SYNTHESIS OF SUBSTITUTED THIOUREAS AND THEIR METAL COMPLEXES - SPECTROSCOPIC AND AGROCHEMICAL STUDIES

A thesis submitted in partial fulfilment of
the requirement for the degree of
DOCTOR OF PHILOSOPHY
(Chemistry)

by
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CERTIFICATE

This is to certify that the thesis entitled "SYNTHESIS OF SUBSTITUTED THIOUREAS AND THEIR METAL COMPLEXES - SPECTROSCOPIC AND AGROCHEMICAL STUDIES" submitted by Kanwaljit Singh Uppal ID No. 80RM21008 for the award of Ph.D. degree of the Institute, embodies original work done by him under my supervision.

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Date April 13, 1984

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(K.S. UPPAL)

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF SYMBOLS

β	: Bending mode of frequency
ϵ	: Extinction coefficient
ν	: Stretching mode of frequency
δ	: Chemical shift
^3J	: Vicinal spin-spin coupling constant
nm	: Nanometer
M	: Molar
ΔG°	: Free energy of formation
λ_{max}	: Wave length of maximum absorption
mM	: milimolar
Hz	: Hertz
Al	: Allyl
Me	: Methyl
Ph	: Phenyl
Cl	: Chloro
Py	: Pyridyl
o	: ortho
m	: meta
p	: para

CHAPTER I

GENERAL INTRODUCTION

1.1 Metal Complexing Nature of Sulphur Donor Ligands

1.1.1 Literature Survey

1.1.2 Thiourea Derivatives

1.2 Thiourea Derivatives in Biological and Other Applications

1.3 Conformational Studies on 'Thioamide' Group of Thiourea Derivatives

1.4 The Present Work

1.1 Metal Complexing Nature of Sulphur Donor Ligands

Ligands with sulphur as donor atom have been less extensively studied as compared to those having oxygen and nitrogen as donors. The past two decades has however seen a tremendous increase in the studies on sulphur containing ligands and their metal complexing behaviour. These studies have made it possible, to a great extent, to fill in the gap and has contributed to a considerable extent to the elucidation of the nature of metal-ligand bonds and the spectroscopic properties of complexes formed. They have also provided valuable correlations regarding the Lewis acid-base nature of donor and acceptor species and have provided information on $d_{\pi}-d_{\pi}$ bonding (Livingstone, 1965).

In this section sulphur donor ligands and their complexes with special emphasis on thiourea and substituted thiourea has been briefly surveyed.

1.1.1 Literature Survey

The complexing behaviour of sulphur has been widely reported, starting with its simplest ligand sulphide ion (S^{2-}) to derivatives of thioethers (R_2S) (Retgers, 1927; Jorgensen, 1963; Jensen, 1944; Mann and Puredic, 1935; Hayter and Humiec, 1964; Tschugaev and Subbotin, 1910; Tschougaeff, 1908, 1912).

The polarisability of sulphur decreases in the order (Williams, 1959)

$$S^{2-} \rangle\ RS^{-} \rangle\ R_2S$$

Sulphide ion gives complexes with most of the metals as an insoluble metal sulphides viz: Hg(II), As(III), Ge(IV), Sn(IV), Mo(VI), W(VI) and Re(VII), (Livingstone, 1965). The mercaptide ion (RS^{-}) which is a unidentate sulphur donor are highly polarisable and form complexes with those metals which fall under soft acid category according to Pearson (1963). Sulphur is a soft base, according to the same classification.

The dialkyl sulphides also known as thioethers (R_2S) do not coordinate very strongly to metals apart from Pt(II), Pd(II), Rh(III), Ir(III) and Hg(II). Tschugaev et al (1910), Jensen (1935) and Fritzmann (1911) have investigated the complexes of thioethers using different techniques.

Metals, in general, can be divided into two classes

a) those which form more stable complexes with ligand whose coordinating site is an atom, which is the first member of a group of the periodic table viz: coordinating nitrogen/ oxygen.

b) those which form stable complexes with the second or subsequent members.

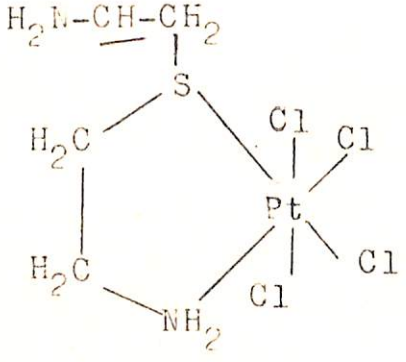
For example the class (a) metals forms more stable complexes with O than S, Se or Te of the VI group of the periodic table.

The above mentioned mercaptide ion forms a strong bond with typical class (b) metals.

The assigning of metal-N, metal-S or both types of coordination in thiosulphato and thiocyanato complexes has been a matter of controversy amongst various workers. (Livingstone, 1965; Turco and Pecile, 1961; Brown and Lingafelter, 1963).

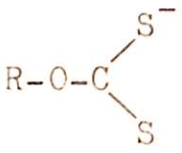
In general the thiocyanate ion coordinates to (a) class metals through nitrogen and to (b) class metals through sulphur, but X-ray analysis by Turco and Pecile (1961) has revealed some contradictory observations. The thiosulphato complexes, which mostly act as an unidentate ligand coordinate through sulphur.

Thioether group containing ligands with one addition donor atom (viz some β-amino-thioethers) often coordinate more strongly than thioethers. The Pt(IV) complex (I) is such an example, which has been investigated in considerable details (Gorick, Fernelius and Douglas, 1954; Mann, 1930).

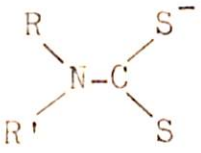


I

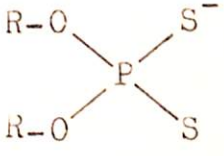
Another group of sulphur compounds, alkyl xanthates (II), dialkyl-dithiocarbamates (III) and dithiophosphates (IV) form complexes by chelation forming a four membered ring. (Malatesta, 1940; Glen and Schwab, 1950; Delepine, 1958; Busev and Ivanyutin, 1960; Jorgensen, 1962; Kida and Yoneda, 1955).



II



III



IV

Thiourea derivatives, which form the bulk of work reported in these areas have been discussed separately in the next section 1.1.2.

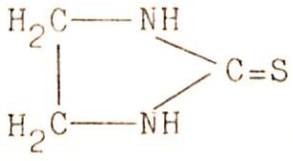
1.1.2 Thiourea derivatives

Among the sulphur containing ligands thioureas and substituted thioureas have evoked considerable interest amongst the various workers in this field. (Nardelli, Chierici and Braibanti, 1928, 1956; Rivest, 1962: Holt and Carlin, 1964; Kashyap, Taneja and Banerji, 1975; Prasad and Banerji, 1976; Burman and Sathyanarayana, 1982).

The interest in complexes of thiourea has been mainly due to the conflicting evidences regarding the donor atom, which is either sulphur (Bystrov, 1960; Nardelli, Cavalca and Braibanti, 1956; Foss and Hauge, 1959; Yamaguchi et al, 1958)

or nitrogen (Rivest, 1962). It has now been recognised that thiourea and substituted thiourea derivatives can coordinate through nitrogen and sulphur both and form a chelate ring in suitably substituted thioureas derivative (Prasad, 1973; Prasad and Banerji, 1976).

One of the most widely studied ligand is ethylene thiourea (V)



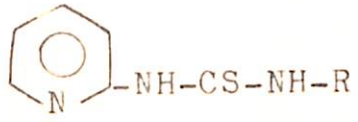
V

Carlin and Holt (1963) and Nardelli et al (1958) have studied ethylene thiourea complexes with Fe(II), Co(II) and Ni(II). Morgan and Burstall (1928) investigated the Cu(I), Ag(I) and Au(I) complexes of ethylene thiourea.

Some of the most group of thiourea ligands are N,N' disubstituted thiourea derivatives. Variation of substituent at, N and N' by alkyl, aryl or heterocylic unit has led to characterization of numerous transition metal complexes. Holt and Carlin (1964) have made detailed studies on the Ni(II) complexes of 1-(1-napthyl)-2-thioureas. Rivest (1962) has shown N,N'-diethyl thiourea and N,N'-diphenyl thiourea to be bidentate chelating agent coordinating through sulphur and nitrogen.

Hirsch (1961) has studied N,N'-diaryl-N-hydroxy thiourea complexes with Co(II), Ni(II) and Cu(II), where coordination was through sulphur and oxygen.

Of more recent origin are the ligands with heterocyclic, particularly pyridyl unit (VI).



VI

These ligands show strong chelating nature and form six member ring structure, as revealed by Kashyap et al (1975) for N-aryl, N'-2-(5 halo-pyridyl thiourea with Cd(II) and Hg(II), Prasad et al (1976) for 1-substituted-3-(-2 pyridyl)-2-thiourea with Co(II) and Ni(II) and Burman et al (1982) for N,N'-di(2-) pyridyl thiourea with Fe(III) and Fe(II).

Apart from this bis (thiourea) ligands have also attracted workers for metal comple-xation. For example acetylacetone (bis thiourea) by Ali et al (1983) and 1-benzoyl-2-monothiobi-uret by Sinha et al (1983).

1.2 Thiourea Derivative in Biological and Other Applications

Work on the synthesis, characterization and physicochemical parameters of these thiourea derivatives has considerably helped in providing the essential theoritical framework for their application. It is now known that thioureas

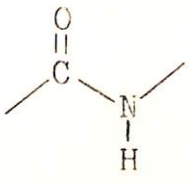
are used as corrosion inhibitors (Iovchev, 1982a, 1982b; Saha et al 1982a, 1983), Fireproofing of synthetic fibres (Teijin ,1981), deposits in thin solar films (Bhatnagar, 1978) and commercially in dyes, photographic films, elastomers, plastics and textile (Schroeder, 1955) industries. Thiourea derivatives are also known to be insecticides (Chatterjee et al, 1980), preservatives (Tokushu and Seizo, 1981), fungicides (Abuzar and Sharma, 1981, Eicken and Pommer, 1981), antiviral (Galabov, 1979), herbicides (Vassilev et al 1982a) and compounds with manifold pharmaceutical importance in medicine (Pandeya et al, 1981; Schroeder, 1955).

It can thus be seen that this group of compounds has found application in numerous fields of human activity.

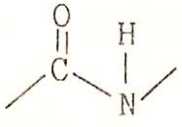
1.3 Conformational Studies on 'Thioamide' Group

Thioamide group (-NH-CS-) has been a subject of conformational studies by various workers (Burman et al, 1982; Vassilev et al, 1982c; Galabov, 1978). Just as in protein, where the conformational studies has established that amide group of the peptide bond has cis and trans conformations, so also in thioamide group:

Amide group in proteins:

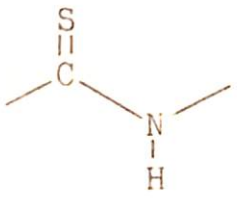


trans

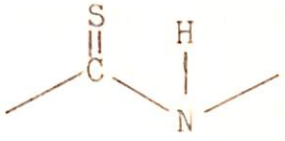


cis

Thioamide group in thioureas:



trans



cis

This can reveal new models to explain numerous biological activities, since they form the skeleton of these thiourea derivatives.

The different conformations of thioureas is due to the restricted C-N bond rotation. This is dependent upon the substituents at N-position (Neuman Jr. and Young, 1965a) and availability of lone pair of electrons for delocalization (Gonzalez and Yutronic, 1983). (Discussed in detail in Chapter III).

1.4 The Present Work

The present work deals with all the three aspects referred above. The main aim of the project has been to test the agrochemical behaviour of the thioureas as growth regulators and herbicides. Synthesis of new bis (thiourea) derivatives, has been undertaken and their complexing behaviour with Co(II), Ni(II), Cd(II) and Zn(II) in solution phase was studied.

Detailed conformational studies by I.R. and N.M.R. methods was done for different thiourea derivatives to assign them appropriate spatial geometry.

The work has been presented in an order, starting with methods of preparation, their characterization, metal complexing behaviour, conformational studies and ending with the agrochemical nature of thiourea derivatives.

CHAPTER II

SYNTHESIS OF SUBSTITUTED THIOUREA AND THEIR CHARACTERIZATION

2.1 Introduction

2.2 Aim of the present Synthetic work

2.3 Reaction
- 2.3.1 Literature Survey
- 2.3.2 Mechanism of the Reaction

2.4 Experimental
- 2.4.1 Material
- 2.4.2 General Method of Preparation
- 2.4.3 Physico-chemical Studies: Elemental analysis, m.p., IR, UV and NMR
- 2.4.4 Chloramine-T Oxidation Titration Studies

2.5 Discussion

2.1 Introduction

Organic synthesis can be considered to be largely responsible for the phenomenal development of biotechnology.

Wöhler (1828) by his remarkable synthesis of urea from ammonium cyanate showed that compounds considered to be capable of being manufactured only in plants can be synthesized in the laboratory. Synthesis therefore lays the foundation towards establishing a new group of biologically active chemicals.

Advancements in technology and availability of better analytical tools has enabled the development of a wider and more varied reaction conditions for synthesis and more precise methods of determination of structures.

2.2 Aim of the present synthetic work

As emphasised elsewhere the use of thiourea has been reported extensively in various types of biological, pharmaceutical and industrial applications (Sections 1.2 and 5.1). The aim of the present work has been to test the growth regulatory and herbicidal activity of thiourea derivatives synthesized, and attempt to identify the substituents which impart maximum toxicity in herbidical usage.

In this attempt three series of substituted thioureas N-Allyl, N-Methyl and N-Phenyl were chosen with different isomers of substituted

phenyl and pyridyl nucleus at N'position. These have been synthesized by methods used by earlier workers (Saha, 1981; Bhatnagar, 1978).

R-NH-CS-NH-R'

R = Allyl;

Methyl;

Phenyl;

R' = 

X = H,o,m,p-Cl and o,p-Methyl

Y = H,3,4 and 6-Methyl

In the second phase of synthesis work, eleven new thiourea derivatives were synthesized for the first time:

1.	Diphenyl bis (Allyl thiourea)	DBAT
2.	Diphenyl bis (Methyl thiourea)	DBMT
3.	Diphenyl bis (Phenyl thiourea)	DBPT
4.	p-Sulfa benzene bis (Allyl thiourea)	SBAT
5.	p-Sulfa benzene bis (Methyl thiourea)	SBMT
6.	p-Sulfa benzene bis (Phenyl thiourea)	SBPT
7.	N-Allyl, N'-(orthohydroxy benzene keto) thiourea	AOKT
8.	N-Methyl, N'-(orthohydroxy benzene keto) thiourea	MOKT
9.	N-Phenyl, N'-(orthohydroxy benzene keto) thiourea	POKT
10.	N-Methyl, N'-(acetamidophenyl) thiourea	MAPT
11.	N-Phenyl, N'-(acetamidophenyl) thiourea	PAPT

These were used for their metal complexation studies as discussed in Chapter IV.

2.3 Reaction

The general scheme of the reaction can be represented as:

$$\underset{A}{R\text{-}NH_2} + \underset{B}{R'\text{-}NCS} \longrightarrow \underset{C}{R\text{-}NH\text{-}CS\text{-}NH\text{-}R'}$$

where substituents on amine (A) and isothiocynates(B) can be varied to get the desired N,N'disubstituted thiourea derivatives (C).

2.3.1 Literature survey

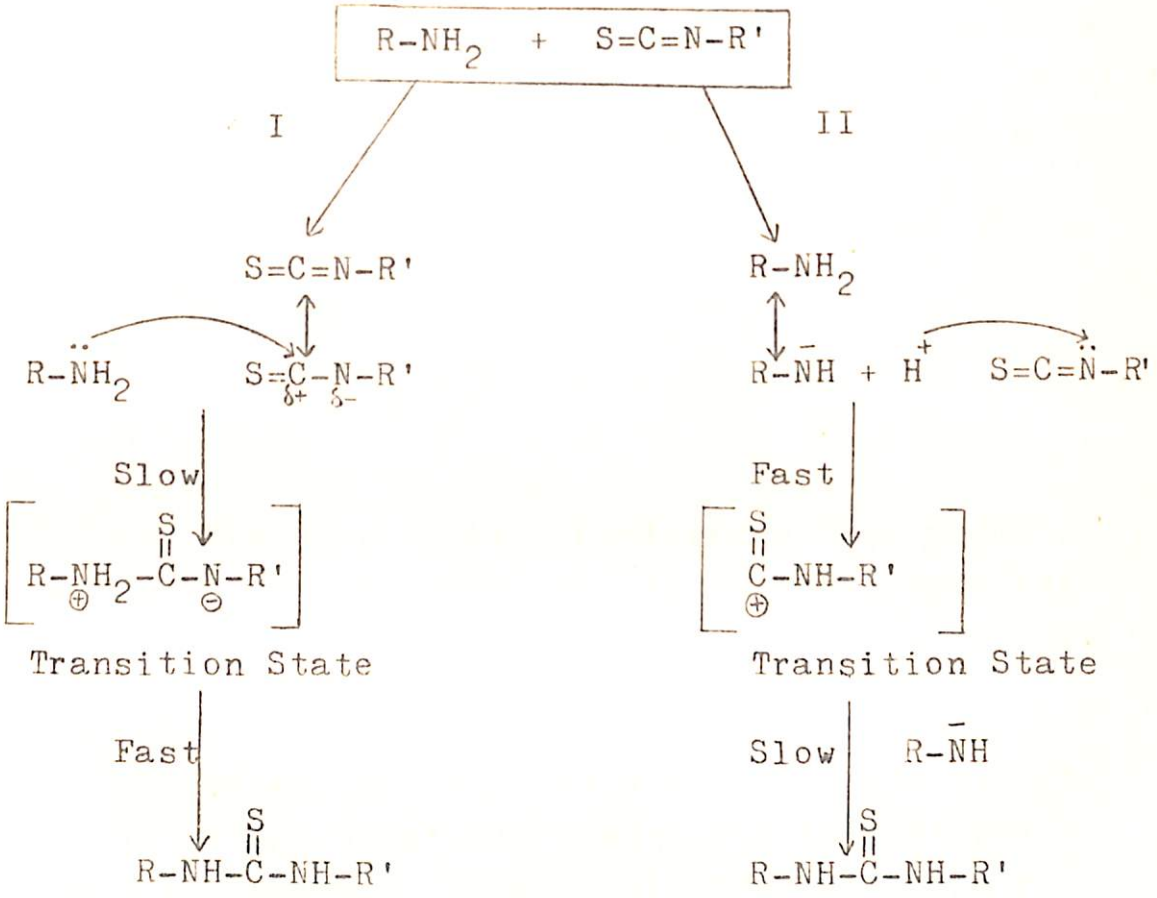
This reaction has been used since the thirties of the present century for the preparation of corresponding substituted ureas (Gilman, 1941). Since then numerous ureas and thioureas derivatives have been synthesized by this scheme (Horning, 1955; Rabjohn, 1963; Baumgarten, 1973; Vassilev et al,1982a,1969a and 1969b; Poradowska et al, 1979; Nair and Desai, 1980; Hoechst, 1980; Saha et al, 1982). This has also been quoted in Vogel, (1956).

The basic chemical for their synthesis is isothiocyanate (also known as mustard oils).

AR/GR quality of this was used in the synthesis to ensure absolute purity of the thioureas synthesized. This enables a precise study of the structure-activity relationship in their biological applications.

2.3.2 Mechanism of the Reaction

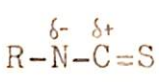
The mechanism proposed for this reaction has been classified as nucleophilic addition to the carbon-hetero double bond (March, 1968).



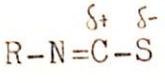
Route I of the scheme is more favourable because of more stabilized dipolar transitional state. The two mechanism I and II are usually not regarded as being very different, and in each case the rate determining step is usually the one involving nucleophilic attack. The only difference is that in I, the reaction is initiated by attack of negative species while in II by positive

species. The certainty of orientation of assymetrical adduct on C=N bond is also obvious due to dipolar nature, where carbon always remains as the positive centre.

The possibility of addition preferably on C=N instead of C=S carbon hetero multiple bond can be explained as being due to the more electronegative nature of nitrogen than sulphur atom causing greater preference for (1) than (2)



(1)



(2)

The possibility involving a free radical mechanism, has however been found to be very rare by Kaplan (1966). This possibility has therefore been ruled out in these synthesis.

Bases and acids catalyze this reaction by facilitating favourable conditions for transition state (Toromanoff, 1962). Electron withdrawing substituents on carbon atom facilitate the reaction while electron donating groups have the reverse effect. Bulkier group on carbon atom also decrease the chances of getting the desired product and may lead to cyclisation if suitable centres are present (Nair and Desai, 1980).

2.4 Experimental

2.4.1 Material

Reagents: Allyl isothiocyanate was used of E.Merck A G Darmstadt, Germany; Methyl isothiocyanate was used of Cambrian Chemicals, England and Phenyl isothiocyanate used was of Koch-Light Laboratories Ltd., England. Different substituted anilines were from 'Fluka' Chemicals, Switzerland and B.D.H. Chemicals, England.

Different solvents and other reagents used were of high quality 'BDH' Analar grade or E.Merck 'GR' grade.

Chloramine-T 'GR' was used of Loba Chemie Industries Co., Bombay.

Instruments: The Arthur H. Thomas Co., USA, Hoover 'UNI-MELT', capillary melting point apparatus and Micro Kjeldahl distilling apparatus, Pregl-Parnas-Wagner were used. Perkin-Elmer SP 1200 model was used for I.R. studies and U.V. studies were done on CARY-17D digital spectrophotometer and Hitachi spectrophotometer (Model - 139) using 0.5 cm matched quartz cuvettes. ^{1}H-N.M.R. studies were carried out on JOEL FX-100 model operating in the Fourier transform mode, at 99.5 MHz for ^{1}H nucleus on the spectrum width of 20 ppm. Computerised print outs were taken with the attached accessory to ensure information of the various chemical shifts with absolute preciseness.

2.4.2 General method of preparation

The reaction was carried out in ethanol or a mixture of ethanol and toluene (3:1), which was found to be the best combination to get maximum yield (80%). All the reagents were distilled and purified to ensure their chemical purity. In some cases refluxing of 30 minutes to one hour was used to produce extreme conditions for carrying out the reaction.

In most of the cases, the thiourea derivative, crystallises as white solid in the mother liquor after cooling in ice water-bath. This solid was filtered out and again recrystallized from ethanol to get pure compound. This was dried and washed with solvent ether and kept under reduced pressure decicator to get it completely dry in vacuum.

Few cases, required about 5-8 days after refluxation to give crystals in the reaction mixtures. Providing suitable nuclei for crystal growth further hasten the phenomena.

2.4.3 Physico-chemical studies

The substituted thiourea and bis thiourea derivatives, prepared were characterized by the studies of elemental analysis, determining melting points and taking the Infra red, Ultra violet and Nuclear Magnetic Resonance spectra of these derivatives.

These observations have been detailed in tables 2.1 to 2.12 and graphically represented in

figs. 2.1 to 2.16 . Spectra's analysis shows assignment of various peaks in U.V. and I.R. range which are relevant to characterize the compound.

The results of N.M.R. spectras are discussed in Chapter III along with conformational studies.

Different relations used for E_T and ϵ values for U.V. spectra are

$$E_T = \frac{2.859 \times 10^5}{\lambda_{max}(A^\circ)} \text{ Kcal/mole}$$

$$\epsilon = A/b.c.$$

where λ_{max}: Wavelength of maximum absorption

A : Absorbance at the particular wavelength

b : Width of the cell

c : Concentration of solute in mole/liter.

2.4.4 Chloramine-T oxidation titration studies

Chloramine-T (Sodium N-Chloro-p-toluene sulphonamide) oxidation is an established method for estimating thiourea derivatives and their metal complexes (Uma and Mayanna, 1980; Avavamudan et al, 1964; Ahmed et al, 1979; Vogel, 1961). This method has been used for the estimation of thioureas, in these studies.

During the course of reaction the chloramine-T is reduced to p-toluene sulphonamide and chloride ion (Bishop and Jennings, 1958).

$$p\text{-}CH_3C_6H_4SO_2NCl + 2H^+ + 2e^- \longrightarrow p\text{-}CH_3C_6H_4SO_2NH + Cl^-$$

Chloramine-T

p-toluene sulphonamide

The titration of thiourea derivatives was done in non-aqueous media, in acetonitrile, since most of the N,N'disubstituted thiourea under study are sparingly soluble in aqueous media. Acetonitrile was chosen because of its reported (Verma and Kumar, 1976) high dielectric constant and resistance to oxidation or reduction.

Aliquots of the solutions of N,N'disubstituted thioureas were taken in dry conical flask and mixed with 5 ml acetonitrile. 10 ml of 0.1N CAT (Chloramine-T) solution (this was prepared in glacial acetic acid containing 10% v/v acetic anhydride, as proposed by Jacob and Nair, 1972) was then added to this. The flasks were then kept aside for 10-15 minutes to attain equilibrium, followed by conventional iodometric method to back titrate the amount of CAT left unutilized.

The amount of the thioureas in mg, was obtained by the relationship

$$x(mg) = \frac{M}{e} \times N\ (V_1 - V_2)$$

where
- N : Normality of thiosulphate solution
- V_1 : Volume of the blank titre
- V_2 : Volume of the test titre
- M : Molecular weight of substituted thiourea
- e : Number of electron change per molecule of substituted thiourea

The results obtained have been detailed in the tables 2.10 to 2.12.

2.5 Discussion

Elemental analysis of thiourea derivatives (Table 2.1) agrees with the calculated values within the permissible limits of errors. A sharp melting point in most of the cases indicates the purity of compound, since impurities always lead to give a range of temperature at which the solid melts. This was also confirmed by chloramine-T studies, revealing 95-98% purity of derivatives. (Tables 2.10 - 2.12).

All the substituted thioureas exhibit an intense absorption maxima in the 265-280 nm, U.V. region as detailed in tables 2.7 to 2.9 and figs. 2.1 to 2.6 . This has been assigned to the thiocarbonyl (C=S) $\pi - \pi^*$ transition (Ahmed and Mandal, 1967). Apart from this other chromophore if present viz C=O, biphenyl etc showed respective absorption maxima in usual manner. This was mostly in the case of bis (Thiourea) derivatives which are synthesized for the first time.

The I.R. spectra of thiourea derivatives (figs. 2.7 to 2.16) are quite complicated. The bands which could be assigned with some certainty are presented in tables 2.4 to 2.6. The bands appearing higher than 3000 cm^{-1} have been assigned to ν (NH) mode (Gosavi et al, 1967; Scheinmann, 1970). There are two such peaks one for trans (higher stretching frequency) and other for

cis (lower stretching frequency) in most of the cases, such assignment has also been done by various workers (Gosavi et al, 1967; Rao et al, 1968; Vassilev et al, 1982c: Suzuki et al, 1960). Two bands in the region 1080 and 730 cm^{-1} are found to have appreciable contribution from the ν (C=S) stretching vibration in thiourea by Gosavi et al (1967) and Yamaguchi et al (1958). These also appear in the present studies. Contribution by the mixed vibrations bands in the region 600 - 1400 cm^{-1} by the so called >N-C=S band (Rao et al, 1962, 1964) is also prominent.

All these observation give strong clues for the support of structures of the thioureas derivatives synthesized.

^{1}H-N.M.R. studies further confirm these results, as discussed in detail in Chapter III.

Table 2.1 Structure, m.p. and Elemental Analysis of N-Allyl Series of Thiourea Derivatives.

Derivative	Structure	m.p. °C	%Nitrogen		%Sulphur	
			Obsd.	Cald.	Obsd.	Cald.
N-Al,N'-Ph tu	$CH_2=CH-CH_2-NH-CS-NH-C_6H_5$	89	14.48	14.57	16.32	16.66
N-Al,N'- oCl Ph tu	$CH_2=CH-CH_2-NH-CS-NH-(C_6H_4-oCl)$	80	12.31	12.36	14.10	14.12
N-Al,N'-mCl Ph tu	$CH_2=CH-CH_2-NH-CS-NH-(C_6H_4-mCl)$	78	12.35	12.36	13.98	14.12
N-Al,N'-pCl Ph tu	$CH_2=CH-CH_2-NH-CS-NH-(C_6H_4-pCl)$	98	12.20	12.36	13.80	14.12
N-Al,N'-oMe Ph tu	$CH_2=CH-CH_2-NH-CS-NH-(C_6H_4-oMe)$	75	13.45	13.59	15.02	15.53
N-Al,N'-pMe Ph tu	$CH_2=CH-CH_2-NH-CS-NH-(C_6H_4-pMe)$	77	13.50	13.59	15.35	15.53
N-Al,N'-2-Py tu	$CH_2=CH-CH_2-NH-CS-NH-2-(C_5H_4N)$	102	21.58	21.75	15.80	16.58
N-Al,N'-(o-OH, benzene keto) tu	$CH_2=CH-CH_2-NH-CS-NH-CO-(C_6H_4-oOH)$	101	11.60	11.82	12.92	13.53
p-Sulfa benzene bis (Allyl tu)	$CH_2=CH-CH_2-NH-CS-NH-C_6H_4SO_2-NH-CS-NH-CH_2-CH=CH_2$	120	14.00	15.45	24.20	23.62
Di Ph bis (Allyl tu)	$CH_2=CH-CH_2-NH-CS-NH-(C_6H_4)_2-NH-CS-NH-CH_2-CH=CH_2$	120	14.21	14.85	12.50	11.33

Table 2.2 Structure, m.p. and Elemental Analysis of N-Methyl Series of Thiourea Derivatives.

Derivative	Structure	m.p. °C	%Nitrogen		%Sulphur	
			Obsd.	Cald.	Obsd.	Cald.
N-Me,N'-Ph tu	$CH_3-NH-CS-NH-C_6H_5$	87	16.78	16.86	19.30	19.27
N-Me,N'-oCl Ph tu	$CH_3-NH-CS-NH-(C_6H_4-oCl)$	103	13.82	13.96	15.20	15.96
N-Me N'-mCl Ph tu	$CH_3-NH-CS-NH-(C_6H_4-mCl)$	91	13.90	13.96	15.45	15.96
N-Me,N'-pCl Ph tu	$CH_3-NH-CS-NH-(C_6H_4-pCl)$	143	13.73	13.96	15.90	15.96
N-Me,N'-oMe Ph tu	$CH_3-NH-CS-NH-(C_6H_4-oMe)$	140	15.50	15.55	17.80	17.77
N-Me,N'-pMe Ph tu	$CH_3-NH-CS-NH-(C_6H_4-pMe)$	123	15.42	15.55	17.65	17.77
N-Me,N'-2-Py tu	$CH_3-NH-CS-NH-2-(C_5H_4N)$	149	23.10	23.46	17.21	17.87
N-Me,N'-(oOH, benzene keto) tu	$CH_3-NH-CS-NH-CO-(C_6H_4-oOH)$	110	13.21	13.35	15.02	15.22
N-Me,N'-(acetamido phenyl) tu	$CH_3-NH-CS-NH-(C_6H_4-pNH-CO-CH_3)$	86	17.22	17.56	16.82	17.34
p-Sulfa benzene bis (Methyl tu)	$CH_3-NH-CS-NH-C_6H_4-pSO_2-NH-CS-NH-CH_3$	135	17.05	17.16	26.20	26.15
Di Ph bis (Methyl tu)	$CH_3-NH-CS-NH-(C_6H_4)_2-NH-CS-NH-CS_3$	122	16.10	16.38	12.50	12.44

Table 2.3 Structure, m.p. and Elemental Analysis of N-Phenyl Series of Thiourea Derivatives.

Derivative	Structure	m.p. °C	%Nitrogen		%Sulphur	
			Obsd.	Cald.	Obsd.	Cald.
N-Ph,N'-Ph tu	C_6H_5-NH-CS-NH-C_6H_5	153	12.20	12.28	13.95	14.03
N-Ph,N'-oCl Ph tu	C_6H_5-NH-CS-NH-(C_6H_4-oCl)	165	10.54	10.66	12.05	12.19
N-Ph,N'-mCl Ph tu	C_6H_5-NH-CS-NH-(C_6H_4-mCl)	124	10.61	10.66	12.20	12.19
N-Ph,N'-pCl Ph tu	C_6H_5-NH-CS-NH-(C_6H_4-pCl)	152	10.59	10.66	12.01	12.19
N-Ph,N'-oMe Ph tu	C_6H_5-NH-CS-NH-(C_6H_4-oMe)	139	11.40	11.57	13.02	13.22
N-Ph,N'-pMe Ph tu	C_6H_5-NH-CS-NH-(C_6H_4-pMe)	142	11.53	11.57	13.25	13.22
N-Ph,N'-2-Py tu	C_6H_5-NH-CS-NH-2-(C_5H_4N)	172	17.40	17.42	13.22	13.27
N-Ph,N'-(oOH, benzene keto) tu	C_6H_5-NH-CS-NH-CO-(C_6H_4-oOH)	130	10.12	10.23	11.57	11.73
N-Ph,N'-(acetamido phenyl) tu	C_6H_5-NH-CS-NH-(C_6H_4-pNH-CO-CH_3)	98	13.65	13.93	11.21	11.65
p-Sulfa benzene bis (Phenyl tu)	C_6H_5-NH-CS-NH-C_6H_4-pSO_2-NH-CS-NH-C_6H_5	160	13.55	13.62	20.60	20.84
Di Ph bis(Phenyl tu)	C_6H_5-NH-CS-NH-(C_6H_4)$_2$-NH-CS-NH-C_6H_5	130	13.42	13.16	9.80	10.02

Table 2.4 I.R. Spectroscopic Data for N-Allyl Series of Thiourea Derivatives.

Assignment	Band Position (cm^{-1}*)						
	CH_2=CH-CH_2-NH-CS-NH-R				AOKT	SBAT	DBAT
	R = Ph	mCl Ph	pCl Ph	2-Py			
ν (NH) Free trans	3360m	3200	3220	-	3350	3425	3340
ν (NH) Free cis	3180	-	3050w	-	-	3330	-
ν (C=C+C=N)	1600	1595	1640	1600	1680	1640	1640
δ_s (NH)	1560	1540	1580	-	1590	1560	1600
δ (NCN+C=S)	1505	1495	1500	1460	1490	1500	1520
δ_a (NH)	1320	1300	1340	-	1370	1310	1310
ν_a (CN)	1240	1235	1240	1250	1260s	1215	1220m
β (CH)	1170	1130	1095	1150	1120	1160	1170
ν (C=S)	760s	770s	825	770	770	755	730
β (NH) out of plane	700	730	715	720m	730	710	-
δ (NCS)	560	555	490	530	570	530	540
(CS) out of plane deformation	490	440	420	410	450	435	440

* w = weak; m = medium; s = strong peaks.

Table 2.5 I.R. Spectroscopic Data for N-Methyl Series of Thiourea Derivatives.

Assignment	Band Position (cm^{-1})*									
	CH_3-NH-CS-NH-R						MOKT	SBMT	DBMT	MAPT
	R = Ph	oCl Ph	mCl Ph	pCl Ph	pMe Ph	2-Py				
ν(NH) Free trans	3280m	3290	3220m	3280	3280	3190	3420s	3330	3205	3280
ν(NH) Free cis	3175	-	3100	-	3100	-	3200	3230	-	-
N-CH_3	2910	2400	2400	2400s	2400s	2400	2740	3010	-	-
ν(C=C+C=N)	1600	1599	1600	1620	1620	1600	1595	1600	1660	1660
δ_s(NH)	1560	-	-	1580	1500	1540	1500	1550w	1595	1580
δ(NCN+C=S)	1495	1450	1460	1500	1460	1495	1413	1525	1500	1520
δ_a(NH)	1290	1300	1290	1340	1340	1325	1320	1340	1345	1330
ν_a(CN)	1250	1260	-	1240	1270	1240	1260s	1245	1250	1255
β(CH)	1155	1145	1150	1145	1140	1160	1170	1160	-	1110
ν(C=S)	800	805	805	830	815	770	750	780	760	755
β(NH) out of plane	725w	740	760	720	735	735	725	730	720	705
δ(NCS)	605	610	525	500	500	575	510	525	535	510
(CS) out of plane deformation	480	440	410	470	465	410	450	410	480	430

* w = weak; m = medium; s = strong peaks.

Table 2.6 I.R. Spectroscopic Data for N-Phenyl Series of Thiourea Derivatives.

Assignment	Band Position (cm^{-1})*										
	C_6H_5-NH-CS-NH-R							POKT	SBPT	DBPT	PAPT
	R = Ph	oCl Ph	mCl Ph	pCl Ph	oMe Ph	pMe Ph	2-Py				
ν(NH) Free trans	3220	3210m	3200w	3220m	3250	3180	-	3400	3300	3305m	3280
ν(NH) Free cis	-	3080w	-	3040w	-	-	-	3200	-	3190	3100
ν(C=C+C=N)	1600	1602s	1595s	1605s	1610s	1600	1605	1600s	1601	1610	1685s
δ_s(NH)	1595	1590w	-	1590m	-	-	1570	1501	-	1580	1595
δ(NCN)	1550	1500m	1490m	1495	1500	1505	1540	1450	1390	1370	1410
δ_a(NH)	1360	1380	1320w	1360	1340	1320	1360	1310	1305	-	1320
ν_a(CN)	1290	1250w	1250	1245w	-	1260s	1270	1240	1280	1290	1280
β(CH)	1080	1180	1085m	1090	1045	1140m	1150	1110	1170	1190	1150w
ν(C=S)	770	760s	760s	770s	730	750	775	860	820	825	850
β(NH) out of plane	700	700	700s	710m	-	690	730	750	740	790	720
δ(NCS)	510	510m	520w	560w	500	540s	510	510	-	510	510
(CS) out of plane deformation	490	430	440m	410	430	420w	430	450	410	405	410

* w = weak; m = medium; s = strong peaks.

Table 2.7 U.V. Spectroscopic Data for N-Allyl Series of Thiourea Derivatives.

Derivative $CH_2=CH-CH_2-NH-CS-NH-R$	λ_{max} (nm)	ϵ_{max} (1 $mol^{-1} cm^{-1}$)	E_T (Kcal mol^{-1})
R = Ph	300	9500	95.3
R = oCl Ph	290	8800	98.5
R = mCl Ph	310	9600	92.2
R = pCl Ph	300	10400	95.3
R = oMe Ph	295	7700	96.9
R = pMe Ph	290	10500	98.5
R = 2-Py	290	4700	98.5
	335	7900	85.3
AOKT	250	8800	114.3
	270	7000	105.8
	305	11200	93.7
SBAT	250	12000	114.3
	285	10200	100.3
DBAT	250	13000	114.3
	290	10300	98.5

Table 2.8 U.V. Spectroscopic Data for N-Methyl Series of Thiourea Derivatives.

Derivative CH_3-NH-CS-NH-R	λ_{max} (nm)	ϵ_{max} (1 $mol^{-1} cm^{-1}$)	E_T (Kcal mol^{-1})
R = Ph	295	7800	96.9
R = oCl Ph	280	11100	102.1
R = mCl Ph	290	9700	98.5
R = pCl Ph	270	9400	105.8
R = oMe Ph	285	10400	100.3
R = pMe Ph	290	8800	98.5
R = 2-Py	280	6300	102.1
	320	7400	89.3
MOKT	315	12600	90.7
SBMT	250	11100	114.3
	290	12600	98.5
	320	12100	89.3
DBMT	300	12500	95.3
MAPT	250	13000	114.3
	270	12800	105.8

Table 2.9 U.V. Spectroscopic Data for N-Phenyl Series of Thiourea Derivatives.

Derivative Ph-NH-CS-NH-R	λ_{max} (nm)	ϵ_{max} ($l\ mol^{-1} cm^{-1}$)	E_T ($Kcal\ mol^{-1}$)
R = Ph	270	8100	105.8
R = oCl Ph	285	6600	100.3
R = mCl Ph	290	8600	98.5
R = pCl Ph	290	7000	98.5
R = oMe Ph	280	7900	102.1
R = pMe Ph	270	10200	105.8
R = 2-Py	280	7100	102.1
	310	7400	92.2
POKT	305	12800	93.2
SBPT	285	11700	100.3
DBPT	290	12400	98.5
	310	10300	92.2
PAPT	280	12800	102.1

Table 2.10 Estimation of N-Allyl Series of Thiourea Derivatives by Chloramine-T Oxidation Method.

Derivative $CH_2=CH-CH_2-NH-CS-NH-R$ R	Amount of Derivative taken (mM) I	Duration of reaction (Minutes)	Amount of CAT used up (mM) II	Equiv.of* CAT used per mole of derivative II/I	Amount of Derivative found (mM)	% Purity
Ph	0.1250	15	0.9250	7.4	0.1234	98
o-Cl Ph	0.1475	10	1.2240	8.3	0.1434	97
m-Cl Ph	0.1325	10	1.0600	8.0	0.1279	96
p-Cl Ph	0.1275	10	0.9945	7.8	0.1251	98
o-Me Ph	0.1050	15	0.8610	8.2	0.0970	92
p-Me Ph	0.1125	15	0.9675	8.6	0.1084	96
2-Py	0.0925	15	1.1180	12.0	0.0876	94
2-(4Me Py)	0.1150	15	1.3915	12.1	0.1066	92
2-(6Me Py)	0.1025	15	1.2197	11.9	0.0982	95

* It is also the number of electron change per mole of derivative in CAT redox reaction.

Table 2.11 Estimation of N-Methyl Series of Thiourea Derivatives by Chloramine-T Oxidation Method.

Derivative CH_3-NH-CS-NH-R R	Amount of Derivative taken (mM) I	Duration of reaction (Minutes)	Amount of CAT used up (mM) II	Equiv. of* CAT used per mole of derivative II/I	Amount of Derivative found (mM)	% Purity
Ph	0.1085	15	1.3454	12.4	0.1079	99
o-Cl Ph	0.1175	15	1.0105	8.6	0.1156	98
m-Cl Ph	0.1065	15	0.7881	7.4	0.1026	96
p-Cl Ph	0.1025	15	0.9122	8.9	0.0999	97
o-Me Ph	0.0926	15	1.1204	12.1	0.0887	95
p-Me Ph	0.0815	15	0.9454	11.6	0.0784	96
2-Py	0.0802	15	0.9864	12.3	0.0779	97
2-(3Me Py)	0.0975	15	1.0920	11.2	0.0959	98
2-(4Me Py)	0.0998	15	1.0379	10.4	0.0968	97
2-(6Me Py)	0.0825	15	1.0642	12.9	0.0796	96

* It is also the number of electrons change per mole of derivative in CAT redox reaction.

Table 2.12 Estimation of N-Phenyl Series of Thiourea Derivatives by Chloramine-T Oxidation Method.

Derivative C_6H_5-NH-CS-NH-R R	Amount of Derivative taken (mM) I	Duration of reaction (Minutes)	Amount of CAT used up (mM) II	Equiv. of* CAT used per mole of derivative II/I	Amount of Derivative found (nM)	% Purity
Ph	0.0986	15	1.1043	11.2	0.0915	92
o-Cl Ph	0.0998	15	1.1776	11.8	0.0973	97
m-Cl Ph	0.1002	15	1.2525	12.5	0.0953	95
p-Cl Ph	0.1025	15	1.2505	12.2	0.0981	95
o-Me Ph	0.0926	15	1.0926	11.8	0.0853	92
p-Me Ph	0.0846	15	1.0067	11.9	0.0766	90
2-Py	0.0947	15	1.0985	11.6	0.0837	88
2-(3Me Py)	0.0828	15	0.9936	12.0	0.0739	89
2-(4Me Py)	0.0898	15	1.0526	11.8	0.0823	91
2-(6Me Py)	0.0845	15	1.0055	11.9	0.0749	88

* It is also the number of electrons change per mole of derivative in CAT redox reaction.

