CHAPTER - II

SYNTHESIS OF 1-(4'-CHLORO-2'-TOLYL) -4,4,6-TRIMETHYL (1H,4H)-2-PYRIMIDINE-THIOL AND ITS CHARACTERISATION

C H A P T E R - I I

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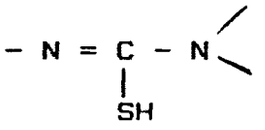
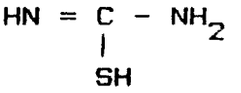
INTRODUCTION

2-Mercaptopyrimidines is a class of compounds known as cyclicthioureas. This constitutes a remarkably versatile class of analytically useful reagent. It is prepared by condensation of isothiocyanates with amines as a fine crystalline compounds. The active grouping for chelation is shown below in structure,



which is analogous to the grouping in thiourea shown in thiol[1] form such as



The mercaptopyrimidines act as a chelating agent for metal ions by bonding through S atom sometimes N atom or possibly both jointly.[2] In most of the cases they behave as unidentate ligand by complexation through S atom of thiol group.[3]

The analytical application of this class of compounds was explored by Singh et al as selective spectrophotometric reagent for the determination of some platinum group metals[4-6]. They[7] further reviewed chemistry of substituted mercaptopyrimidines. However the use of such compounds as extractants for platinum group metals and gold has been reported for the first time in our laboratory[8-10]. The literature as well as our investigations on the use of mercaptopyrimidines in the extraction, separation and determination of Noble metals in particular revealed that the thioligands possess a fascinating analytical potentialities. This prompted us to undertake the studies on synthesis of mercaptopyrimidine with chlorophenyl substituent at position 1 of mercaptopyrimidine moiety. With improved method for synthesis of mercaptopyrimidines reported by Mathes a large number of compounds, their derivatives and the analytical utilities in the extractive photometric determinations of metals have been recently reported.

Like heterocyclicthiols, mercaptopyrimidines have been shown to be useful as vulcanization accelerators[11]. The compounds are biologically important as they have been reported to have antibacterial activity.[12-13] A number of papers have appeared on pharmacology of these compounds. Derivatives of pyrimidinethiols have been reported as anti-wear additives for lubricating oils, photographic adjucants[14-15]. There is a report on the use of these compounds as

an intermediate in the preparation of fungicidal compounds.[16]

SYNTHESIS OF 1-SUBSTITUTED PYRIMIDINETHIOL

1-(4'-chloro-2'-tolyl)-4,4,6-trimethyl (1H,4H)-2-pyrimidinethiol was prepared by the method of Mathes[17-20]. The synthesis was carried out in two steps. In the first step, 2-methyl-2-isothiocyanato-4-pentanone was prepared according to Singh[21], while in the second step the product was condensed with 4-chloro-2-methyl aniline to obtain 4'-chloro-2'-tolyl TPT.

A) SYNTHESIS OF 2-METHYL-2-ISOTHIOCYANATO-4-PENTANONE

49.0 g (0.5 mole) of sulphuric acid dissolved in 50 ml of water was added over a period of 15 min to 98 g (1 mole) of mesityl oxide (4-methyl-3-penten-2-one) at 15^{o}. 76 g (1 mole) of ammonium thiocyanate dissolved in 25 ml of water was added quite rapidly to this mixture at room temperature. After stirring for 15 min the upper red, oily layer was separated and was washed with water until free from acid. The compound was dried by keeping it with anhydrous sodium sulphate over night. The yield of the product was 85%.

Anal. calculated for $C_{17}H_{11}NOS$:- C,53.51; H,7.00; N,8.91, O,10.2; S,20.38.

Found : C,53.47; H,7.07; N,8.94; O,10.20; S,20.40.

B) Synthesis of 1-substituted mercaptopyrimidines (4'-chloro 2'-tolyl TPT from 2-methyl-2 isothiocyanato and 4-chloro-2-methyl aniline :

To synthesise 4'chloro-2'-tolyl TPT 2-methyl- 2-isothiocyanato-4 -pentanone (3.14 g, 0.02 mole) was mixed with 4-chloro-2-methyl aniline (2.80 g, 0.02 mole) dissolved in 50 ml ethanol. 15-25 drops of conc H_2SO_4 were added to the reaction mixture. The mixture was refluxed for 20-25 min and cooled. The crystalline product was recrystallised from glacial acetic acid, washed with water and air dried. The compound is colourless with sharp M.P. 234^{o} and practical yield was 65%.

