CHAPTER - II

SYNTHESIS OF REAGENTS AND THEIR CHARACTERISATION

C H A P T E R - I I

SYNTHESIS OF REAGENTS AND THEIR CHARACTERISATION

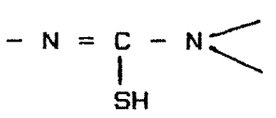
I. 1-(2'-Chlorophenyl)-4,4,6-trimethyl (1H,4H)-2-pyrimidinethiol, abbreviated as 2'-chloro PTPT

II. 1-(4'-Bromophenyl)-4,,6-Trimethyl (1H,4H)-2-Pyrimidinethiol, abbreviated as 4'-Bromo PTPT

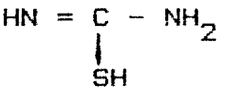
Synthesis and Characterisation of 2'-chloro PTPT and 4'-bromo PTPT :

INTRODUCTION

2-Mercaptopyrimidines is a class of compounds known as cyclic-thio-ureas, constitute a remarkable versatile class of analytically useful reagents. They are 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 made by Singh et al as selective spectrophotometric reagent for the determination of some platinum group metals[3-6]. The analytical aspects of chemistry of substituted mercaptopyrimidines was also reviewed by Singh[7] et al. However the use of such compounds as extractants for platinum group metals and gold has been reported for the first time in this 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 thioligands with bromo-phenyl substituted at position 1 of mercaptopyrimidine moeity. With improved method for synthesis of mercaptopyrimidines by Mathes a large number of compounds, their derivatives and the analytical utilities in the extractive photometric determination 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 in the use of these compounds as an intermediate in the preparation of fungicidal compounds.[16]

SYNTHESIS OF 1-SUBSTITUTED PYRIMIDINETHIOL

1-(2'-chlorophenyl)-4,4,6-trimethyl (1H,4H)-2-pyrimidinethiol and 1-(4'-Bromophenyl)-4,4,6-trimethyl (1H,4H)-2-pyrimidinethiol were 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 Bruson[21], while in the second step the product was condensed with o-chloroaniline and p-bromoaniline to obtain 2'-chloro PTPT and 4'-bromo-PTPT respectively.

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

24.5 g (0.5 mole) of sulphuric acid dissolved in 50 ml of water was added over a period of 15 min to 49 g (1 mole) of mesityl oxide (4-methyl-3-penten-2-one) at 15^{o}. 38 g (1 mole) of ammonium thiocyanate dissolved in 100 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 for over-night. The yield of the product was 80% with respect to mesityl oxide.

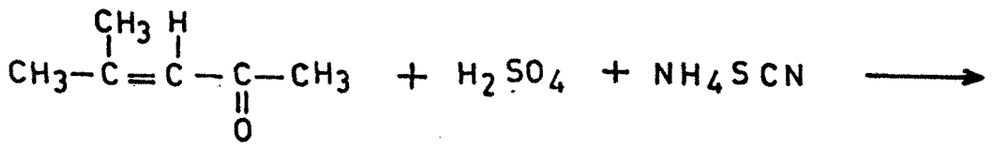
Anal. calculated for $C_7H_{11}NOS$:- C,53.51; H,7.00; N,8.91, O,10.2; S,20.38.

Found : C,53.48; H,7.06; N,8.9; O,10.18; S,20.38.

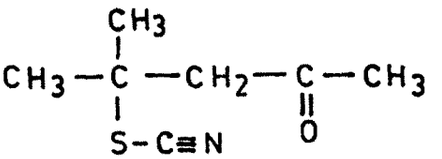
B) Synthesis of 1-substituted mercaptopyrimidines (2'-chloro PTPT) and (4'-bromo PTPT) from 2-methyl-2-isothiocyanato--4- pentanone and o-chloroaniline or p-bromoaniline :

To synthesise 2'chloro-PTPT or 4'-bromo-PTPT, 2 methyl-2-isothiocyanato-4 -pentanone (3.14 g, 0.02 mole) was mixed with 2-chloroaniline (2.55 gm, 0.02 mole) or 4'-bromoaniline (3.44g, 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 precipitated. The product was recrystallised from glacial acetic acid, washed with water and air dried. The compounds are colourless with sharp M.P. 205^o and 188^o respectively. The practical yield on the basis of amine taken were 49% and 68% respectively.