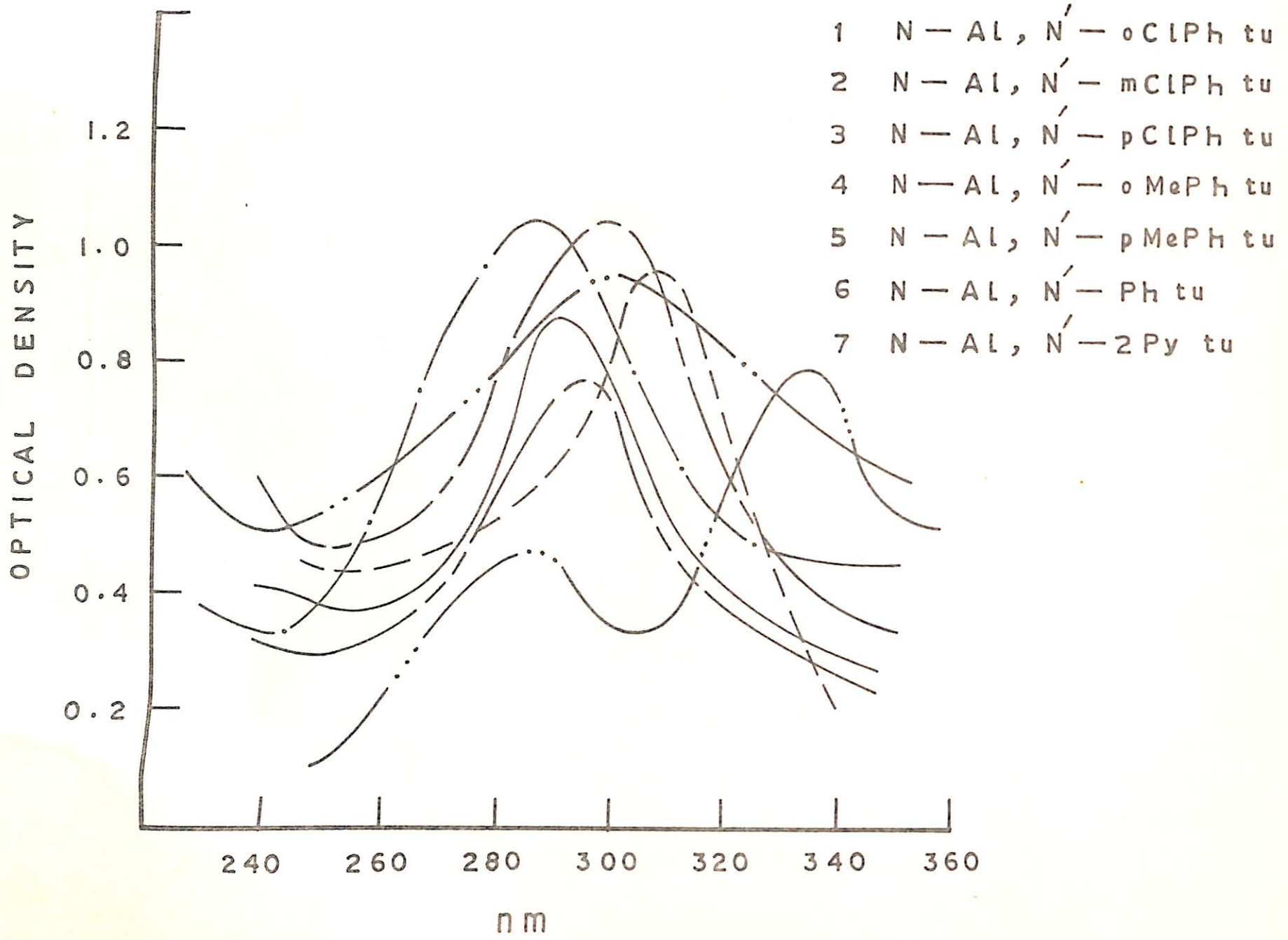


Fig. 2·1 U. V. Spectra of N—Allyl series of substituted thiourea

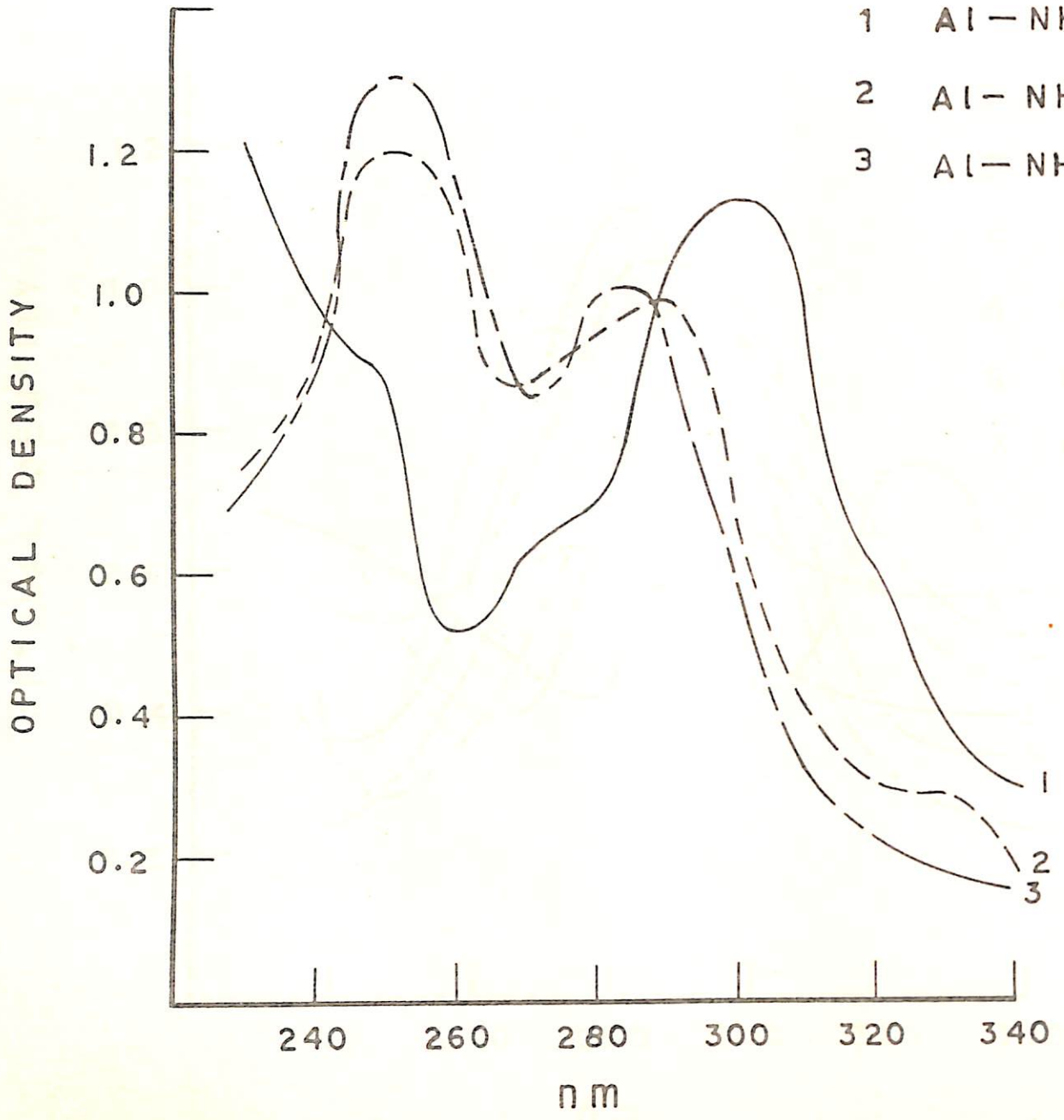


Fig. 2.2 U. V. Spectra of N—Allyl series of substituted thiourea

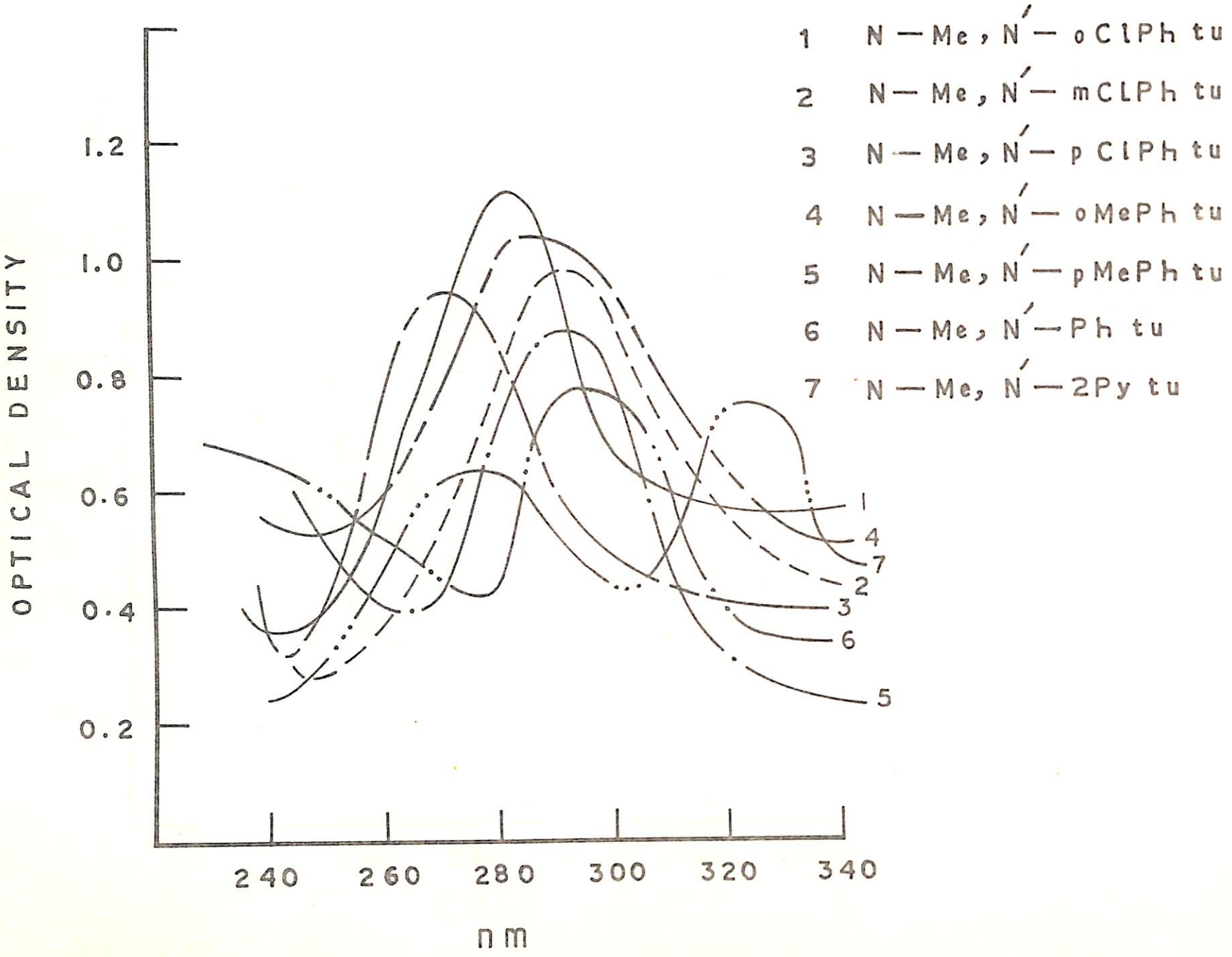


Fig. 2.3 U. V. Spectra of N — Methyl series of substituted thiourea

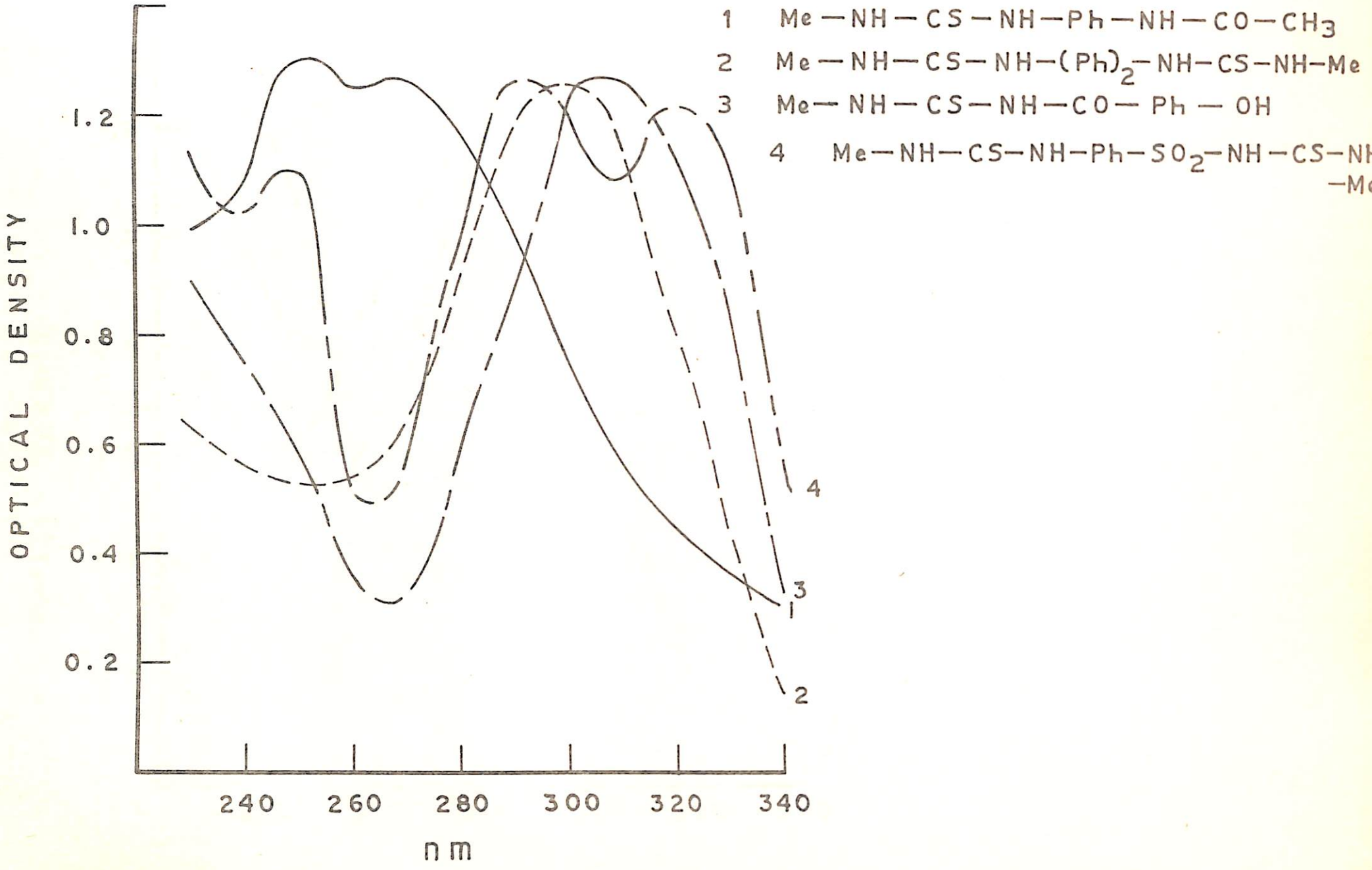


Fig. 2.4 U. V. Spectra of N—Methyl series of substituted thiourea

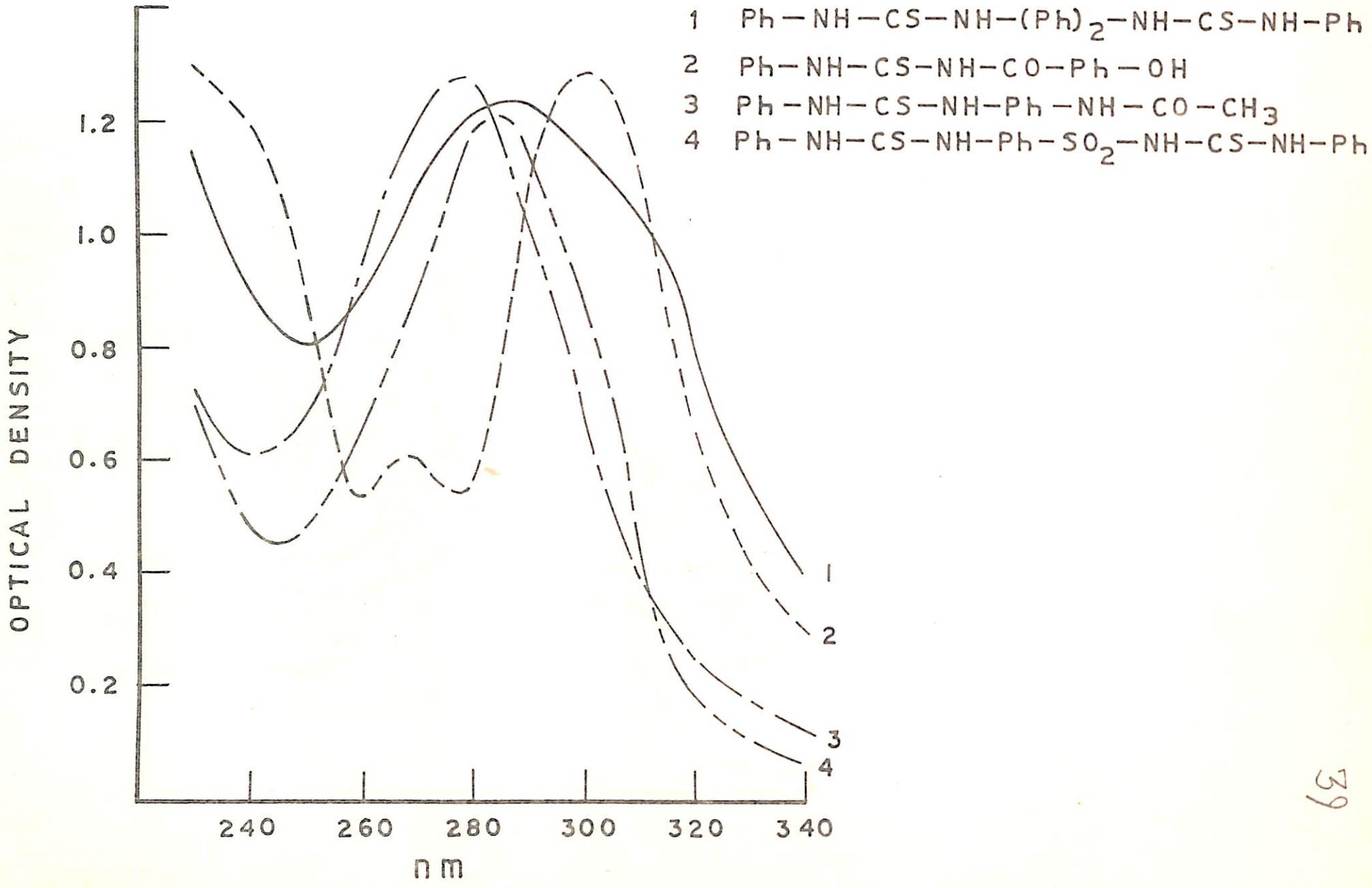


Fig. 2.5 U. V. Spectra of N— Phenyl series of substituted thiourea

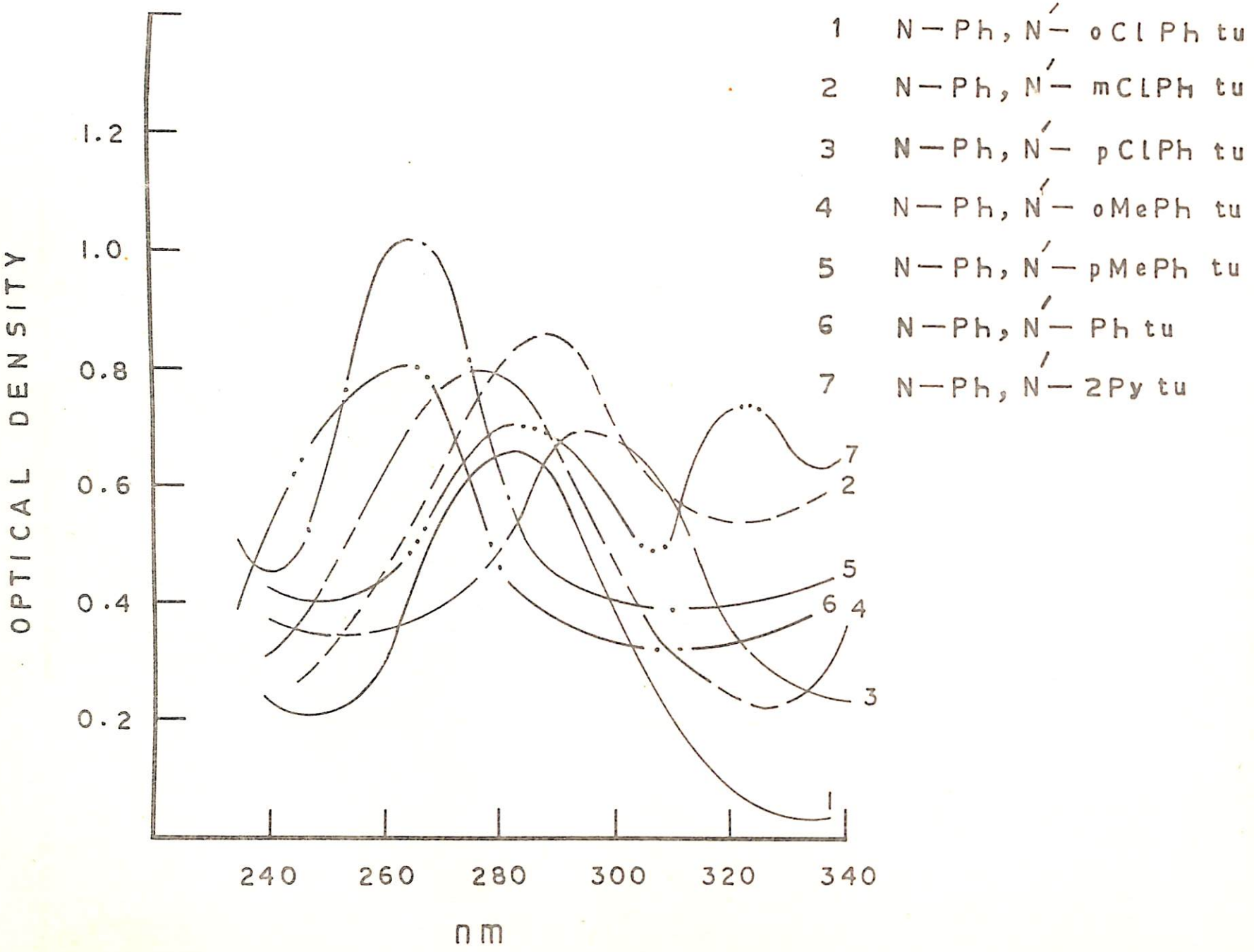


Fig. 2.6 U. V. Spectra of N—Phenyl series of substituted thiourea

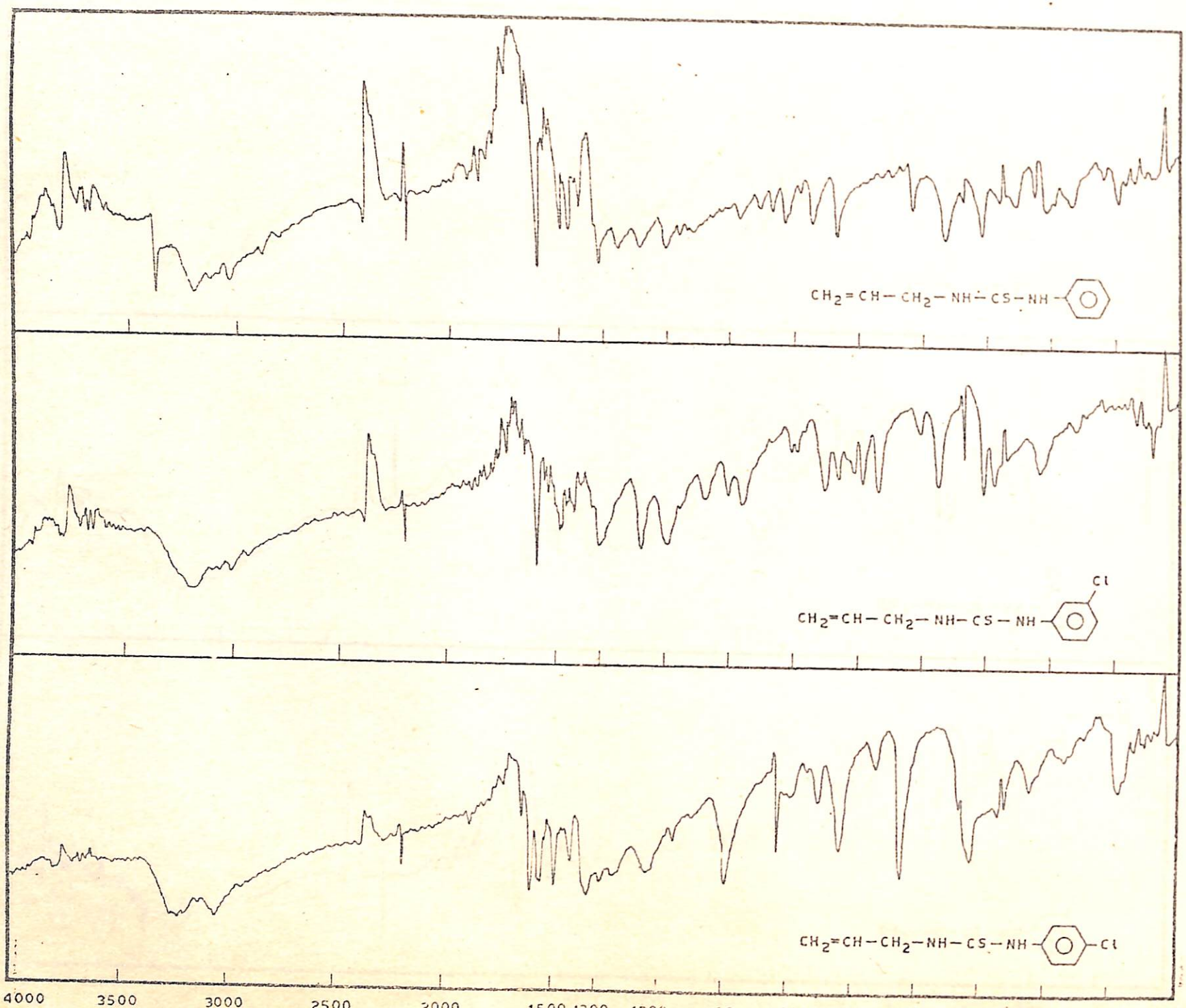


Fig. 2.7 I. R. Spectra of Substituted thioureas in KBr Pellet

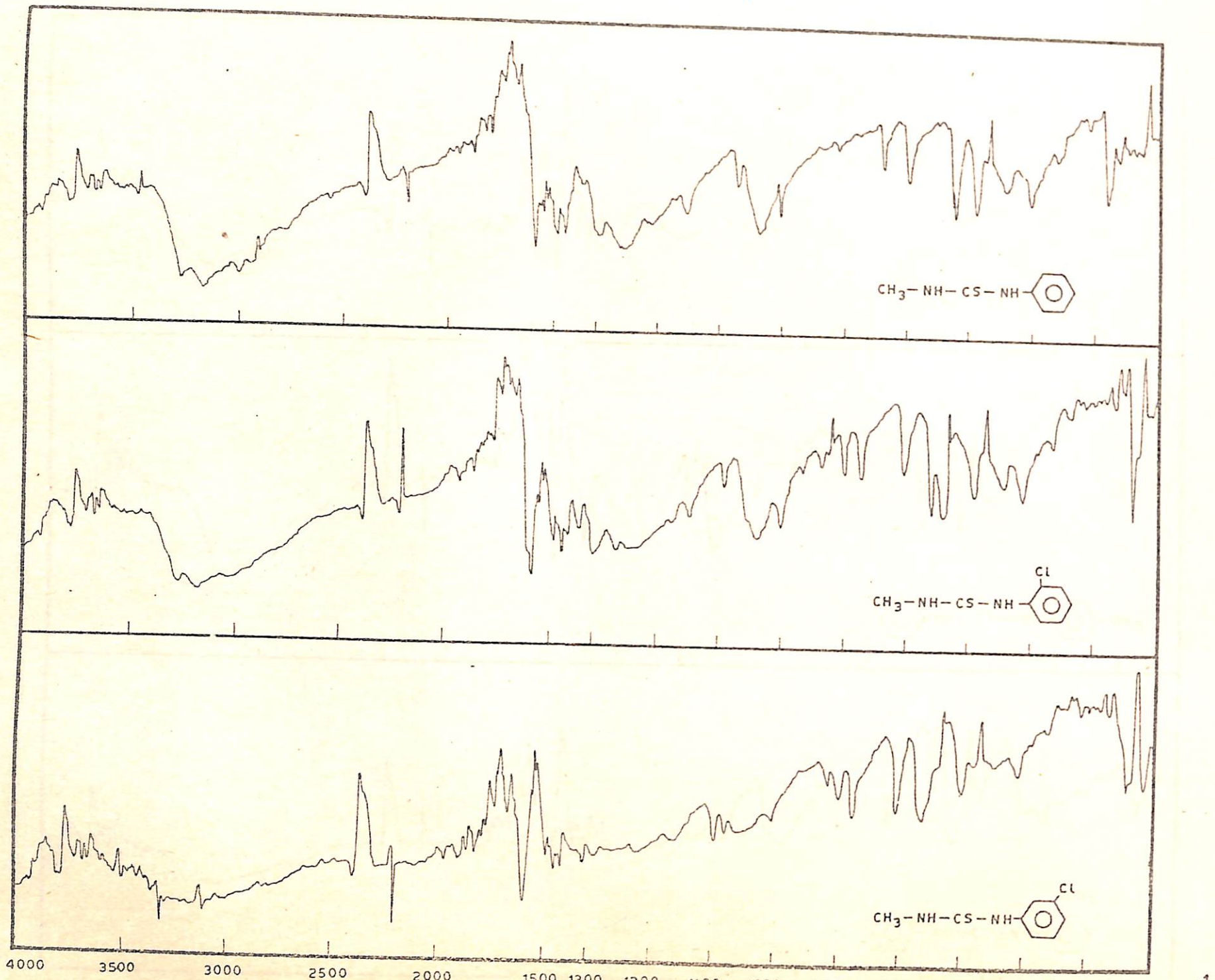


Fig. 2.8 I. R. Spectra of Substituted thioureas in KBr Pellet

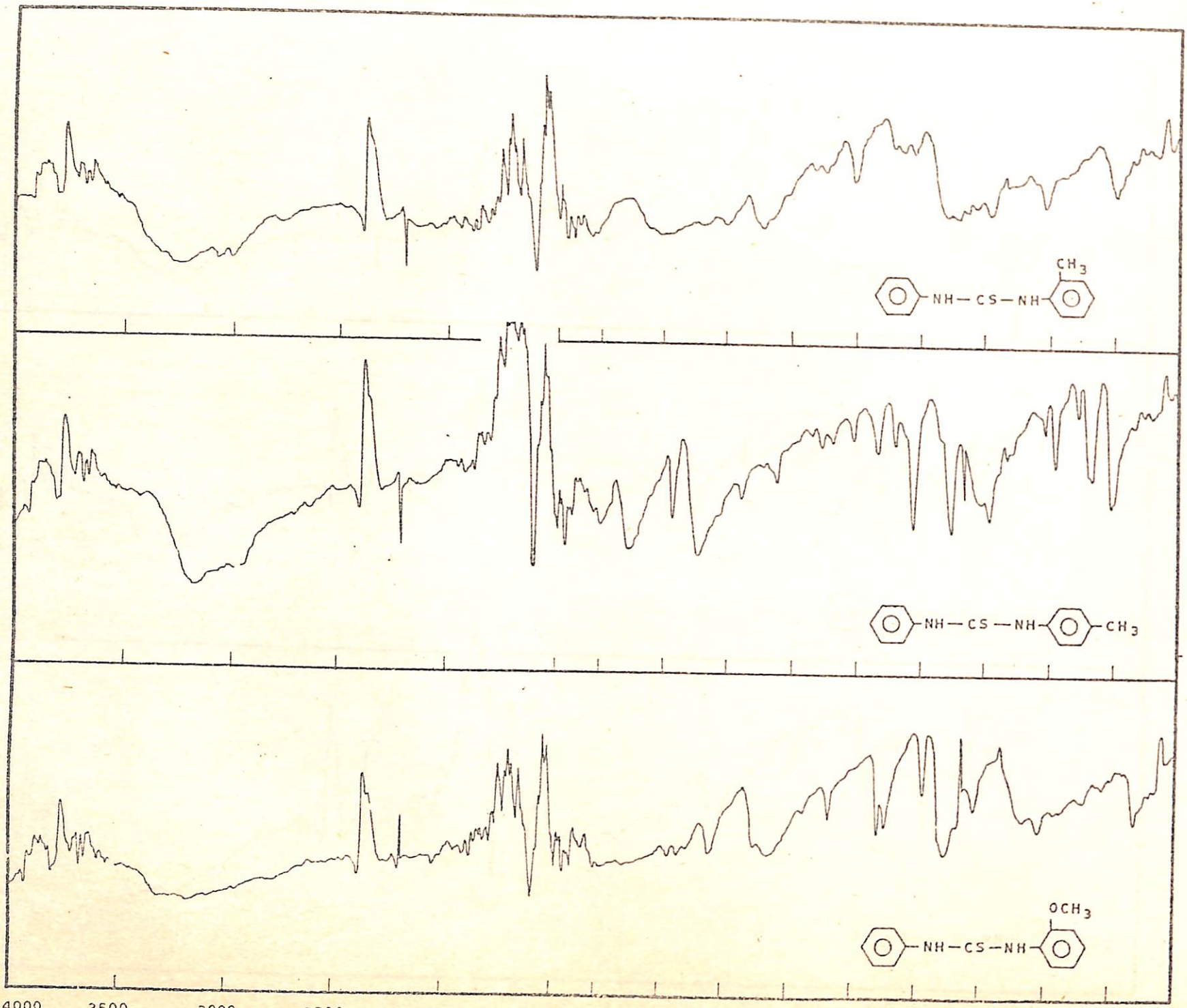


Fig. 2·9 I. R. Spectra of Substituted thioureas in KBr Pellet

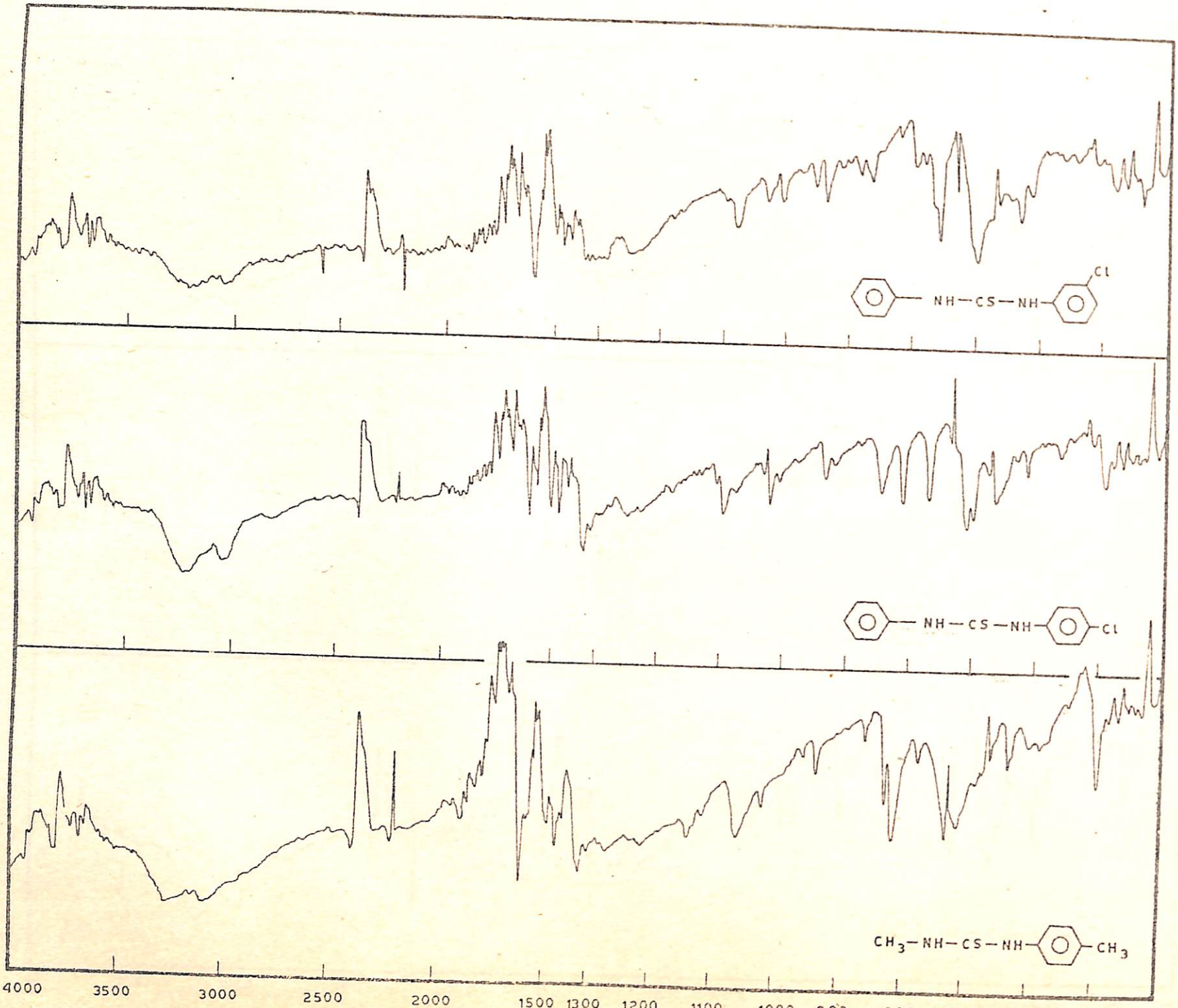


Fig. 2.10 I. R. Spectra of Substituted thioureas in KBr Pellet

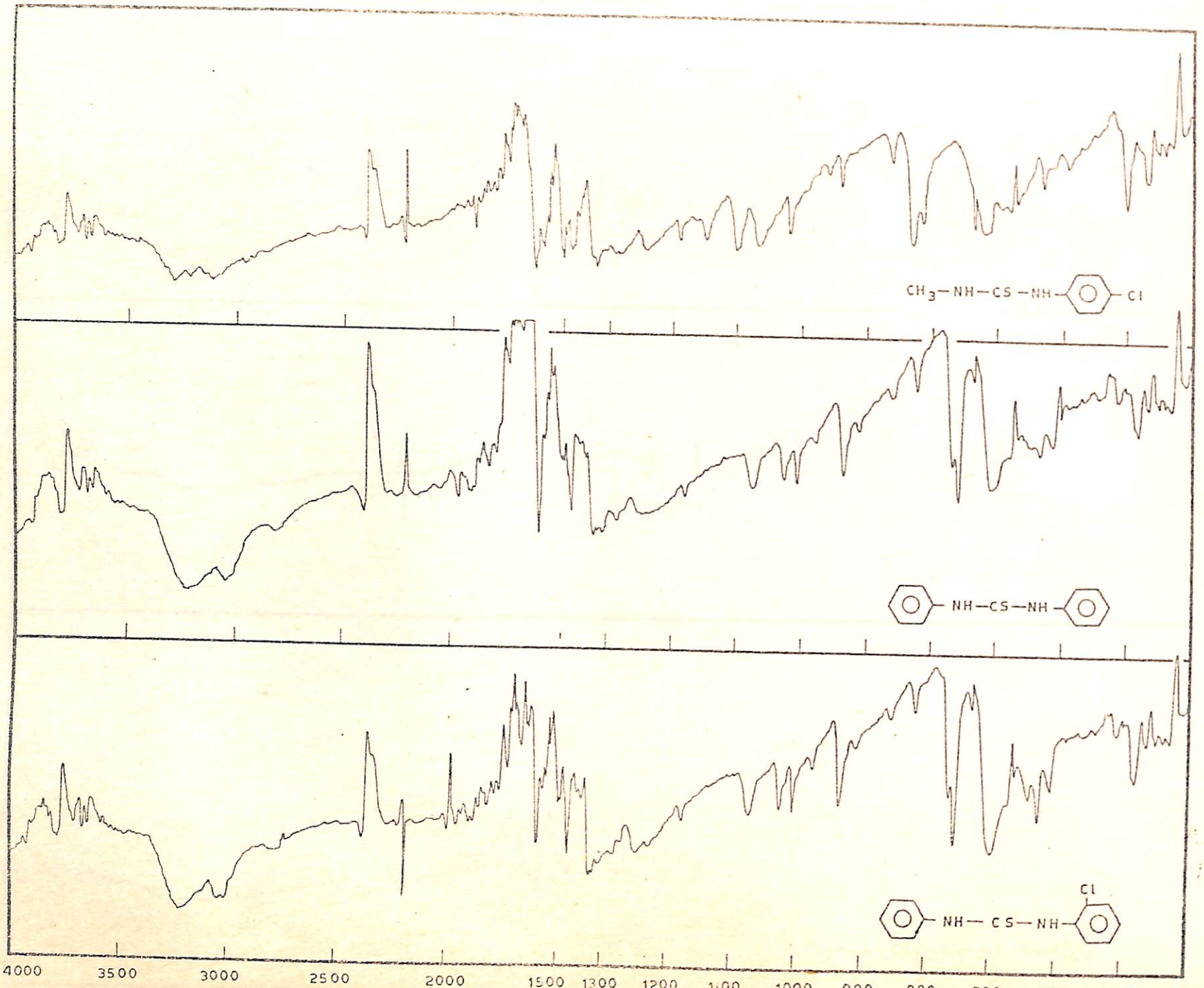


Fig. 2·11 I. R. Spectra of Substituted thioureas in KBr Pellet

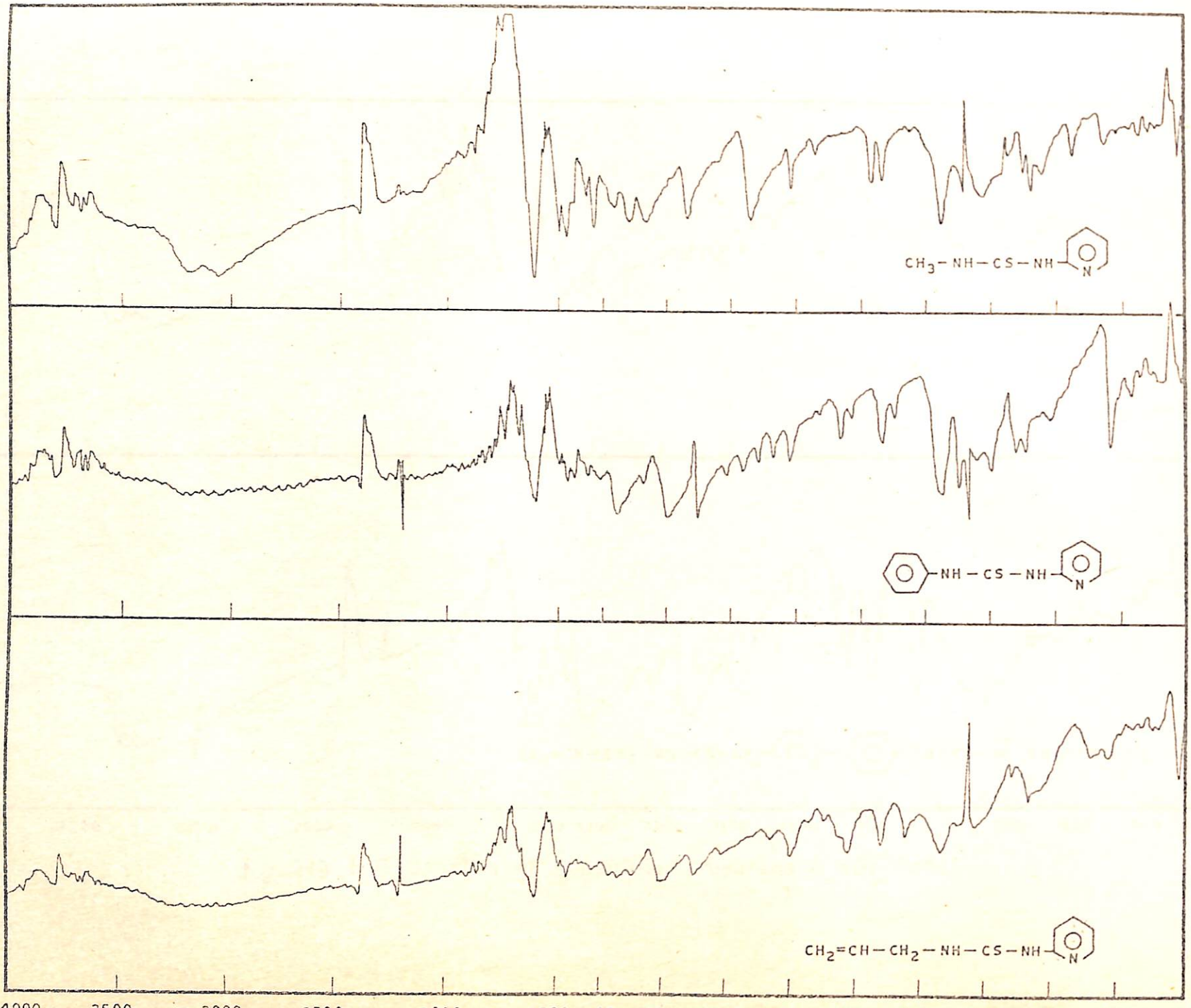


Fig. 2·12 I. R. Spectra of Substituted thioureas in KBr Pellet

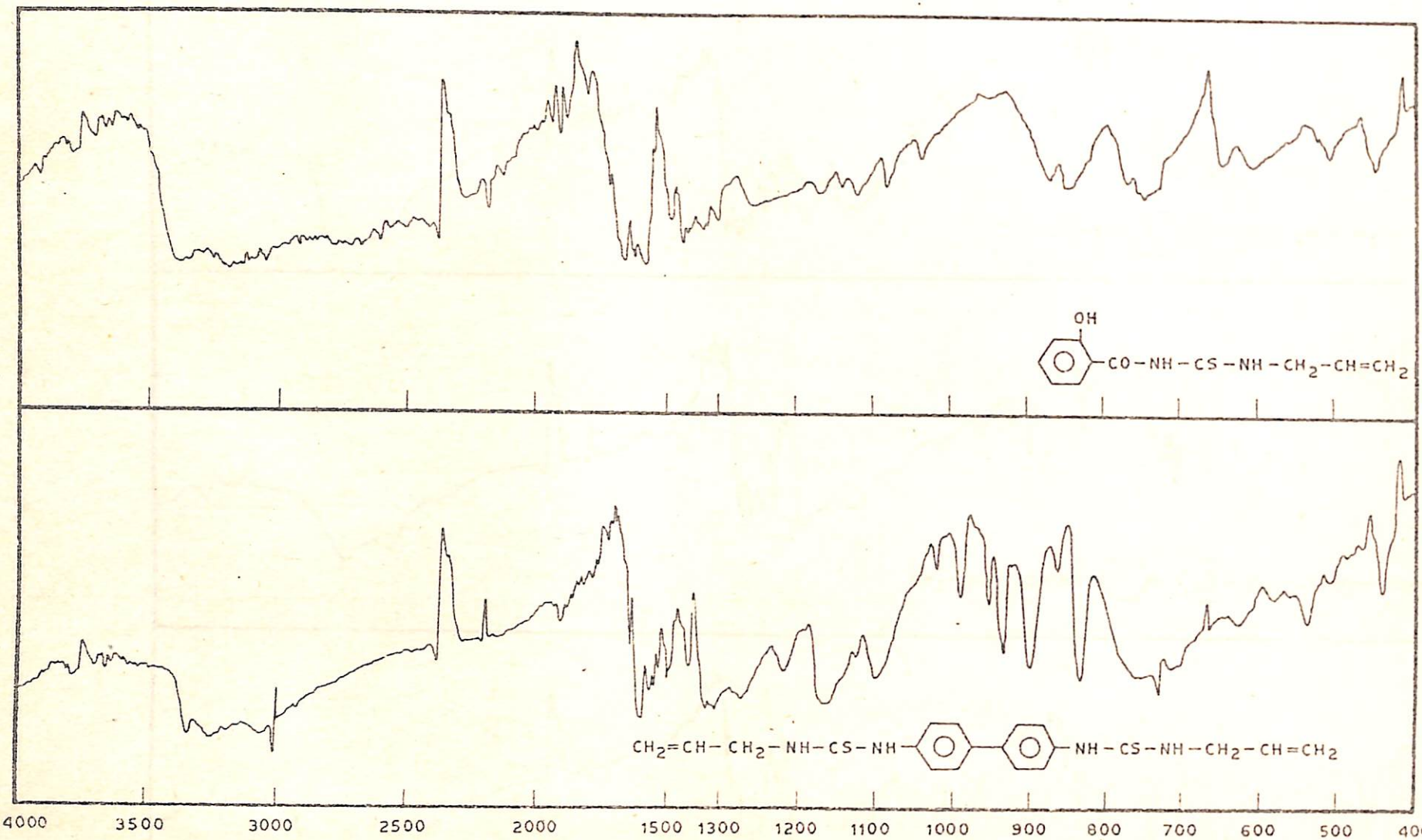


Fig. 2·13 I. R. Spectra of Substituted thioureas in KBr Pellet

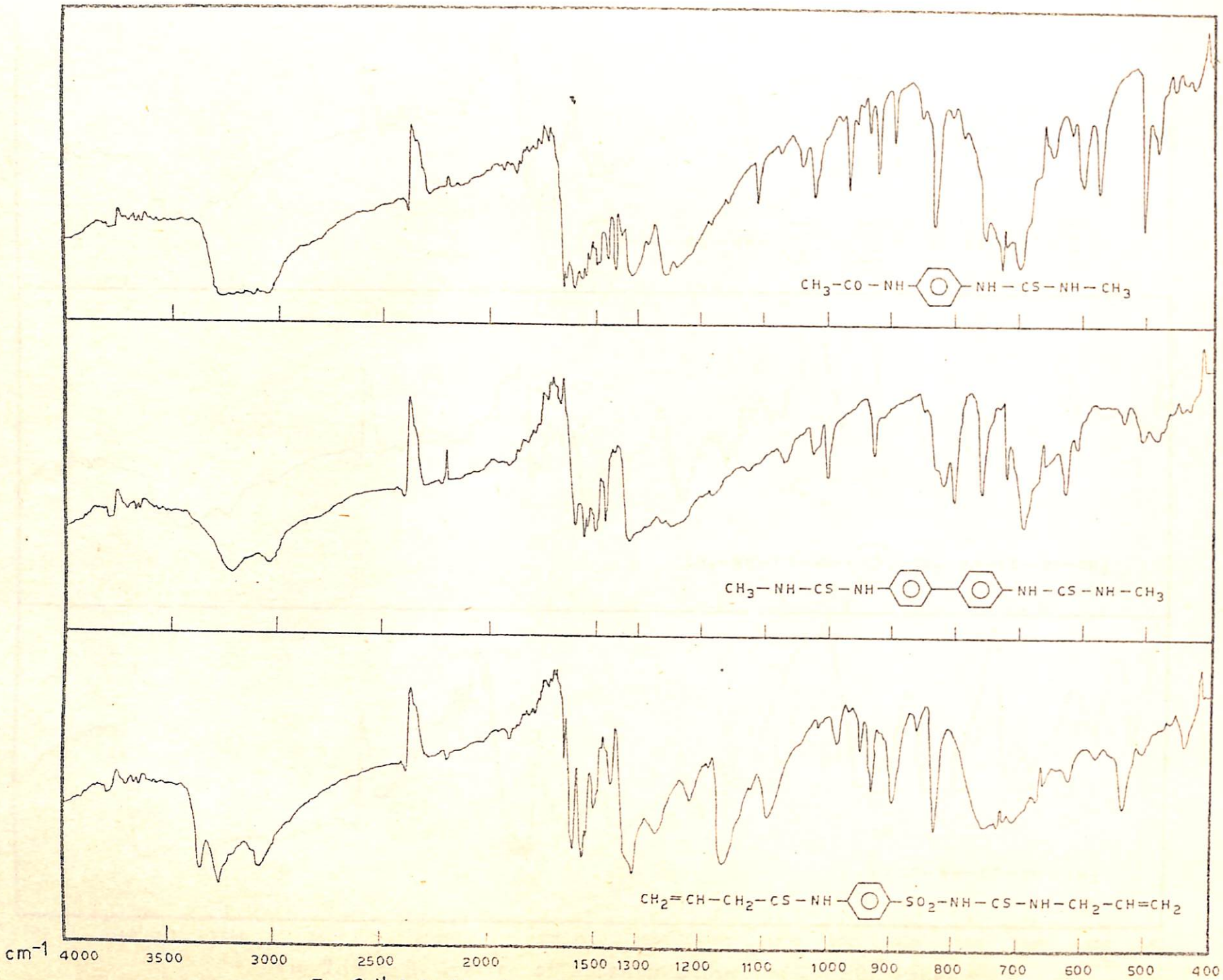


Fig. 2.14 I. R. Spectra of Substituted thioureas in KBr Pellet

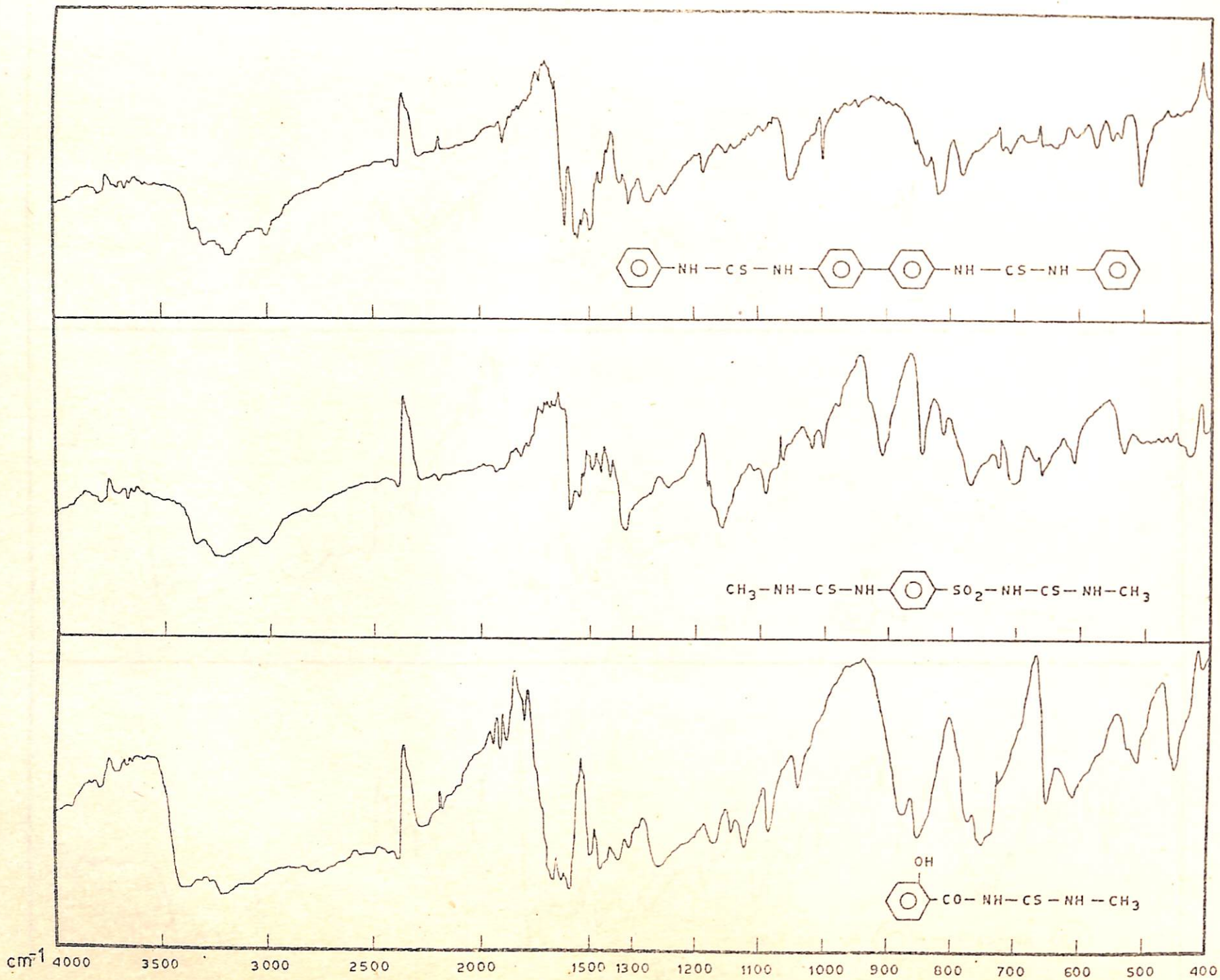


Fig. 2·15 I. R. Spectra of Substituted thioureas in KBr Pellet

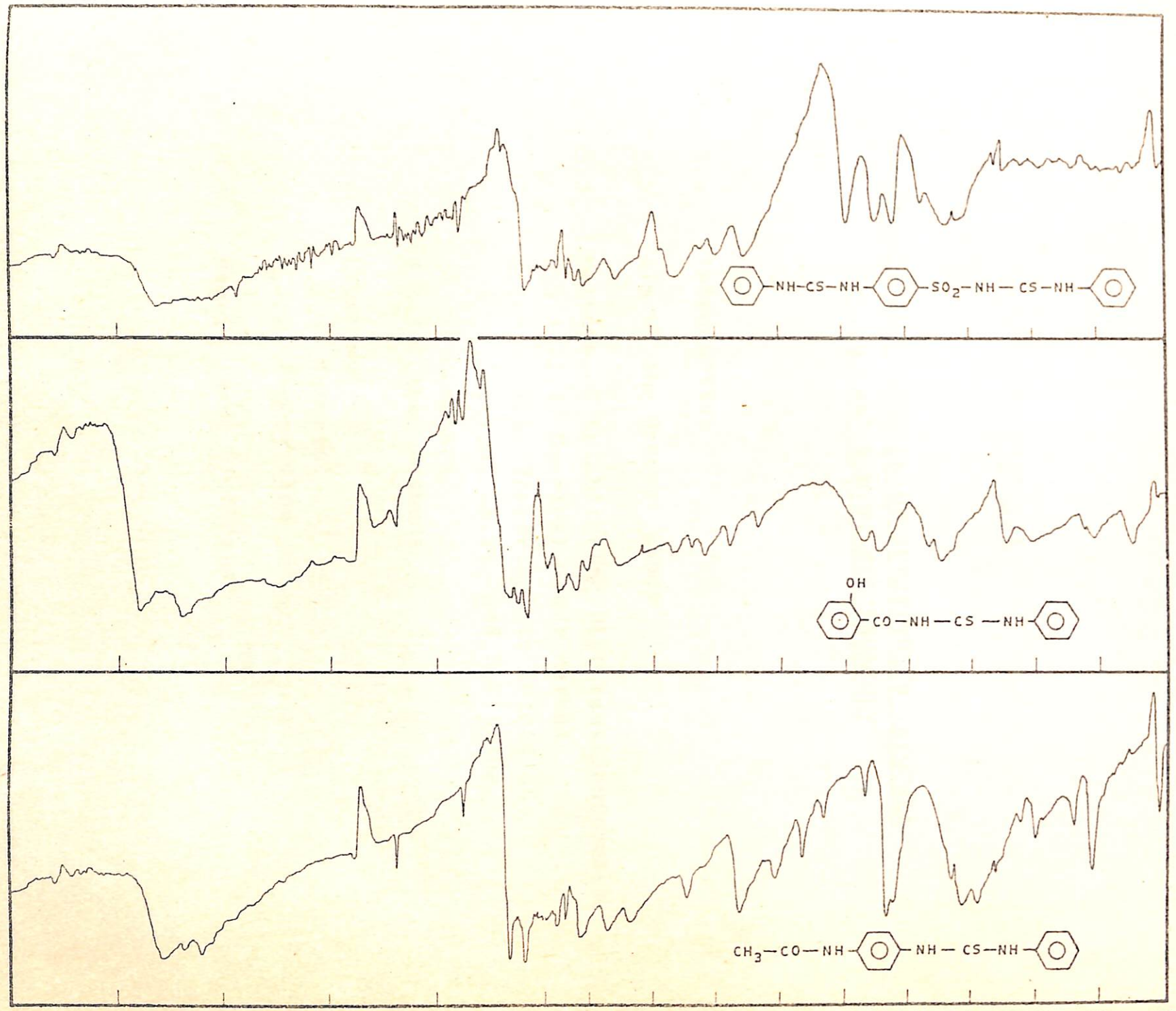


Fig. 2·16 I. R. Spectra of Substituted thioureas in KBr Pellet

CHAPTER III

CONFORMATIONAL STUDIES OF SUBSTITUTED THIOUREA BY I.R. AND N.M.R. SPECTROSCOPY

3.1 Introduction

The conformational isomerism of the thioamide group has been the subject of numerous studies (Hallam and Jones, 1970, ; Suzuki et al, 1960: Rae, 1967).