Molecular formula of resultant compound is

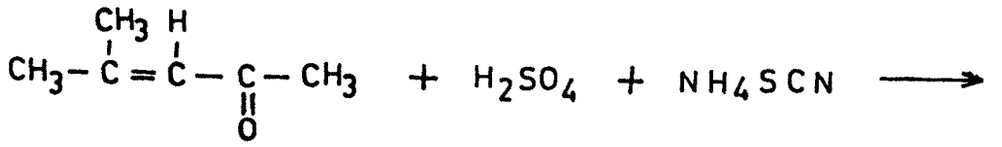
$C_{14}H_{17}N_2SCl$, mol. wt. 280.5

Anal. calculated for $C_{14}H_{17}N_2SCl$

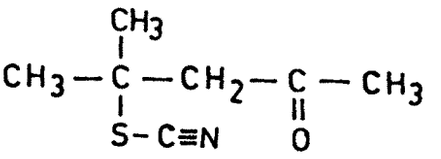
$C_{14}H_{17}N_2SCl$: C,59.89; H,6.06; N,9.98; S,11.41; Cl,12.66.

Found : C,59.85; H,6.06; N,10.0; S,11.43; Cl,12.60.

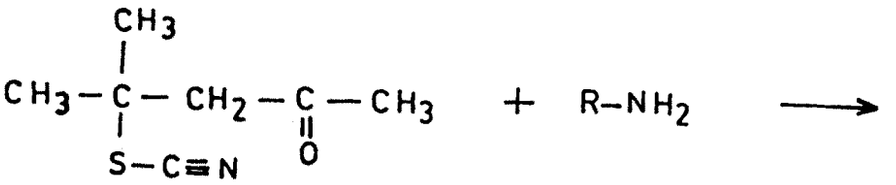
REACTIONS

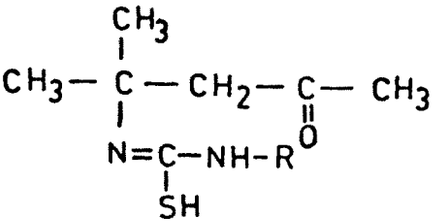


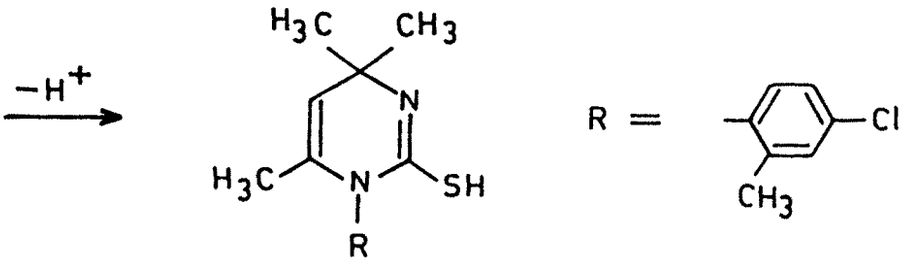
Mesityl Oxide



2-Methyl-2-isothiocyanato-4-pentanone







1-(4′-Chloro-2′-tolyl)-4,4,6-trimethyl (1H,4H)-2-Pyrimidinethiol.

Properties of 4'-chloro-2'-tolyl-TPT

The pyrimidinethiol is colourless, fine crystalline shining solid with a sharp M.P. 234°. The compound is soluble in chloroform, DMF, DMSO and 1,4-dioxan. It is insoluble in water and sparingly soluble in ethanol, acetone and MIBK. Its solution in DMF, chloroform, ethanol and DMSO is stable at room temperature for about 48 hrs and hence does not need protection from light.

UV spectrum of 4'chloro-2' tolyl- TPT

The absorption spectra of 4'-chloro-2'-tolyl TPT in chloroform is shown in Fig.1.The spectrum shows that the reagent exhibits sharp absorption maxima at 279 nm with the molar extinction coefficient 1.86×10^4 L mol^{-1} cm^{-1}.

Determination of purity of 4'-chloro 2'-tolyl-TPT

Aromatic pyrimidinethiols are much more acidic than corresponding phenols, hence the thiol group as an acid has been determined titrimetrically by several authors[22-23]. The purity of pyrimidinethiol was determined by non-aqueous titration of the thiol group using Azo-violet (p-nitrophenyl-azoresorcinol) indicator, according to the method of Verma.[24]