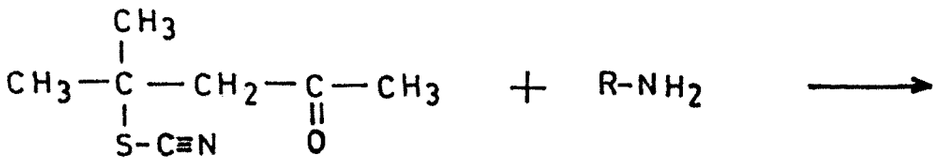
REACTIONS

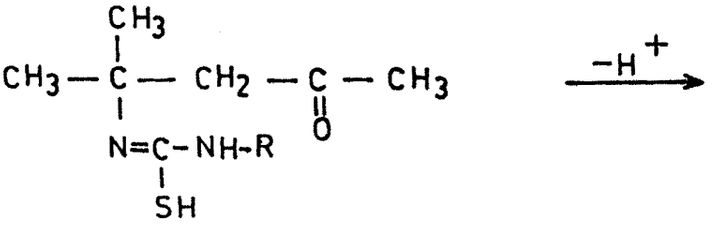


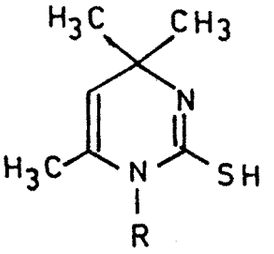
Mesityl Oxide

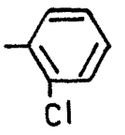


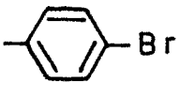
2-Methyl-2-isothiocyanato-4-pentanone







I R = 

II R = 

Molecular formula of resultant compound are

I. Anal. calculated $C_{13}H_{15}N_2SCl$, mol.wt. 266.5.

C, 58.53; H,5.63; N,10.51; S,12.01; Cl,13.32 .

Found : C,58.40; H,5.63; N,10.50; S,12.00, Cl,13.40.

II. $C_{13}H_{15}N_2SBr$, mol. wt. 311.

Anal. calculated for $C_{13}H_{15}N_2SBr$

$C_{13}H_{15}N_2SBr$: C,50.17; H,4.82; N,9.0; S,10.29; Br,25.72.

Found : C,50.20; H,4.86; N,8.9; S,10.30; Br,25.74.

Properties of 2'-chloro-PTPT and 4'-bromo-PTPT

The pyrimidinethiols are colourless fine crystalline shining solids with a sharp M.P. 205° and 188° respectively. The compounds are soluble in chloroform, DMF, DMSO and 1,4-dioxan. They are insoluble in water and sparingly soluble in ethanol, acetone and MIBK. Their solutions in DMF, chloroform, ethanol and DMSO are stable at room temperature for about 48 hours and hence does not need protection from light.

UV spectrum of 2'chloro PTPT and 4'-bromo-PTPT

The absorption spectra of pyrimidinethiols I and II in chloroform are shown in Fig.1 and 2 respectively. The spectra show that the reagents exhibit sharp absorption maxima at 330

