drug compound

Aliquots of solutions of each derivative/compound in 80% *tert*.-butanol were taken and mixed with standard sodium hydroxide (3 ml, 0.01M) and hydrogen peroxide (1ml, 10%) both in 80% *tert*.-butanol and kept in an microwave for 60 sec. to ensure completion of the reaction. Each solution was mixed with sodium sulphite (1 ml, 10% in 80% *tert*.-butanol) and again kept for 2 min. Finally each solution was mixed with a drop (~100 µl) of carbon disulphide and the volume made to 6 ml with 80% *tert*.-butanol. The photometric titrations were performed with standard benzyl mercaptan in the same manner as described above.

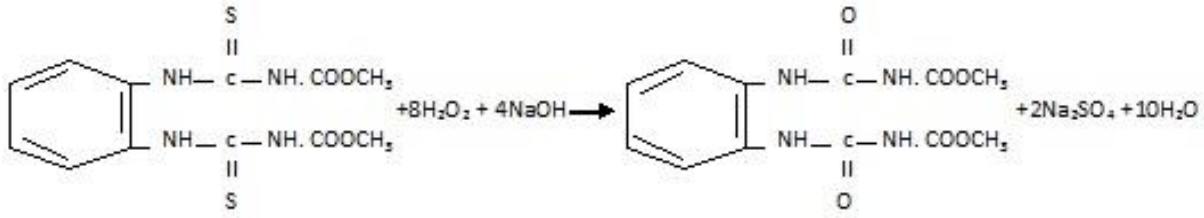
V. FORMULATION ANALYSIS

One formulation each of thiophanate-methyl fungicide (containing 70% active ingredient, WP) a thiopentone sodium drug viz injection (containing 0.5 g active ingredient per vial) were used. A single large sample of each formulation was weighed and dissolved in known volume of 80% *tert.*-butanol. The residue, if any, was washed with 2-3 times with the *tert*.-butanol and filterate alongwith washings were diluted to a known volume with the same solvent. Suitable aliquots of each formulation were taken and processed for analysis by photometric titrations in the same manner as described above. The results are given in Table 1.

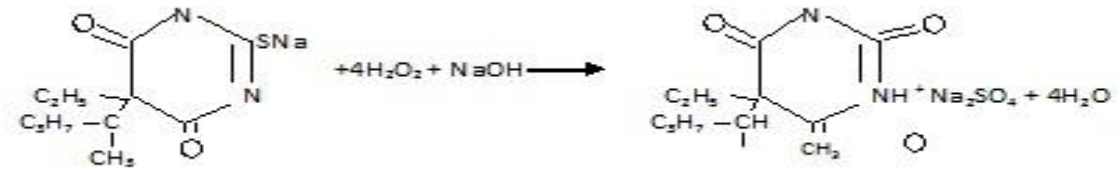
VI. RESULTS AND DISCUSSION

The quantitativeness of the transformation of sodium hydroxide into bright yellow sodium benzyl trithiocarbonate (the basis of the proposed method) has been verified by titrating sodium hydroxide in the presence of carbon disulphide against standard benzyl mercaptan. The alkali in the range 0.4 to 2.0mg have been determined with a maximum relative standard deviation (RSD) of 0.7%. The proposed method has primarily been developed for the analysis of thiourea-based commercial products viz. fungicide and drug with thiourea function present in them serving as the basis of analysis. In order to establish the generality and versatility of the method, it was thought advisable to standardize it with a number of reference compounds bearing the same function. In this endeavor, a number of thioureas have been determined by this method. The maximum RSD calculated from the pooled data of all the titrations performed with 0.75 and 2.25 mg of phenyl, 0-methoxyphenyl, 0-ethoxyphenyl, totyl, o-phenylene-bis-thiourea, were 0.8%. Thiophanate methyl and thiopentone sodium in the range 1 to 3 mg could be determined with a maximum RSD of 0.7% by this method. When applied to the analysis of commercial formulations of thiophanate methyl and thiopentone sodium for active ingredient contents, the recoveries were in the range 99.1-99.6% of the nominal content with RSD's in the range 0.4-0.6% (Table 1).

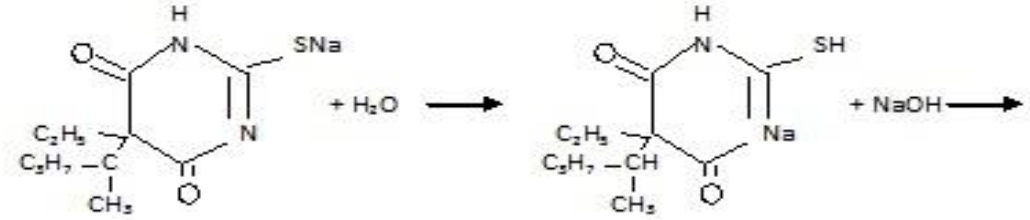
The results indicate that each molecule of thiophanate methyl in the oxidative desulphurization reaction consumes 4 moles of sodium hydroxide, which is in conformity of the presence of two thiourea functions in it. However, the oxidative desulphurization of thiopentone



Sodium involves one mole of the alkali. It is important to mention here that the second molecule of



sodium hydroxide is formed from the drug compound which hydrolyses in aqueous tert.butanol as:



That thiocarbonyl sulphur undergo above oxidative desulphurization to sulphate is well known[7].

The proposed method possesses significant advantages over the commonly used methods [5, 6] for the analysis of these commercial products in terms of the simplicity, rapidity and ruggedness of the procedure. Since the method does not require the preparation of calibration graph (generally required in Spectrophotometric analysis) and for which standards of high purity are needed makes the method all the more rapid. The smooth and quantitative transformation of sodium hydroxide into sodium benzyl trithiocarbonate, instant development of yellow colour and its excellent solution stability, well-established stoichiometry of the reactions involved and non-interference from the reaction products are some other special attributes of the present method.

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Table 1: Assay results of some commercial formulations of thiophanate methyl and thiopentone sodium

Formulation	Based on active Ingredient	Recovery *, %	
		Present method	Literature method [5, 6]
Topsin-M	70%	99.1 (0.4)	98.9 (0.8)
Intraval sodum	0.5 gm per vial	99.6 (0.6)	99.0 (0.7)

* Values are mean of five terminations with standard deviation (±).