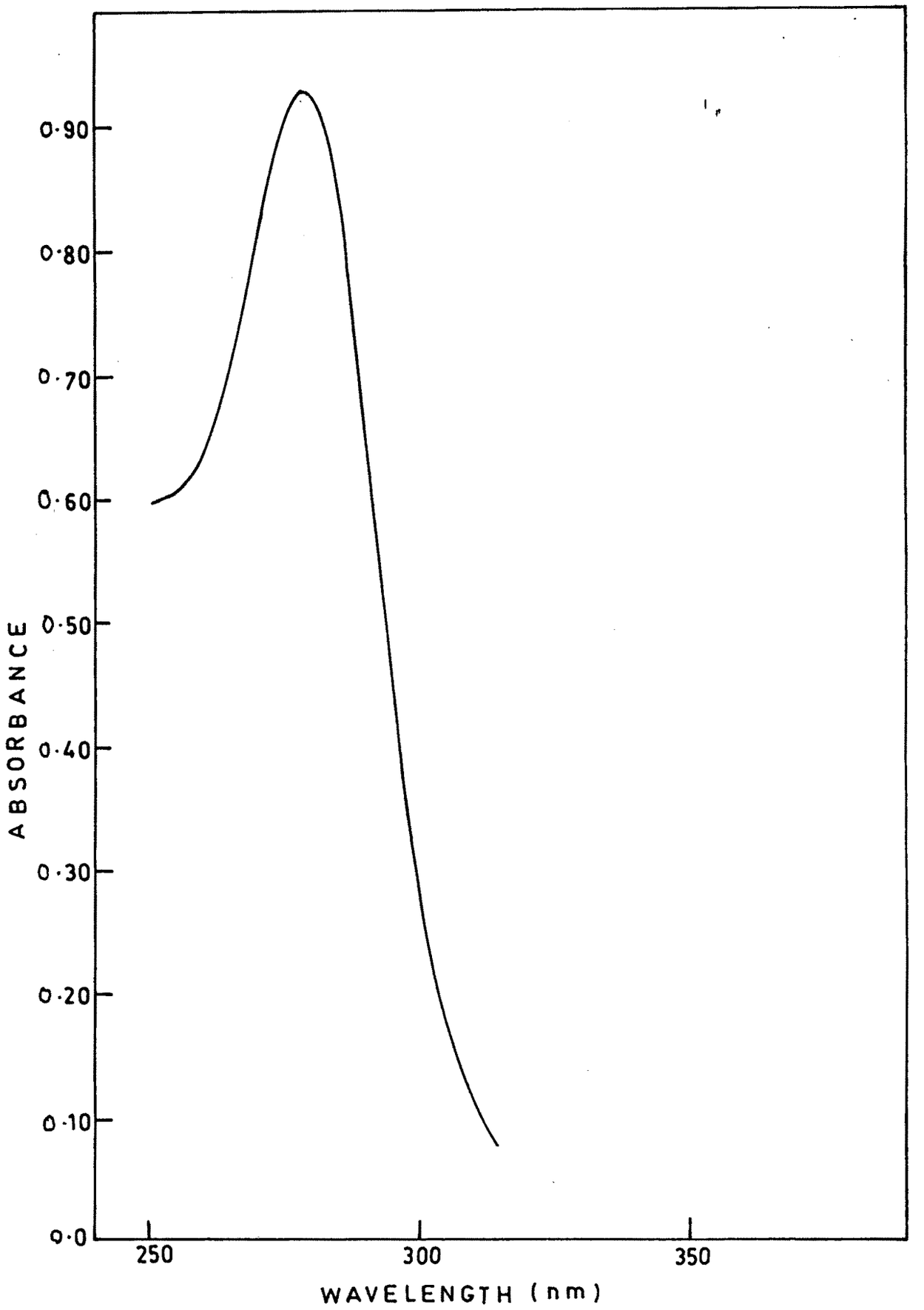


FIG.1 – ABSORPTION SPECTRUM OF PYRIMIDINETHIOL $5{\cdot}0 \times 10^{-5}$ M IN CHLOROFORM .

EXPERIMENTAL

Reagents :

Sodium methoxide solution : 0.05 M sodium methoxide in benzene-methanol was prepared as described by Fritz and Lisicki[22] and standardised against benzoic acid in acetone using Victoria blue as an indicator.

Indicator :

0.1 % solution of Azo-violet in acetone was used.

Procedure : A solution of 4'-chloro-2'-tolyl TPT containing 21-25 mg in 25 ml of N,N'-dimethyl formamide (DMF) was prepared. The appropriate aliquots were taken for titration with 0.05 M sodium methoxide by using 3-4 drops of the indicator solution. The colour changes from red to blue.

The results of the purity carried out in the triplicate analysis indicate that the compound is99.55 pure. The overall standard deviation calculated from pooled data for 20 mg of the compound used was 0.02 mg. The results are shown in Table No.1.

Table - 1 : Titration of pyrimidinethiols with sodium methoxide solution in DMF using azo-violet indicator.

Pyrimidinethiol	Pyrimidinethiol		Percentage recovery
	Taken, mg	Found, mg	
I)	21.00	20.90	99.52
4'-chloro-2'tolyl TPT	23.00	22.88	99.47
	25.00	24.92	99.68

(Triplicate analysis)

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