Literature shows that the "-CS-NH-" i.e. thioamide group can be found in both cis and trans conformations, in contrast to the amide group, "-CO-NH-", which is normally in the trans form, for example proteins, and substituted ureas (Mido, 1974; Russell and Thompson, 1956; La Planche and Rogers, 1964)

This has been explained as being due to partial double bond character of C-N bond due to delocalization of the electron pairs on nitrogen. (Neuman Jr. and Young, 1965a). The order of free energy of C-N bond rotation has been reported highest for thioamides in comparison to amides and amidines (Neuman et al 1965b). This has been found to be 13.5 Kcals/mole by Burman & Sathyanarayana,(1982).

Apart from the substituent on nitrogen and carbon, the donor and acceptor nature of the medium increases or decreases respectively the increment of energy barrier for the rotation around the C-N bond (Gonzalez and Yutronic, 1983; Kleinpeter et al, 1982).

Studies on the conformations of substituted thioureas (Sulliran and Price, 1975; Isaksson and Sandstrom, 1970: Gosavi et al,1967)

reveal the existence of several forms, cis-cis, cis-trans, trans-cis and trans-trans, where the thioamide hydrogen and the thiocarbonyl sulphur take cis and trans position with respect to each other. The relative proportions of each conformer depend mainly on the type of substituent. (Vassilev et al, 1982c: Emsley et al, 1972)

3.2 Aim of the Present Study

The spatial arrangement of amide group "CO-NH" when present in biologically indispensible constituent of living species: proteins, in the form of peptide linkage, has given many structural and functional behaviours to this most versatile biopolymer. Similarly conformational studies of thioamide group, which constitutes many biologically important compounds, including thiourea derivatives, will make a worth while contribution.

An appreciable amount of work has already been done as evident from section 3.1, this work is an attempt of similar studies with new set of thiourea derivatives and their metal complexes.

3.3 Methods of Establishing Different Conformers

Various methods (Lau, 1961; Klyne, 1954; Elliel et al, 1965) are known for undertaking conformational study of a compound. A few of them which have been made use of in the present studies are discussed here in detail.

Those forms which can be separated and are not interconvertable by C-N bond rotation are known as configurational isomers. Interconvertible forms which cannot be separated, under ordinary conditions, are known as conformational isomers. (March, 1968). The N, N' disubstituted derivatives of thioureas are conformational isomers (Vassilev et al, 1982c; Galabov et al, 1978).

3.3.1 I.R. Spectral study method

Geometric isomers cannot be easily identified by chemical analysis. The only reliable method is to detect the formation of a ring structure which is indicative of a cis conformation (Nakagowa and Onoue, 1965, 1966).

Conformers on the other hand can be identified conveniently by infra red absorption spectra. Each conformer has its own characteristic infra red spectrum, and the peak positions are often different. For instance the C-F bond in equatorial fluorocyclohexane absorbs at 1062 cm^{-1}, while the axial C-F bond absorbs at 1129 cm^{-1} (Larnaudie, 1952).

The polarization of the double bond in geometrical isomers due to field effects of various group, has also led to increase in the absorption frequency in I.R. range (Paperno et al, 1979).

3.3.2 N.M.R. Method of chemical shift and splitting constant

There are several ways in which N.M.R. may be used to determine conformation. A proton on a

double bond carbon has a different chemical shift depending on whether it is cis or trans with respect to a particular group. For example in case of 1,2 dimethyl stilbenes (Inamoto et al, 1963) and peptide bond of N-monosubstituted amides (LaPlanche, 1964).

The nature of the substituent on carbon carrying hydrogen atom also leads to difference in chemical shifts, example isomers of trichloroethane. (Paperno et al, 1979).

The extent of splitting of two peaks by spin-spin coupling varies with the different spatial orientation of hydrogen atom. The one which is in cis position will split the corresponding peak to a lesser extent than that in the trans position (Scheinmann, 1970: Jackman and Wiley, 1960). Thus the splitting constant (J) values in the range of 2 to 11 Hz indicate cis form, while that between 11 to 18 indicate the trans form (Paperno et al, 1979).

Lastly advantage is taken, of low temperature spectral measurement, which enables one to get different peaks for two easily interconvertable conformers. (Jackman, 1964; Phillips, 1962).

3.3.3 Other methods

Some other methods like dipole moment measurement (Aroney, Izak and LeFevre, 1962),

X-ray and electron diffraction techniques (Lyle et al, 1962), optical rotatory dispersion (ORD) (Djerassi, 1960) and chemical methods involving correlation with known compounds and reaction by routes of known mechanism (March, 1968) have been used.

It is well known that conformational assignment can only be done on the basis of information obtained from several measurements, as conformational assignment cannot be made on the basis of a single measurement.

3.4 Experimental

3.4.1 Material

Reagent: Deutro-chloroform (Sigma Chemical Company, U.S.A.) was used as solvent for all the N.M.R. measurement. Tetra methyl silane (TMS), from the same company, was used as reference.

Instrument: All the ^{1}H-N.M.R. spectra were taken on JOEL FX 100 model working on fourier transform mode at 99.5 MHz with deutrium locking. The 5 mm tube was used for sampling. The spectrum width sweep taken was 1000 and 2000 Hz.

I.R. spectras were taken in SP 1200 model using K Br pellet medium, in the range of 400 to 4000 cm^{-1}.

3.4.2 Observation

The ^{1}H-N.M.R. spectra of thiourea derivatives were analysed and peaks were assigned as different chemical shifts to each of the group of protons in the same chemical environment.

The vicinal spin-spin coupling constants (^{3}J) were calculated with the help of observed field strength and chemical shifts (in Hz) for each of the multiplet, provided by the in built computerised print out from the N.M.R. spectrometer. These observations have been detailed out in tables 3.2 to 3.4.

These values were helpful in interpreting various conformational and structural nature of these compounds, which have been discussed later in section 3.5.

The I.R. spectra measurements which has already been detailed out in tables 2.3 to 2.6 were used, specially with emphasis on the ν(NH) bonds, which reveals the geometrical isomeric nature due to $\gtrless C=N^{\pm}\lessgtr$ partially double bond.

3.5 Result and Discussion

The existence of different conformations of -CS-NH- group (known as thioamide group) is manifest in the I.R. spectra by the appearance of two distinct ν(NH) maxima near 3200 cm^{-1} and 3400 cm^{-1}. (Hallam and Jones, 1970; Suzuki

et al, 1960: Rae, 1967: Gosavi et al, 1967; Galabov et al, 1978: Vassilev et al, 1982c). This is evident from the I.R. spectra presented in Chapter II from figs. 2.1 to 2.16. The peak at higher frequency is attributed to the trans form while at lower frequency is due to the cis form (Hallam and Jones, 1970). This assignment of the two bands is supported by most workers, some ambiguity however remains to be solved (Rae, 1967: Mido, 1974).

In the table 3.1 the characteristic N-H frequencies of different thiourea derivatives studied in K Br pellet are given. It will be evident that all N-alkyl -N'aryl or pyridyl thioureas with an alkyl group bigger than methyl group (viz. allyl and phenyl) possess two N-H bands. This is evidently due to two different -CS-NH- conformations. The variation in the polar substituents from chloro to methyl on aromatic and pyridyl ring do not have any contribution, which is evident from only single ν(NH) band in a few derivatives, despite of their presence (Vassilev, 1982c). Although shift in the ν(NH) frequency is do observed to the extent of ± 3 cm^{-1}, which is quite minor.

Further detailed study of Vassilev(1982c) on some N,N disubstituted thioureas by taking spectra in varying polarity solvents has revealed that these derivatives show different conformation, are not due to stabilized trans-cis

conformers but due to their participation in an equilibrium between several rotational isomers viz

cis-cis; cis-trans: trans-cis and trans-trans.

In the present studies this was found to be correct in all cases excepting those which had a stabilized conformation. This was established by supplementing the above studies by ^{1}H-N.M.R. measurements.

As evident from the tables 3.2 to 3.4, a peak of NH proton was obtained with a chemical shift (δ) between 6.0 to 10.0 ppm. In some of the cases there are two different peaks, which proves that the derivative exist as a stabilized conformer in one of the above mentioned forms. The cases where only one peak of NH proton was obtained, agree with the Vassilev (1982c) and Galabov (1978) finding, for existence of an equilibrium between different forms.

Tables 3.2 to 3.4 which shows the data on N.M.R. spectra shown in figs. 3.1 to 3.10, also reveal the vicinal spin-spin coupling constant values(^{3}J), for various coupled peaks. Since the J_{AX} value usually falls less than 1, this cannot be considered in the case of first order only and multiplets due to higher order spin-spin coupling are expected; leading to peaks with greater number of splits than expected.

Where the value of ^{3}J is between 2 and 10, it can be concluded that the two groups are cis to each other; whilst those showing a ^{3}J value between 11 and 18 give indication of trans orientation.

A study of ^{1}H-N.M.R. spectra of few metal complexes of N'-pyridyl substituted thiourea derivatives show the shift of NH proton peak by 5-7 ppm towards the higher values. (Figs. 3.11to 3.15). This can be attributed to involvement of N atom in complex formation.

Table 3.1 N-H Stretching Frequencies of Alkyl, Aryl Thioureas, R'-NH-CS-NH-Ar.

R'	Ar	(NH) cis (cm^{-1})	(NH) trans (cm^{-1})
Al	Ph	3180	3360
Al	m-Cl Ph	-	3200
Al	p-Cl Ph	3050	3220
Al*	2-(4Me Py)	3100	3300
Al*	2-(6Me Py)	3210	3420
Me	Ph	3175	3280
Me	o-Cl Ph	-	3290
Me	m-Cl Ph	3100	3220
Me	p-Cl Ph	-	3280
Me	2-Py	-	3190
Me*	2-(3Me Py)	-	3400
Me*	2-(4Me Py)	-	3300
Me*	2-(6Me Py)	-	3250
Ph	Ph	-	3220
Ph	o-Cl Ph	3080	3210
Ph	m-Cl Ph	-	3200
Ph	p-Cl Ph	3040	3220
Ph*	2-(3Me Py)	3200	3430
Ph*	2-(4Me Py)	3250	3400
Ph*	2-(6Me Py)	3150	3435

* Data taken from elsewhere (Saha, 1981).

Table 3.2 ^{1}H-N.M.R. Studies Data of N-Allyl Series of Thiourea Derivatives.

Derivative CH_2=CH-CH_2-NH-CS-NH-R R	^{1}H Chemical Shift (δ ppm) range*										^{3}J Values (Hz)					
	NH		Py - ^{1}H			Ph	CH	$=CH_2$	$-CH_2$	CH_3						
			ortho	meta	para											
	a_1	a_2	b	c	e	f	g	h	i	j	J_{ai}	J_{gi}	J_{gh}	J_{bc}	J_{ce}	
Ph	8.2	-	-	-	-	7.1-7.5 (m)	5.6-6.0 (m)	5.0-5.2 (d)	4.3	-	-	-	9	-	-	
m-Cl Ph	8.7	6.2	-	-	-	7.1-7.4 (m)	5.7-6.0 (m)	5.1-5.2 (d)	4.2	-	-	-	10	-	-	
p-Cl Ph	8.0	-	-	-	-	7.1-7.4 (m)	5.7-6.0 (m)	5.0-5.2 (d)	4.2-4.3 (d)	-	5	5	11	-	-	
2-Py	-	-	8.2 (d)	6.9-7.1 (t)	7.3-7.8 (m)	-	5.9-6.3 (m)	5.2-5.4 (t)	4.4-4.5 (t)	-	4	1	6	5	7	-
2-(4Me Py)	-	-	7.9-8.0 (d)	6.7 (d)	-	-	5.8-6.2 (m)	5.1-5.3 (t)	4.3-4.4 (t)	2.3	5	5	15	7	-	-
2-(6Me Py)	9.4	-	-	6.7 (d)	7.2-7.5 (m)	-	5.8-6.2 (m)	5.1-5.4 (t)	4.3-4.4 (t)	2.4	2	5	14	-	8	-

* d = doublet; t = triplet; m = multiplet, of peaks.

Table 3.3 ^{1}H-N.M.R. Studies Data of N-Methyl Series of Thiourea Derivatives.

Derivative CH_3-NH-CS-NH-R R	^{1}H Chemical Shift (δ ppm) range*								^{3}J Values (Hz)			
	NH		Py - ^{1}H			Ph	$N-CH_3$	CH_3	J_{ag}	J_{bc}	J_{ce}	J(Ph)
			ortho	meta	para							
	a_1	a_2	b	c	e	f	g	h				
Ph	8.3	-	-	-	-	7.2-7.5 (m)	3.1	-	-	-	-	10
o-ClPh	8.2	6.1	-	-	-	7.0-7.3 (m)	3.1 (d)	-	2	-	-	10
m-Cl Ph	8.4	6.1	-	-	-	7.0-7.3 (m)	3.1	-	-	-	-	12
p-Cl Ph	8.3	6.0	-	-	-	7.1-7.4 (m)	3.1	-	-	-	-	9
2-Py	-	-	8.0-8.1 (d)	6.8-7.0 (m)	7.5-7.7 (t)	-	3.2 (d)	-	5	6	7	-
2-(3Me Py)	-	7.8	7.9-8.0 (d)	6.7-6.9 (t)	7.3-7.4 (d)	-	3.2	2.3	4	5	8	-
2-(4Me Py)	9.6	-	7.9-8.0 (d)	6.6-6.7 (t)	-	-	3.2 (d)	2.3	4	6	-	-
2-(6Me Py)	9.3	-	-	6.7 (d)	7.2-7.5 (m)	-	3.2 (d)	2.4	4	-	8	-

* d = doublet; t = triplet; m = multiplet, of peaks.