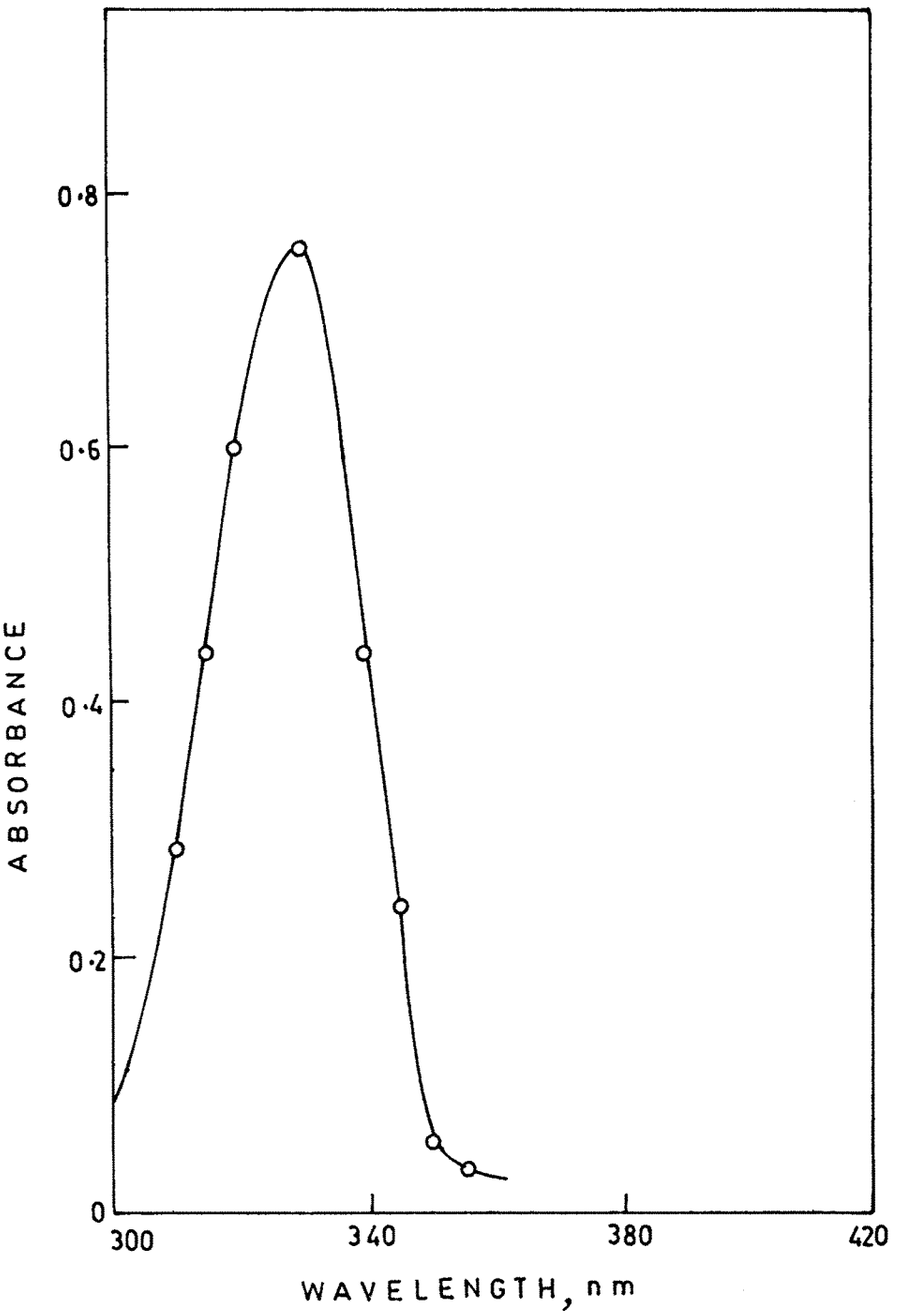


FIG. 1 — ABSORPTION SPECTRA OF 2′-CHLORO-PTPT IN CHLOROFORM. $2{\cdot}5 \times 10^{-3}$ M.