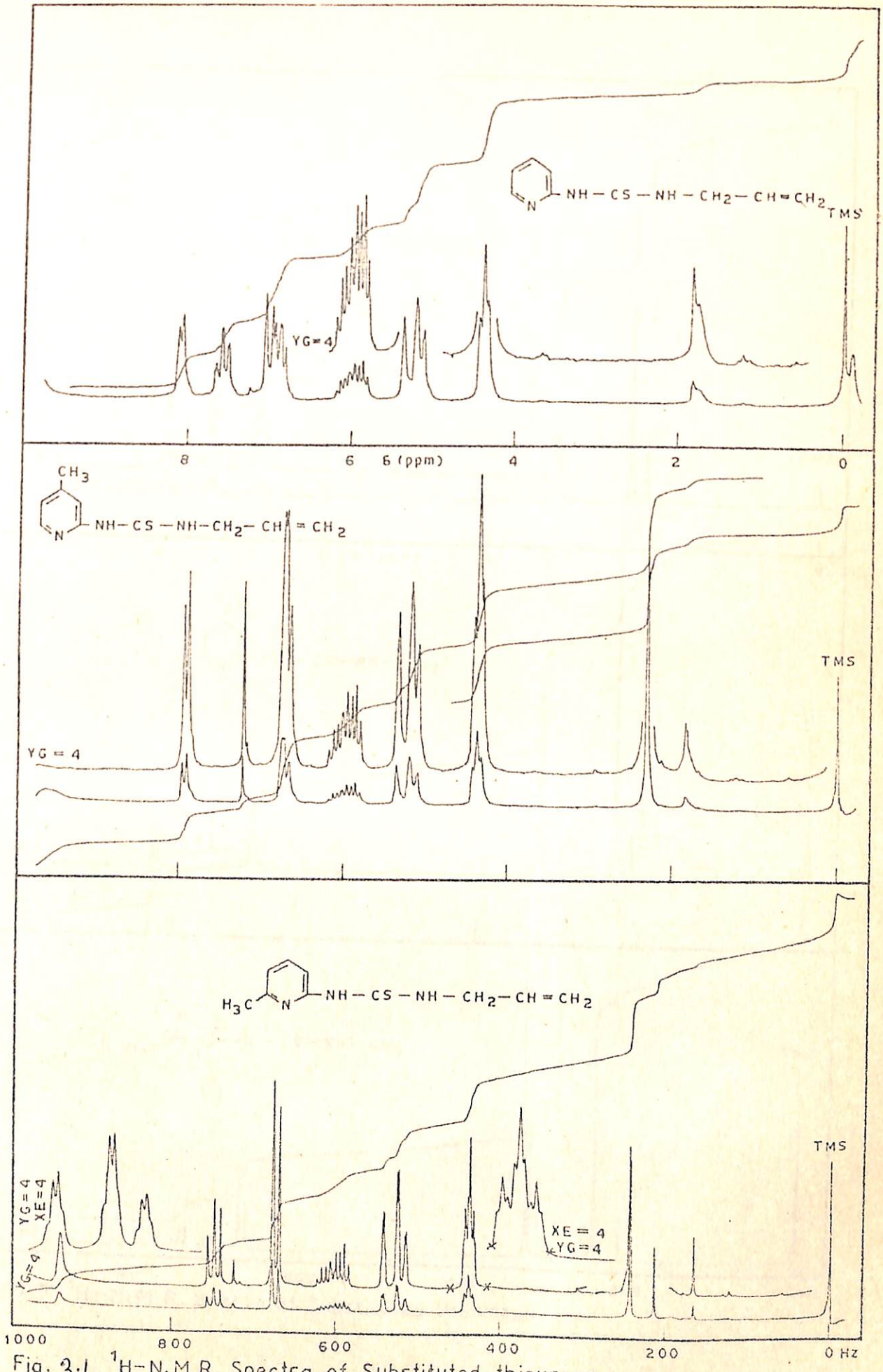


Fig. 3.1 ^{1}H-N.M.R. Spectra of Substituted thioureas

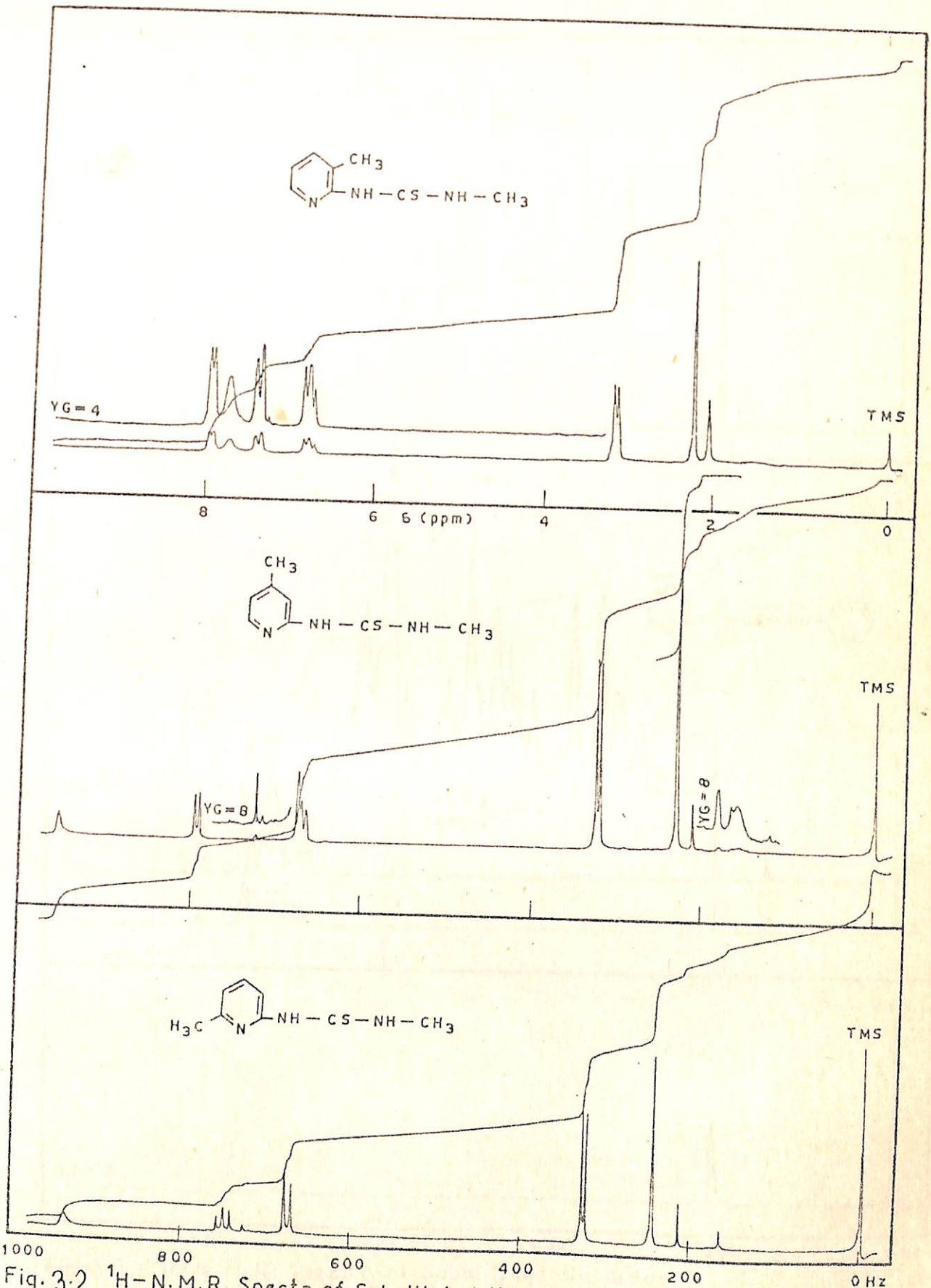


Fig. 3.2 ^{1}H-N.M.R. Specta of Substituted thioureas

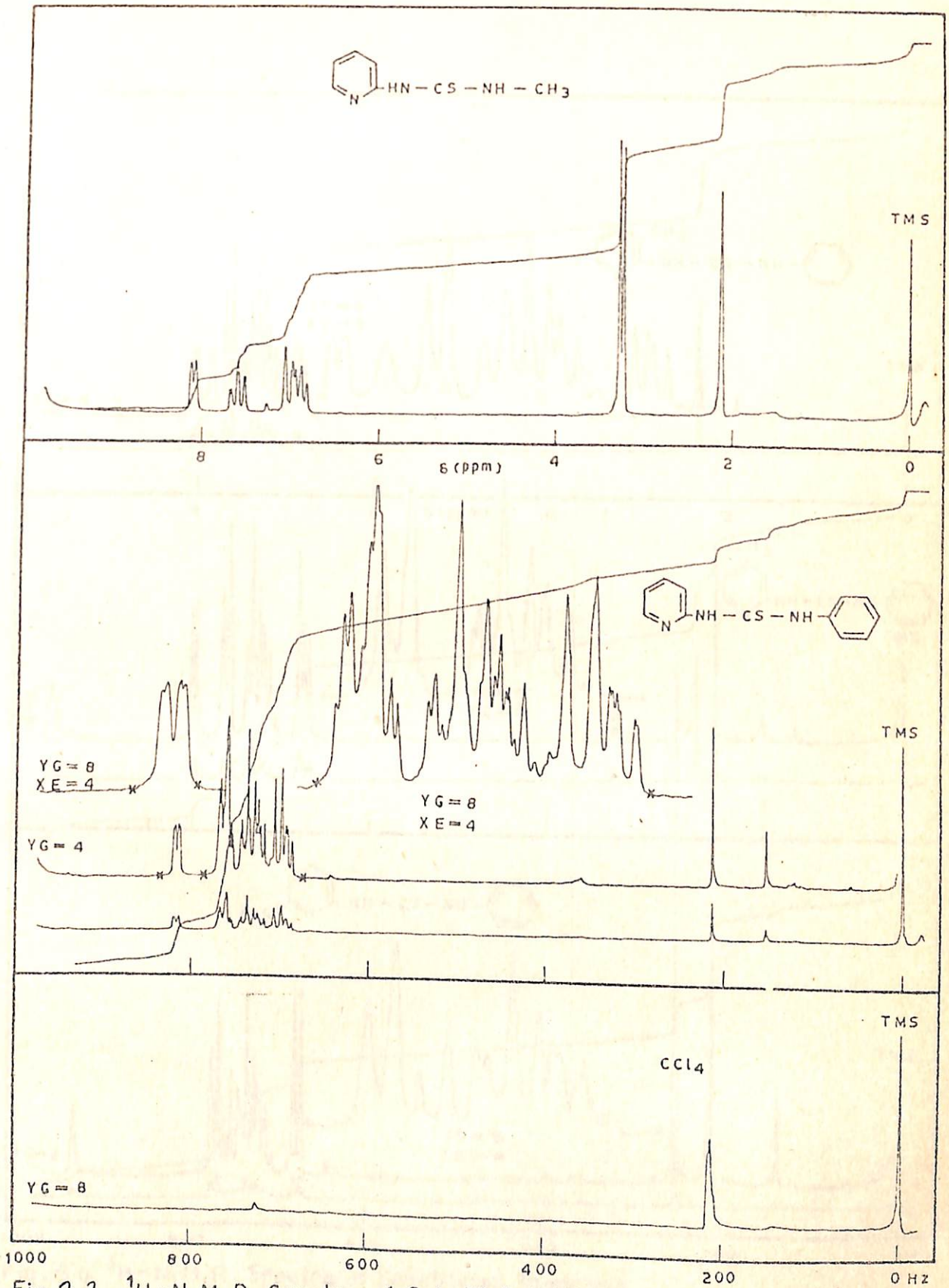


Fig. 3·3 ^{1}H-N.M.R. Spectra of Substituted thioureas

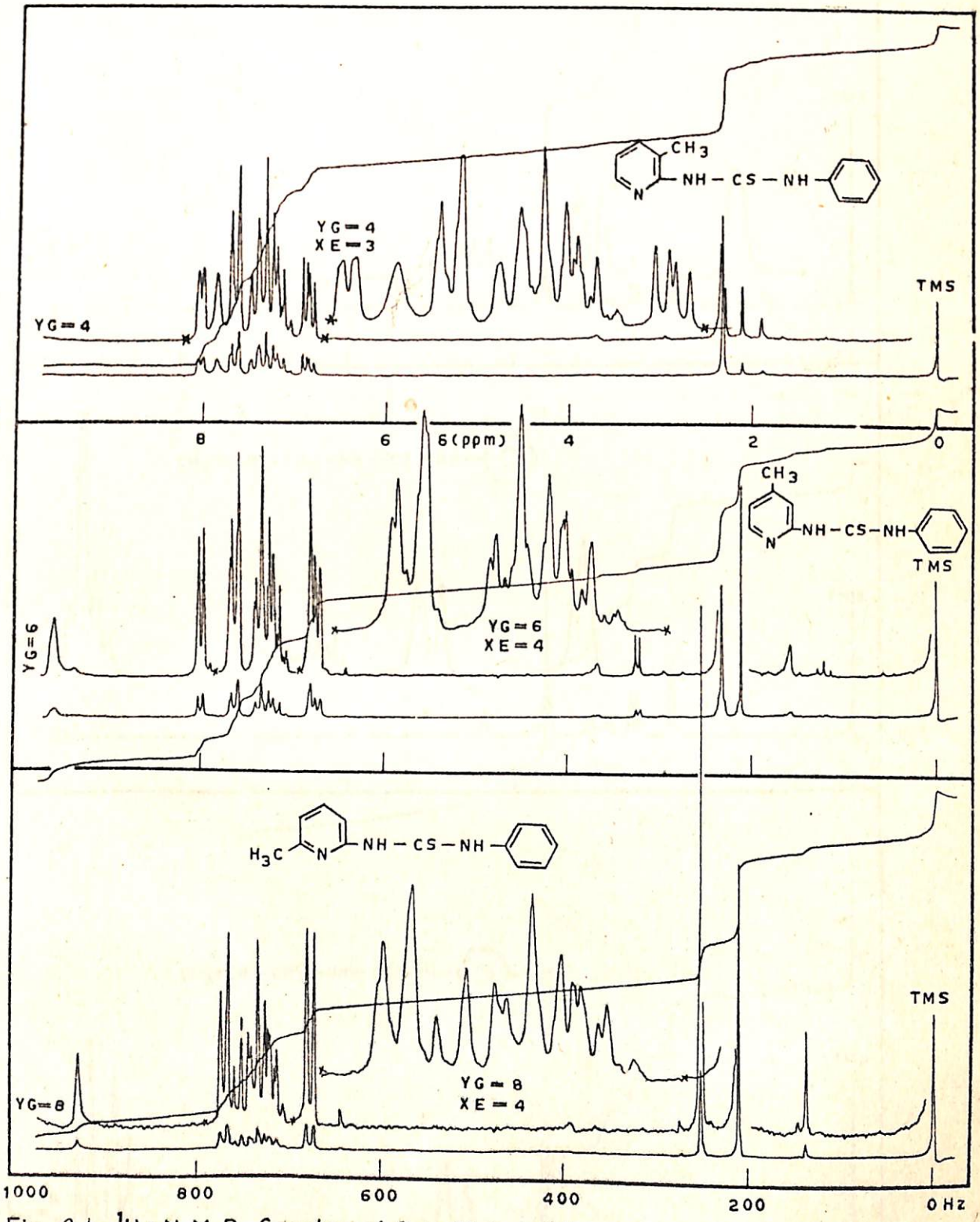


Fig. 3·4 ^{1}H – N.M.R. Spectra of Substituted thioureas

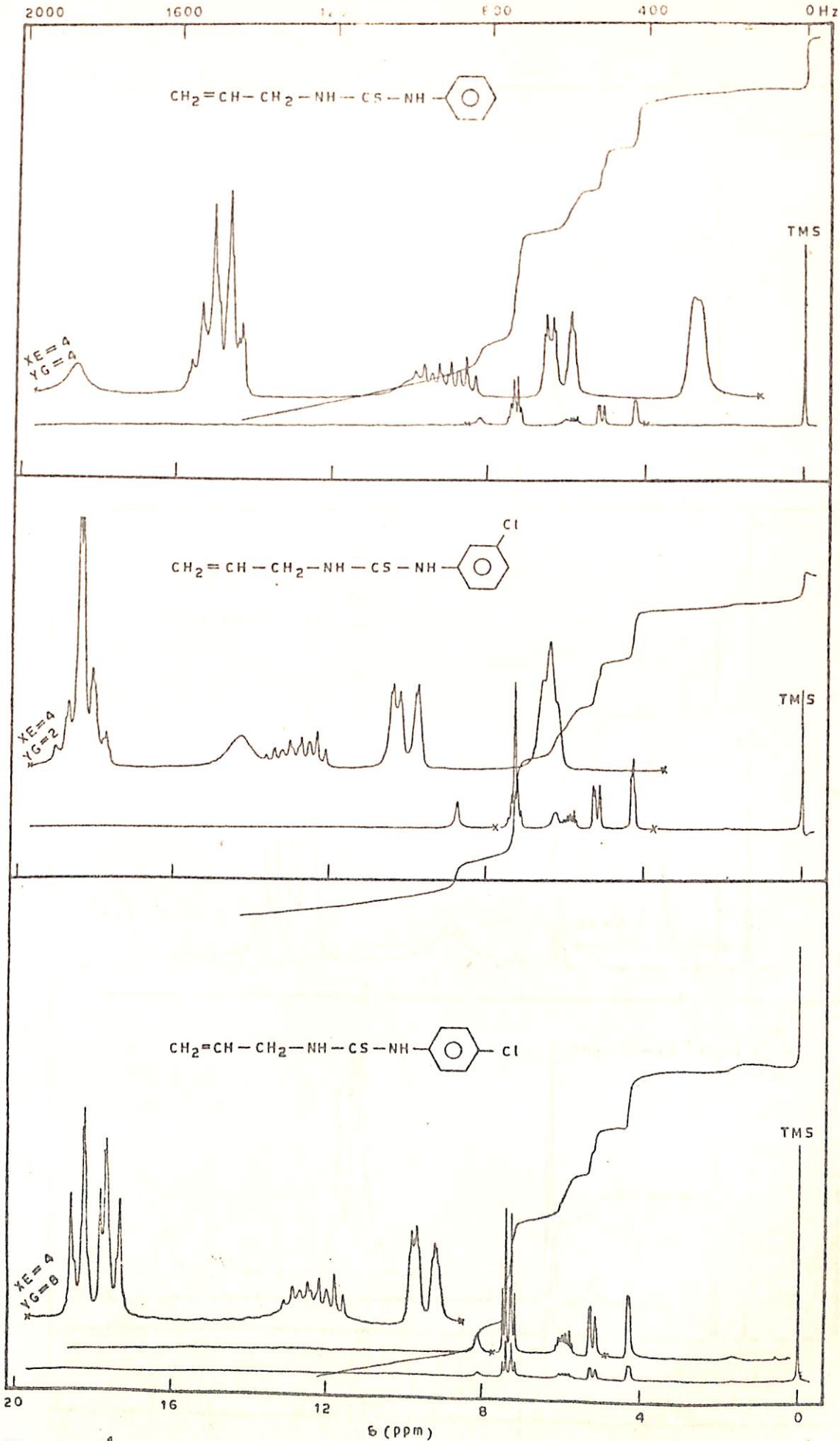


Fig. 3.5 ^{1}H – NMR Spectra of substituted thiourea derivatives

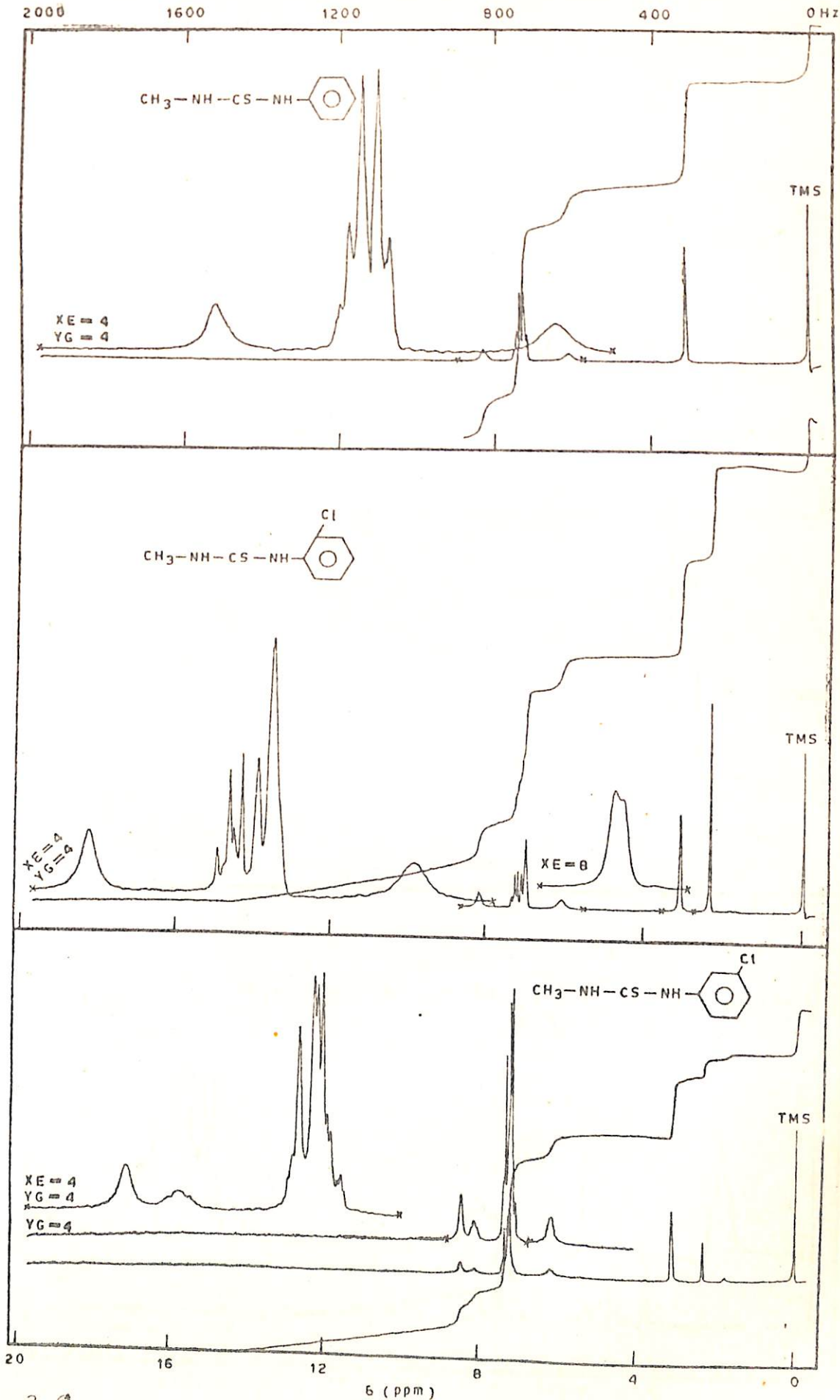


Fig. 3.6 ^{1}H-NMR Spectra of substituted thiourea derivatives

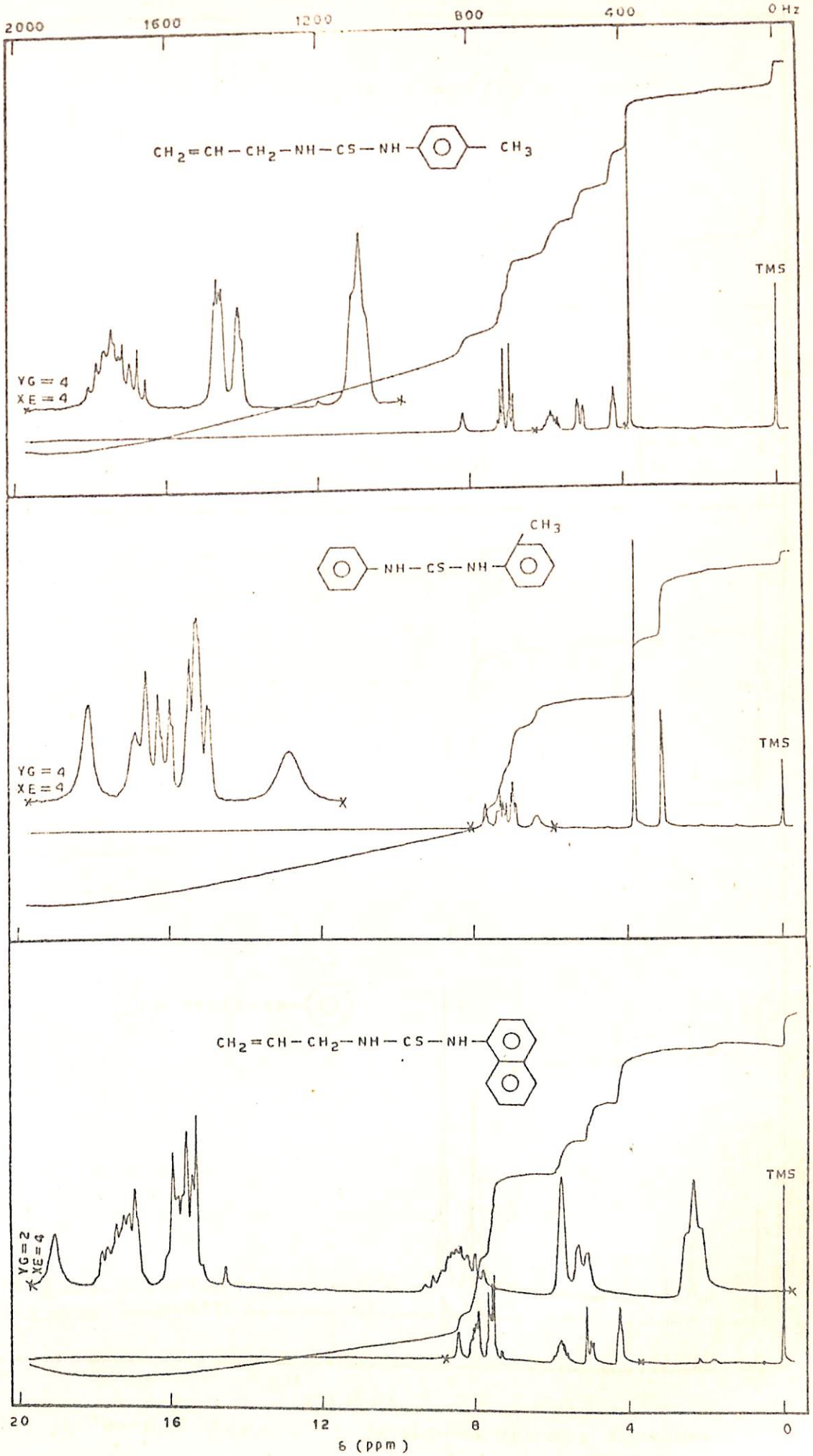


Fig.3.7 ^{1}H-NMR Spectra of substituted thiourea derivatives

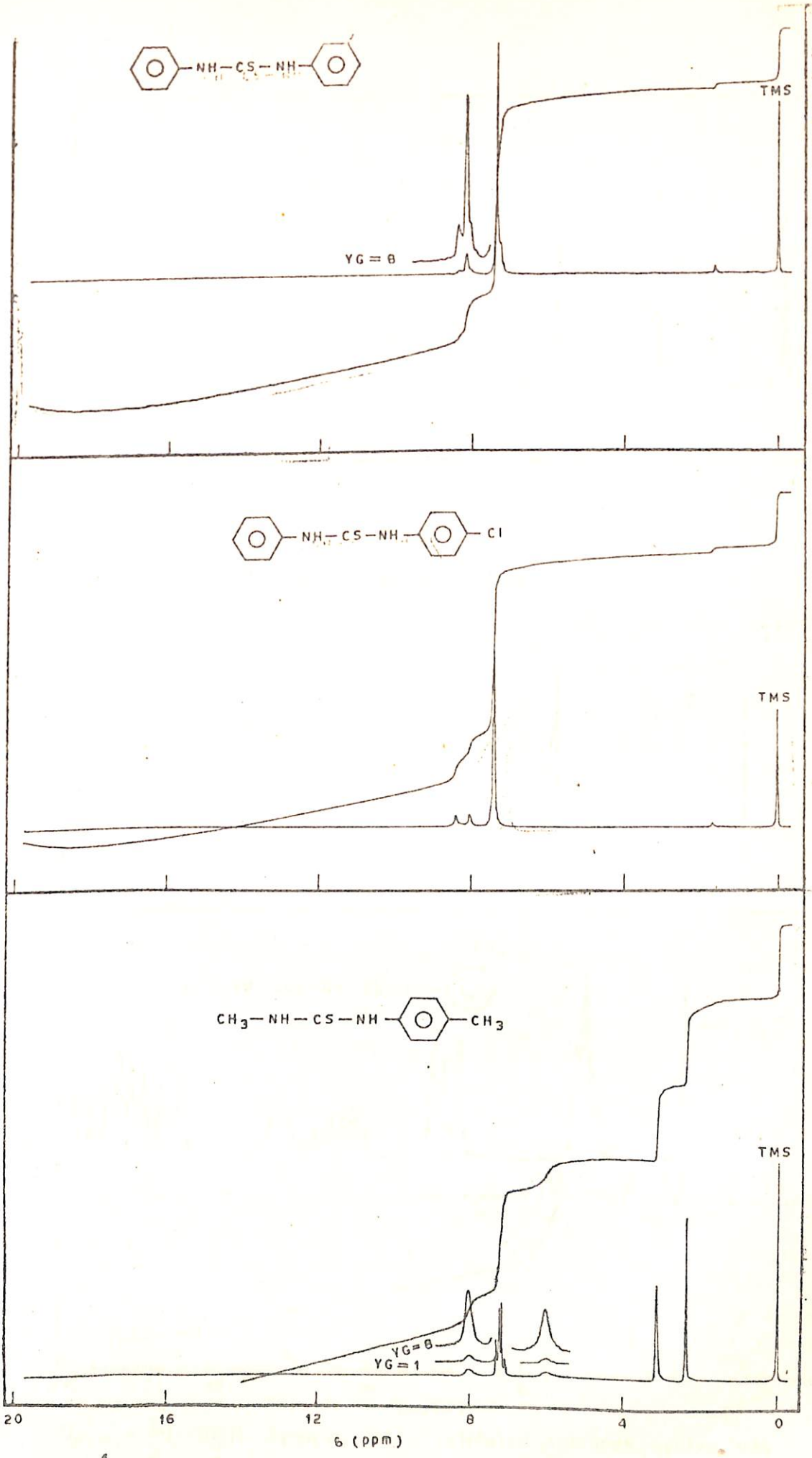


Fig.3.9 ^{1}H-NMR Spectra of substituted thiourea derivatives

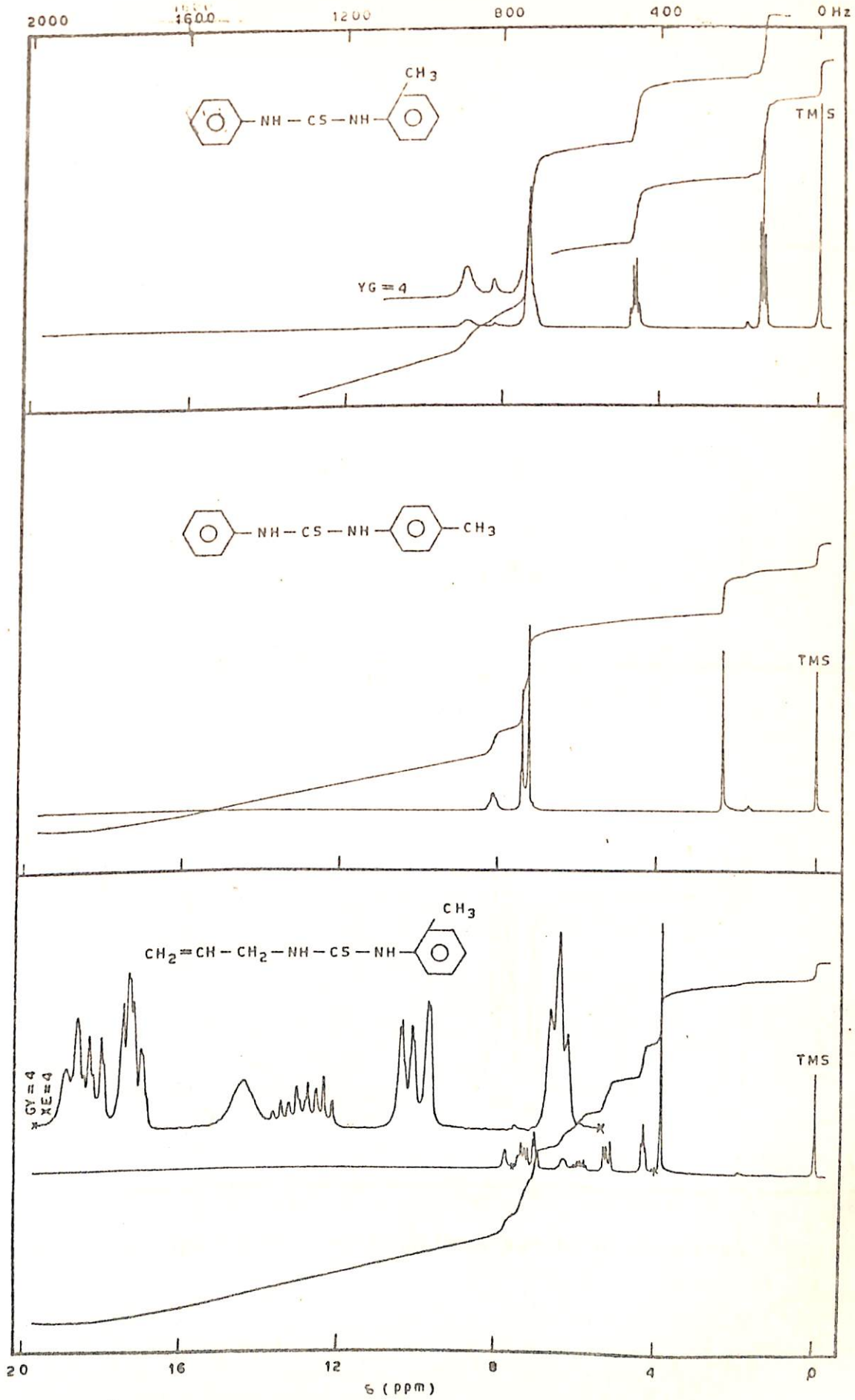


Fig. 3.10 ^{1}H–NMR Spectra of substituted thiourea derivatives

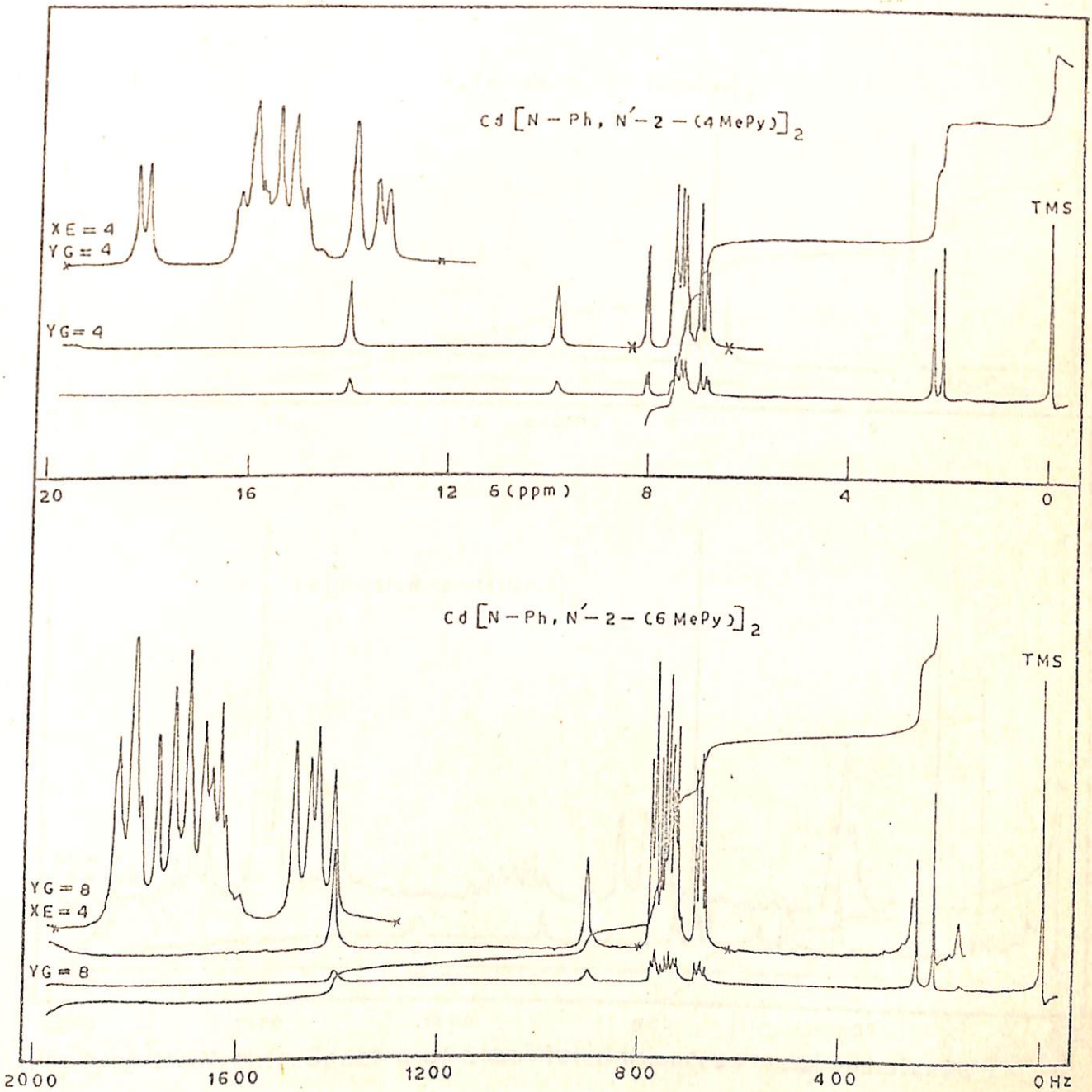


Fig. 3.11 ^{1}H-N.M.R. Spectra of Substituted thioureas metal complexes

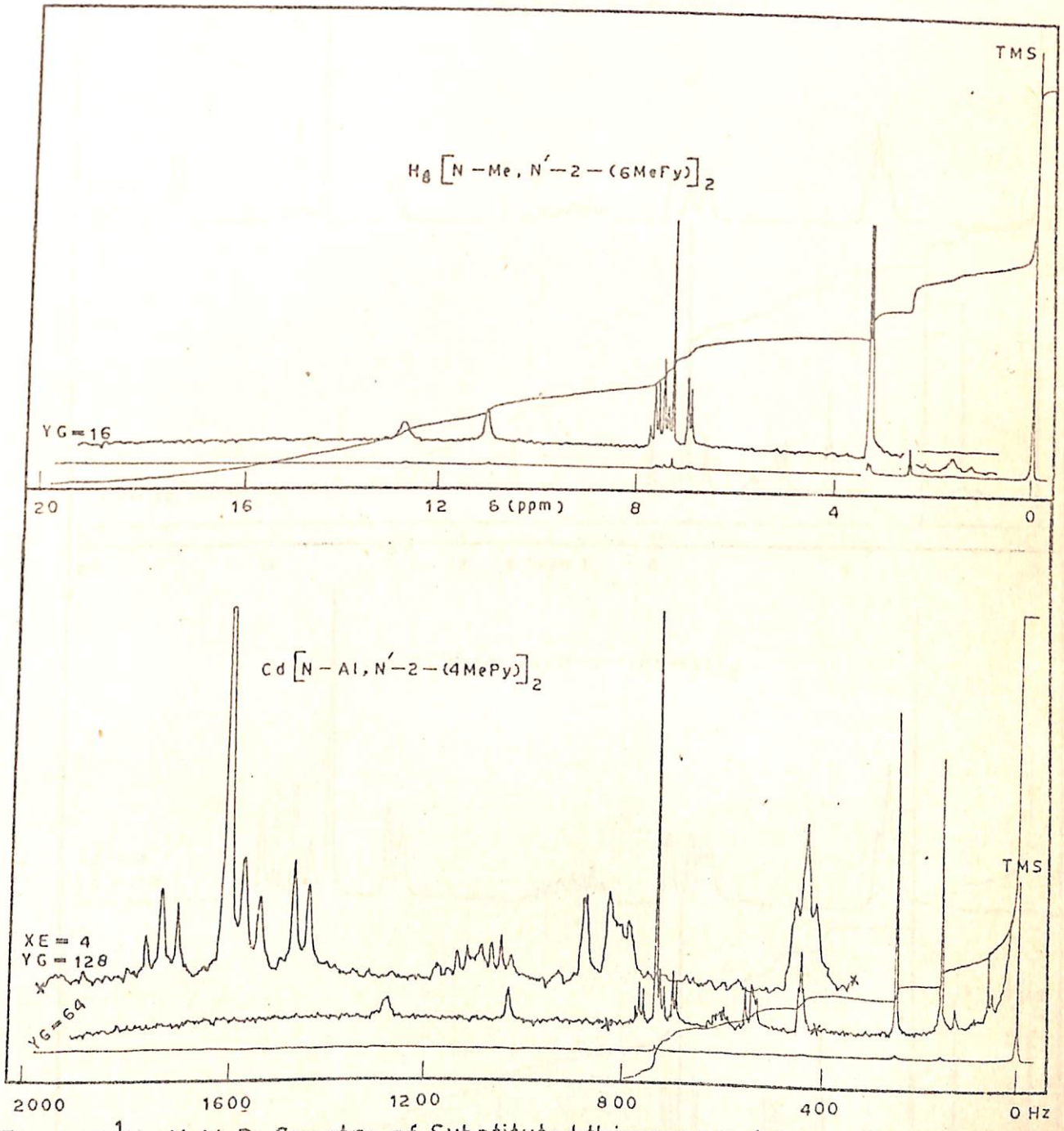


Fig. 3·12 ^{1}H-N.M.R. Spectra of Substituted thioureas metal complexes

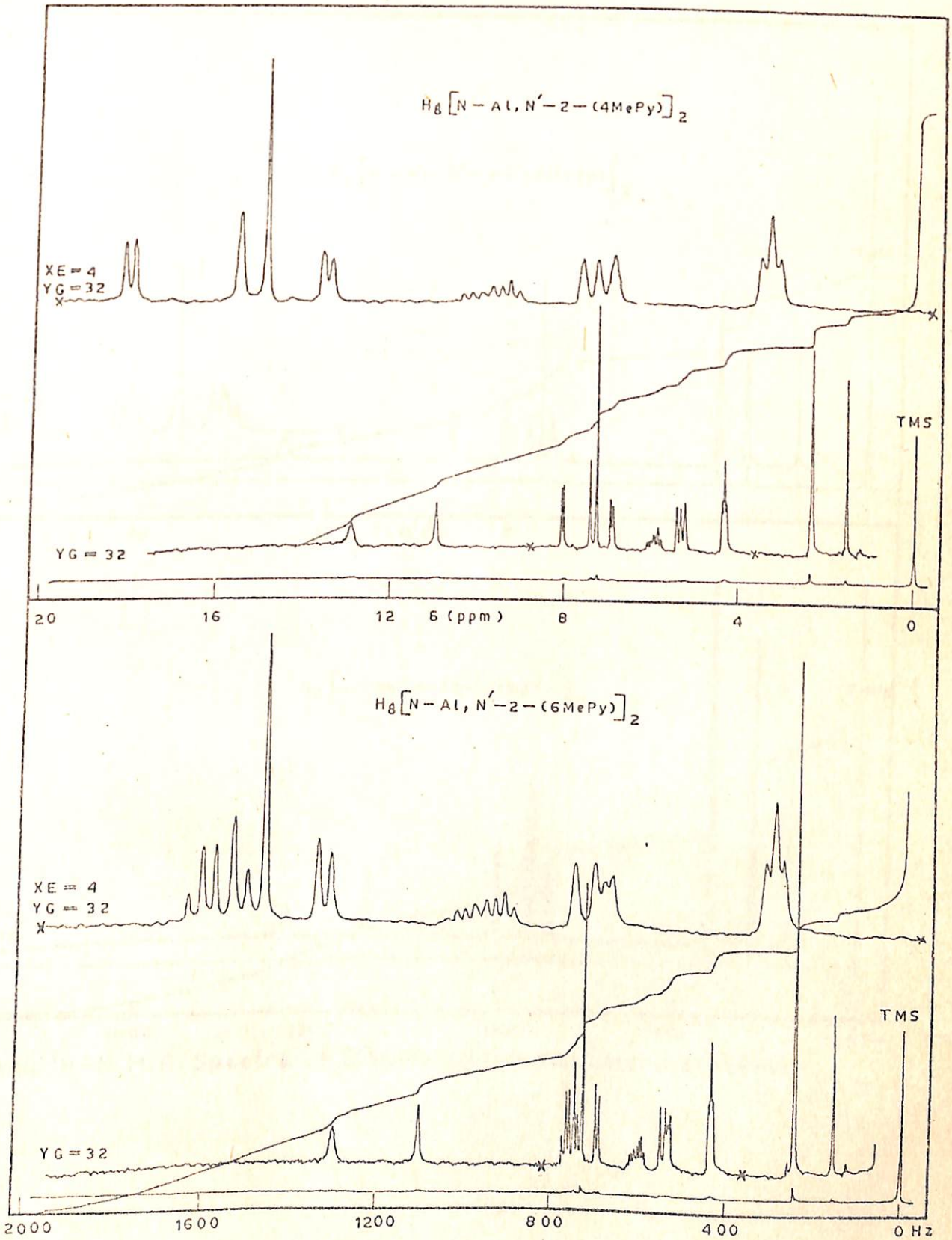


Fig. 3·13 ^1H-N.M.R. Spectra of Substituted thioureas metal complexes

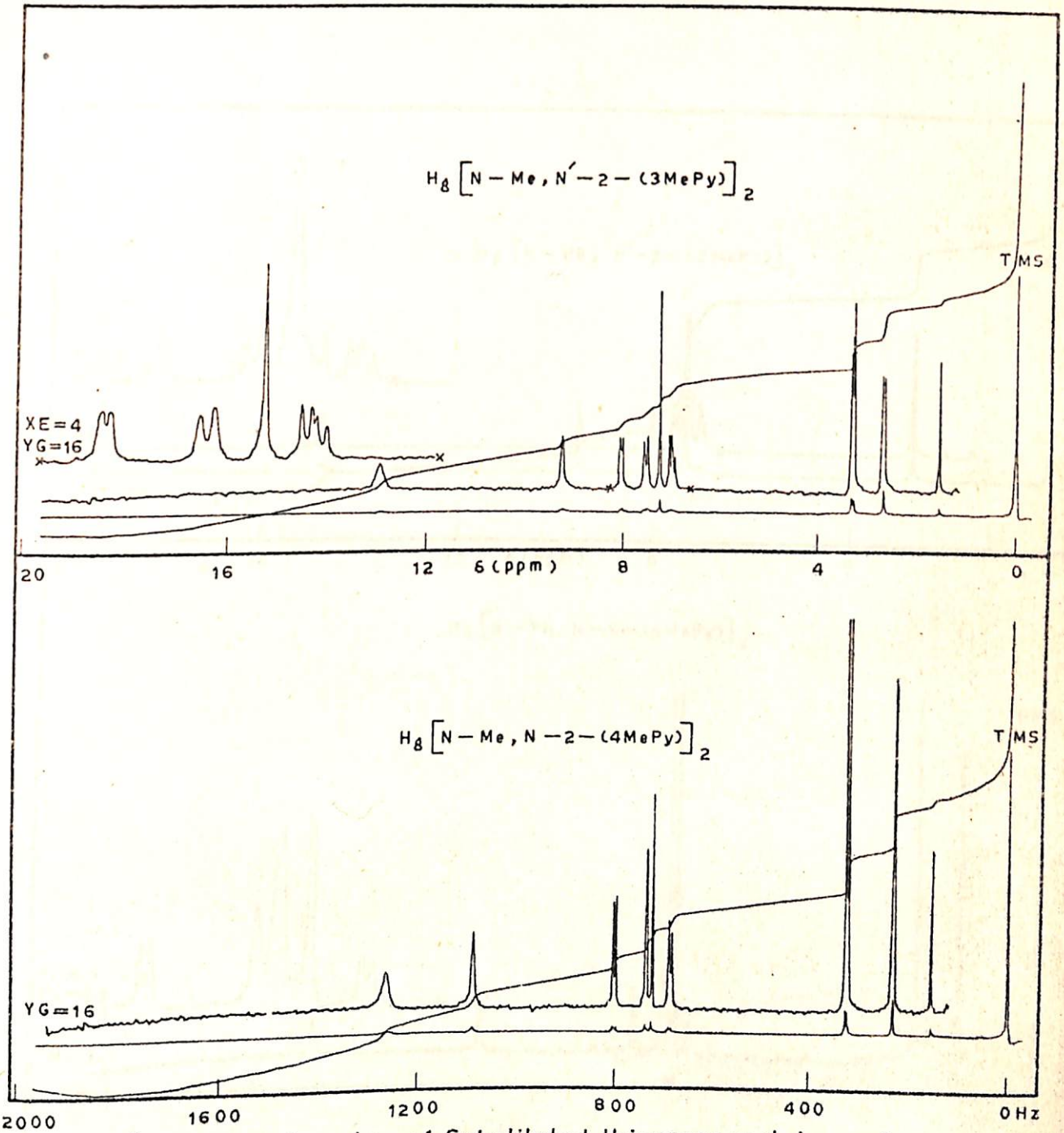


Fig. 3.14 ^1H-N.M.R. Spectra of Substituted thioureas metal complexes

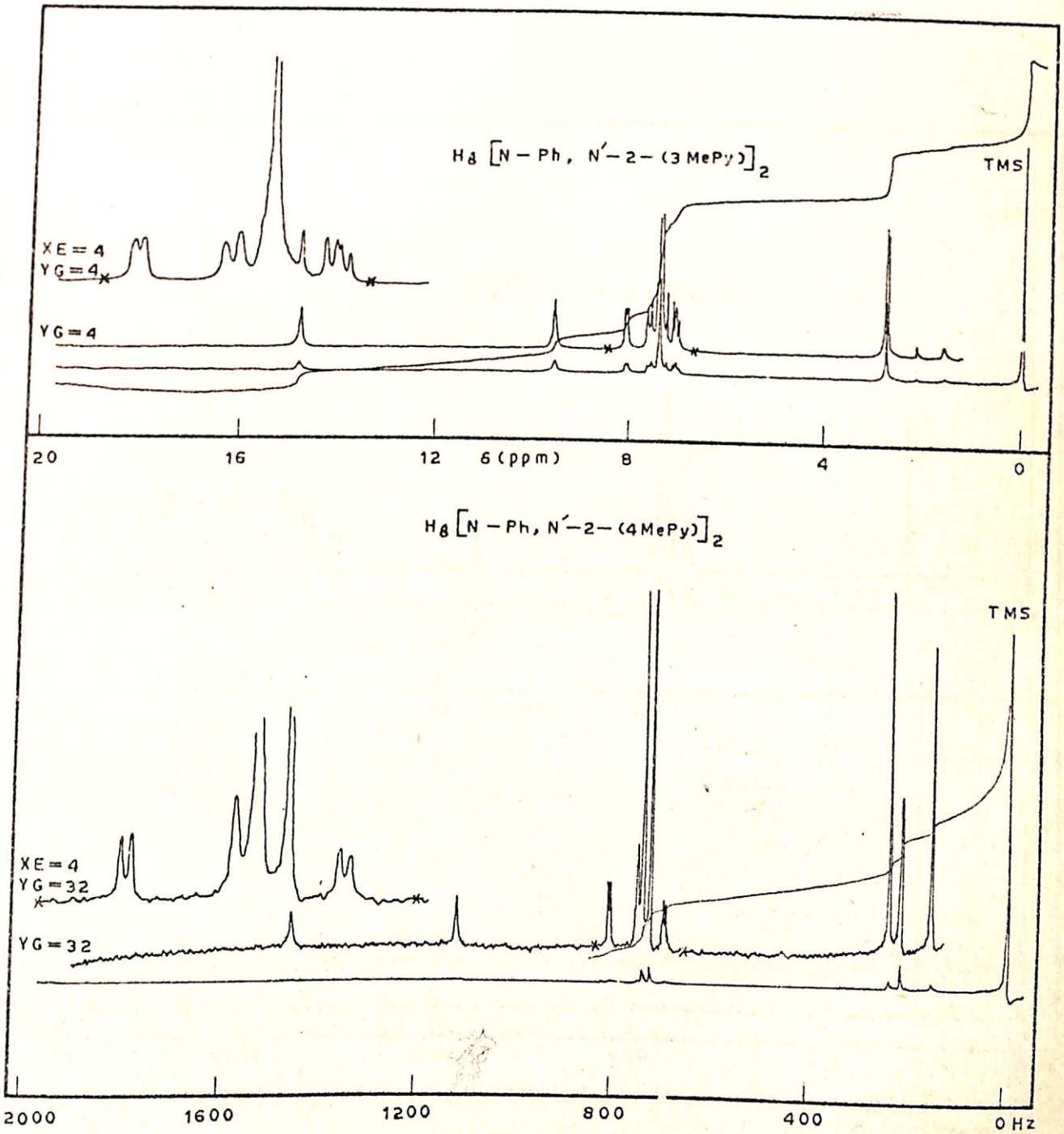


Fig. 3·15 ^{1}H–N.M.R. Spectra of Substituted thioureas metal complexes

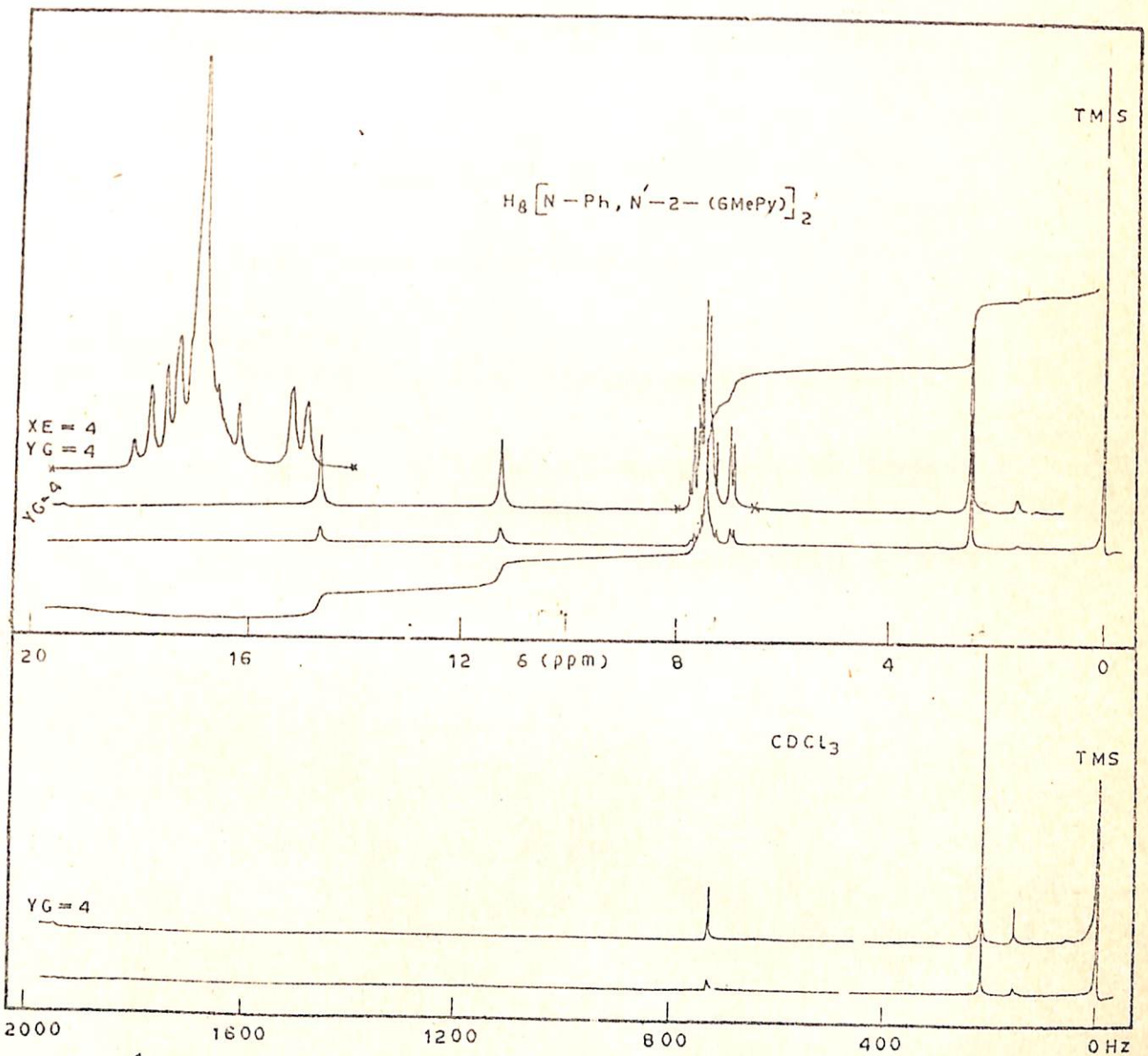


Fig. 3·16 ^1H-N.M.R. Spectra of Substituted thioureas metal complexes

CHAPTER IV

SPECTROPHOTOMETRIC STUDY ON THE COMPLEXES OF SUBSTITUTED THIOUREA WITH Cd(II), Ni(II), Co(II) AND Zn(II) TRANSITION METALS IN SOLUTION.

4.1 Introduction

The rapid advances and the varied character of the work being done in the realm of coordination chemistry has largely been responsible for the renaissance of inorganic chemistry. Expansion of this area of scientific endeavour has been fostered by world wide interest. The field of coordination chemistry has grown in a half century (begining with theories by Werner, 1920 and Sidgwick, 1927, on basic concepts) from a well defined and limited area of inorganic chemistry to permeating all types of human activity.

With the availability of physico-chemical methods and progressively reinnovated instruments for investigation, complex formation in the solution has now become a challenging area of research, leading to valuable contribution for the past three decades (Yoe and Jones, 1944; Moore and Anderson, 1945; Harvey and Manning, 1950; Mukherji and Dey, 1958; Banerji and Dey, 1961; Sinha and Agarwal, 1983).

Transition metal complexation with thiourea and substituted thiourea has been a topic of interest for the past several years. The work reported presents almost unambiguously the complexing behaviour of substituted thioureas as ligands.

Starting with findings of thiourea complexation through sulphur (Yamaguchi, 1958)

followed by reports on coordination through nitrogen (Rivest, 1962) and then proposals of coordination through nitrogen or sulphur depending upon the nature of transition metal and chemical environment (Lane and Mizushima, 1959), today we have a much clearer picture of the chelating behaviour of these thiourea derivatives (Kashyap, Banerji and Taneja, 1974).

Synthesis of various substituted thiourea derivatives with heterocyclic and other similar multidentate substituents has also led to an interesting investigation on their metal complexation behaviour (Prasad, 1973; Kashyap, 1974; Ali et al, 1983: Roy et al, 1980 and Dutta et al 1981).

4.2 Aim of the present studies

Most of the work reported, as discussed in previous section 4.1, done on metal complexation studies of substituted thiourea is based on solid state.

The complexing properties of these complexes and behaviour in solution has not attracted much attention, due to highly insoluble nature of these complexes.

Since the thiourea derivatives have now been discovered as having excellent biochemical properties (Chapter V), it has become important to find out their complexing nature in solution. This will also provide the much needed theoritical framework required for such work.

In the present work, spectrophotometric studies have been made on newly synthesised thiourea and bis thiourea derivatives for their metal complexation behaviour in alcoholic aqueous medium, in view of the solubility of the compounds. In the course of studies, composition, free energy of formation and stability constants of Cd(II), Co(II), Ni(II) and Zn(II) complexes were determined.

The thiourea derivative chosen, also had substituents, sulfonamide, salicylic acid and benzidine in their nucleus, all of these have been found of medicinal importance (Schroeder, 1955). This work will further augment the study of their application in medicine to understand the mechanism of action of these compounds.

4.3 Methodology

4.3.1 Complex formation studies

Studies on metal complexation were carried out using spectrophotometric methods in the UV-VIS range, using standard methods (Person, 1965; Foley and Anderson, 1949). The visible range of 400 to 800 nm is most suitable for studying coloured complexes. In the case of colourless complexes studies have been carried out in the UV range 220 - 400 nm using standard methods used by other workers (Sinha and Agarwal, 1983).

The ligands under investigation showed absorption maxima at 250 and 290 nm. (see Chapter II). Verification of Beer's law by these thiourea

derivatives was checked. The Beer's law was applicable in the concentration range 1.0×10^{-5} to 1.0×10^{-3}M, and all studies have been made in this concentration range.

The formation of the complexes was established by Person (1965) and Foley et al (1949) methods.

4.3.2 Composition of ligand - metal complexes

Numerous procedures are known to have been employed using absorption measurements for the calculation of the composition of the complexes viz: Job's method of continuous variation (Job, 1924 and Vosburgh et al, 1942), mole ratio method (Yoe and Jones, 1944), slope ratio method (Harvey and Manning, 1950) and limiting logarithmic method (Moore and Anderson, 1945).

The most widely used method is that of limiting logarithmic, which has been improved upon by Sinha and Agarwal (1983).

Principle as proposed by Moore et al (1945): From the equation for the equilibrium constant for the system

$$mA + nB \rightleftharpoons A_m B_n$$

one may obtain

$$\log \left[A_m B_n\right] = m \log \left[A\right] + n \log \left[B\right] - \log K$$

if $\left[A\right]$ kept constant and $\left[B\right]$ varied a plot of $\log \left[A_m B_n\right]$ verses $\log\left[B\right]$ will be a linear and

similarly for plot of log $[A_m B_n]$ verses log$[A]$ in constant $[A]$ conditions.

Now if plot of some quantity such as 'optical density' which is directly proportional to the $[A_m B_n]$ be plotted against log$[B]$, a straight line should be obtained, whose slope will be n. In the same manner we can find m.

Modification to logarithmic method: The basic principle used is the same as described above, where log of optical density of the set of solutions was plotted against log of concentration, one with constant metal ion and variable ligand concentration and other with a constant ligand and variable metal ion concentration.

But to get exactly linear plot, instead of limiting cases as is usually the case, application of least square method was done by regression analysis to get the calculated values for the most ideal case. (Sinha et al, 1983). Ratio of slopes of these straight line obtained gave the stoichiometry of complexes in terms of metal:ligand ratio.

4.3.3 Stability constant and free energy of the complexes

Stability constant: The stability constant of various metal ligand complexes studied in solution was determined from intercepts of linear plots obtained by method discussed in section 4.3.2.

From the two relations

$$\log \left[\text{Optical Density}\right] = n \log \left[L\right] + \text{Constant 1}$$

$$\log \left[\text{Optical Density}\right] = m \log \left[M\right] + \text{Constant 2}$$

Constant 1 and constant 2 could be determined as intercept of the straight line, since it is a case of

$$y = mx + c$$

where

$$\text{Constant 1} = m \log \left[M\right] - \log K \quad \text{and}$$

$$\text{Constant 2} = n \log \left[L\right] - \log K$$

Thus knowing the values of constant 1, constant 2, [M] and [L], one can always find out the log K, which is the stability constant of these complexes in solution.

The free energy of formation of the complex can be calculated from the expression

$$-\Delta G^{\circ} = RT \text{ Ln } K$$

where

ΔG° = free energy of formation
R = gas constant
K = stability constant
T = absolute temperature

4.4 Experimental

4.4.1 Material

Spectrophotometric studies were carried out on CARY-17D digital spectrophotometer and Hitachi spectrophotometer (Model-139) using 0.5 cm matched quartz cuvettes.

Metal chlorides of A.R. grade of bivalent cadmium, nickel, cobalt and zinc was prepared in A.R. ethanol and triple distilled water (1:1) solvent.

All the observations were carried out in a thermostatically controlled air-conditioned laboratory, maintained at 20 $\pm$ 2°C.

4.4.2 Observation

In all eleven thiourea derivatives listed earlier in Chapter II (section 2.2) were studied.

Samples of substituted thioureas and metal chlorides solutions in a mixture within range of 5 x 10^{-5}M to 0.5 x 10^{-5}M concentrations were studied. As described in the method earlier (section 4.3.2), the ligand concentration was kept constant at 5 x 10^{-5}M with varying concentration of metal chlorides once, and next, the reverse was done.

The shift in peaks as well as absorbance were scanned and recorded for the range 230 nm to 340 nm. The absorbance at λ_{max} for different concentrations were observed and used in the

logarithmic method (as discussed in section 4.3.2) to get the linear plots, which have been detailed out in figs. 4.1 to 4.15.

Regression by least square method was carried out with the help of computer (see Appendix B for listing of program).

The ratio of slopes, which represent the metal : ligand ratio and the values of stability constant (log K) and free energy of formation ($-\Delta G^{\circ}$) were calculated by method discussed earlier (section 4.3) and these have been detailed out in tables 4.1 to 4.4.

4.5 Result and Discussion

The formation of complexes was established on the basis of shifts in the absorption maximas of ligands. The bands of the ligand at 250, 300 and 320 nm in different thiourea derivatives shifted to the lower wavelength gradually on increasing the addition of ligands (i.e. thiourea derivatives) to the fixed concentrations of the metal ions resulting in large increase in absorbance, alongwith the shifts in the λ_{max}. In another set of experiments varying amounts of metal ion are added to a fixed amount of ligand where a decrease in the absorbance is observed figs. 4.1 to 4.15.

There was no absorbance shown by metal ion solution at the concentrations used.

The shift of ± 5 to ± 10 nm was observed in the region of λ_{max} of the ligand by the addition of 0.01 mM of ligand to the metal ions solution or by 0.01 mM of the metal ions to the ligand solution.

The appearance of a new band by complexation of N-methyl, N'-(acetamido phenyl) thiourea with Co, Ni and Cd, replacing minor shoulder at 270 nm further confirm the complex formation.

Similarly a gradual disappearance of bands shown by ligands by complexation was observed, viz: 270 nm and 320 nm band of N-phenyl, N'-ortho hydroxy benzene keto) thiourea POKT . This also gives a confirmed evidence of complex formation. (Sinha et al, 1983)

The appearance of an isobestic point, which indicates more than one type of complexes in equilibria (Griffiths and Symons, 1960), was also observed in a number of cases. (figs. 4.1 to 4.15).

The stoichiometric composition of these complexes showed either 1:1 or 1:2 metal : ligand ratio. In a large majority of cases cobalt showed complexing tendencies similar to nickel and the same was observed in case of zinc and cadmium. This is in agreement with the chemistry of these metals (Cotton and Wilkinson, 1976).

The stability constant (log K) values and free energy of formation ($-\Delta G^{o}$) data were consistent with the findings of other workers

(Sinha et al, 1983), which reveals that the stability constant and free energy of formation increases with the increase in the stoichiometry (Tables 4.1 to 4.4). This has got thermodynamical basis (Kuriacose and Rajaram, 1972), which predicts greater $-\Delta G^{\circ}$ values by increase in number of bond formation.

No definite conclusion regarding exact coordination site and structure of complexes could be established as these call for a more extensive study of the complexation, which is not the purpose of these studies.

The results obtained can however be channelised to a new field in area of complexing behaviour of thiourea derivatives in solution, which has considerable biological potential and far reaching implications.

Table 4.1 Metal Complex Formation Data for di Phenyl bis (Thiourea) Derivatives.

Derivative	Metal	Composition ratio(M:L)	log K	$-\Delta G^{\circ}$ (Kcal mol^{-1})
DBAT	Co	1:2	14.8	19.7
	Ni	1:2	13.4	17.8
	Zn	1:1	10.1	13.4
	Cd	1:1	9.2	12.2
DBMT	Co	1:2	12.6	16.8
	Ni	1:2	11.5	15.3
	Zn	1:1	9.6	12.8
	Cd	1:1	9:1	12.1
DBPT	Co	1:2	11.6	15.4
	Ni	1:1	10.9	14.5
	Zn	1:1	8.7	11.6
	Cd	1:2	11.3	15.0

Table 4.2 Metal Complex Formation Data for N'-(ortho-hydroxy benzene keto) Thiourea Derivatives.

Derivative	Metal	Composition ratio(M:L)	log K	$-\Delta G^{\circ}$ (Kcal mol^{-1})
AOKT	Co	1:2	10.6	14.1
	Ni	1:2	10.7	14.2
	Zn	1:2	11.7	15.6
	Cd	1:1	8.3	11.0
MOKT	Co	1:2	11.1	14.8
	Ni	1:2	11.8	15.7
	Zn	1:1	3.7	4.9
	Cd	1:2	12.1	16.1
POKT	Co	1:2	14.6	19.4
	Ni	1:2	16.7	22.3
	Zn	1:2	11.9	15.8
	Cd	1:1	10.3	13.7

Table 4.3 Metal Complex Formation Data for p-sulfa benzene bis (Thiourea) Derivatives.

Derivative	Metal	Composition ratio(M:L)	log K	$-\Delta G^{\circ}$ (Kcal mol^{-1})
SBAT	Co	1:1	7.8	10.4
	Ni	1:1	7.5	10.0
	Zn	1:1	5.8	7.7
	Cd	1:1	4.6	6.1
SBMT	Co	1:1	9.3	12.4
	Ni	1:1	8.4	11.2
	Zn	1:2	11.5	15.3
	Cd	1:2	12.8	17.0
SBPT	Co	1:1	7.7	10.2
	Ni	1:1	10.0	13.3
	Zn	1:2	15.9	21.2
	Cd	1:2	13.5	18.0

Table 4.4 Metal Complex Formation Data for N'-(acetamido phenyl) Thiourea Derivatives.

Derivative	Metal	Composition ratio(M:L)	log K	$-\Delta G^{\circ}$ (Kcal mol^{-1})
MAPT	Co	1:2	13.9	18.5
	Ni	1:1	10.6	14.1
	Zn	1:2	11.4	15.2
	Cd	1:2	14.3	19.0
PAPT	Co	1:1	7.5	10.0
	Ni	1:1	8.8	11.7
	Zn	1:1	8.0	10.6
	Cd	1:1	10.5	14.0

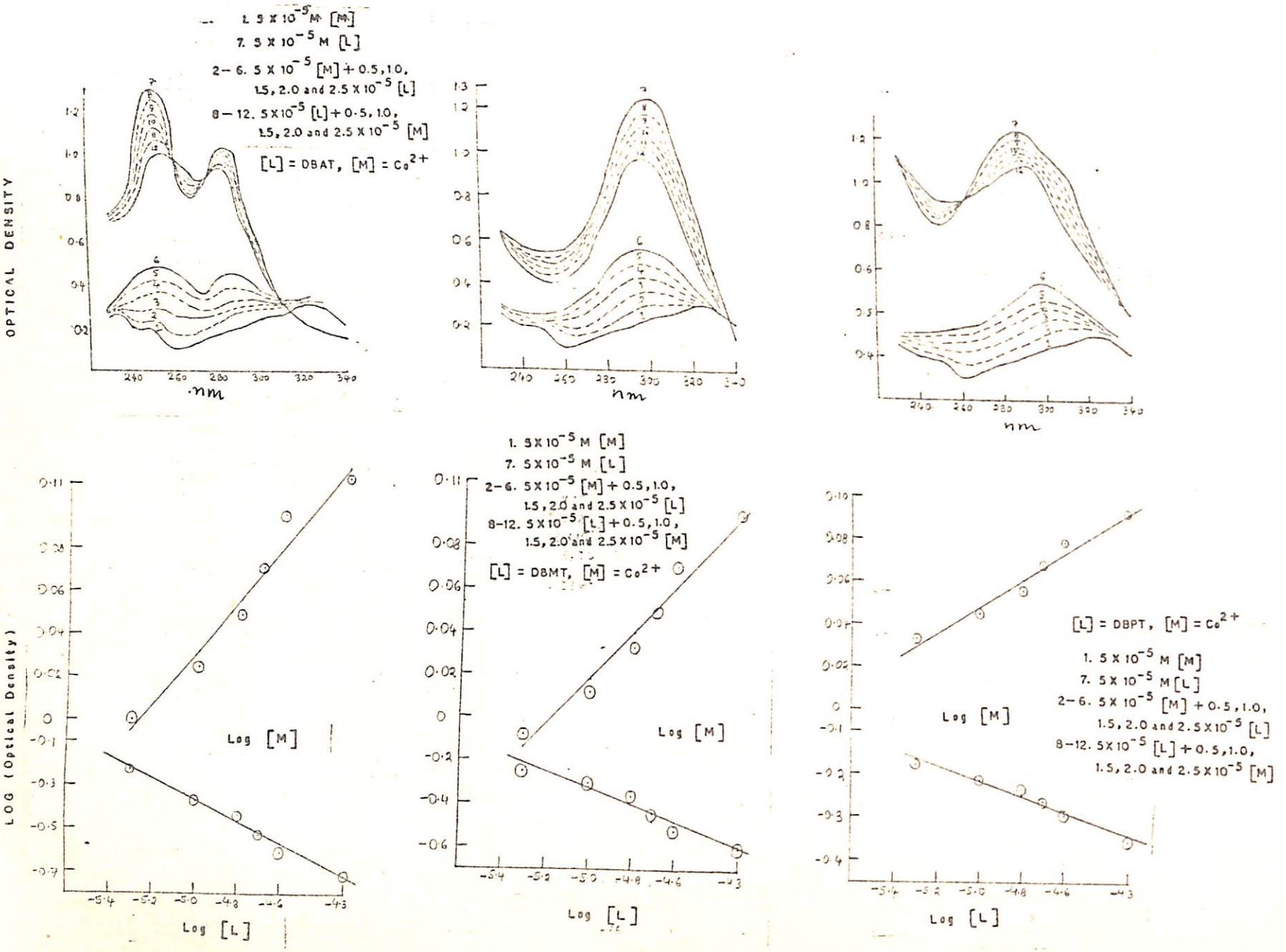


Fig. 4.1 Metal Complexation Studies of thiourea derivatives

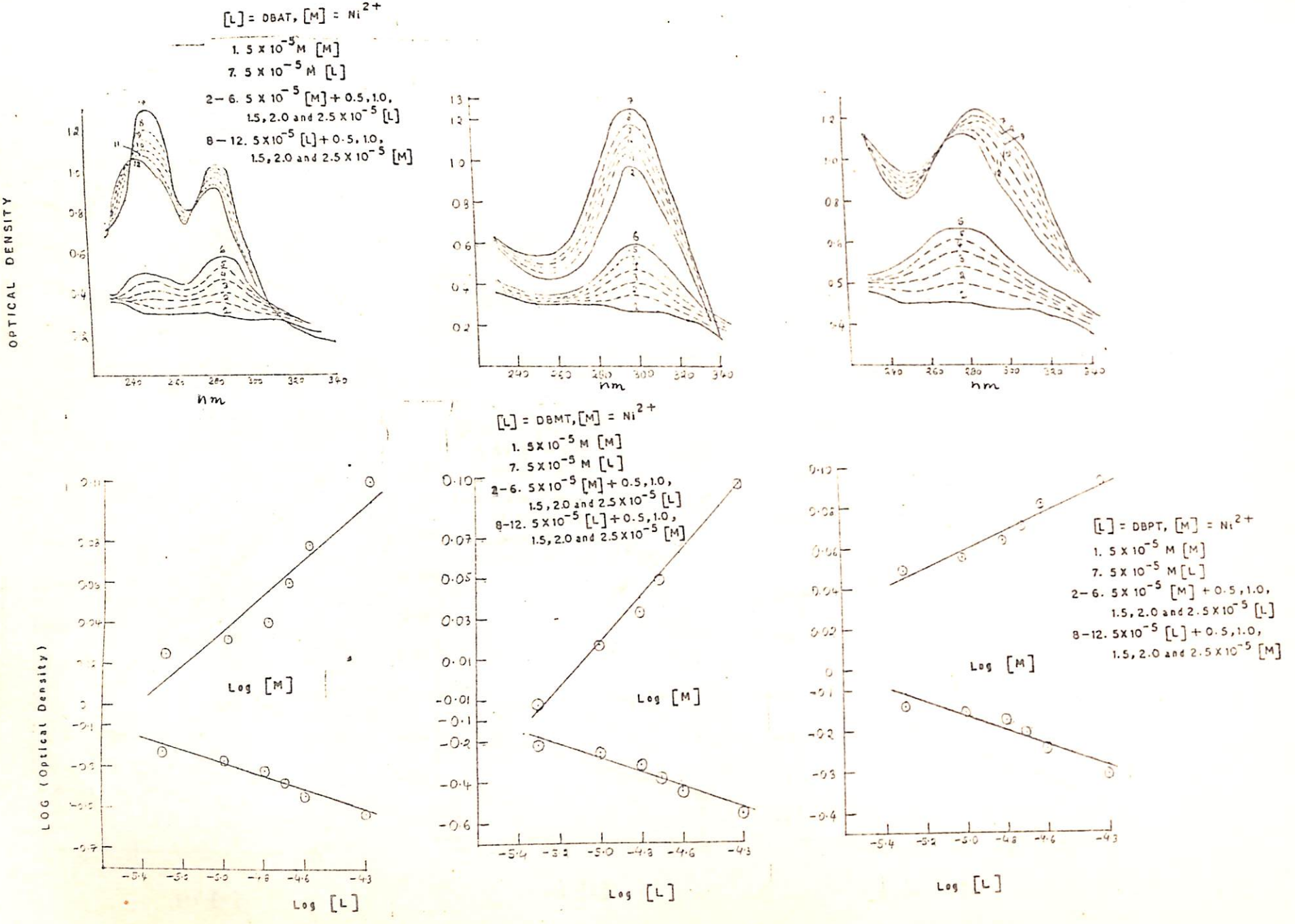


Fig. 4.2 Metal Complexation Studies of thiourea derivatives

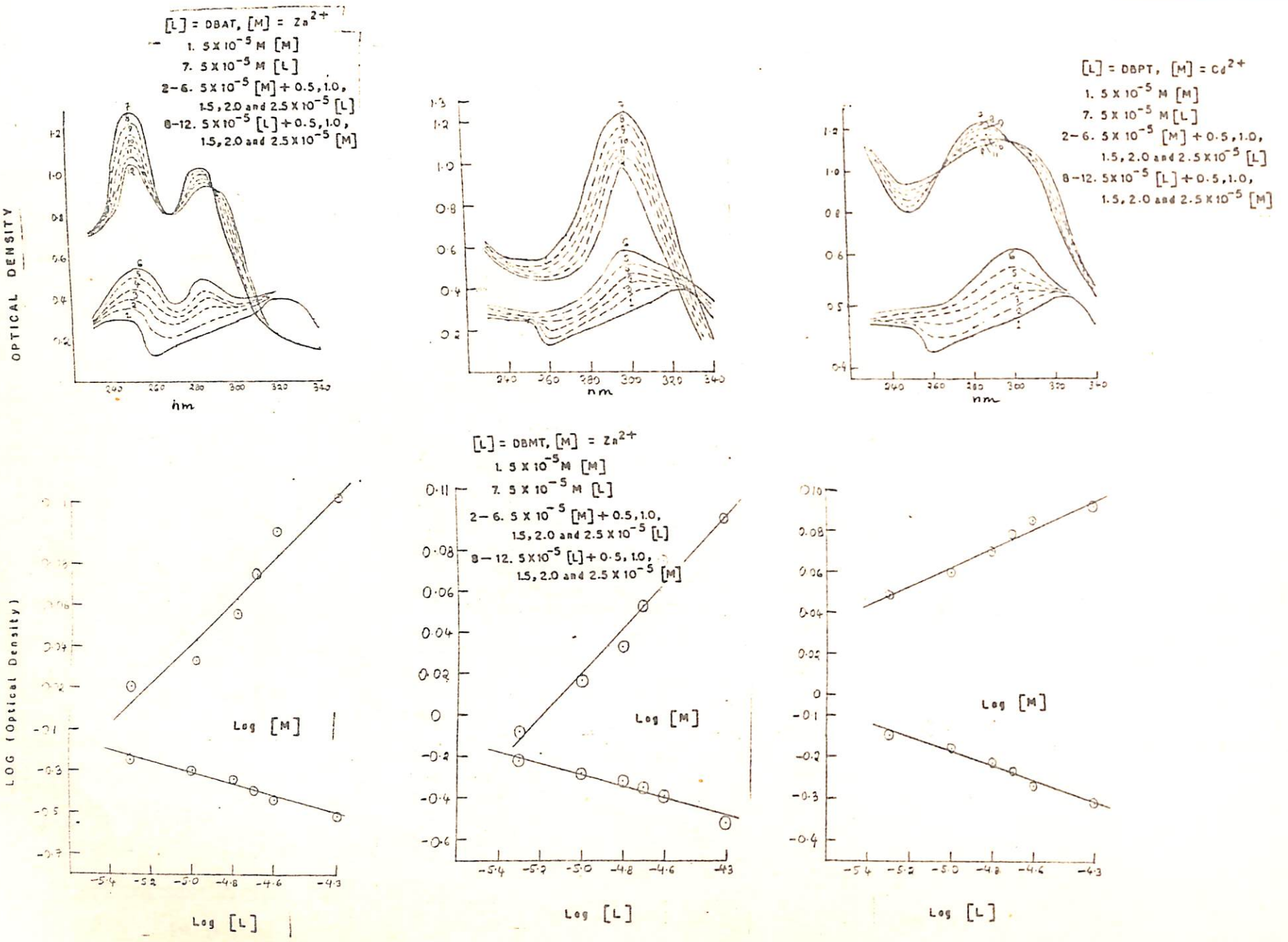


Fig 4.3 Metal Complexation Studies of thiourea derivatives

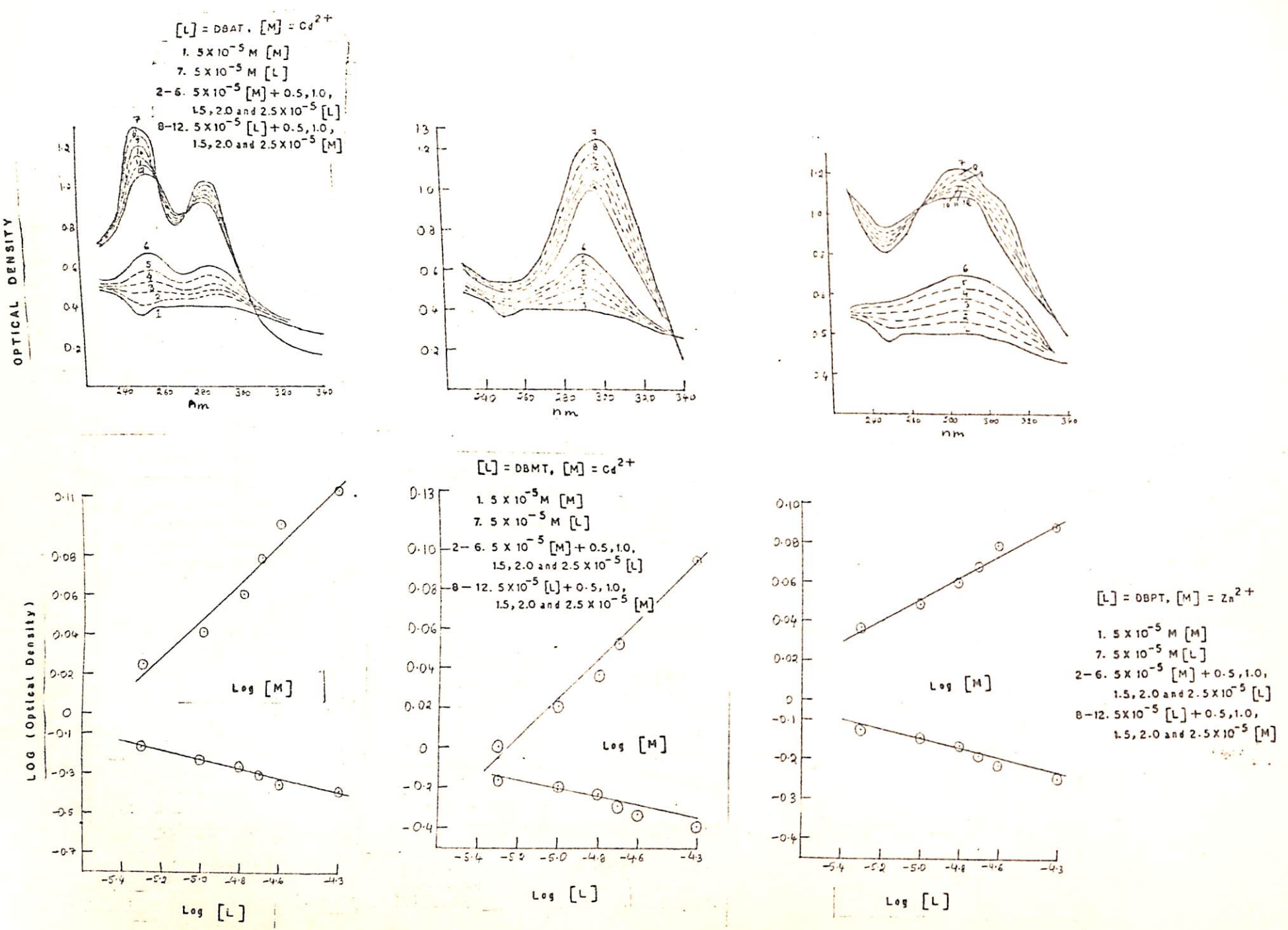


Fig. 4.4 Metal Complexation Studies of thiourea derivatives

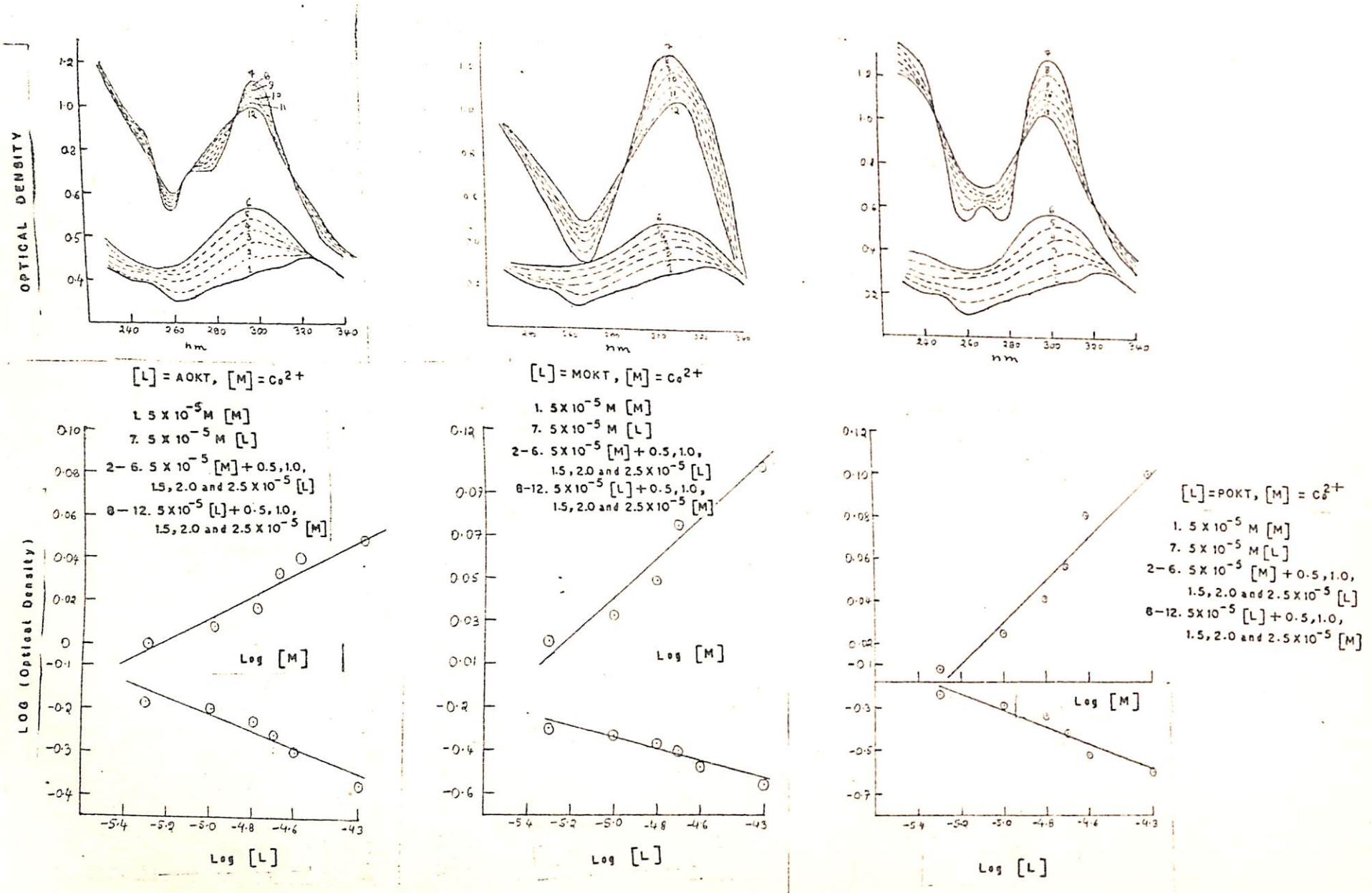


Fig. 4.5 Metal Complexation Studies of thiourea derivatives

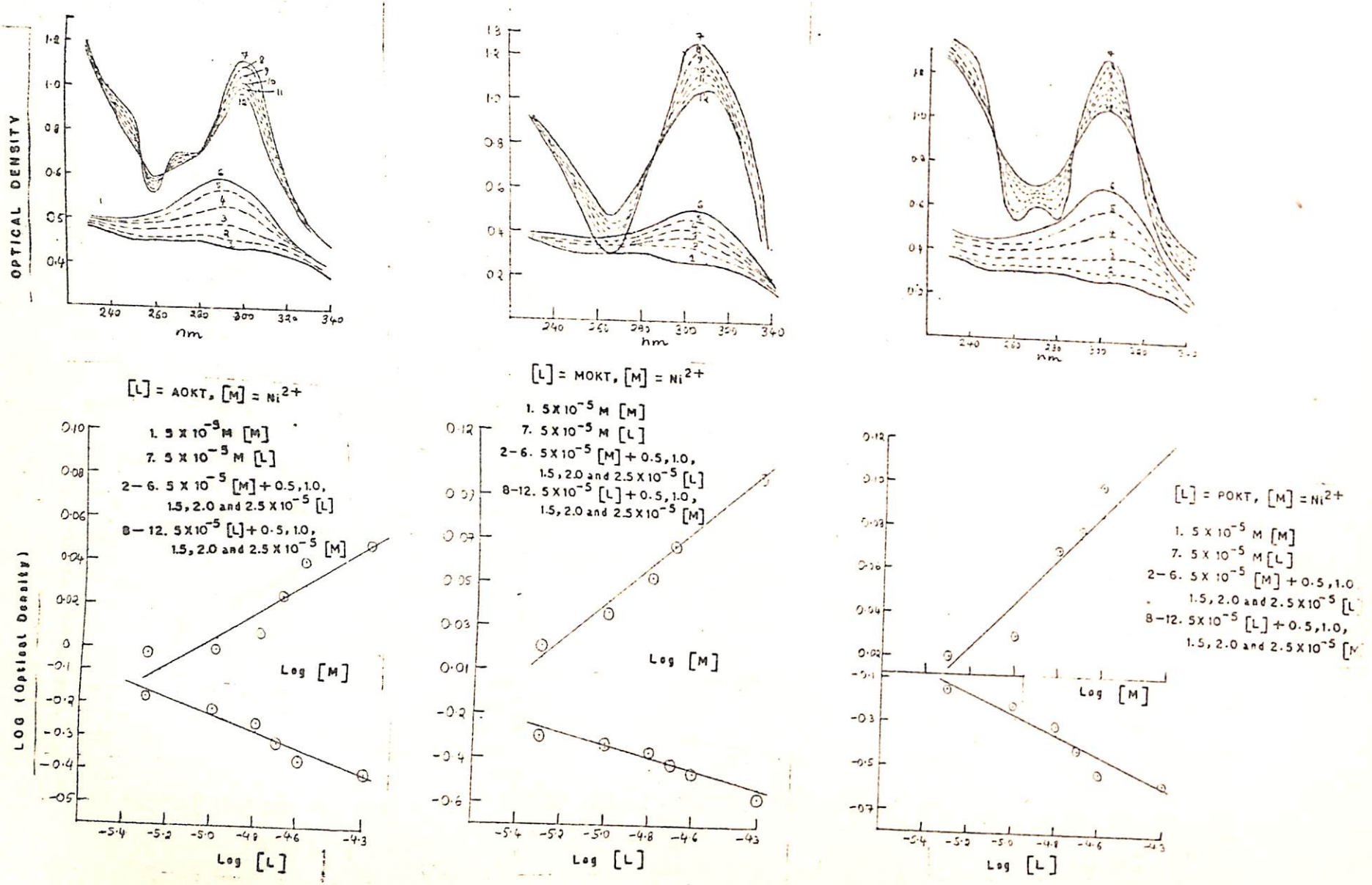


Fig.4.6 Metal Complexation Studies of thiourea derivatives

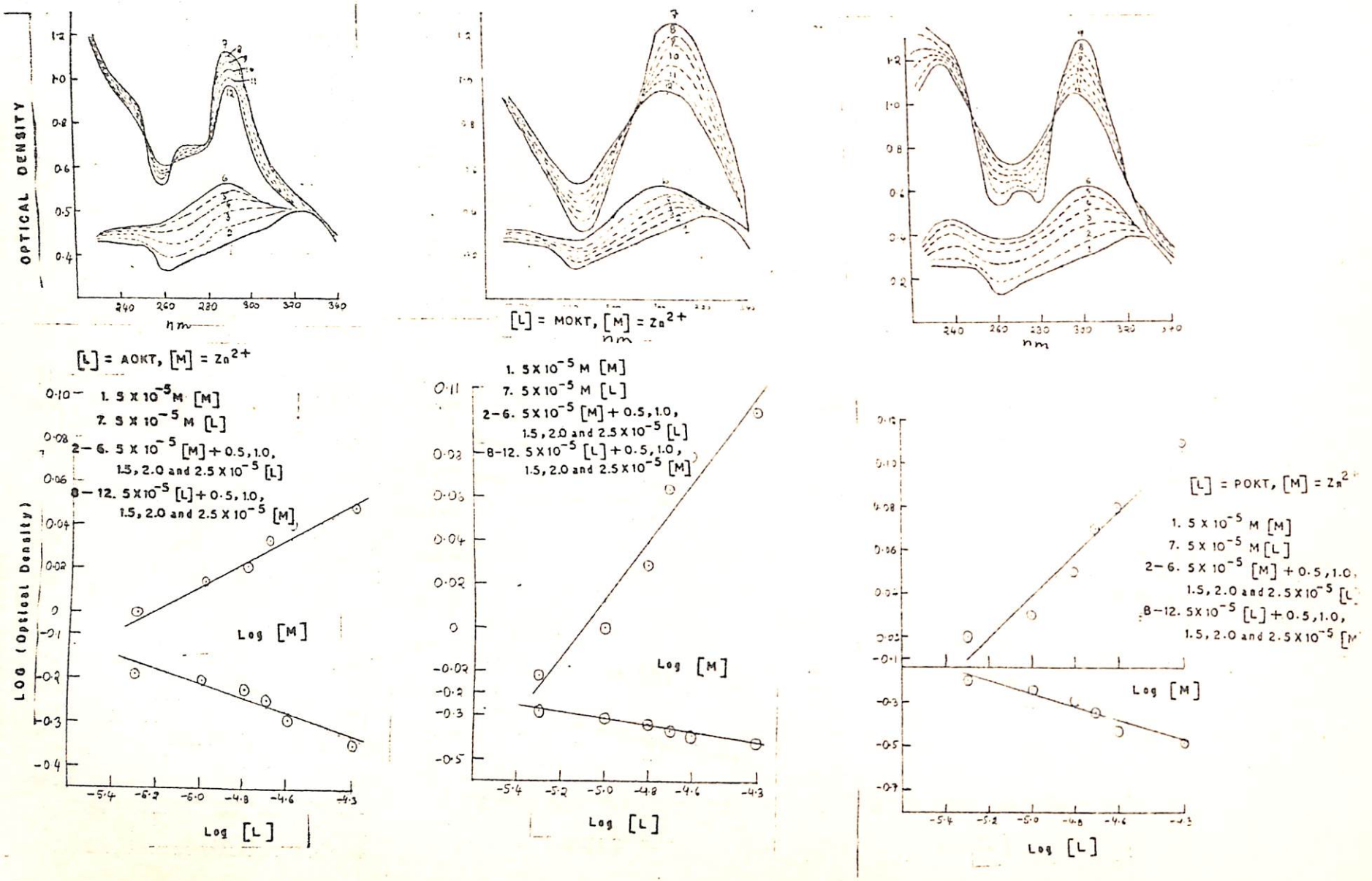


Fig. 4.7 Metal Complexation Studies of thiourea derivalives

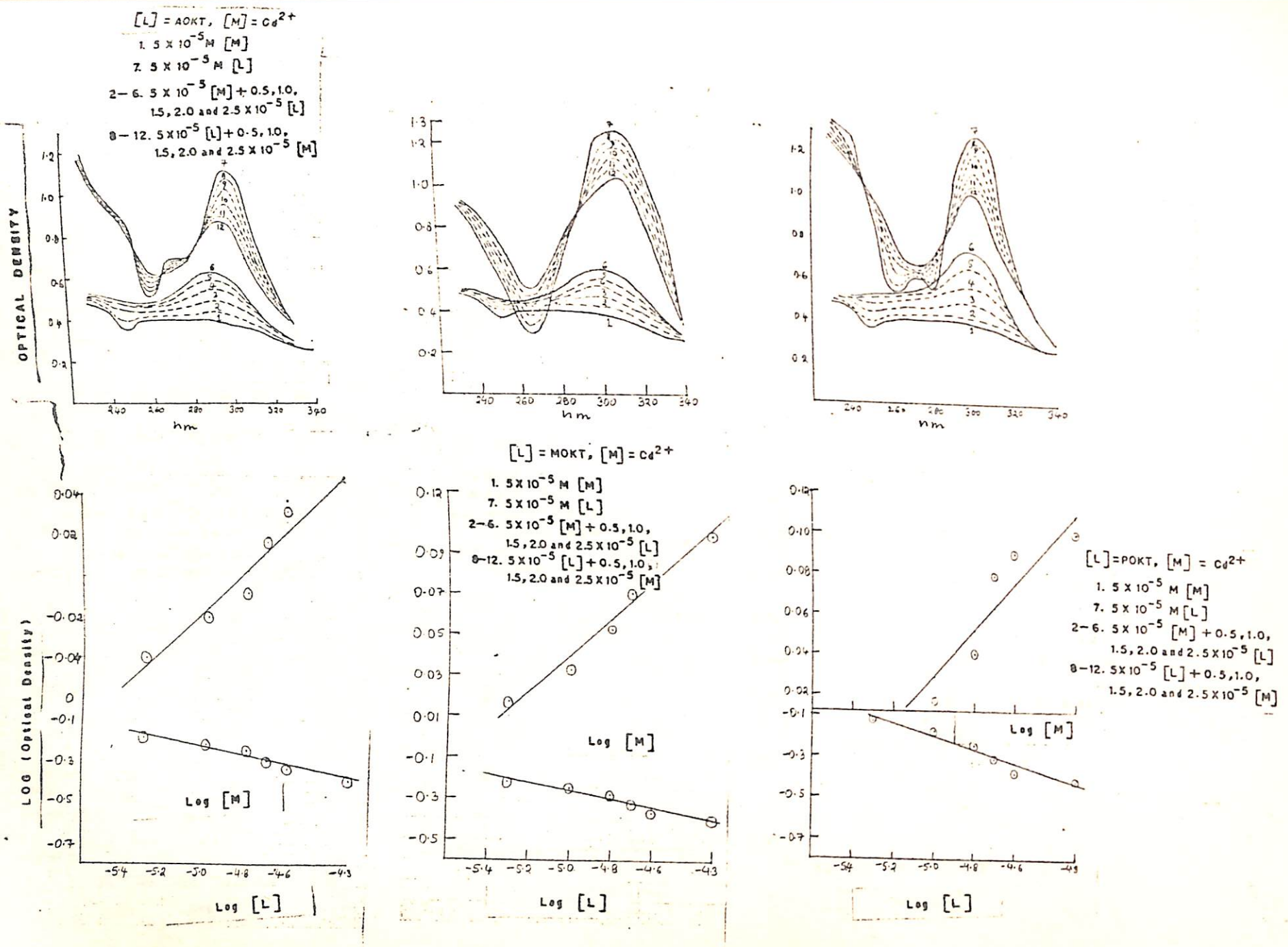


Fig. 4.8 Metal Complexation Studies of thiourea derivalives

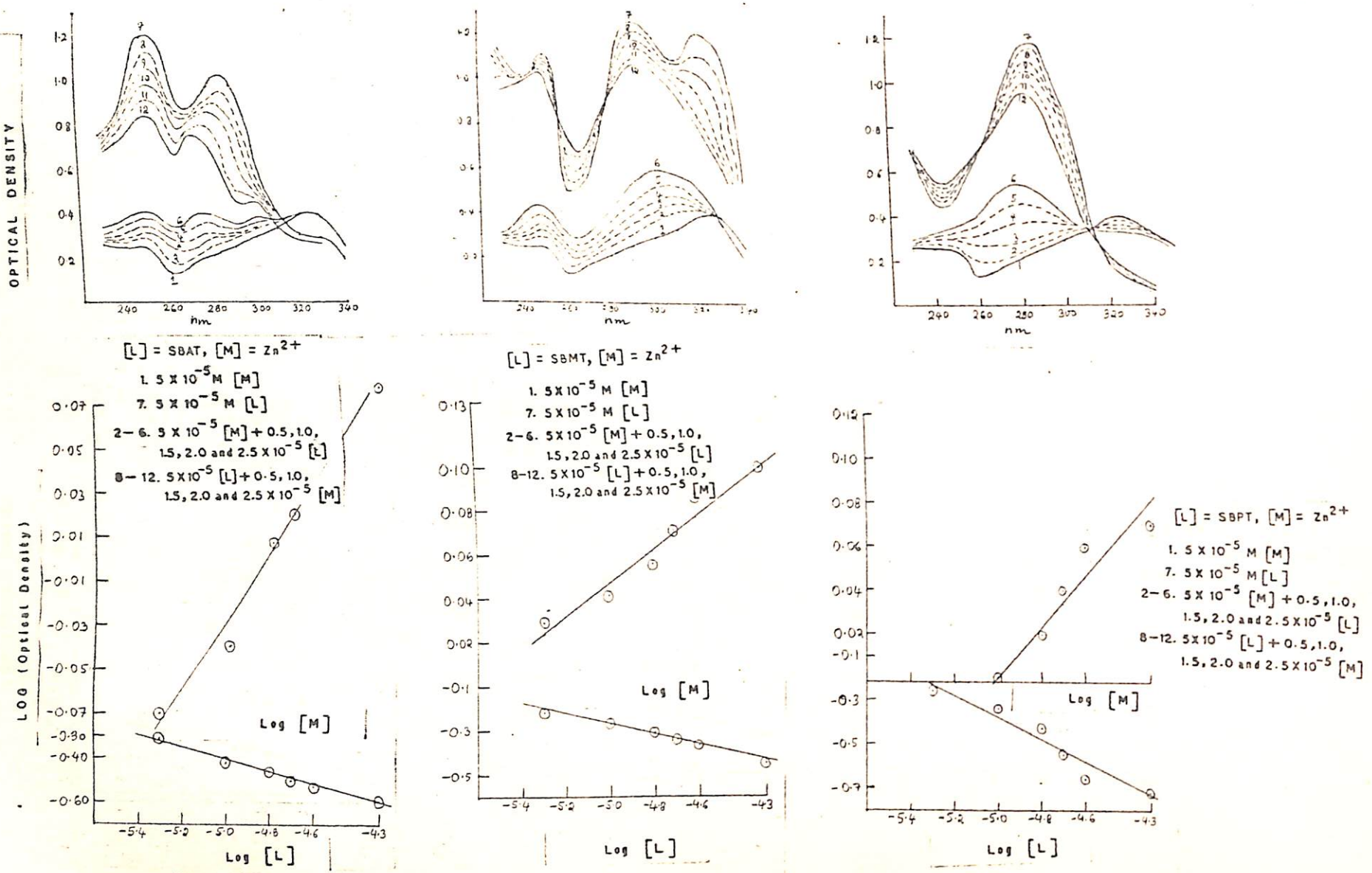


Fig.4.9 Metal Complexation Studies of thiourea derivalives

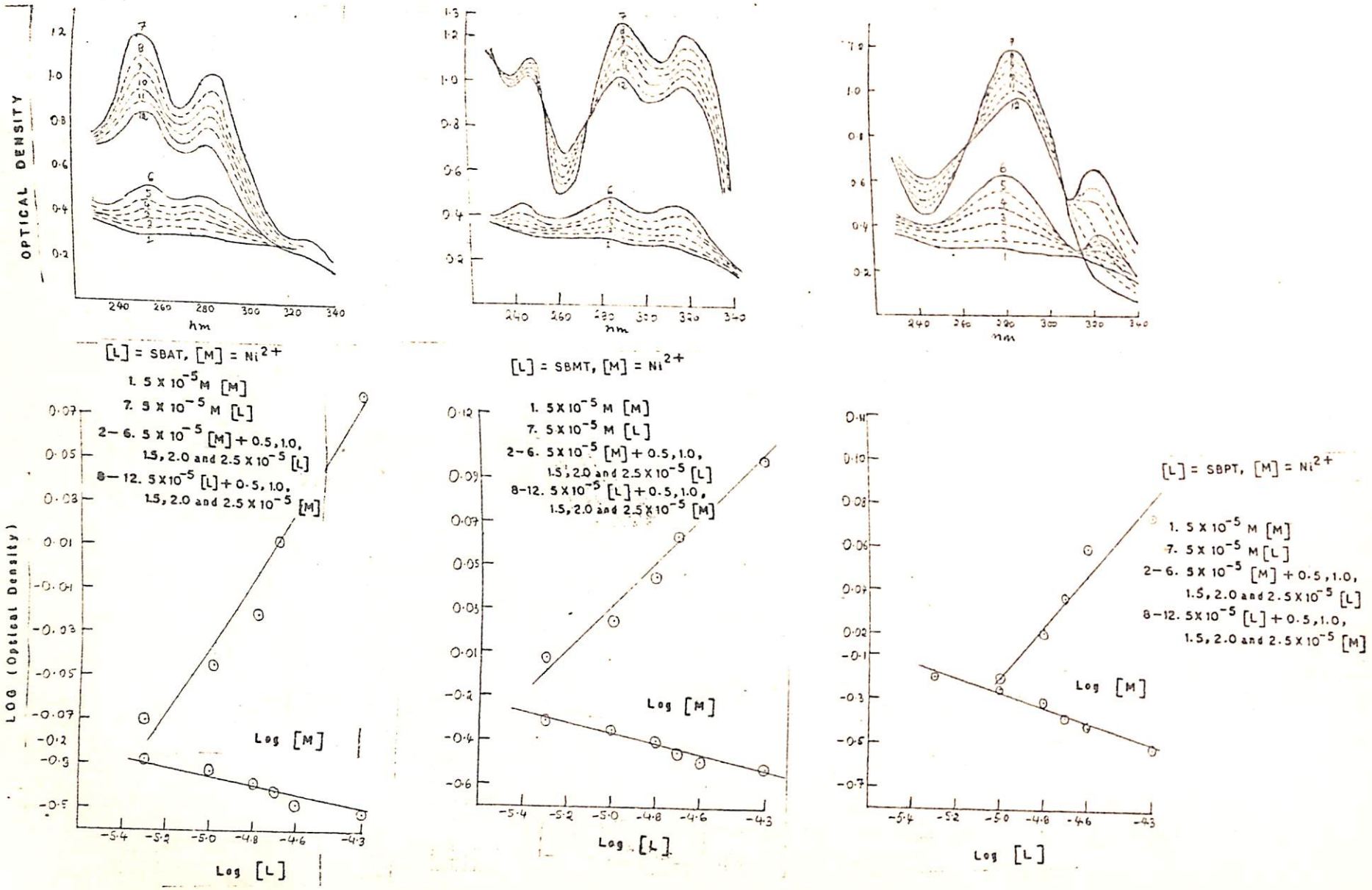


Fig 4.10 Metal Complexation Studies of thiourea derivatives

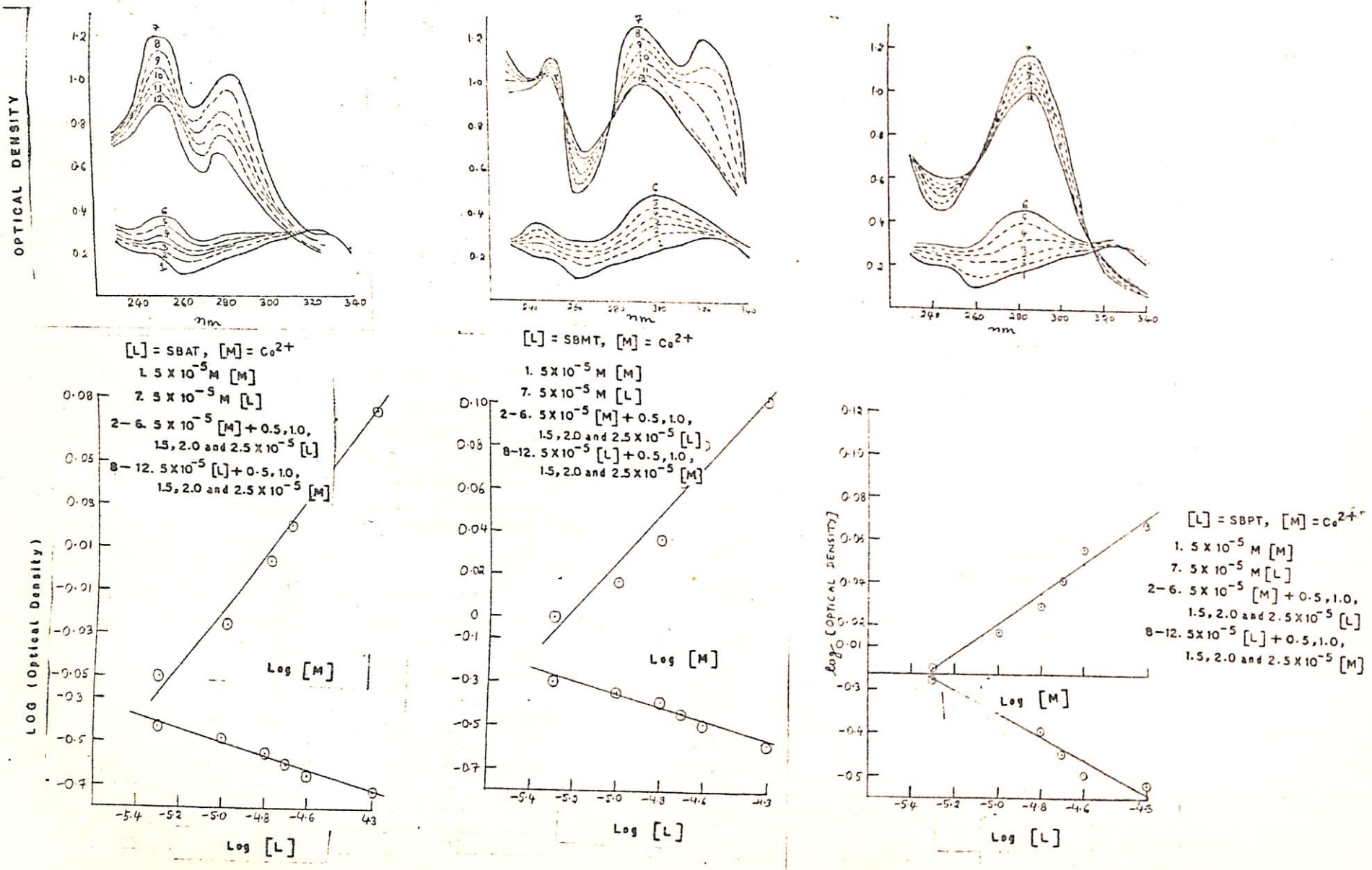


Fig. 4.11 Metal Complexation Studies of thiourea derivalives

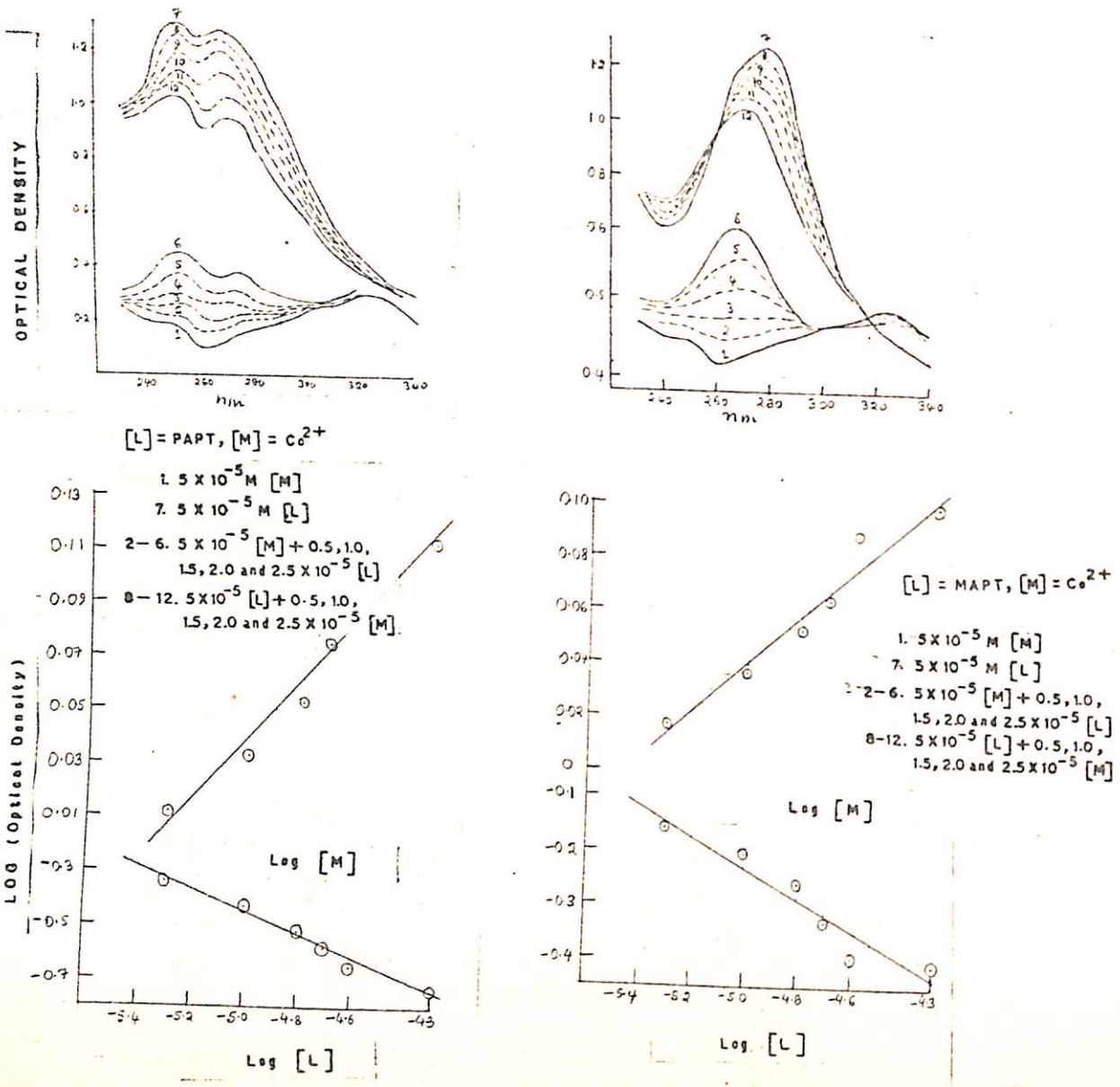


Fig. 4.12 Metal Complexation Studies of thiourea derivatives

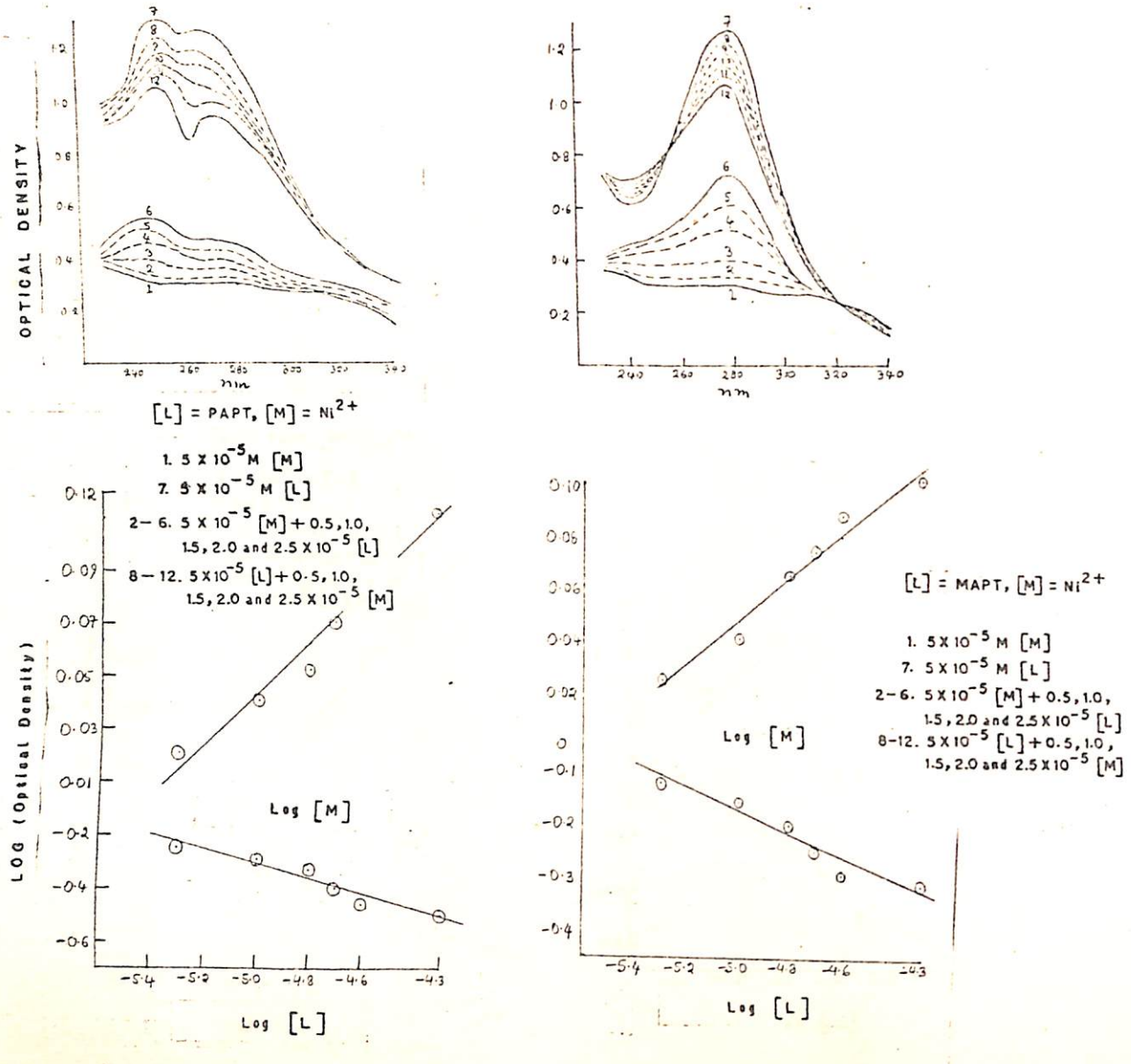


Fig.4.13 Metal Complexation Studies of thiourea derivalives

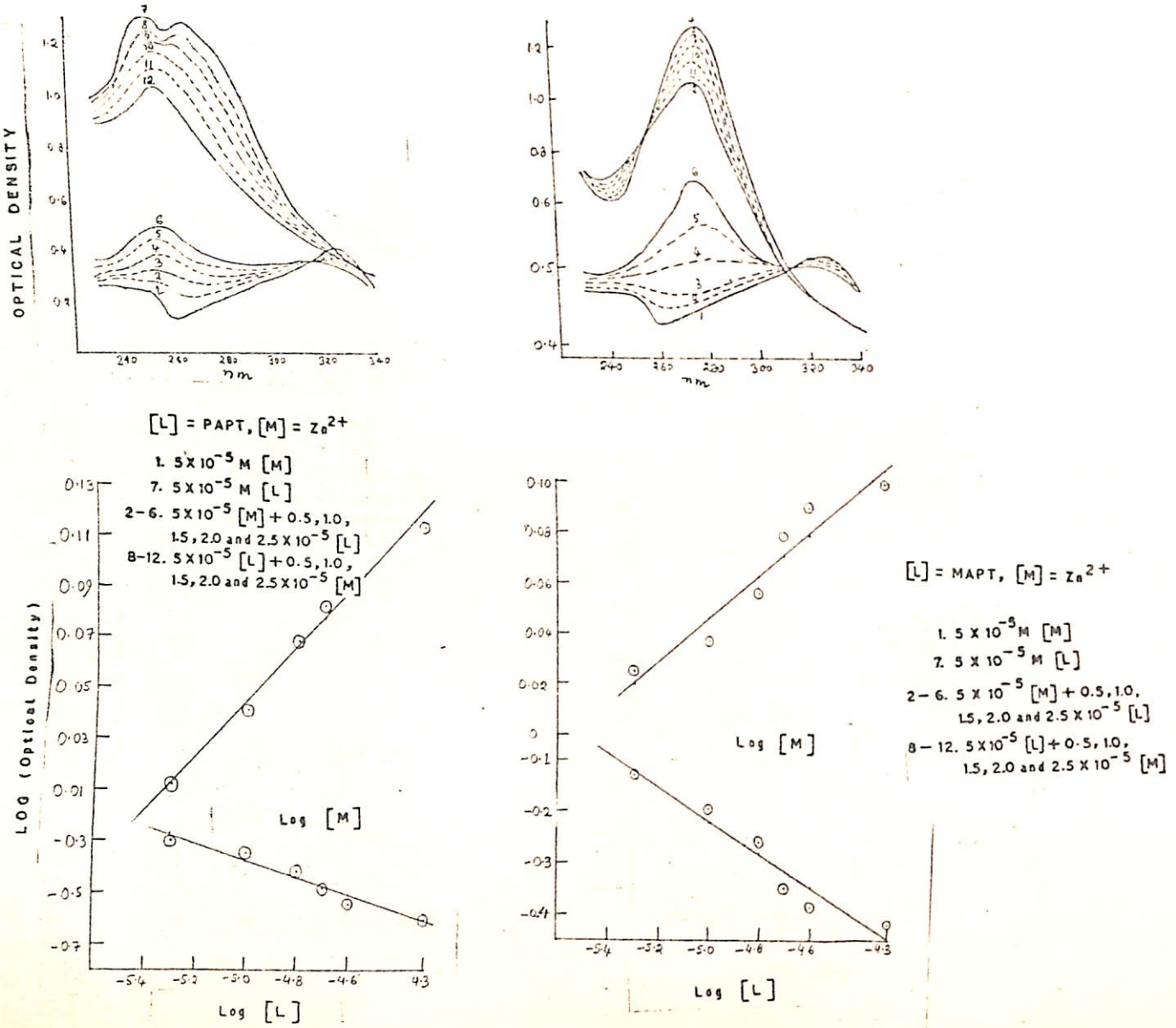


Fig. 4.14 Metal Complexation Studies of thiourea derivalives

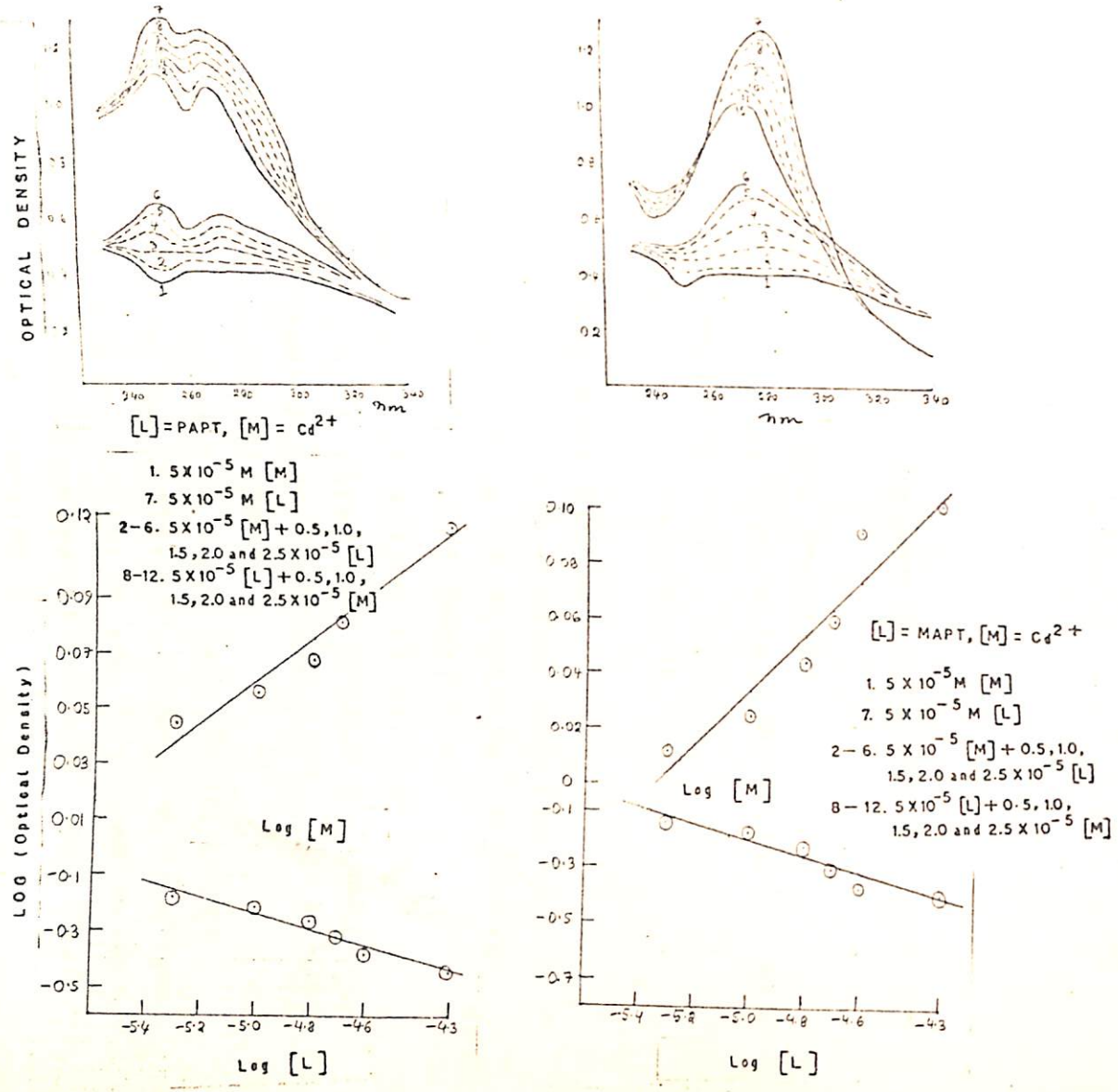


Fig. 4.15 Metal Complexation Studies of thiourea derivatives

CHAPTER V

AGROCHEMICAL STUDIES OF N,N' DISUBSTITUTED THIOUREAS

5.1 Introduction

5.2 Seed Treatment and Growth Regulatory Activity Studies

- 5.2.1 Definition and Theories
- 5.2.2 Experimental - Material, Methodology and Observations.
- 5.2.3 Results and Discussions.

5.3 Herbicidal Activity Studies

- 5.3.1 Definition of Herbicide and its Role
- 5.3.2 Different Type of Herbicidal Activity
- 5.3.3 Mode of Action of Herbicides
- 5.3.4 Mechanism of Action of Herbicides
- 5.3.5 Methods of Screening Herbicidal Activity
- 5.3.6 Representative Chemical Nuclei of Established Herbicides
- 5.3.7 Experimental - Material, Methodology
- 5.3.8 Testing the Efficacy of Agar Bed Method and Comparison with the Soil Bed Method
- 5.3.9 Activity Experiments for Pre- and Post Emergence Herbicide
- 5.3.10 Dose Response Curve Studies and LD_{50} Values
- 5.3.11 Observations
- 5.3.12 Activity Score
- 5.3.13 Selective Activity Index (S.A.I.)
- 5.3.14 Results and Discussion

5.4 Antimicrobial Activity Studies

5.4.1 Aim of Such Study

5.4.2 Experimental - Material, Methodology and Observations

5.4.3 Results and Discussion

5.1 Introduction

Thiourea and its derivatives have been found to be of immense importance in industrial uses viz in dyes, photographic films, elastomers, plastic and textiles (Schroeder, 1955). Their role in biological activity have also been extensively reported, as has been reviewed by Pandeya et al (1981). Diverse types of biological activities are associated with thioureas example, N,N'-di-(p-n-butoxyphenyl) thiourea (Wagner and Winkelmann, 1969) and butamelide (Galstukhova et al, 1972) are antitubercular agents, while substituted benzyl thioureas (Mackay et al, 1959) and bedionel (Patsch and Hoehne, 1967) are effective antibacterials. N-(2 hydroxy phenyl)-N'-benzyl (Shindarov et al, 1972) and N-(2-adamantyl) thioureas (Kreutzberger and Schroeders, 1973) show virustatic activity. Amathiozone (Diphenyl thiourea) (Crowther et al, 1948) and thiambutosine (Ellard, 1966) are given in place of sulphones as antimalarial drugs and for controlling Mycobacterium leprae. Thus we find the 'thiourea' group of compounds are coming up as very useful pharmaceutical agent.

Apart from these activities a new area of interest has emerged, in recent years in the agricultural application of thiourea and substituted thiourea derivatives.

Thiourea has been used for a long period for seed treatment to break the dormancy and enhancing the growth rate. (Joshi, Mishra and Gaur, 1978). But substituted thiourea derivatives have found application

as herbicidals at moderately higher concentration (Uppal, Saha and Banerji, 1983). The increasing number of patents (Damm et al, 1980; Fancher and Schor, 1982; Grohe and Paul, 1983) of such derivatives itself reveals their importance. At present only one thiourea derivative by the trade name of 'METHIURON' has been commercially marketted by Uniroyal (U.K.) and recommended by British Standards Institution. But more of the potent compounds remain to be established.

Extensive work has been reported in literature for the herbicidal nature of numerous thiourea derivatives (Vassilev et al, 1982b, 1980, 1969a, 1969b, 1969c; Pandey et al, 1979; Khalifa and Kadaus, 1979).

The present work is related to the agrochemical studies of N,N'disubstituted thiourea derivatives. It has been devided into three sub-sections: Seed treatment and Growth regulating activity, Herbicidal activity and Antimicrobial activity.

5.2 Seed treatment and Growth regulatory activity Studies

5.2.1 Definition and theories:

The seed treatment of various crop seeds is done by various chemicals, whenever it is required to break the dormancy and enhance the germination as well as growth activity. A survey of the literature revealed a list of such chemicals (Table 5.1). Thiourea has also got its place and have been shown to be used in more than sixty percent of such studies with various seeds, as detailed in table 5.2 (Choudhary and Chakrawar, 1981; Chohan and Dhillon, 1970).

Table 5.1 Various Chemical used in Seed Treatment Studies.

Compounds	Relative % of use*
Thiourea	60
Gibberellic acid	80
Etherel (2-chloro ethyl phosphoric acid	30
6-Benzyl adenine	30
Kinetin	40
NAA (Naphthalene acetic acid)	70
Potassium nitrate	60
Sulphuric acid	40
IAA (Indole ascorbic acid)	50
Boric acid	40

* Data presented from an analysis of the literature.

Table 5.2 Thiourea as a Growth Promotor.

Plants Seeds	% Activity*
Wild oat	20
Calosia argentea	33
Crotolaria tunecea	10
Atropa belladona	50
Medicago species	60
Datura innoxia	30
Dichanthius annulatum (Herbage grass)	40
Dioscorea rotundia poir (White yam)	40
Lettuce seeds	60
Cocklebus seeds	50
Rangpur lime	30
Cicer ariltinum	56
Soybean	60

* Data presented from an analysis of the literature.

Most of these chemicals viz: Gibberellins, Kinetins, Naphthalene acetic acid, Indole ascorbic acid, etc are the established growth regulators. There is hardly any physiological process from seed dormancy to senescence which is not affected by these chemicals (Leopold, 1971; Wright, 1967).

Hormone action is concentration dependent (Thimann, 1937; Leopold, 1955) has not only been verywell confirmed but it is also now universally accepted as one of the most important factors controlling the action of both the growth hormones and their synthetic analogues known as growth regulators. Such an activity was also revealed in our work on substituted thioureas (Uppal, 1984).

Dormancy in seeds is mainly due to rudimentary and physiologically immature embryos, mechanically resistant and impermeable seed coats and the presence of germination inhibition etc (Barton, 1965). It has also been postulated that dormancy is due to the accumulation of the products of anaerobiosis (Vegis, 1964). Seed dormancy is also attributed to the presence of inhibitors in one or more parts of the seed and this has been recently reviewed by Taylorfon and Hendricks(1977).

The work presented in this section deals with studies on hormonal activity of substituted thioureas.