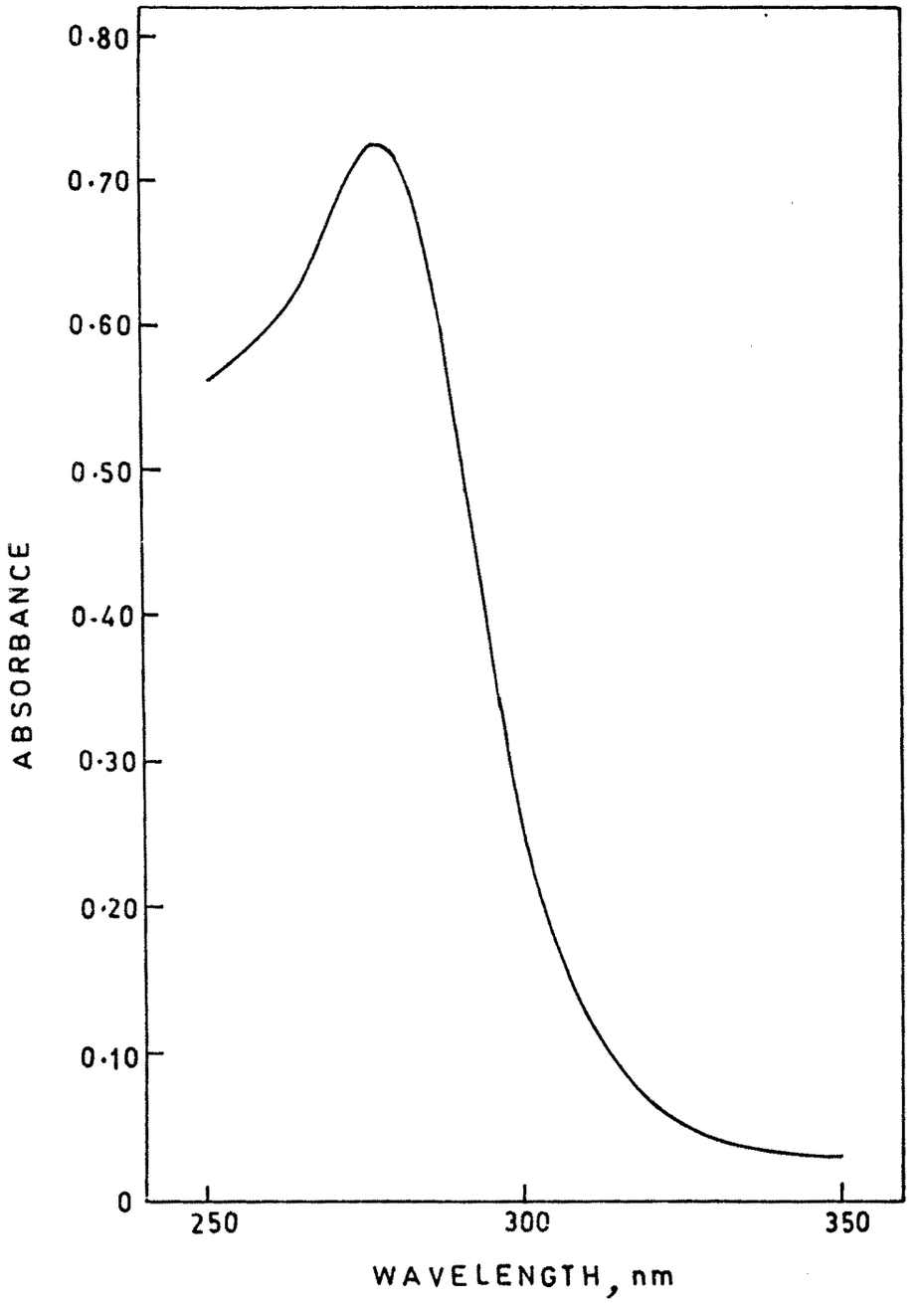


FIG. 2 — ABSORBANCE SPECTRUM OF 4′-BROMOPTPT IN CHLOROFORM. $5{\cdot}0 \times 10^{-5}$ M.

and 278 nm with the molar extinction coefficients 300 and 1.46 x 10^4 L mol^{-1} cm^{-1} respectively.

Determination of purity of 2'-chloro PTPT and 4-bromo-PTPT

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

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 2'-chloro-PTPT or 4'-bromo-PTPT containing 20-25 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 change was from red to blue.

The results recorded in Table 1 of the purity carried out in the triplicate analysis indicate that the compounds are 99.71 and 99.6% pure. The overall standard deviation calculated from the pooled data for 25 mg of the compound used was 0.02 mg.

Table - 1 : Titration of pyrimidinethiols with sodium methoxide solution in DMF

Pyrimidinethiol	Pyrimidinethiol		Percentage recovery
	Taken, mg	Found, mg	
I)	21.00	20.94	99.71
2'-chloro-PTPT	23.00	22.91	99.60
	25.00	24.96	99.84
II)	20.00	19.92	99.6
4'-Bromo-PTPT	22.00	21.90	99.5
	24.00	23.95	99.8

(Triplicate analysis)

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