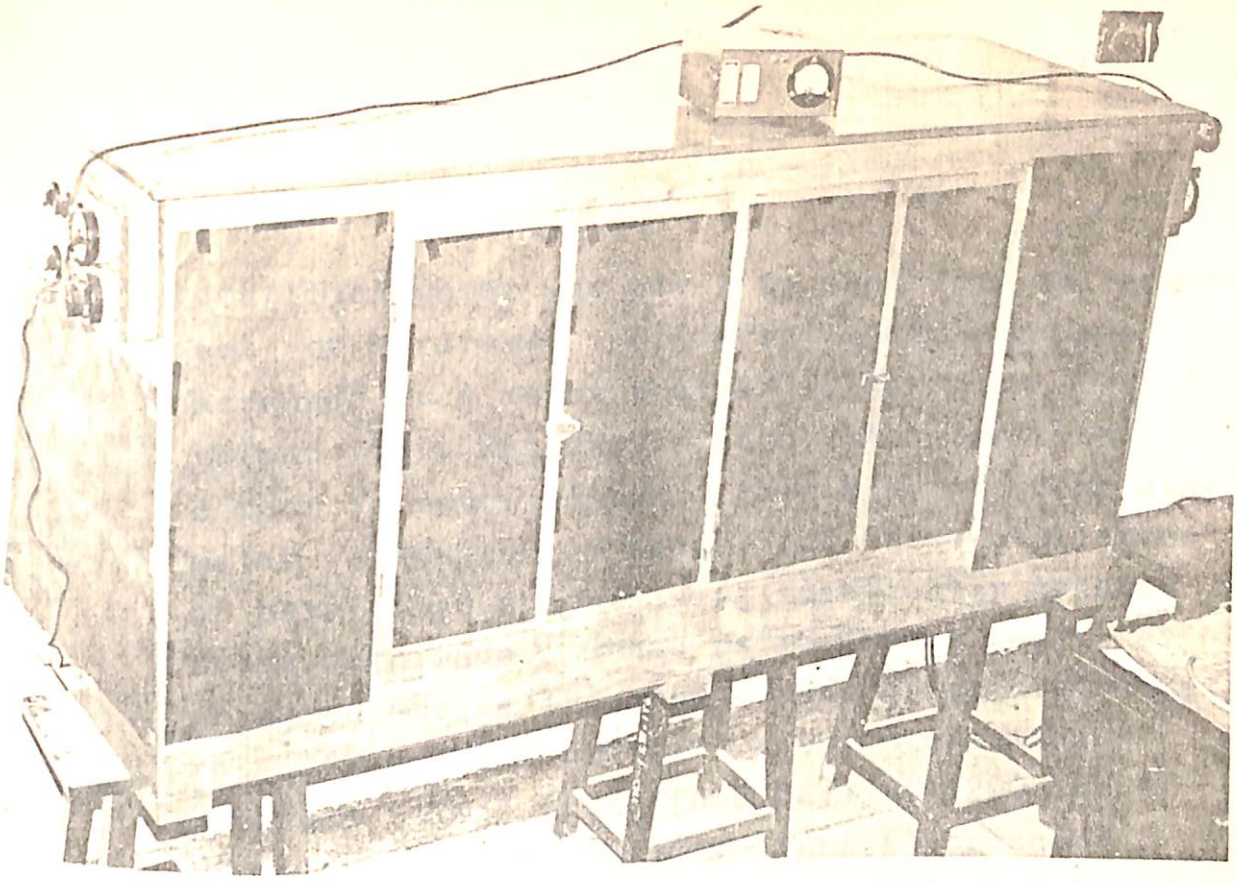
5.2.2 Experimental

Material: All the glassware used was of corning (Borosil Glass Works Ltd., Bombay), and caliberated according to Internationally accepted standards. Special care was taken to use only triple distilled water washed and sterilized petri dishes with sterilized cotton pads. The sterilization was carried out at 15 Lbs pressure and 160°C high temperature in gravity displacement autoclave (National Steel Equipment Co., Bombay).

A suitable growth chamber was fabricated, with controlled light, temperature and humidity conditions for simulating the ideal climatic conditions (fig. 5.1). All the weighings were done on semi-micro electrical balance (Sartorius, Germany) to ensure accuracy. Before using the thiourea derivative, recrystallization from A.R. ethanol solvent was carried out to obtain the maximum purity.

Identified seeds of Barley (Hordeum vulgare L.) of K-125 variety were obtained from National Seed Corporation, Pusa, New Delhi, for these studies.

Methodology: Solutions of different concentrations, 10, 100 and 500 ppm of substituted thiourea were prepared. Barley seeds were soaked in distilled water before treatment for a period of 24 hours, to prepare them for germination. The seed treatment was carried out with different doses of thioureas for a period of $2\frac{1}{2}$ hours at a temperature of 26 ± 1°C. A treatment of simple



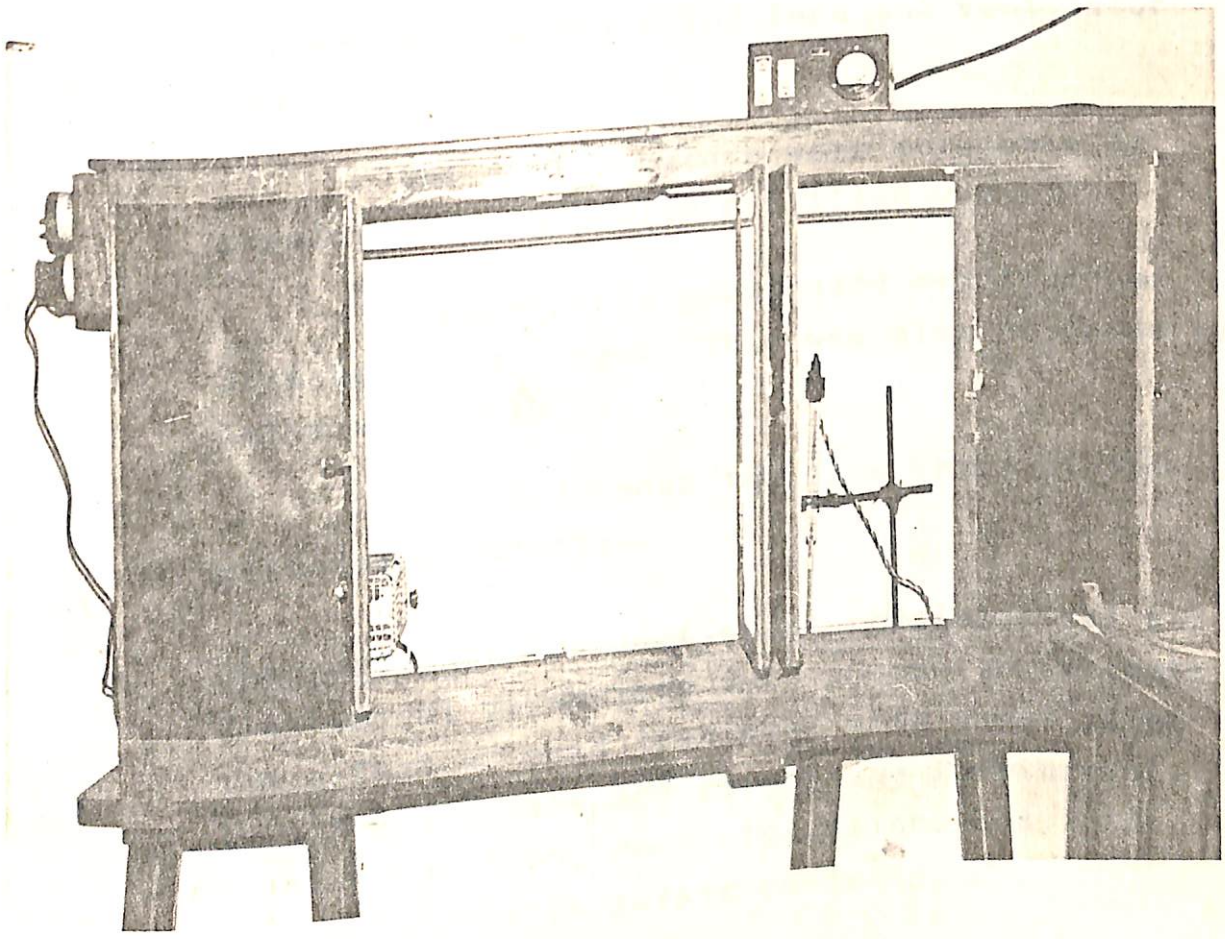


Fig. 5.1 Growth Chamber; Overview (top), Open Chamber view (bottom).

distilled water was given to seeds for the control set of replicas. Different seeds were now arranged over moist Whatman filter paper (W & R Balson Ltd., England) padded with sterilized cotton in petri dishes. Each dish of 10 cm diameter contained 15 seeds, and three replicates of petri dishes containing identically treated seeds were made. These petri dishes were arranged inside the growth chamber maintained at 26 $\pm$ 1°C and 70% humidity with intermitted exposure (12-13 hours in a day) of 4200 lux light on the floor by day light fluorescent tubes (Sylvania Ltd., Bombay). All glass windows were pasted by black paper to restrict entry of light from outside. Proper ventilation of fresh air was maintained using fans and ventilator holes.

The filter papers were moistured at regular intervals with distilled water.

A completely germinated seedling was obtained in 10 days. This was also reported by Kalia et al (1970).

Fig. 5.2 shows the flow chart of the methodology adopted.

Observations: Four different physiological and biochemical parameters were chosen to estimate the effect of seed treatment with substituted thioureas. These are percentage germination, shoot elongation, root elongation, and total protein and carbohydrate contents.

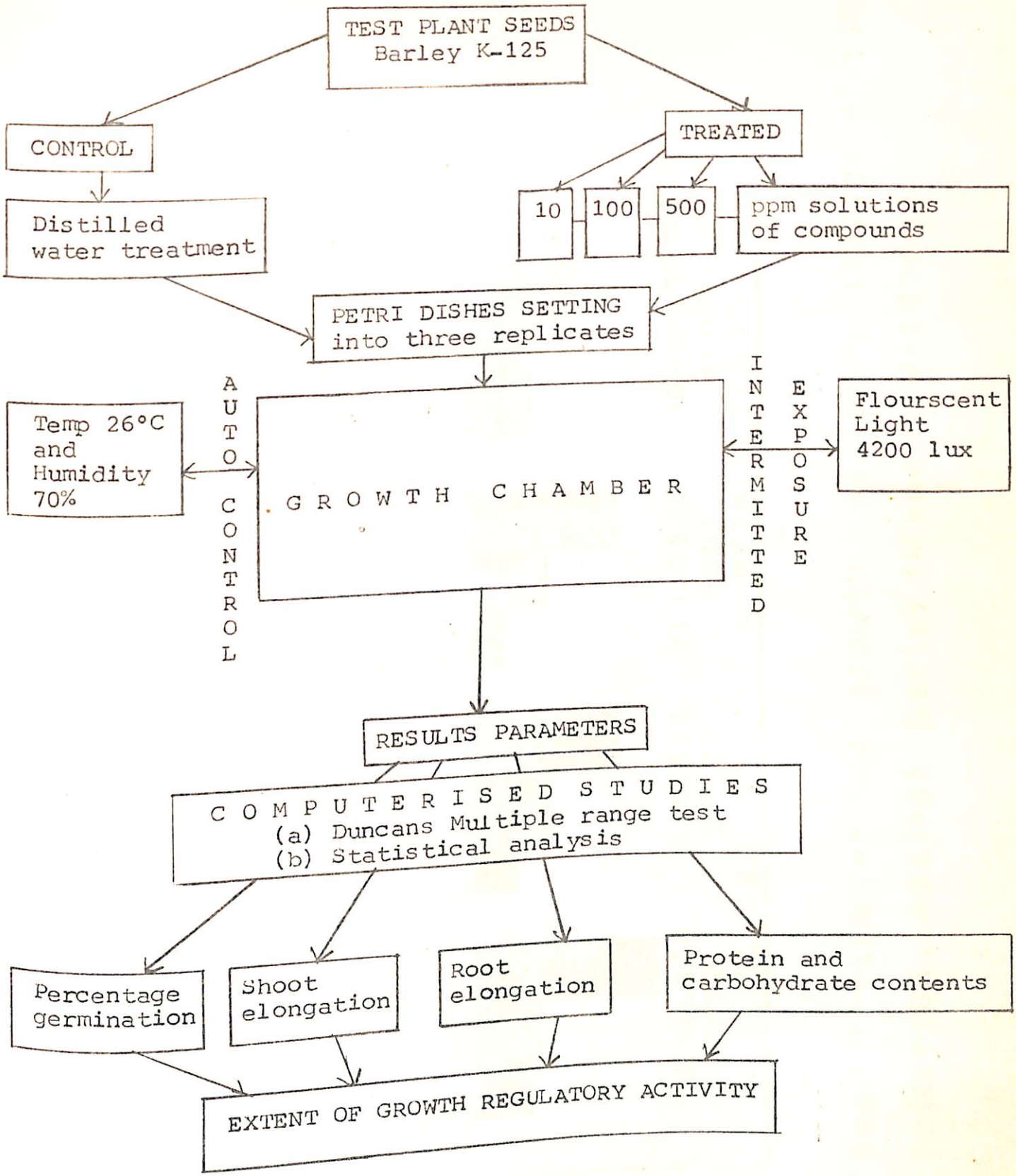


Fig. 5.2 Flow Chart Diagram of Growth Regulatory Acticity Studies Methodology.

$CH_2=CH-CH_2-NH-CS-NH-R$; R = Ph [1], H [2], p-Me Ph [3] and o-Me Ph [4]

$CH_3-NH-CS-NH-R$; R = 2-(6MePy) [1], 2-(3MePy) [2], 2-(4MePy) [3] and 2-Py [4]

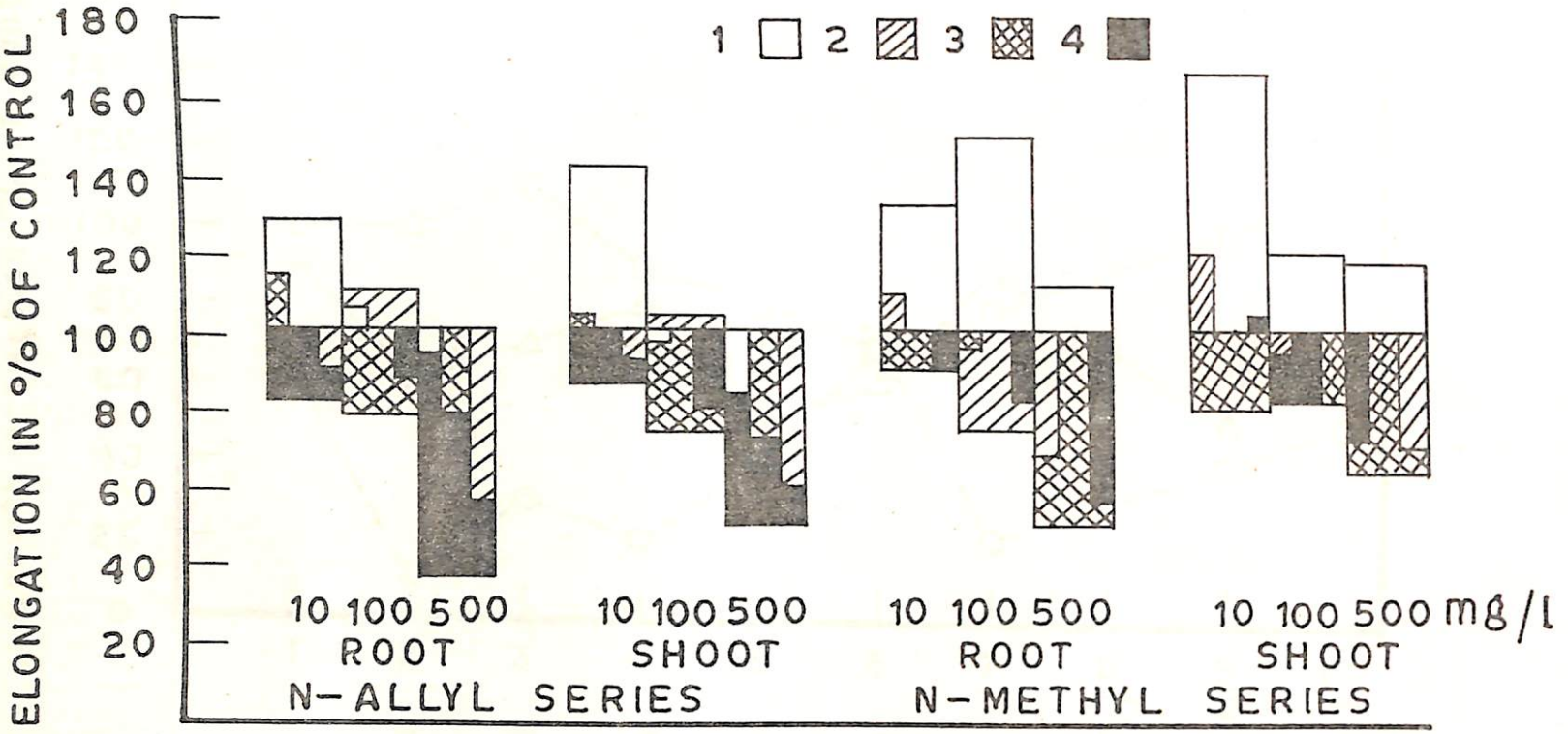


Fig. 5.3 Seed treatment and growth regulatory studies of substituted thioureas, against Barley (Monocotyledons)

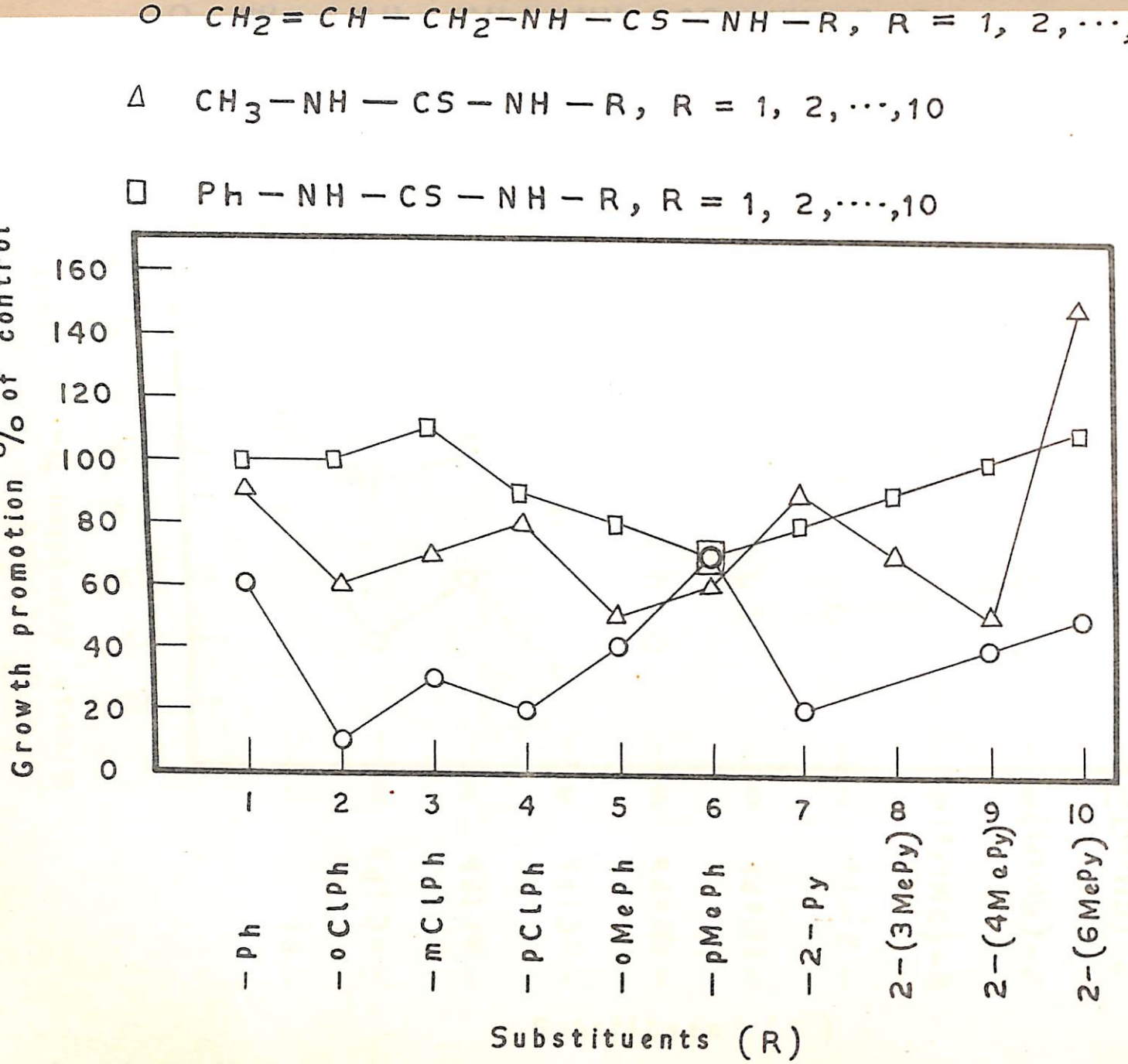


Fig. 5.4 Seed treatment studies for growth promotion activity on Barley (Monocotyledons) with substituted thioureas

△ $CH_3-NH-CS-NH-R$, R = 1, 2, ···, 10

□ $Ph-NH-CS-NH-R$, R = 1, 2, ···, 10

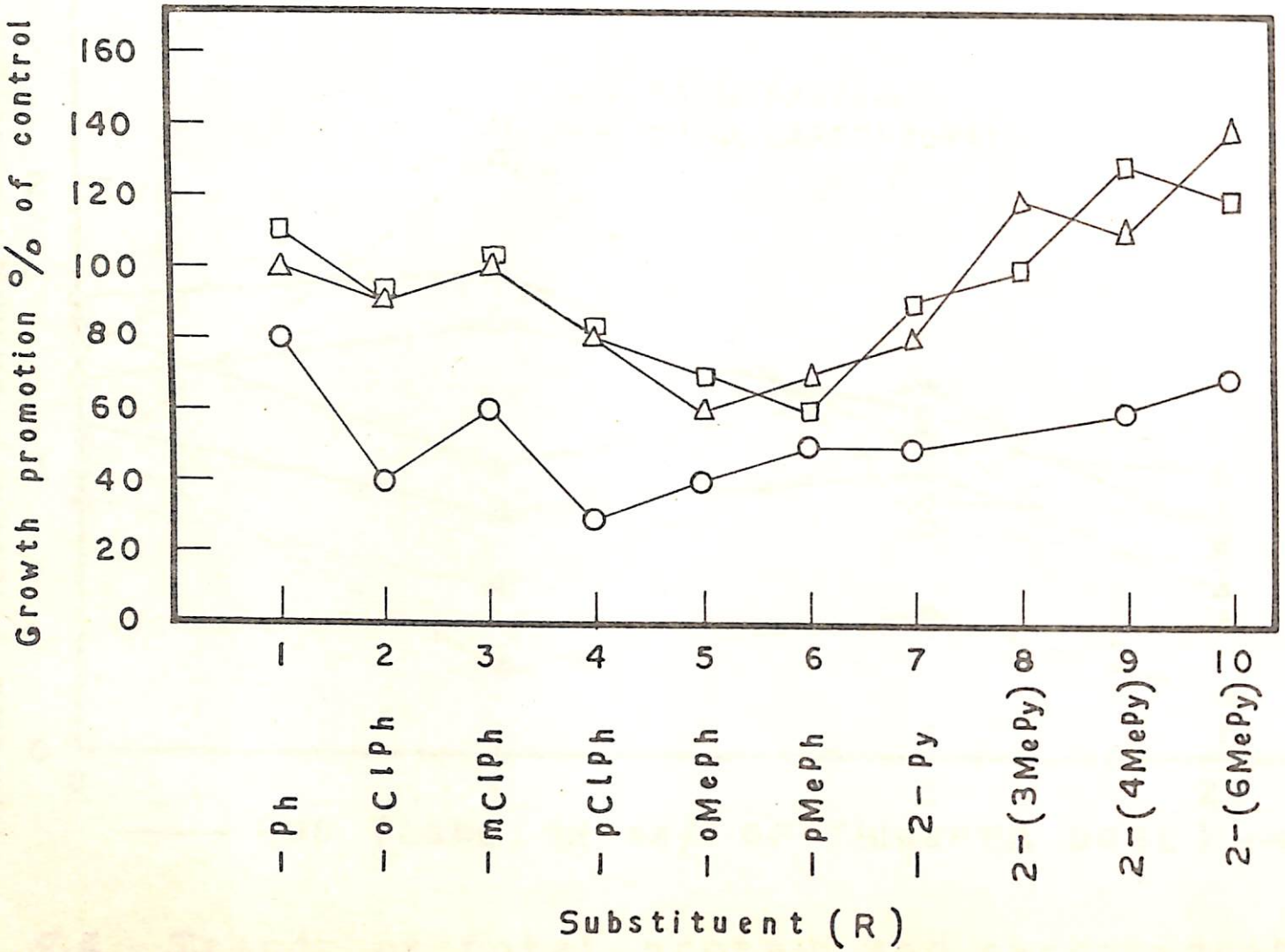


Fig. 5.5 Seed treatment studies for growth promotion activity on Mustard (Dicotyledons) with substituted thioureas

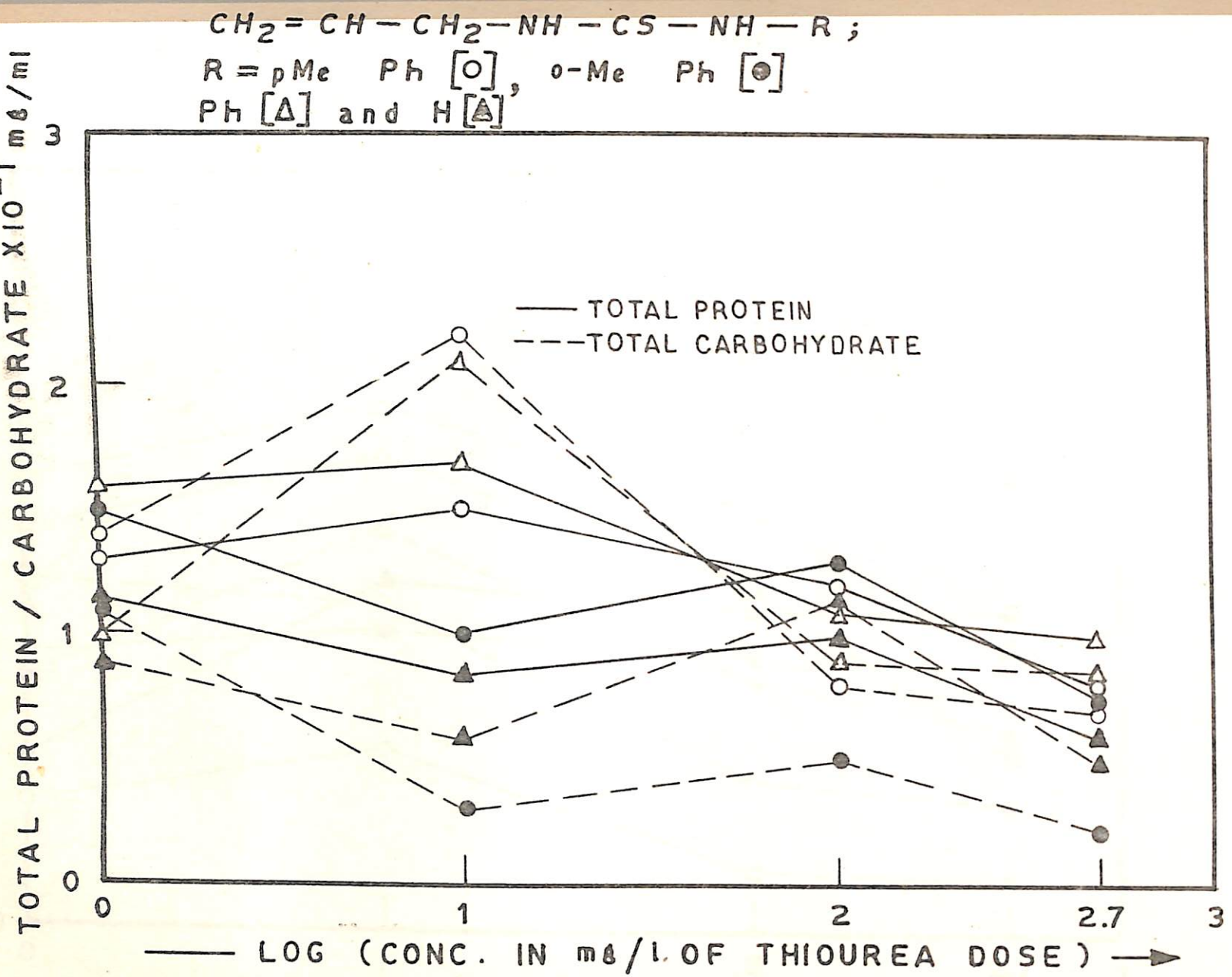


Fig. 5.6 Trends of total protein and carbohydrate contents of Barley seedlings on different substituted thiourea doses.

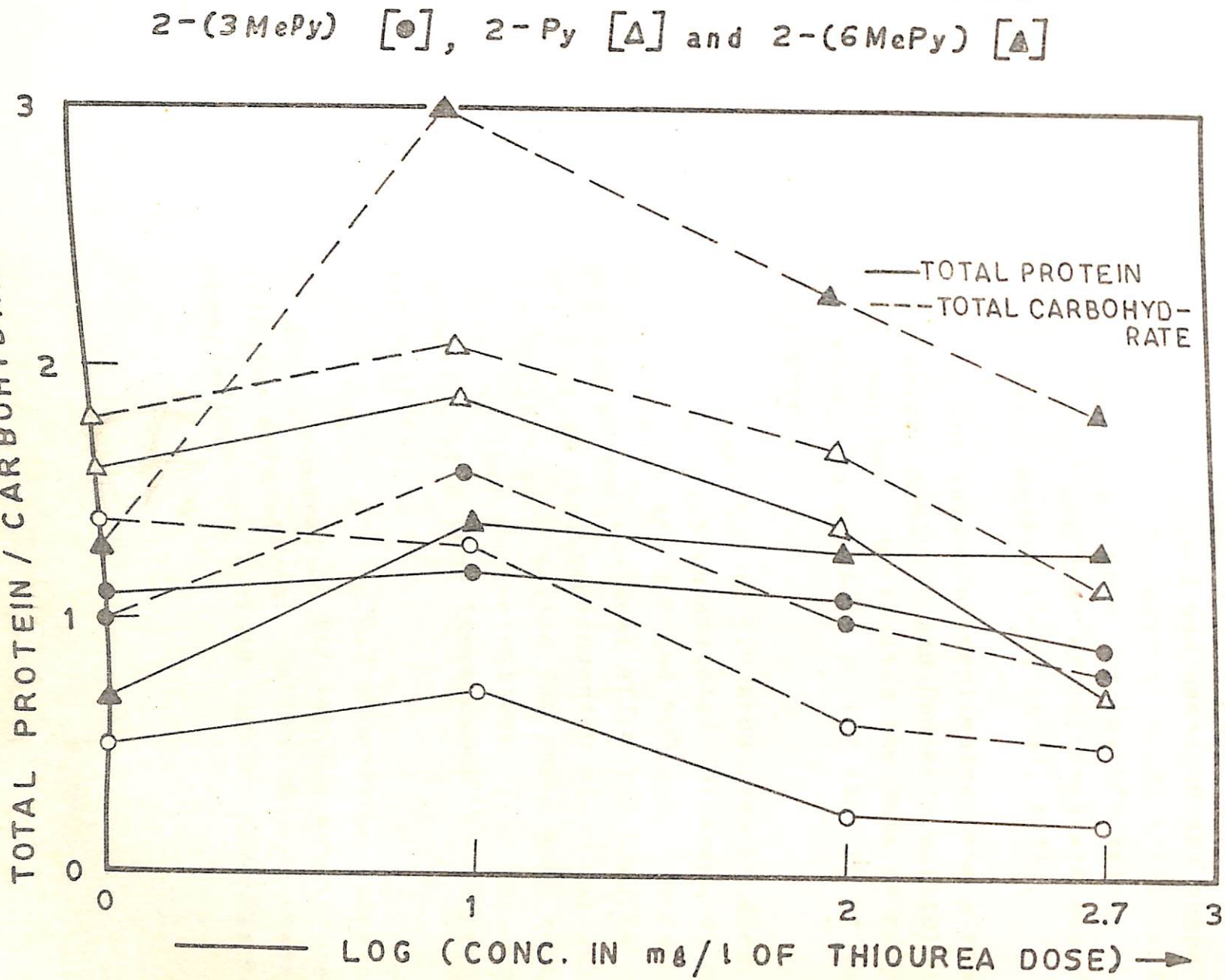


Fig. 5.7 Trends of total protein and carbohydrate content of Barley seedlings on different subtituted thiourea doses.

The percentage germination was found by counting the seeds germinated (those showing atleast protruding of radical and plumule) of treated and control. Increase in shoot and root length of each seed was measured and compared with control. The estimation of total content of protein was done by Lowry's method (Lowry et al, 1951) and that of carbohydrate was done by Anthrone method (Good et al, 1933).

The values of replicates were given statistical analysis and Duncan's multiple range test treatment, by feeding the data to computer (HP 1000, see Appendix B for listing of the programme).

Figs. 5.3 to 5.5 show the studies carried out with substituted thioureas at concentration of 10, 100 and 500 ppm. These observations showed the most effective results at the level of 10 ppm, consequently all other thiourea derivatives were tested for their seed treatment effect at this concentration. This facilitated screening of a very large number of thiourea derivatives.

Figs. 5.6 to 5.7 show these results at 10 ppm concentration for various substituted thiourea derivatives. Tables showing these observations are included in the Appendix A

5.2.3 Result and Discussion

The results obtained reveal that substituted thioureas can be used as effective seed treatment agents for enhancing the germination and growth of seedling, only at a concentration of 10 ppm. Studies with thiourea derivatives at higher concentration of 100 and 500 ppm has been found to be toxic in many cases. (Figs. 5.3 to 5.5), while thiourea itself has been reported to be growth promotor at concentration of 100 ppm and more upto 70% over control. (Yadav et al, 1979; Choudhari and Chakrawar, 1981, 1982).

Thus we find that the substitution at N,N' position of thiourea (H_2N-CS-NH_2) leads to the enhancement in the toxicity of the compound, as revealed by the present studies.

Some useful conclusions could be drawn by present studies when seed treatment with 10 ppm substituted thiourea derivatives was done.

It was generally observed that the growth promoting activity depends upon substituent at N position in the order

Ph > Me > Allyl

Thus the N-phenyl series of substituted thioureas were found to be the best potential growth promotor at 10 ppm concentration.

Further substitution of phenyl on N'position was found to be more useful than pyridyl. But further substituents on these rings lead to enhanced activity in pyridine and reduced growth promoting activity in phenyl. Thus N-phenyl, N'-2-(6MePy) thiourea was found as the most potent growth promotor. (Fig. 5.6). These substituents in aromatic and heterocyclic ring which varied from alkyl to halogens, led to the results where we see that a halo substituent leads to the reduced activity and alkyl (viz Methyl) substituent leads to the enhanced growth promoting activity (Fig. 5.7).

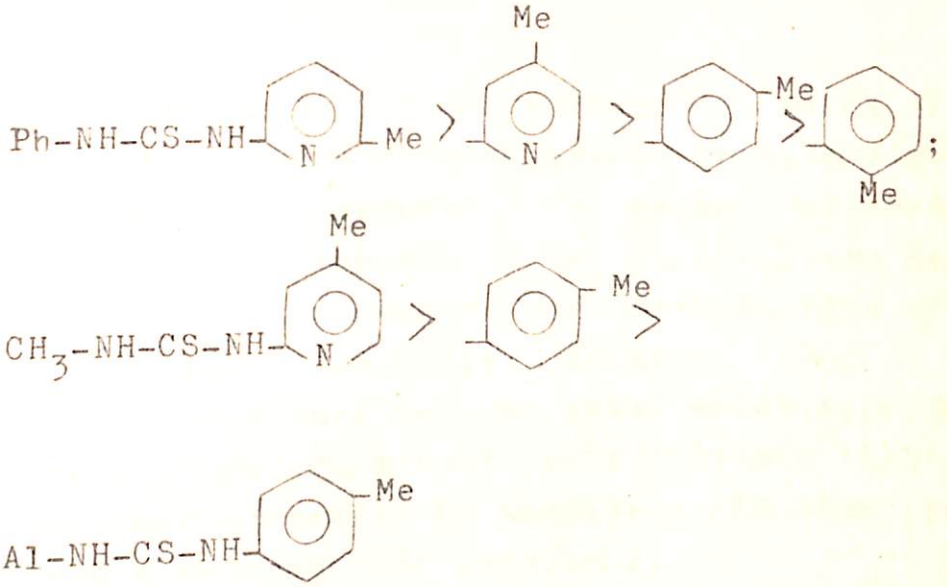
Further studies on the seed treatment of two different plants, Barley (Monocotyledon) and Mustard (Dicotyledon) were found to have different extent of activity for the three series of thiourea derivative studied.

For N-Phenyl series: Growth activity in monocotyledons was more than dicotyledons.

For N-Methyl series: Growth activity in dicotyledons was more than monocotyledons.

For N-Allyl series: Growth activity in dicotyledons was more than monocotyledons.

From these studies, the growth promoting activities of the different compounds tested can be arranged in following descending order:



5.3 Herbicidal Activity Studies

5.3.1 Definition of herbicide and its role

Herbicides are the chemicals which are used to kill the unwanted green vegetation (herbs). The most common class of plants of this nature are called 'weeds'.

The weeds are important to all agriculturists. Weed control is one of the most expensive step in crop production. Weeds may poison or seriously slow down weight gains of the livestock. They cause allergies (Klingman, 1973) such as hay fever and poison ivy. They infest lawns and gardens. Weeds create problems in recreating areas such as golf course, parks and fishing and boating areas. They are troublesome along highways, railroads, in industrial areas and in irrigation and drainage systems.

Of the total annual loss of agricultural produce from various pests in India, weeds account for 45%, insects 30%, diseases 20% and other pests 5% (Rao, 1983).

The impact of the presence of weeds on crop production is very considerable. Estimates suggest that weeds are responsible for an over all reduction of more than 10 percent in the yield of the major world crops, thus causing considerable loss of food supplies annually. (Roberts, 1982). Much of this loss occurs because weeds which deprive the crop of water, mineral nutrients and light which would otherwise be available and thus prevent it from achieving full potential.

There is further augmentation to the damage caused by these weeds when they serve as hosts for many organism which attack crops, including insects, nematodes, fungi, bacteria and viruses (Roberts, 1982: Chiarappa, 1972).

Herbicides thus forms an important agrochemical playing a vital role in agriculture. The most important agents generally understood to be included within the meaning of the nearly interchangeable terms 'pesticides' and 'agrochemicals' are herbicides, insect control agents, fungicides and plant growth regulators. The two most important in terms of global use are herbicides (an estimated U.S. $ 4.9 billion in sales at the user's level in 1980) and insect control agents (U.S. $ 3.9 billion) (Addor, 1982).

To cite an example, advent of 2,4-D herbicides in the year 1947 as the first commercially available one, led to the revolutionization of agriculture so much that food shortage plagueing

North America and Europe at the conclusion of World War II disappeared within a few years. This was possible because 2,4-D weed control led to increase in yield by 600 to 900 kg/ha of wheat crop (Freed, 1980). The use of herbicide in India has gained momentum only in recent years.

It has now been realized that the use of chemical weed control has great advantages over eradication by manual means.

5.3.2 Different types of herbicidal activity

Herbicides activity has been found to belong to one of the two catagories:

1. Total or non-selective herbicides
2. Selective herbicides.

Total or non-selective herbicides: When these herbicides are applied, it kills all types of vegetation present. These are used on railway tracks, garden paths and industrial sites.

Most of inorganic herbicides viz. copper sulphate, ferrous sulphate, borax, sodium chlorate and ammonium sulphate are the non-selective herbicides used for the non-crop areas. This is because of their slow and persisting action.

Few other organic herbicides viz. glyphosate, dalapon and aminotriazole are used as non-selective doses for crop area, due to their quick herbicidal activity.

The mode of action of these herbicides are by both foliage and soil treatment of the vegetation to be checked.

Selective herbicides: This class of compounds are more important and have numerous established names, which are well known. Selective herbicides are intended to suppress or kill some plants without seriously affecting others which are the non-target plants, thus showing selectivity between the undesired plants (i.e. weeds) and the crop.

This type of herbicides also acts by the foliage and soil treatment methods.

Selective herbicides may be further classified according to their time of application, at a particular stage of development of crop.

1. Pre-sowing or Pre-plantation activity: When the herbicide is applied before the crop is sown or planted, it is referred to as Pre-sowing or Pre-plantation type of herbicides. Some of the common examples are: 2,4-D for field bindweed and TCA (Trichloro acetic acid) for controlling Grasses like common couch and wild oat.

2. Pre-emergence activity: When the herbicide is applied after the crop is sown but before it has emerged. Here too the treatment may be contact foliage, translocated foliage or residual, according to the stage of development of the weeds and the nature of herbicides. For example paraquat as contact foliage treatment, simazine and atrazine on maize.

3. Post-emergence activity: When the herbicide is applied after the crop has emerged from soil. Contact foliage, translocated foliage and residual

treatments are all possible. For example bromoxynil and ioxynil are contact foliage treatment type, 2-methyl-4-chlorophenoxy acetic acid for translocated foliage type treatment and 2,4-Dichlorophenoxy acetic acid (2,4-D) to control broad leaf weeds.

5.3.3 Mode of action of herbicides:

The various types of herbicides classified above act upon the unwanted weeds, by different modes and are classified as:

1. Contact foliage type
2. Translocated foliage type
3. Residual type.

Contact foliage type: In this mode the herbicide affects only the part of the plant receiving direct treatment with the herbicide.

Translocated foliage type: Where the herbicide after entering the plant is transported within it and affects sites elsewhere. These may be in shoot or roots.

Residual type: In this mode the herbicides act through the medium of soil and continue to exert an effect on germinating weeds for a period of time after application, depending on the rate of dispersion and breakdown.

The mode of action of all these herbicides have been shown in fig. 5.8

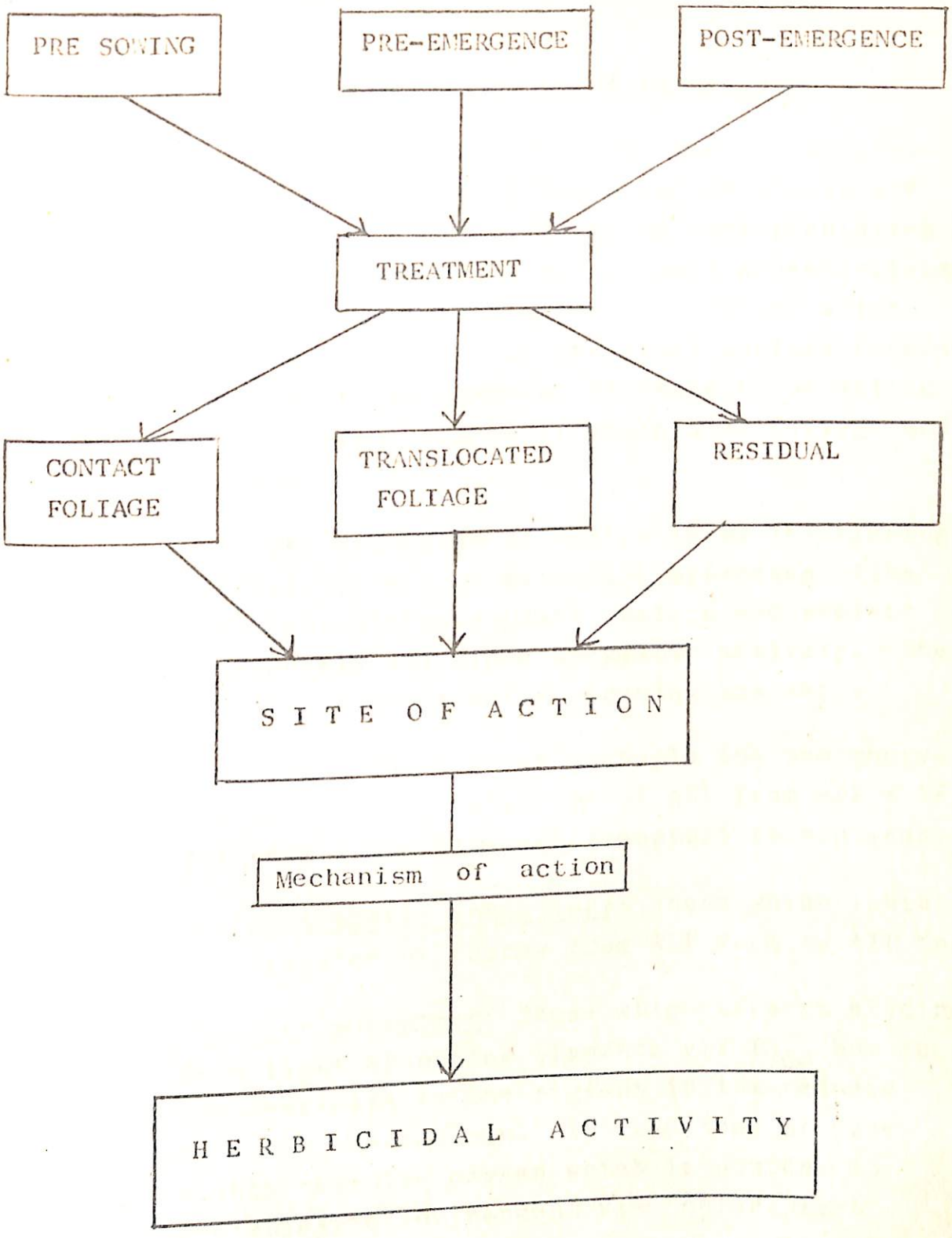


Fig 5.8 Mode of action of Herbicides

5.3.4 Mechanism of action of herbicides

Herbicides bring about various physiological and biochemical effects on the growth and development of emerging seedling (pre-plantation and pre-emergence activity) as well as established plants (post-emergence activity), either after coming into contact with the plant surface (contact foliage) or after reaching the site(s) of action within the plant tissue (translocated foliage and residual).

The mechanism of action is by interfering in different steps of metabolic processes like respiration, photosynthesis protein and nucleic acid synthesis and other enzymatic activity. The herbicides as interfering agents, act as:

1. Uncoupler: Those which uncouple the phosphorylation and thus formation of ATP from ADP + iP, but permit the electron transport to continue.

2. Energy transfer inhibitors: Those which inhibit the transfer of energy from ADP form to ATP form.

3. Electron acceptors: Those which take up electron from light absorbing pigments viz P_{700} but do not dessipate to the pigment in the reduced form viz ferredoxin. Instead they produce highly reactive oxygen which is noxions to protoplasmic environment viz chloroplast leads to chlorosis.

4. Electron inhibitors: Those which inhibit the transport of electron in chain from lower to higher potential pigment.

Various steps in metabolic processes referred above, which are the possible sites of herbicides attack can be summarised as below:

In Respiration and mitochondrial activity: Here herbicides act either in the form of electron transport inhibitors, or uncouplers. In the former case they interfere in the electron transport chain in mitochondria while uncouplers act on the mitochondrial membrane - the place of ATP synthesis. For example carbamates and phenyl ureas.

In Photosynthesis: In this case herbicides act as electron transport inhibitor in photosystem II (P.S. II), where water is releasing oxygen (Hill reaction); as uncouplers and energy-transfer inhibitors for the non-cyclic phosphorylation in P.S. II and cyclic phosphorylation in P.S. I and lastly as electron acceptor at the ferredoxin reduced substance site. For example substituted ureas, uracils, triazines, etc.

In Protein and nucleic acid synthesis: No specific site of action can be pointed, in general the various steps of protein synthesis on ribosomes and nucleic acid contents, specially of RNA is most affected. Effects on this, thus leads to pronounced growth regulatory factor. For example phenoxy acids, carbamates, benzoic acids, glyphosate, etc.

The mechanism of action as shown by herbicides thus depends upon two factors - mobility of herbicide in the plant tissue (Apoplast-xylem and symplast-phloem) and the nature of chemical nucleus.

A comprehensive list of major classes of herbicides and their mode of action has been tabulated in table 5. 3

5.3.5 Methods of screening herbicidal activity

The evaluation of a new herbicide, from the first indications of activity in the laboratory to its commercial utilization is a process which normally takes around four years. It is a complex process, characterized by the interaction of a large number of disciplines ranging from agronomy to chemistry and toxicology. The cost of developing and marketting a new herbicide is considerable.

A study conducted in USA (National Agricultural Chemicals Association, 1970) revealed that the total number of compounds screened per year increased by about 4% (60,000 to 62,000) between 1967 and 1970, while the number of compounds which needed to be examined to produce a successful product increased by 36% (5,481 to 7,430). Similarly the average time required to produce a successful product increased from 5 years to more than 6 years in 1970 and the cost by 60% from 3.4 to 5.5 million U.S. dollars.

One may broadly list the various stages involved in the search of a new herbicide:

1. Synthesis of new compounds
2. Screening at preliminary level.

3. Testing of more selected compounds for field studies.

4. Toxicological evaluation, degradation and residual studies.

5. Scaling up for commercial production.

Synthesis of new herbicides: This is the first step towards search for new herbicides. The choice of chemical nucleus to be synthesised broadly falls into three groups

1. Random or speculative screening
2. Directed screening and
3. Basic research screening.

In the random screening, the compounds which arise from sources not directly connected with the search for new herbicides are submitted for a test for herbicidal activity. In directed screening approach, the synthetic chemist studies the literature on compounds known to be active and deduce from this that certain combinations of chemical groups are likely to produce herbicidal activity. The third approach of basic research to screen choice of chemical is probably the most intellectually satisfying method and is based on the study of the biochemistry of the plant. At this stage it must be admitted that so far the first two approach has only lead to successful finding of new herbicides but more information regarding their herbicidal activity has been obtained by the third method.

The present work was started initially with thiourea derivatives synthesised for other research studies, but once their herbicidal activity was found, more new derivatives were synthesised following the directed approach.

Screening at preliminary level: The primary purpose of this stage of screening test is to sort out those compounds which are worth further investigation. Since large number of such compounds are to be screened, the quantity of many of which is small, the test should, therefore, be capable of giving a clear indication of activity from milligram quantities of compounds. The different methods, adopted by various workers can be summarised as:

1. In vitro experiments involving the use of isolated enzyme systems or organelles for testing the inhibition of growth (Thompson, Swanson and Norman, 1946), photosynthesis (Truelove, Davis and Jones, 1974) or respiration (Kratky and Warren, 1971).

2. In vitro experiments, in which seeds, small seedlings or portion of plant tissue are in direct contact with very dilute solutions or deposits of active material.

3. In vivo experiments, using whole plants growing in water culture.

4. Tests for post-emergence activity through the foliage and pre-emergence activity by direct application to seeds on soil or incorporation

in soil in which seeds are being grown (Richard and Parker, 1978).

5. Testing pre-emergence activity by tests on inhibition of germination and growth of seedlings using an artificial medium incorporating the chemical. Vassilev et al (1969a) have used agar medium for this type of experimental setup.

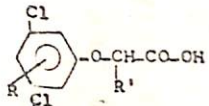
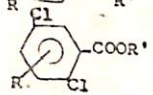
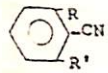
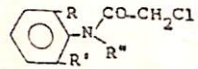
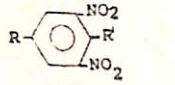
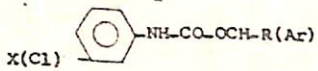
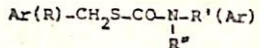
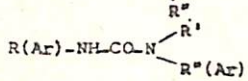
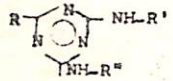
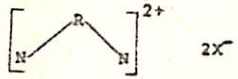
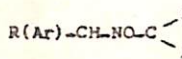
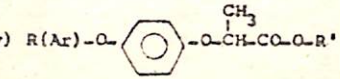
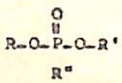
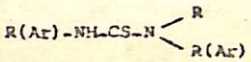
Once the selected compounds have been sorted out by above method, experiments for field studies have to be undertaken followed by the toxicological studies (Roberts, 1982).

5.3.6 Representative chemical nucleus of established herbicides

A brief survey to various group of organic herbicides nucleus will provide information for correlating the structure and herbicidal activity.

At present more than 250 formulations of established herbicides are known. All of them can be grouped together into various chemically related catagories. A selective list of such groups is presented in table 5.3.

Table 5.3 Representative Established Herbicides and Relevant Data.

S.No.	Class	Nucleus	Examples	Year of advent of examples asterisk (*)	Site for mechanism of action
1	Halogenated alkanoic acid	R-CO-O Na	TCA, Dalapon-sodium, Chlorfenprop-methyl*	1967	Proteins synthesis
2	(Aryloxy) alkanoic acid		2,4-D*, MCPC*	1942	Nucleic acid metabolism
3	Arylcarboxylic acid and their esters		2,3,6-TBA*, Picloram	1954	Nucleic acid metabolism
4	Nitriles		Ioxynil, Bromoxynil Dichlobenil*	1960	Electron transport and phosphorylation in chloroplast or mitochondria
5	Anilides		Propachlor*, Alachlor	1967	Cell division and enlargement
6	2,6-Dinitroanilines		Isopropalin, Trifluralin*	1960	Photosynthesis, RNA and protein synthesis
7	Carbamates		Propham*, Chloropropham	1945	Hill reaction, RNA and protein synthesis
8	Thiocarbamates		EPTC*, Molinate	1954	Photosynthesis, respiration, protein synthesis
9	Ureas		Monouron*, Diuron, Linuron	1952	Photosynthesis
10	Triazines		Simazine*, Atrazine	1956	Hill reaction and photosystem II of photosynthesis
11	Quaternary ammonium salt		Diquat*, Paraquat	1957	Cell division and elongation (by free radical formation)
12	Hydroxylamine derivatives		Bromofenoxim*	1969	Hill reaction in photosynthesis and oxidative phosphorylation in mitochondrial respiration
13	Esters of 2-(4-(aryloxy) phenoxy) alkanoic acid		Diclofop-methyl*	1975	ATP production
14	Organophosphorus compounds		Glyphosate*	1971	Aromatic amino acid biosynthesis
15	Thioureas		Methiuron*	1970	Yet to be established

5.3.7 Experimental

Material: Sterilized corning petri dishes were used for preparing artificial bed of agar. Bacteriological grade of agar-agar (B.D.H., England) was used. B.D.H., A.R. grade acetone was used as solvent. Standard herbicides 2,4-D and Diuron ('KARMEX' E.I. DU Pont de Nemours & Co. (Inc), Delaware, USA) were used as reference for test chemicals. Thioureas derivatives were freshly recrystallized from ethanol to ensure purity.

For post-emergence activity, plastic cups of 7 cm diameter and 6 cm depth were used for preparing soil bed. The soil used was of agricultural field, free from chemicals.

The soil was analysed at the Indian Agricultural Research Institute (I.A.R.I.), New Delhi, for its organic and mineral content (Table 5.4). For achieving a uniform spray of herbicides, spraying atomizer (A.H. Thomas Co., Philadelphia, USA) was used.

Growth chamber with controlled temperature at 26 ± 1°C, light exposure (intermitted, 12 hours in a day of 4200 lux by day light fluorescent tubes, Sylvania Ltd., Bombay) and humidity of 70% was used.

Identified seeds of Barley K-125 (Hordeum vulgare L.) and mustard 'varuna' (Brassica compestris L.) were obtained from I.A.R.I., Pusa, New Delhi.

Statistical analysis and Duncan's multiple range test for significance at 5% level were carried out for all the replicate studies, in IBM 1130, Spectrum 3, and HP 1000 computers. (Listing of the program is given in Appendix B).

Methodology

a) Pre-emergence herbicidal activity: Method adopted by Vassilev et al (1982a, 1982b, 1969a, 1969b, 1969c, 1969d, 1969e, 1967a, 1967b) at Institute of Plant Physiology, Sofia, Bulgaria using agar bed incorporated with chemical under test was adopted after testing and obtaining satisfactory reproducible results, for standard herbicides.

1. Preparation of agar bed: Hot agar solution 0.5% (containing 8 gm of agar in 1500 ml of water) was prepared. This was used as stock solution for agar. For preparing bed dispersed with test chemical, 140 ml of hot agar solution was taken and 10 ml of acetone containing the required dosage of test chemical, in this case 2,4-D and Diuron at 10, 100, 150, 200 and 500 mg/liter, was added. This bulk was evaporated to a 90 ml volume to ensured removal of all the acetone (Vassilev et al, 1969e).

This was then transferred to separate petri dishes of 6 cm diameter, each carrying 15 ml of the prepared solution. It was left for cooling so that agar sets up into a soft bed in the dish.

2. Preparation of soil bed: Farming soil from local agricultural fields of Pilani was used. A detailed analysis of which has been discussed earlier and reported in table 5.4. In this case the test chemical is mixed with the soil prior to sowing the seed. In order to economise on chemical usage and avoid solvent induced effects compounds are taken in volatile solvent (in this case acetone was used) and mixed with soil at initial rate of application of 530 mg to 3.8 liter of soil, which correspond to equivalent to a surface application of 56 kg/ha (Saggers, 1976). Thereafter the level of concentration of test chemical can be brought to the desired one. This was distributed in plastic cups of 7 cm diameter and 6 cm depth. Each cup has a volume of approximately 65 ml.

Both agar and soil beds were given identical condition of temperature, (26 ± 1°C), light (4200 lux 12 hours/day) and humidity (70%) in the growth chamber and seeds of Barley K-125 (Hordeum vulgare L.) and mustard 'varuna' (Brassica compestris L.) sown at identical depth of 2 cm. Each one of the beds were given 10 seeds to grow.

All these experiments were carried out in triplicate and with a control (identical treatment, without the presence of test chemical).

Assessment of these was done when a fully grown seedling had appeared with true leaves. The parameters chosen for determining the percent herbicidal activity were, percentage germination, shoot and root elongation.

Flow chart presented in fig. 5.9 gives a quick summary of this method.

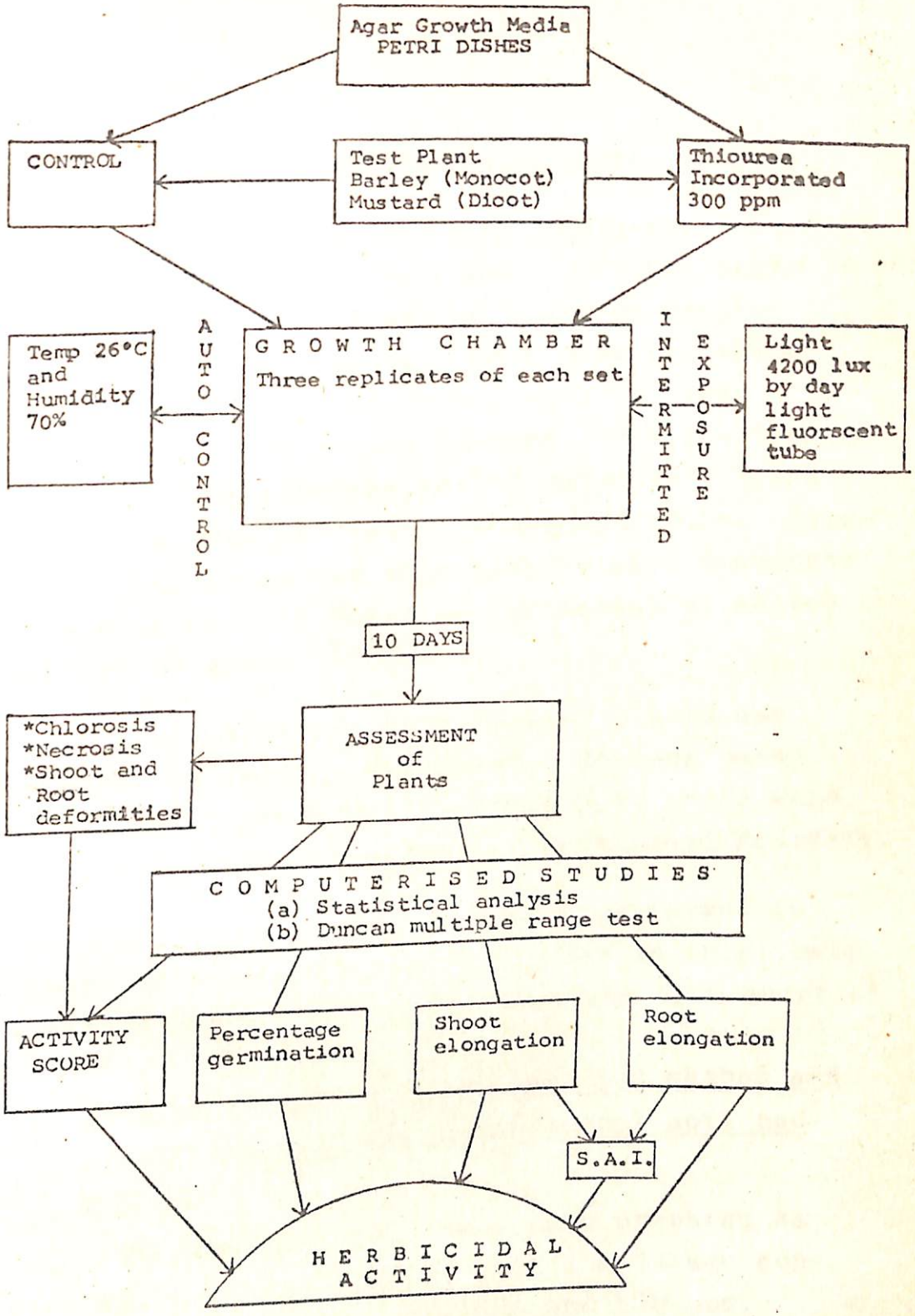


Fig. 5.9 Flow Chart Diagram of Pre-emergence Herbicidal Activity Screening Methodology.

b) Post-emergence herbicidal activity:

1. Preparation of soil bed and treatment: Soil from local agricultural fields (Table 5.4) was taken in plastic cups of 7 cm diameter and 6 cm depth. Seeds of Barley and mustard were grown in these cups. Once a small twig/seedling with first appearance of true leaves emerges, they are treated with spray from atomizer having solutions of test chemicals at desired level of concentration. Solutions of insoluble and sparingly soluble compounds was made using 0.5% Tween 80 surfactant by method described by Rosen (1978).

Assessment of these treated plants was done after 15 days of treatment. Various parameters studied are shown in table 5.5, which were used to calculate the extent of herbicidal activity.

All these experiments were performed in the earlier described growth chamber in triplicate set with a control. Fig 5.10 shows the flow chart of methodology.

5.3.8 Testing the efficacy of agar bed method and comparison with the conventional soil bed method:

The agar and soil beds were prepared as discussed in section 5.3.7, with the dosage concentration of 10, 100, 150, 200 and 500 ppm.

Barley and mustard seeds grown and assessed after 10 days (Kalia et al, 1970).

Table 5.4 Soil and Environmental Conditions for Post-emergence Activity inside the Growth Chamber.

Experiment type	Activity Experiment for Dose Response			Selectivity Experiment at 300 ppm		
Compounds studied	N-Allyl series	N-Methyl series	N-Phenyl series	N-Allyl series	N-Methyl series	N-Phenyl series
Period:						
Date of treatment	2.11.82	4.1.83	20.1.83	24.11.82	23.1.83	5.2.83
Date of main assessment completion	23.11.82	21.1.83	1.2.83	15.12.82	14.1.83	2.3.83
Soil:						
Organic matter (%)	1.8	1.8	1.75	1.8	1.8	1.8
Clay content (%)	13.2	14.0	13.0	13.0	14.5	13.0
pH	6.8	7.0	7.3	6.9	7.1	7.3
Growth Chamber:						
Temperature (°C)	26	26.5	27	25.8	27	27
Relative humidity (%)	71	70	68	70	70	69
Light exposure (lux)	4200	4200	4200	4200	4200	4200
Period of exposure in a day (hours)	12	12.5	11.5	12	13	12

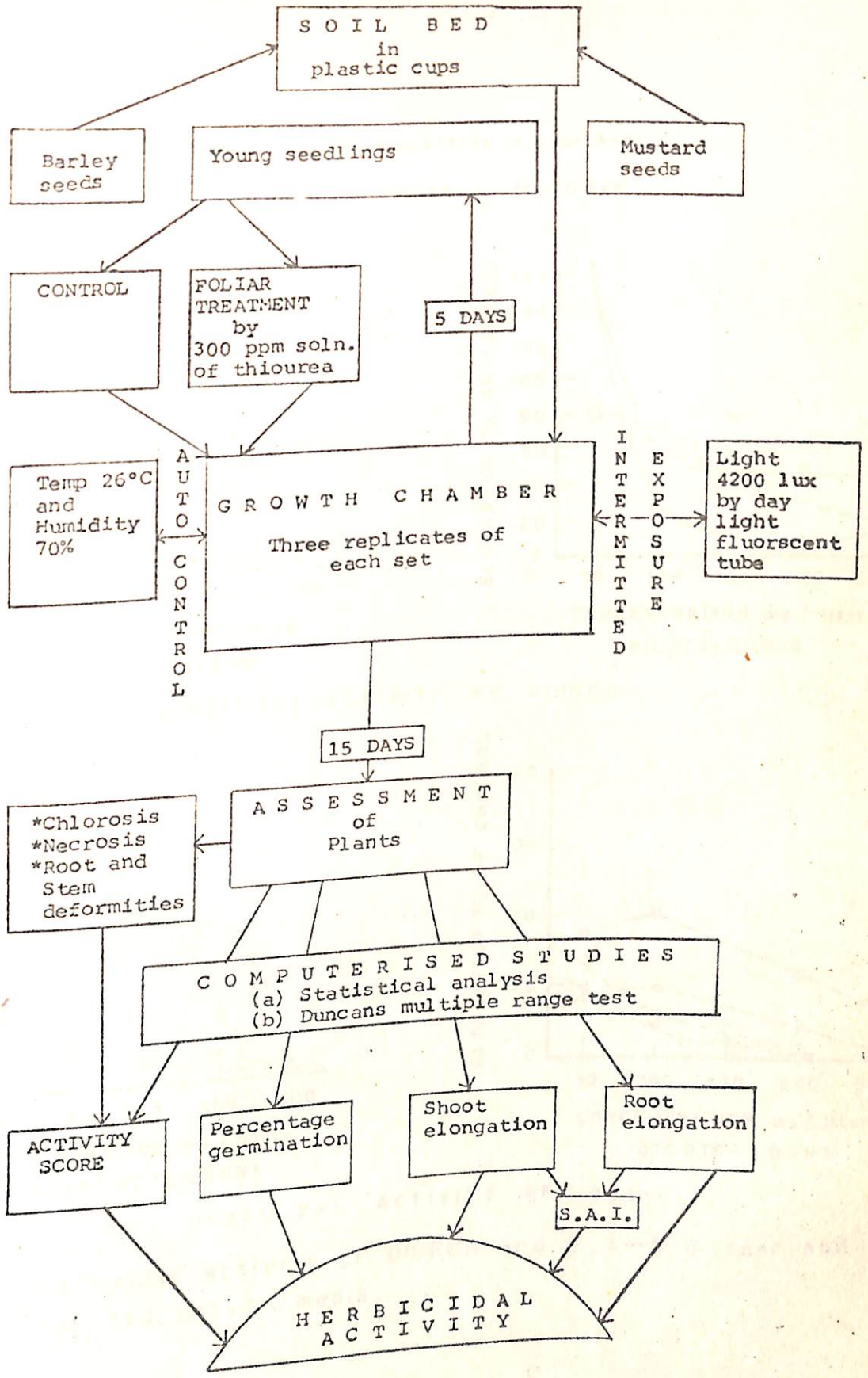


Fig. 5.10 Flow Chart Diagram of Post-emergence Herbicidal Activity Screening Methodology.

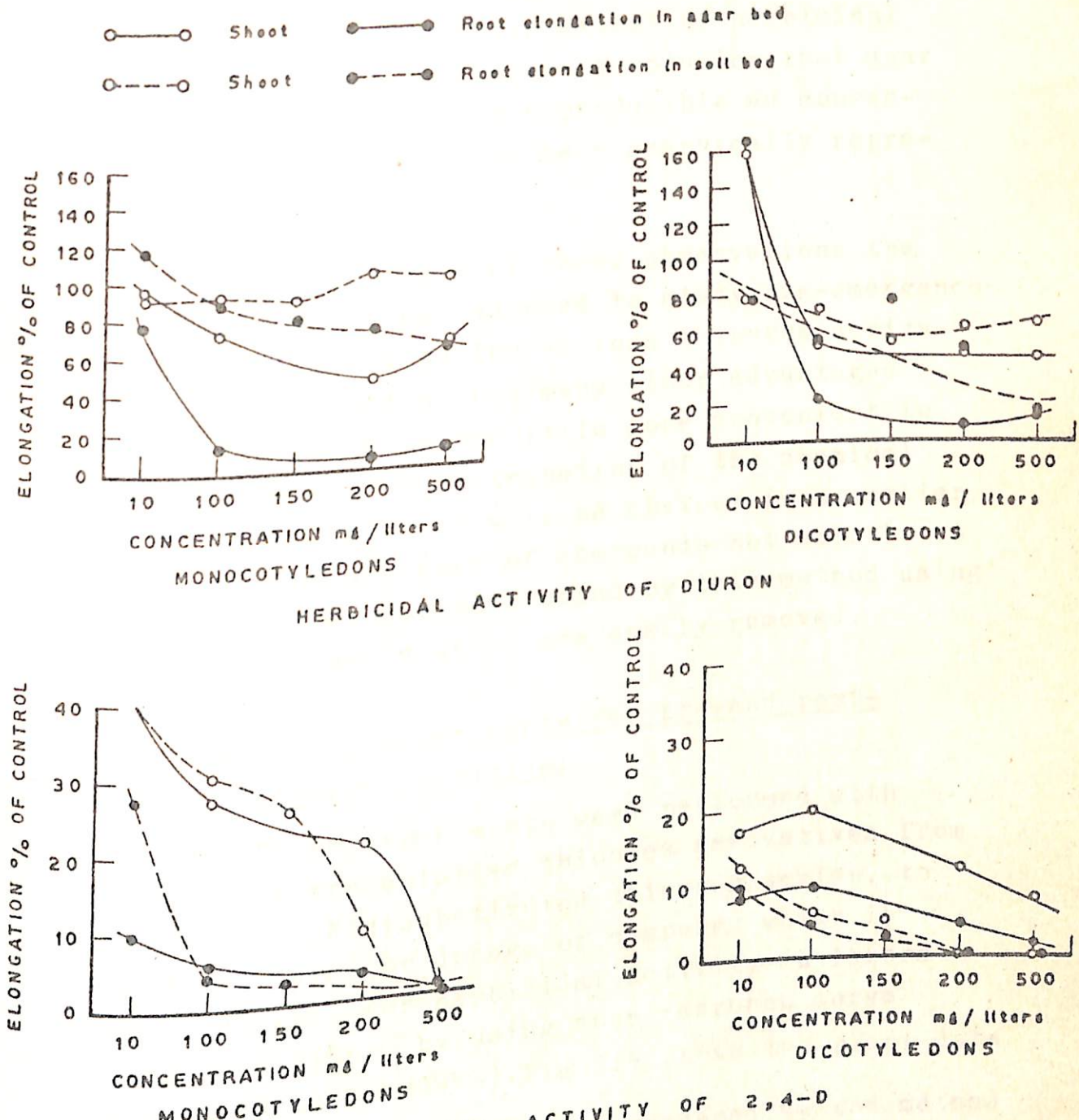


Fig. 5.11 Herbicidal activity of DIURON and 2,4-D in agar and Soil bed Growth media

These studies showed that both the media had almost same trend in extent of herbicidal activity, which led to the conclusion that agar bed method was equally reproducible as conventional soil bed, as has been graphically represented in fig 5.11

On the basis of these observations the agar bed method was adopted to study pre-emergence herbicidal activity for various thiourea derivatives. This method had many other advantages over soil media, since it is more convenient to get homogenity in distribution of the chemical into the media. As will be obvious from earlier observations a number of compounds not soluble in aqueous media, can be studied by this method using volatile solvents which are easily removed.

5.3.9 Activity experiments for pre-and post-emergence herbicide:

These experiments were performed with selected representative thiourea derivatives from different N,N'disubstituted thiourea series, to test the level or dosage of compound which is most suitable for herbicidal activity in laboratory conditions, by using dose response curve method (Roberts, 1982). Fig 5.5 shows the plant data.

Pre-emergence: Agar bed were prepared by the method described earlier (section 5.3.7) for six thiourea derivatives, belonging to N-allyl or methyl or phenyl substituted, N'-phenyl or pyridyl substituted series. Concentration was kept at 10, 100, 500 and 1000 ppm for each of them.

Table 5.5 Plant Data for Herbicidal Activity Experiment.

Species	Source*	No.per		Depth of planting		Stage of Growth**			Parameters studied.
		Pre emergence treatment	Post emergence treatment	Pre (Agar bed) cm	Post (Soil bed) cm	Post-emergence treatment	Assessment Pre	Assessment Post	
Barley (Hordium vulgare L.)	K-125 NSC	10	10	0.5 - 1.0	2.0	1½ - 2	4-5	4-5½	Percentage germination; Shoot elongation; Root elongation; Total protein content; Total carbohydrate content; Chlorosis symptoms; Necrosis symptoms; Other deformities
Mustard (Brassica compestris L.)	Varuna NSC	10	10	0.5 - 1.0	2.0	2	3-4	4-4½	

* NSC : National Seed Corporation, Pusa, New Delhi.

** Leaves numbers are exclusive of cotyledons.

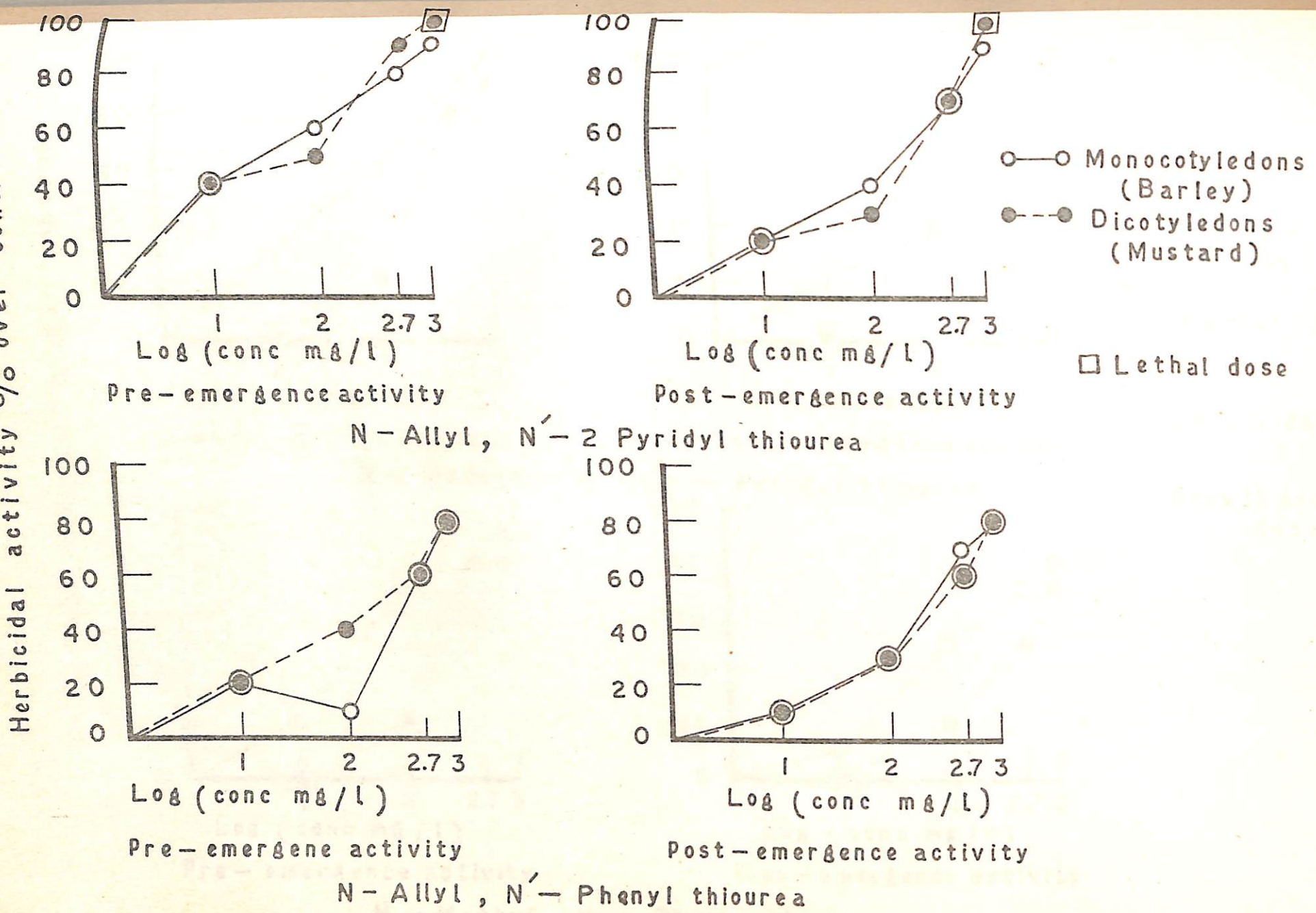


Fig. 5.12 Herbicidal activity experiment for different doses of substituted thioureas

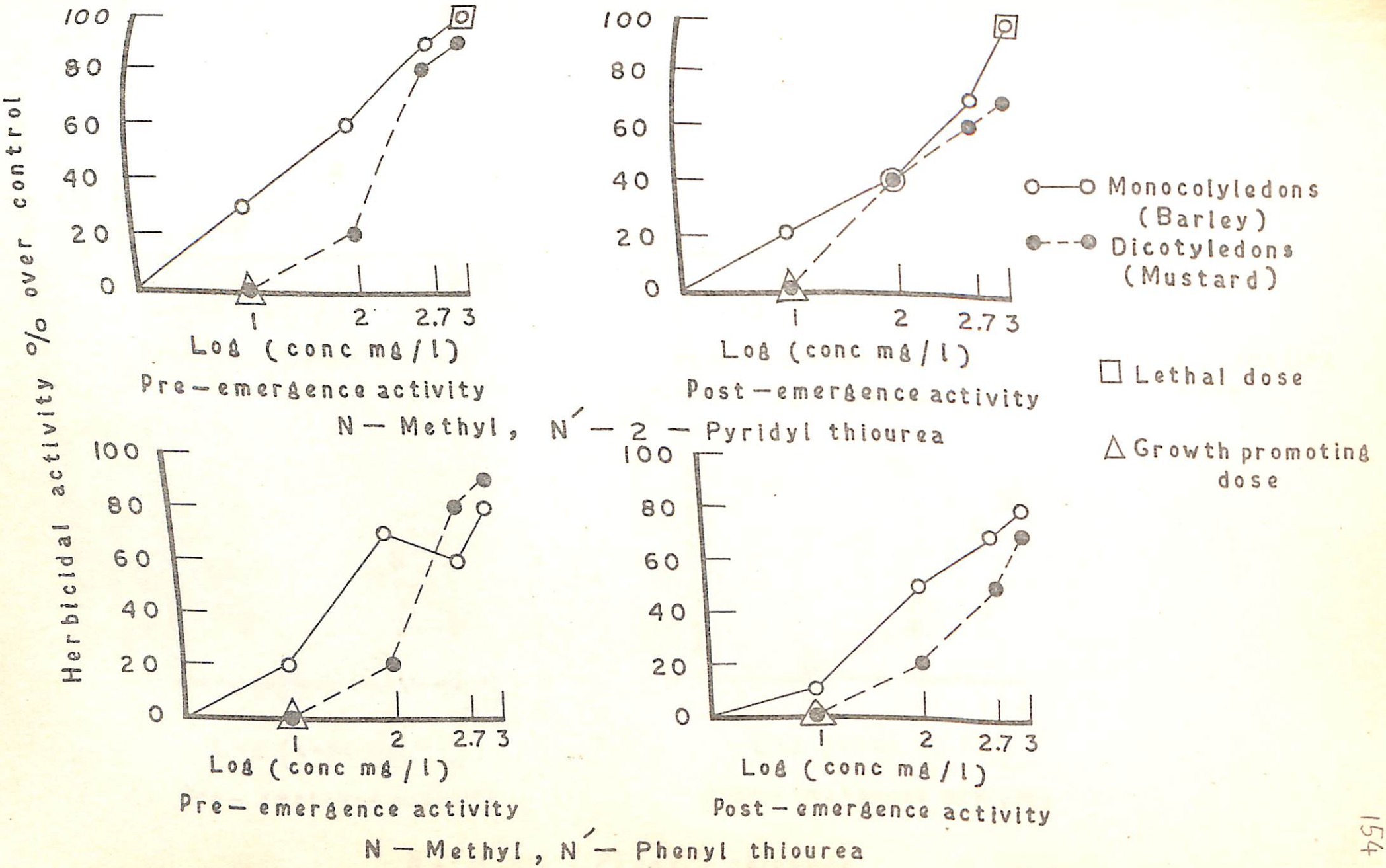


Fig. 5.13 Herbicidal activity experiment for different doses of substituted thioureas

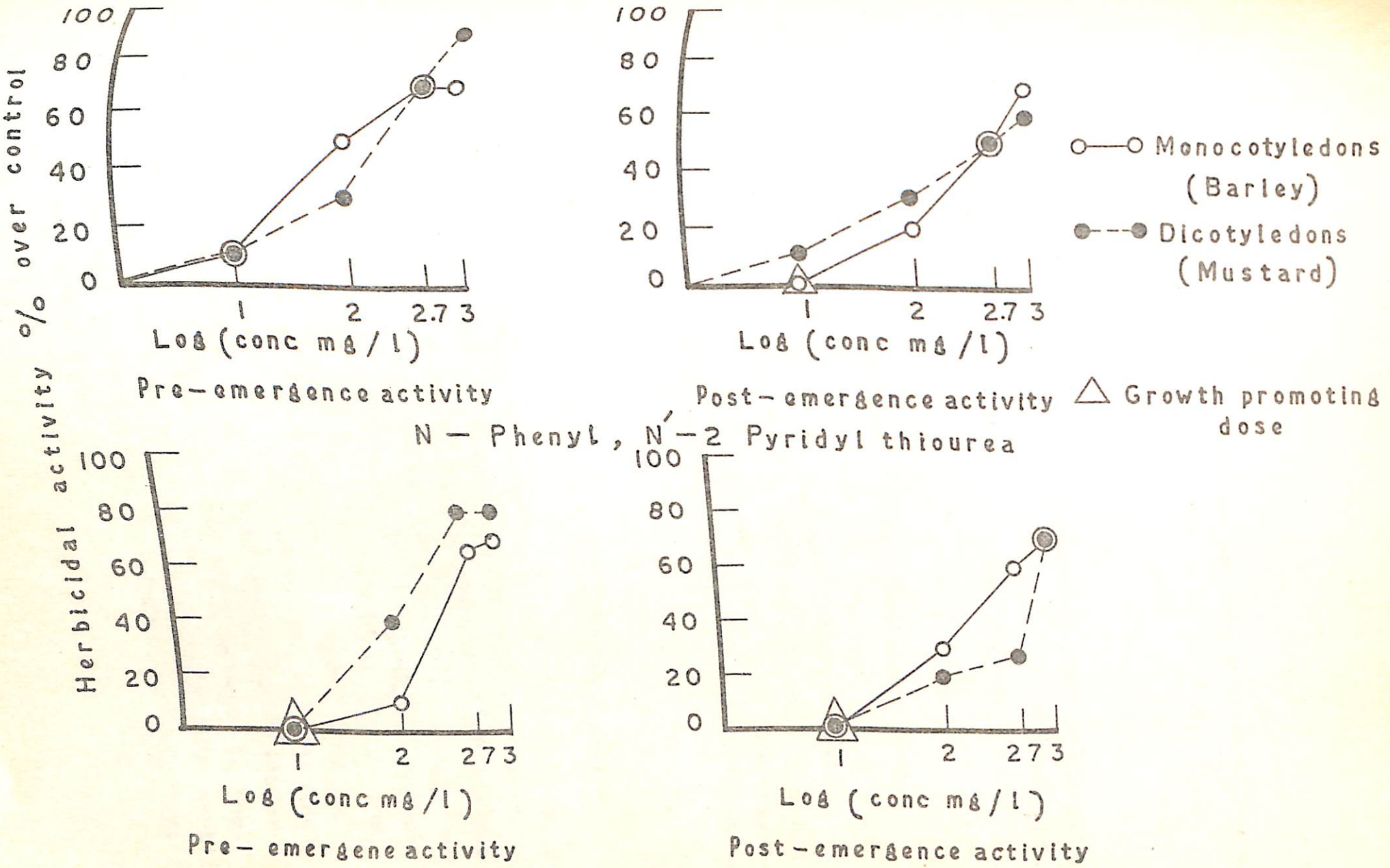


Fig. 5·14 Herbicidal activity experiment for different doses of substituted thioureas

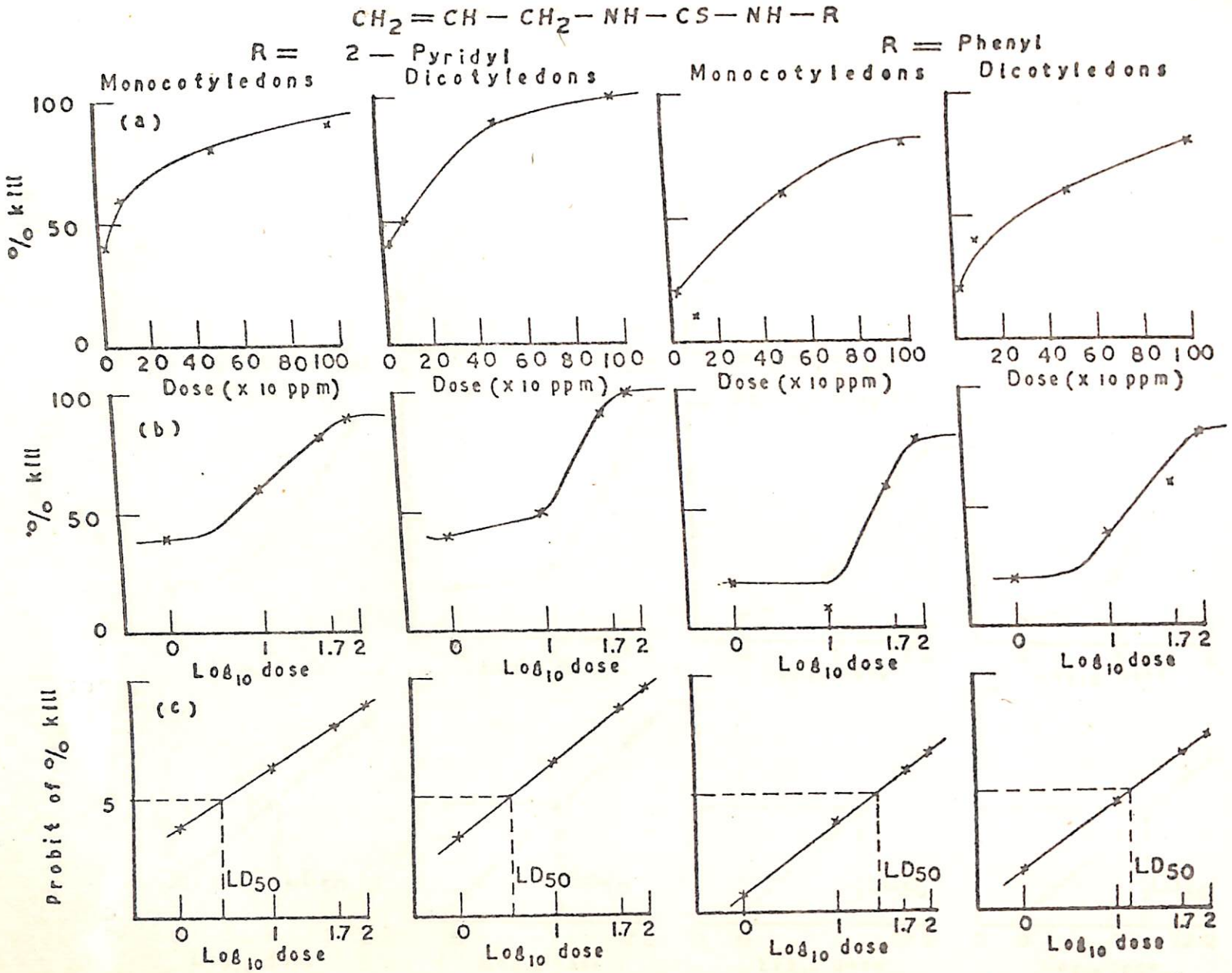
Seeds of both Barley (monocotyledon) and mustard (dicotyledon) were sown on these beds, in triplicate sets of petri dishes for each dosage level.

Observations on grown up seedlings was done after 10 days of time. The results obtained are shown in figs. 5.11 to 5.14 and tables included in the Appendix A .

Post-emergence: Same representative thiourea derivatives were tested for post-emergence herbicidal activity by method described in section 5.3.7 at concentration level of 10, 100, 500 and 1000 ppm. The results obtained have been represented in figs. 5.11 to 5.14 and tables included in Appendix A.

5.3.10 Dose response studies and LD_{50} values

In very many types of work with herbicides if the effect or response is plotted against dose on an arithmetic scale a growth curve is obtained. If the doses are transformed to their logarithms this curve is converted to a symmetrical sigmoid form (Roberts, 1982). A transformation of the percentage activity can often convert this in turn to a straight line, which facilitates the drawing of the line of best fit. The transformation most often used for this purpose is the probit. The best fit for the results with probit lines may be calculated by regression using the least square method.



Fig·5·15 Dose-response relationships : (a) dose on arithmetic scale (b) dose on logarithmic scale (c) probit regression line for Pre-emergence herbicidal activity of N—allyl substituted thioureas

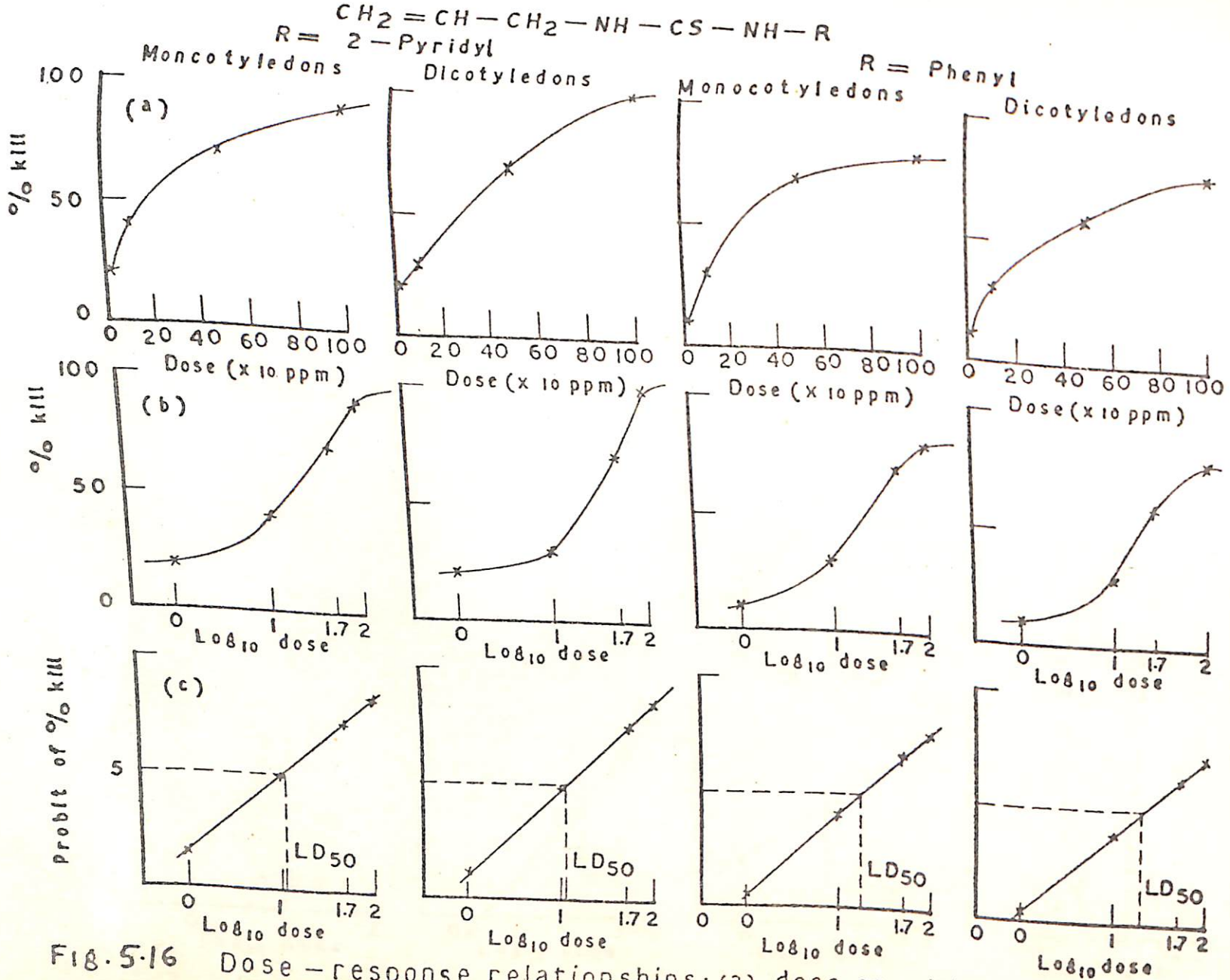


Fig. 5.16 Dose — response relationships: (a) dose on arithmetic scale (b) dose on logarithmic scale (c) Probit regression line, for Post-emergence herbicidal activity of N — allyl substituted thioureas

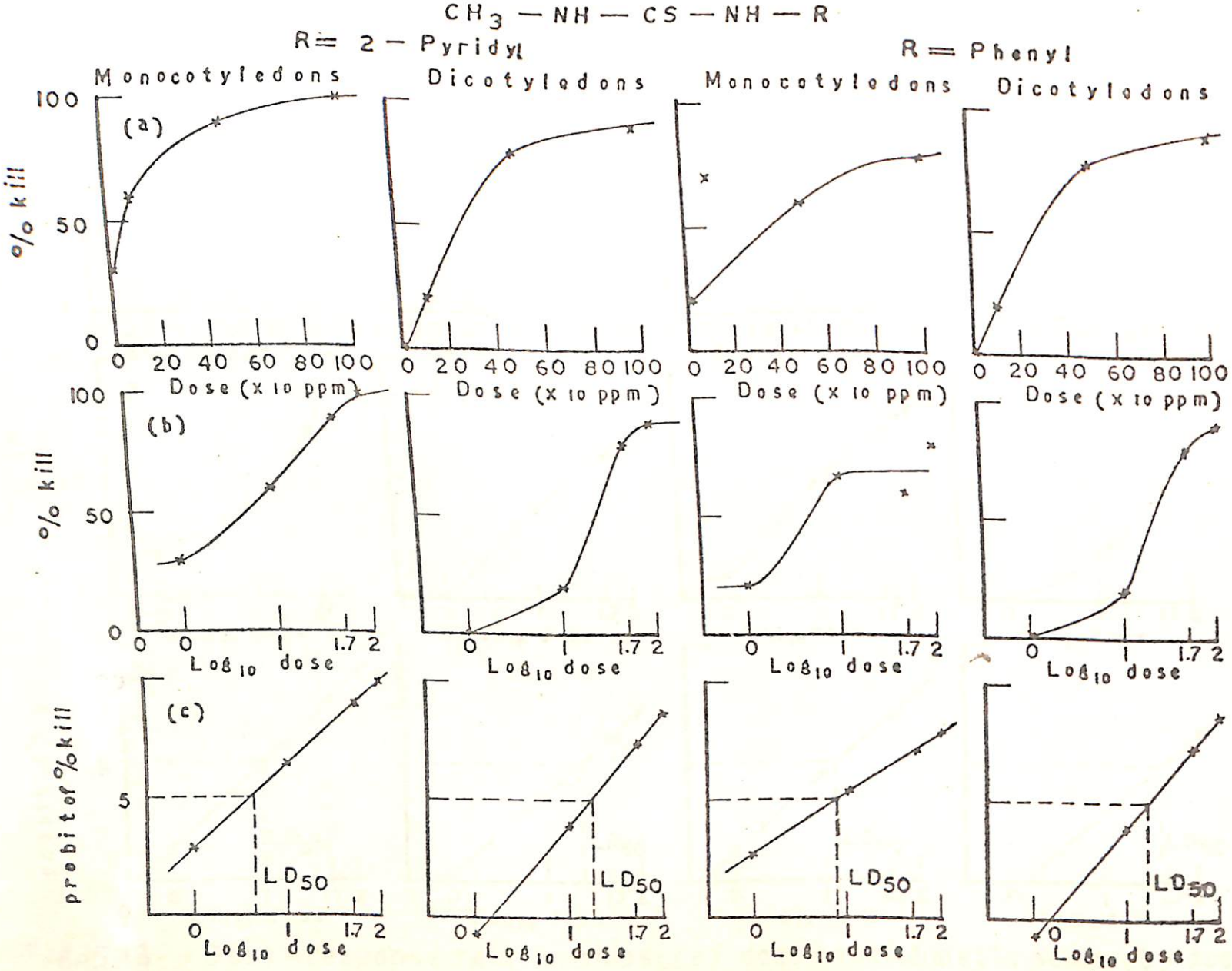


Fig.5.17 Dose—response relationships: (a) dose on arithmetic scale (b) dose on logarithmic scale (c) Probit regression line for Pre—emergence herbicidal activity of N—Methyl substituted thioureas

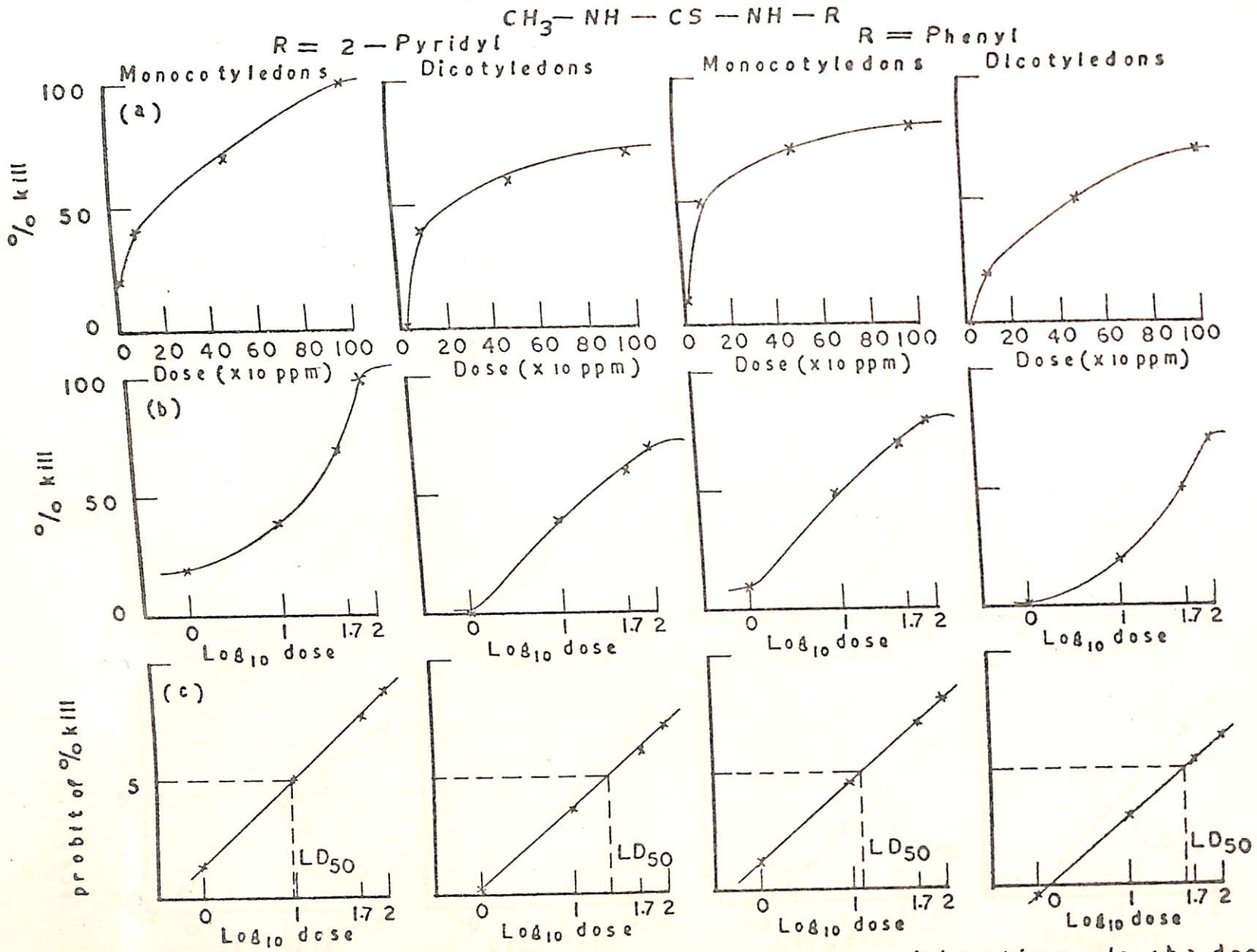


Fig. 5.18 Dose–response relationships: (a) dose on arithmetic scale (b) dose on logarithmic scale (c) Probit regression line, for Post-emergence herbicidal activity of N–Methyl substituted thioureas

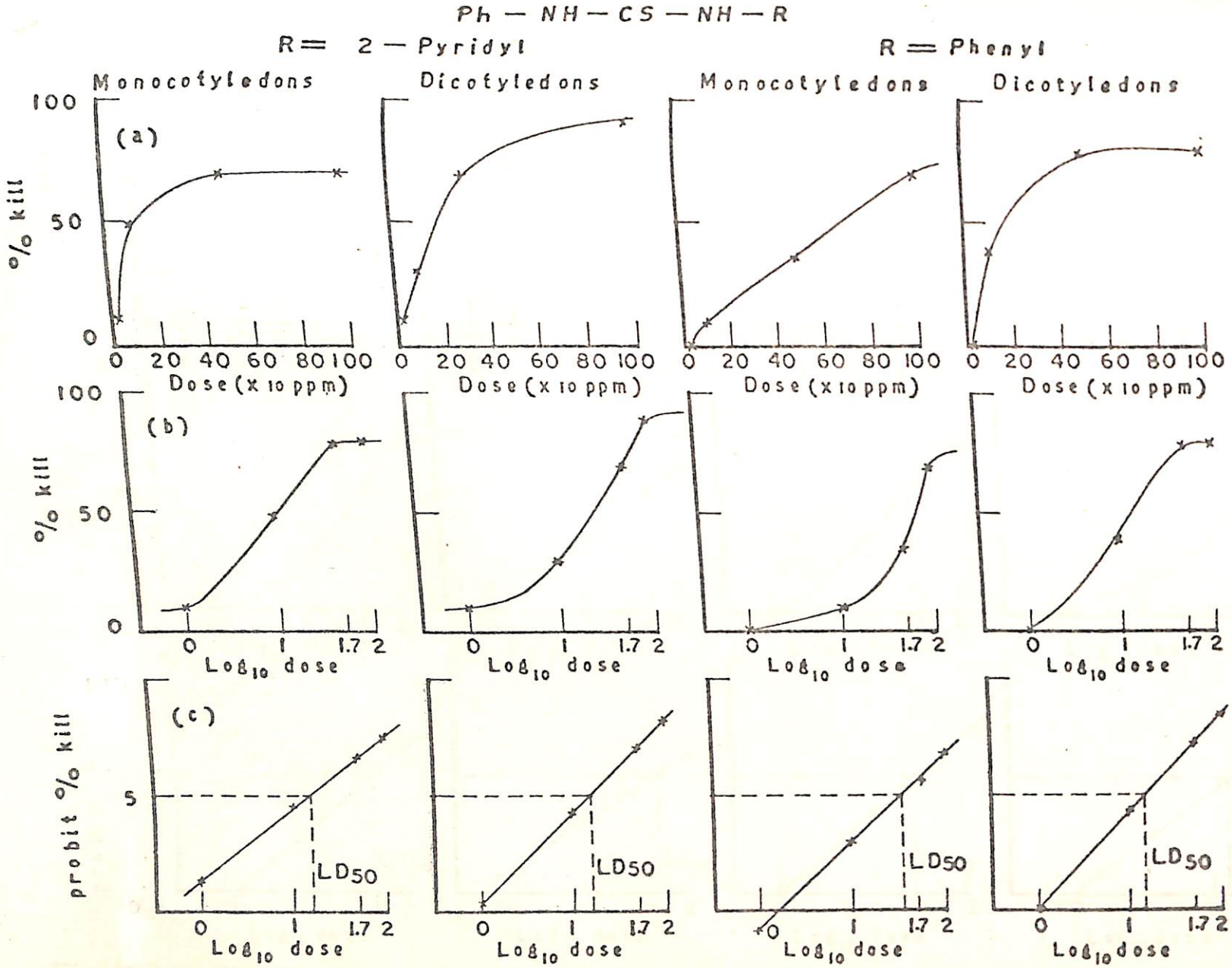


Fig. 5.19 Dose—response relationships: (a) dose on arithmetic scale (b) dose on logarithmic scale (c) probit regression line, for Pre—emergence herbicidal activity of N — Phenyl substituted thioureas

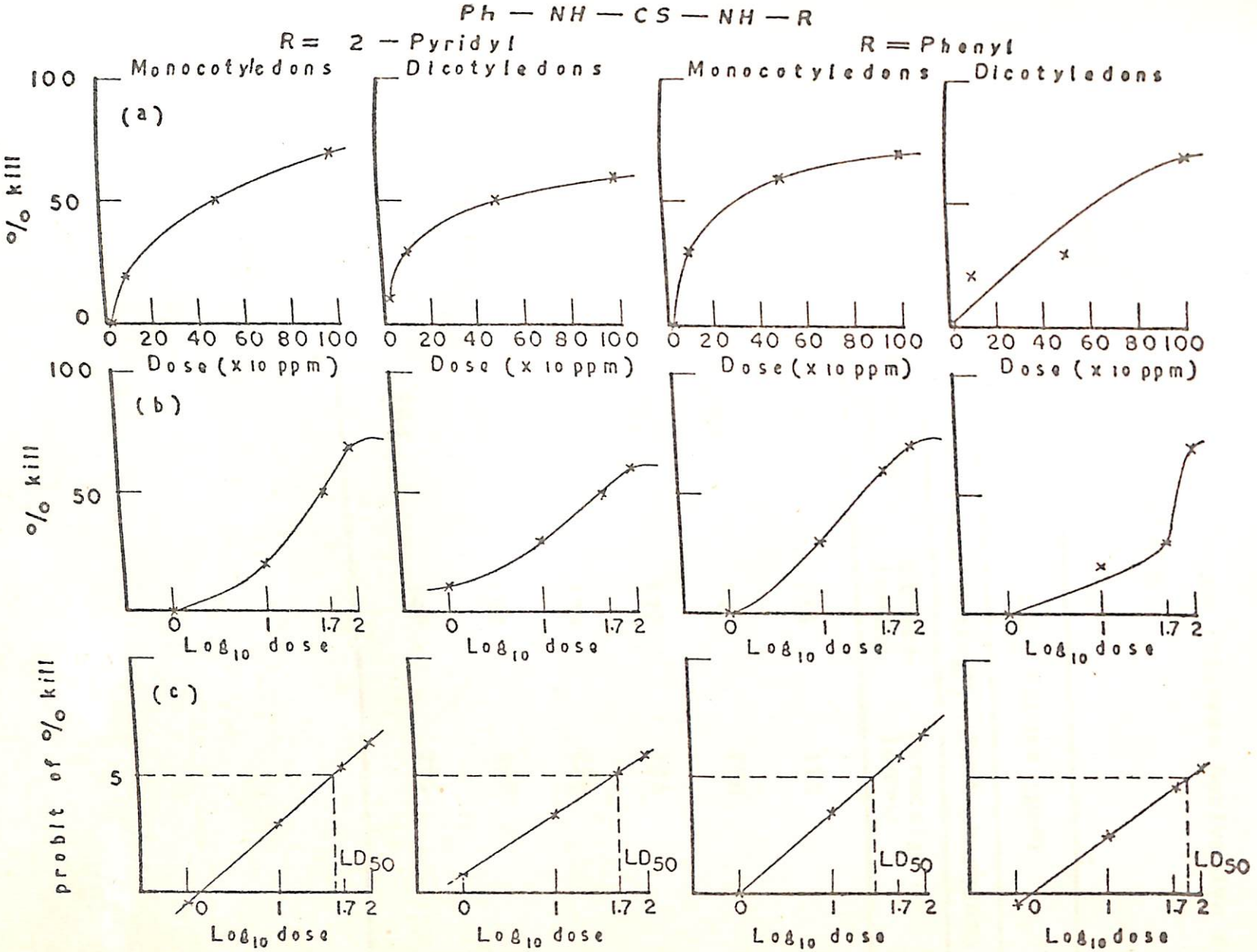


Fig. 5.20 Dose–response relationships: (a) dose on arithmetic scale (b) dose on logarithmic scale (c) probit regression line, for Post-emergence herbicidal activity of N–Phenyl substituted thioureas

Table 5.6 LD_{50} Values of Substituted Thiourea Derivative for their Herbicidal Activity.

Thiourea derivative	LD_{50} Values (ppm)			
	Pre-emergence activity		Post-emergence activity	
	Monocoty-ledons	Dicoty-ledons	Monocoty-ledons	Dicoty-ledons
N-Al,N'-2 Py tu	128	135	112	112
N-Al,N'-Ph tu	280	141	178	200
N-Me,N'-2 Py tu	144	178	193	234
N-Me,N'-Ph tu	179	178	126	468
N-Ph,N'-2 Py tu	158	158	398	501
N-Ph,N'-Ph tu	354	148	281	708

The data obtained from activity experiment and curves are represented in figs. 5.15 to 5.20. The use of IBM 1130 computer was taken for calculating the best fit values by method of regression (listing of program is given in the Appendix B).

The LD_{50} values so calculated (table 5.6) lead to the conclusion that dosage of 300 ppm is the most suitable for this type of chemicals viz. N,N' disubstituted thiourea. For studies for screening pre-emergence and post-emergence herbicidal activity, dosage value of 300 ppm was taken.

5.3.11 Observations

Twentynine N,N'disubstituted thiourea derivatives, divided into three series of N-allyl, N-methyl and N-phenyl thiourea derivatives were tested for the pre and post-emergence herbicidal activity at 300 ppm concentration, by methodology described in section 5.3.7.

All the observationschosen for estimating herbicidal activity are shown in figs. 5.21 to 5.26 along with standard deviations and level of significance.

5.3.12 Activity score

This is the method universally used for a qualitative evaluation of the species for herbicidal activity of treatment.

Each species of plant is assessed on scale which has been varying from 0 - 7

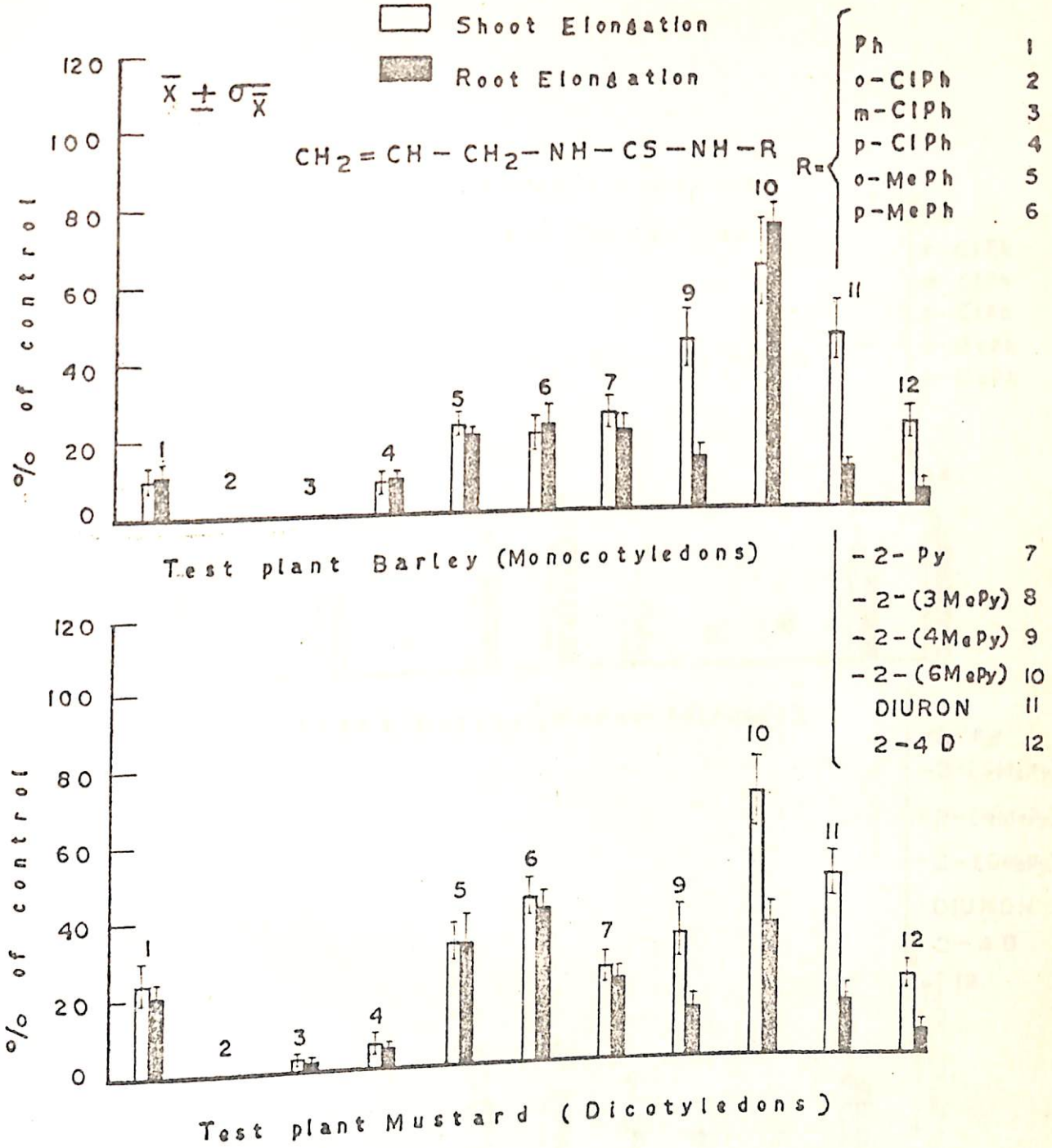


Fig.5.21 Pre-emergence Herbicidal activity of substituted thioureas

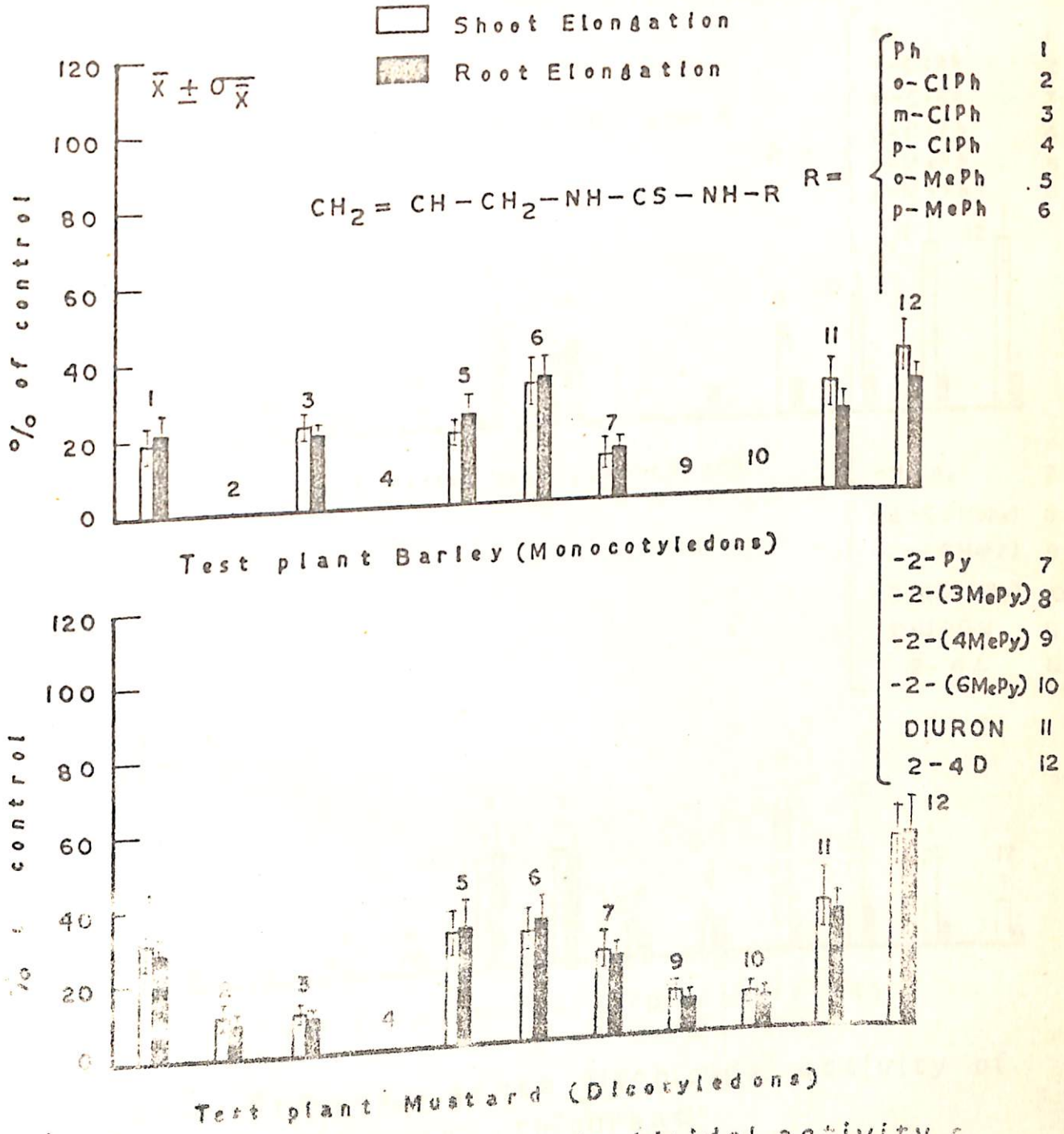


Fig. 5.22 Post-emergence Herbicidal activity of substituted thioureas

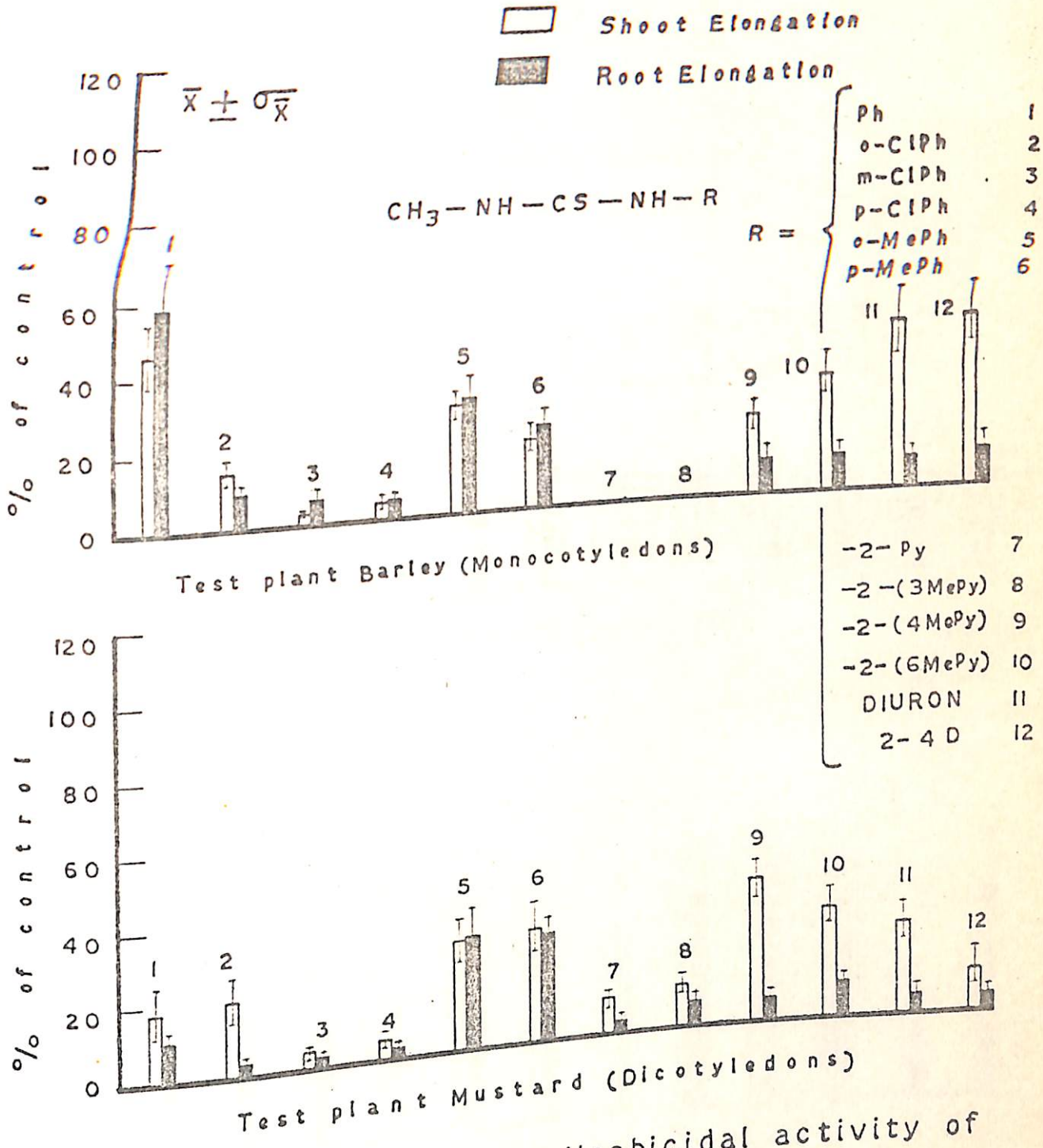


Fig. 5.23 Pre-emergence Herbicidal activity of substituted thioureas

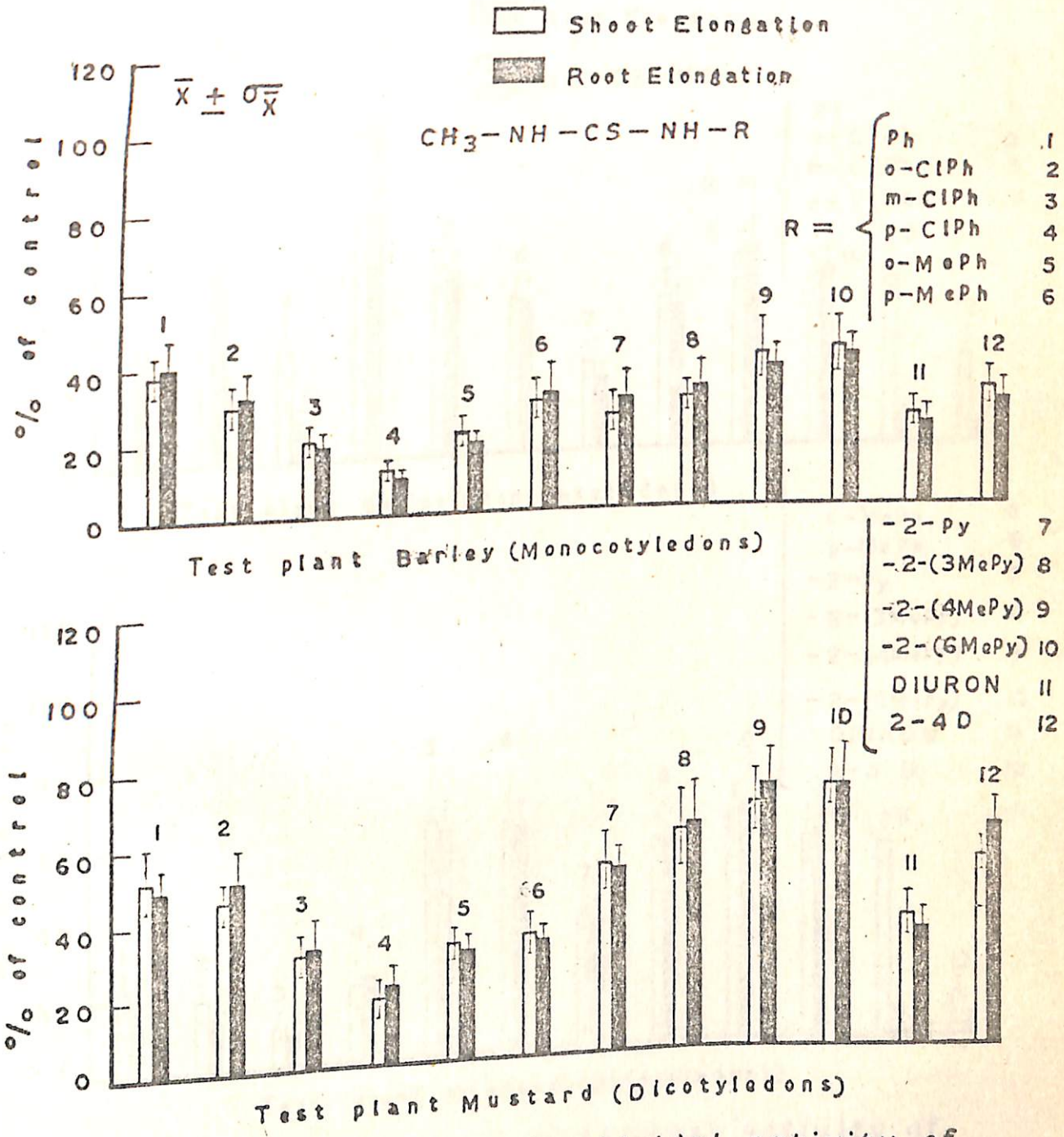


Fig. 5.24 Post-emergence Herbicidal activity of substituted thioureas

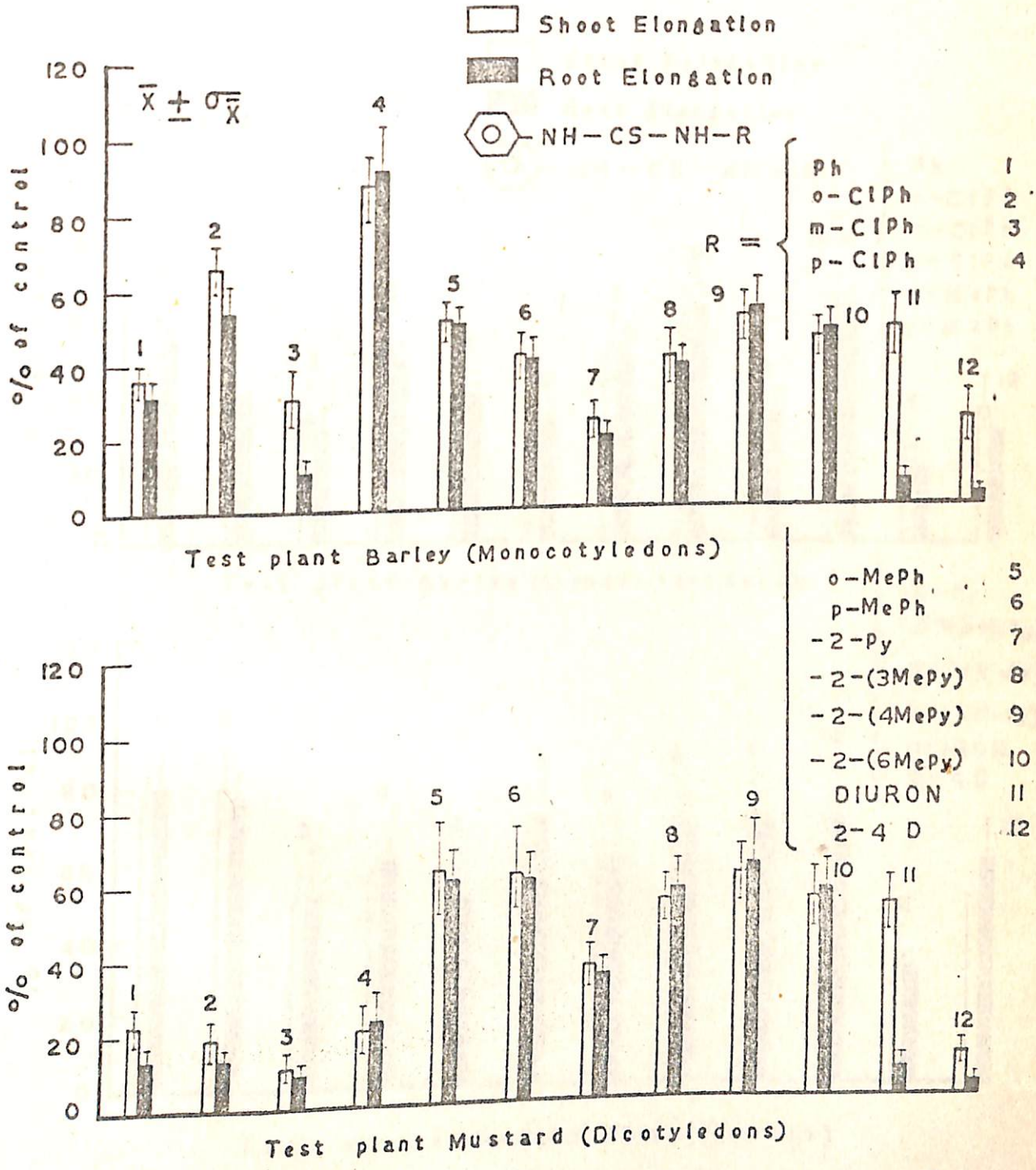


Fig. 5.25 Pre-emergence Herbicidal activity of substituted thioureas

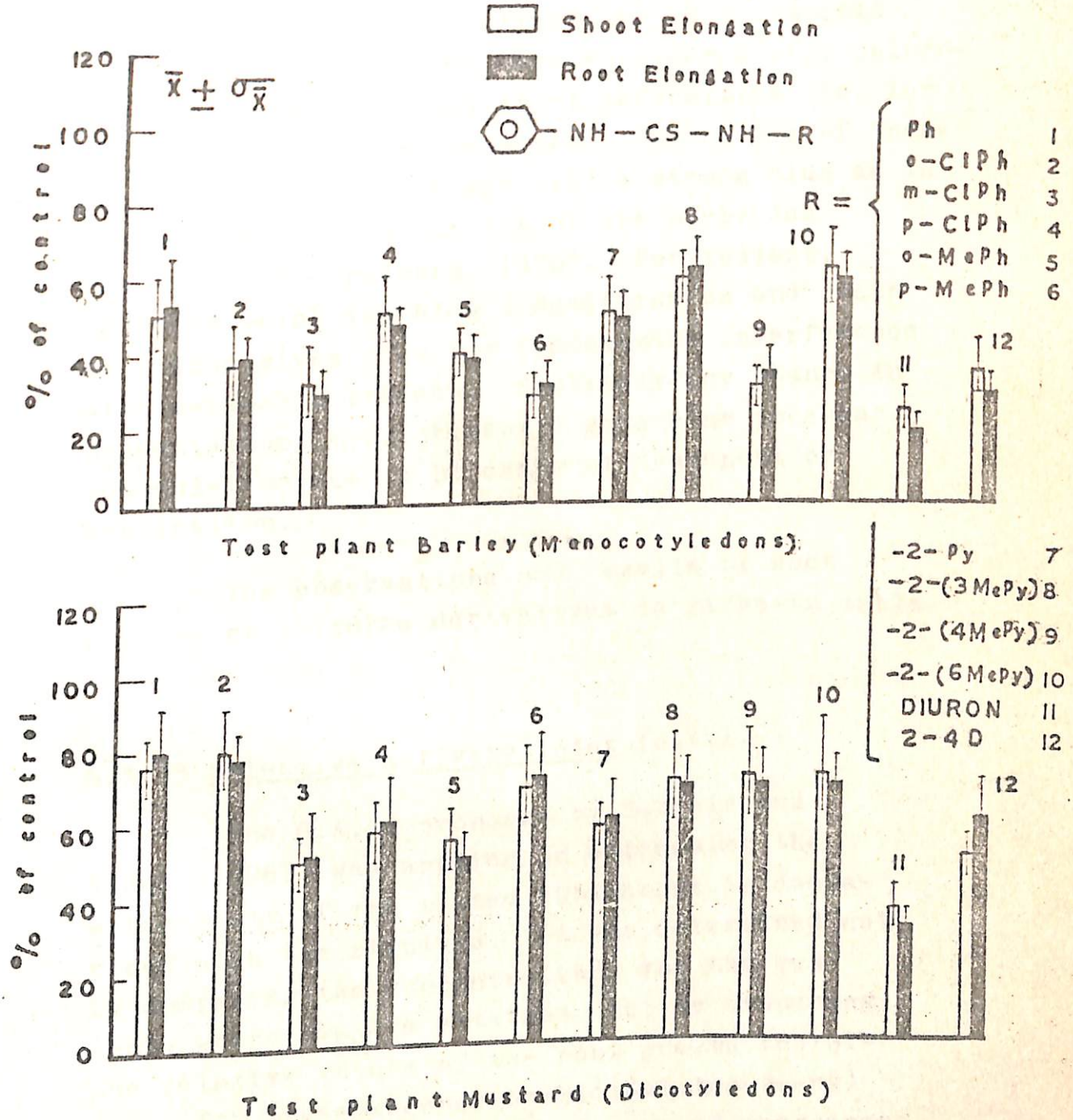


Fig.5.26 Post-emergence Herbicidal activity of substituted thioureas

(Richardson and Dean, 1973), 0 - 100 (Saggers, 1976) and so on. In the present studies a 0 - 10 scale was used, where 0 = no effect and 10 = complete kill. Various symptoms were considered viz. chlorosis, necrosis, root and shoot deformities etc for assigning a comparative score. The nature of these qualitative responses may give a strong clue as to the primary site of action of the herbicide (Ashton 1967, Bradbury, 1970). For instant, necrosis which is a slow discolouration and death of tissue gives clue for fundamental interference with metabolic process. Similarly any change in pigmentation like, chlorosis give clue to sugar accumulation due to blockage of transport or respiration.

The observations and results of such studies on thiourea derivatives is given in table of Appendix A.

5.3.13 Selective activity index (S.A.I.)

The S.A.I. proposed by Rakitin and Rudnik (1967) was applied in expressing the selectivity of the tested substances in comparison with the standard. It was determined not by comparing the concentrations for the two tests where LD_{50} is obtained, but by comparing the relative values of the root growth inhibition (for pre-emergence herbicidal treatment) and shoot growth inhibition (for post-emergence treatment) obtained by experiments at optimal concentration. (See Appendix A)

This method has been extensively used by Vassilev et al (1982a, 1980, 1969a, 1967a, 1965) who have obtained very satisfactory results.

5.3.14 Result and Discussion

Herbicidal activity screening of the thiourea derivative have shown very encouraging results. Some of them were even 100% lethal at the optimum concentration chosen viz 300 ppm (Figs.5.21 to 5.26).

Among the three series of substituted thiourea studied, the N-allyl substituted series of derivatives were found to be most effective. The work of Vassilev (1982a), on similar compounds confirms these observations.

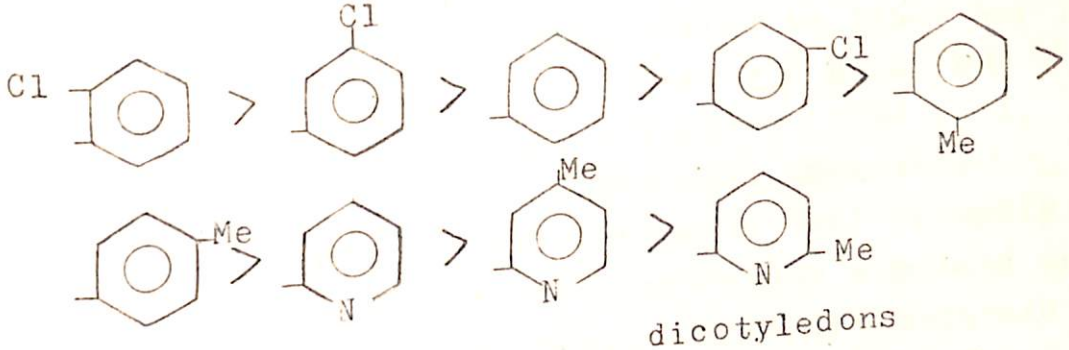
The present studies reveals many interesting trends of herbicidal activity upon structural changes. A comparison of pre-emergence and post-emergence herbicidal activity for both monocotyledon and dicotyledon for each series has also helped in drawing major conclusions on the physiology, biochemistry and mechanism of action of these derivatives. These will be discussed herein after.

N-allyl series of thiourea derivatives: As mentioned earlier, these derivatives were the most effective herbicides. The percent activity observed ranges from 30 to 100% as represented by tables in Appendix A and figs. 5.21 to 5.22 The qualitative assessment showed clear symptoms of chlorosis and necrosis, which was more prominant in case of post-emergent treated plants. Further these herbicides were found to be more effective towards monocotyledons than dicotyledons.

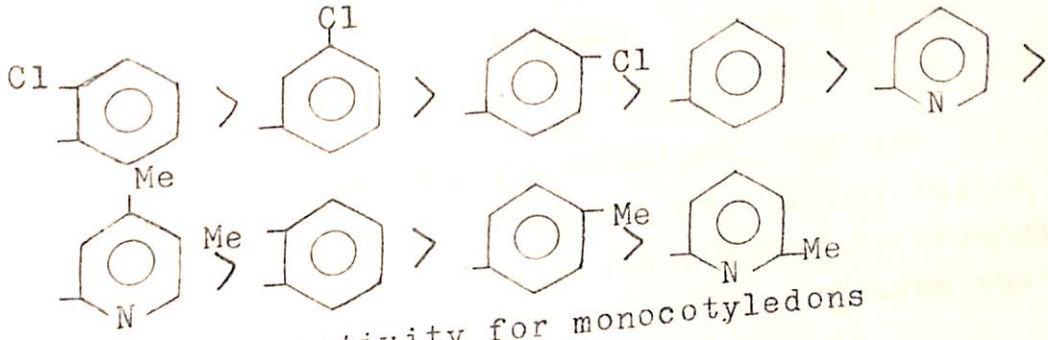
The effect of various substituent at N'-position upon herbicidal activity of compound can be seen from the following descending orders.

$CH_2=CH-CH_2-NH-CS-NH-R$, R varies as:

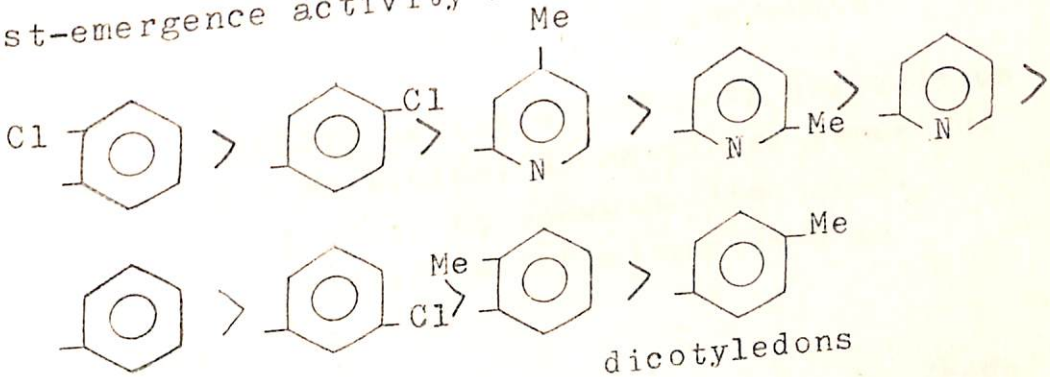
Pre-emergence activity for monocotyledons



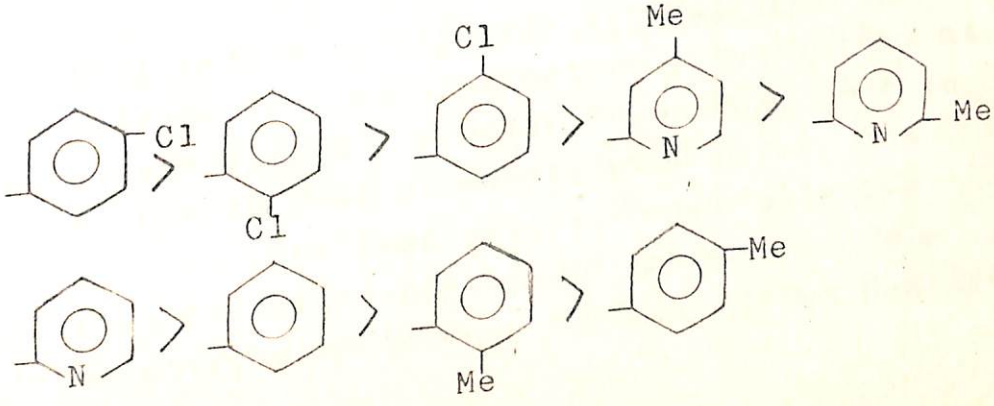
dicotyledons



Post-emergence activity for monocotyledons



dicotyledons



These results lead us to conclude that halo (viz chloro) substituents on phenyl ring at N' position of thiourea derivative are most effective, while alkyl substitution (viz methyl) is the least. Although heterocyclic ring (viz pyridine) with alkyl substituents is least herbicidal in case of pre-emergence (30% kill) but it is interestingly most effective (100% kill, lethal see fig. 5.22) for its post-emergence herbicidal action. This suggests that probably the translocation of this particular compound is best along the phloem cells, which pre-dominate for such function on foliage (leaves & stems) (Roberts, 1982).

From the results obtained, one can generalize by saying that an alkyl substitution on the phenyl or pyridyl ring reduces herbicidal activity AND halogen substitution increases the herbicidal activity of these compounds.

N-allyl series of thiourea derivatives were highly herbicidal as mentioned above but were non-selective as shown by the S.A.I. values represented in tables included in Appendix A.

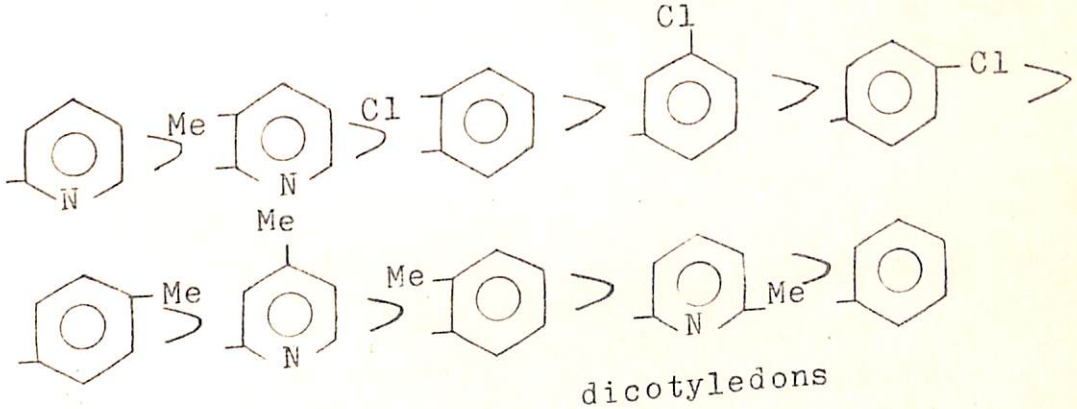
N-methyl series of thiourea derivatives: These derivatives were also effectively herbicidal at the dosage slightly greater than LD_{50}. But in comparison to N-allyl substituted series compounds they were less active, especially for the post-emergence herbicidal activity. This can be attributed to many factors, first N-allyl

derivatives were in general more soluble compounds and thus can be imbibed by the seed coat from the aqueous phase of growth bed in pre-emergence and stomata or similar openings on leave surfaces in post-emergence treatment. Secondly acetylenic H on -CH group of allyl substituent imparts more acidic nature and thus enhances over all effect of herbicidal nature. N-methyl derivatives were herbicidal between 60 to 100% as shown in figs. 5.23 to 5.24 .

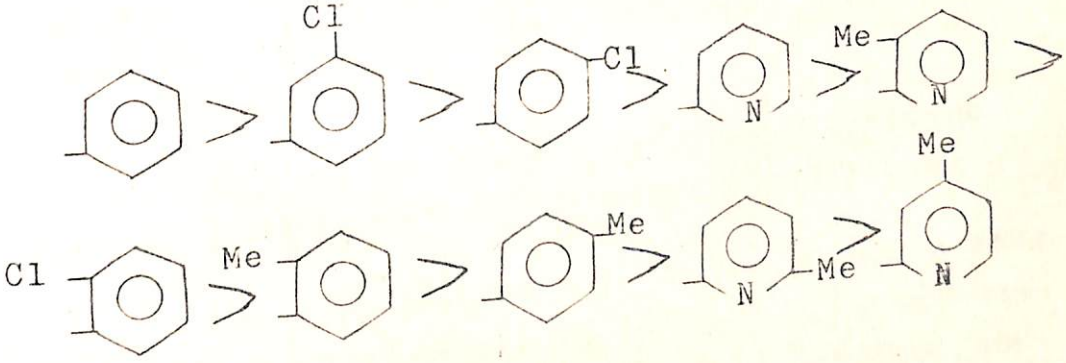
From the results obtained, the following structure - activity correlationship can be obtained.

CH_3-NH-CS-NH-R, R varies as:

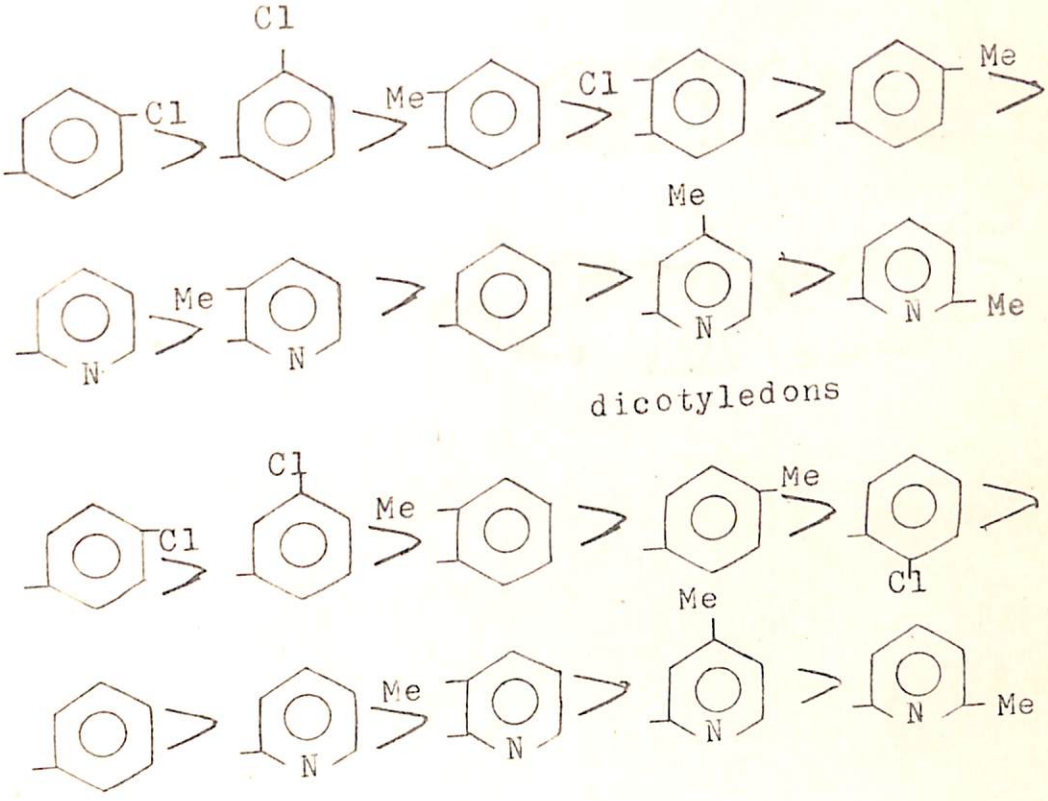
Pre-emergence activity for monocotyledons



dicotyledons



Post-emergence activity for monocotyledons



dicotyledons

From the trends obtained it can be concluded that halogen substitution on phenyl nucleus leads to enhanced herbicidal activity. These are the most active compounds that have been synthesised.

All pyridine and substituted pyridine compounds have been found to be less active.

One more interesting observation in case of N-methyl derivatives is that the para orientation isomer was more active than the ortho, the

reverse is the case in N-allyl derivatives. This leads to the conclusion that it is a clue for the involvement of thiourea herbicides in the enzymatic metabolic processes of the plant, where role of spatial orientation plays a major role in choosing a specific site of action (Roberts, 1977).

Qualitative assessment from activity score showed that the chlorosis in this series was more predominant and certain deformities in shoot (which got shortened and thick) and root (which was thin and elongated) were observed.

The S.A.I. data shown in tables in Appendix A reveals an interesting fact. It was found that N-methyl derivatives with phenyl and halo substituted phenyl nucleus were highly selective towards dicotyledons (S.A.I. ratio 1:5) for their pre-emergence herbicidal activity. This selectivity is far better than the standard herbicide chosen viz 2,4-D. Since the later is a post-emergence treatment herbicide, thus we can safely conclude that the mode of action of thiourea herbicide will be different from this herbicide as the herbicidal action chiefly depend upon mode of translocation (Roberts, 1982).

All other derivatives selectivity was towards the monocotyledons and better in their post-emergence treatment.

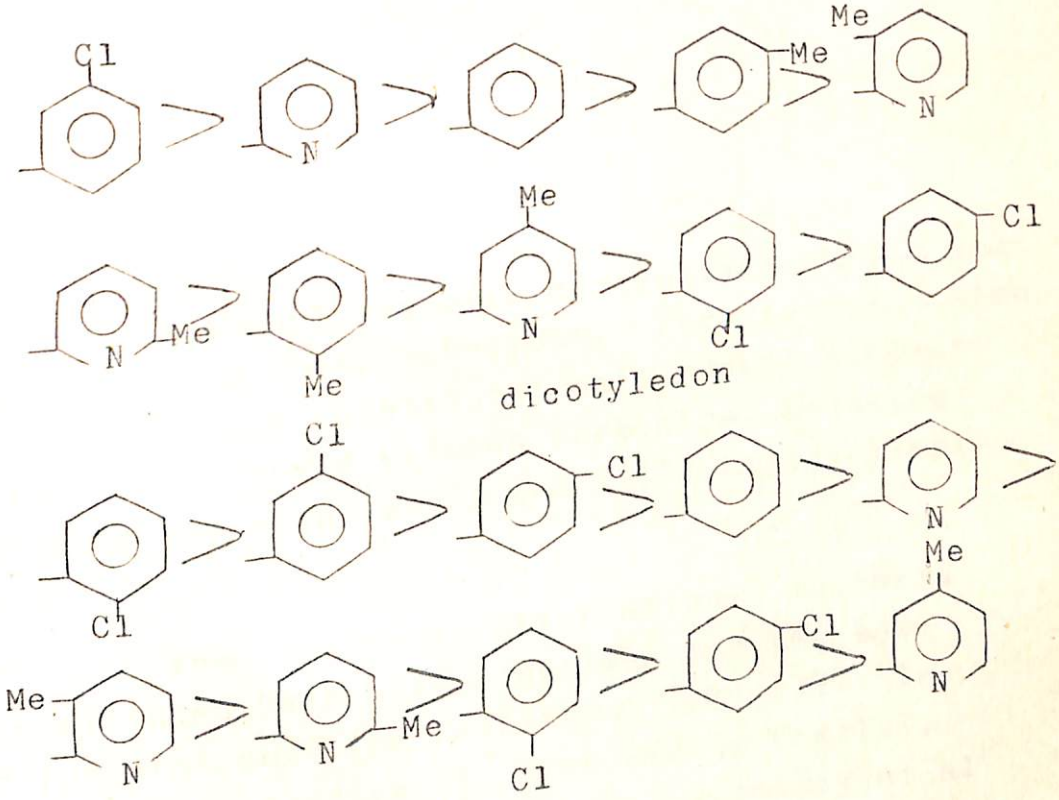
N-phenyl series of thiourea derivatives: These derivatives were found to be least herbicidal in comparison to the other two series. The herbicidal activity ranges from 20% to 90% (figs. 5.25 to 5.26)

Their low herbicidal activity is also revealed by high LD_{50} values of the two parent compounds chosen for dose response studies (table 5.6). These derivatives were also found to be better pre-emergence treatment herbicide, which again agreed with the LD_{50} values (table 5.6) and qualitative activity score shown in tables of Appendix A.

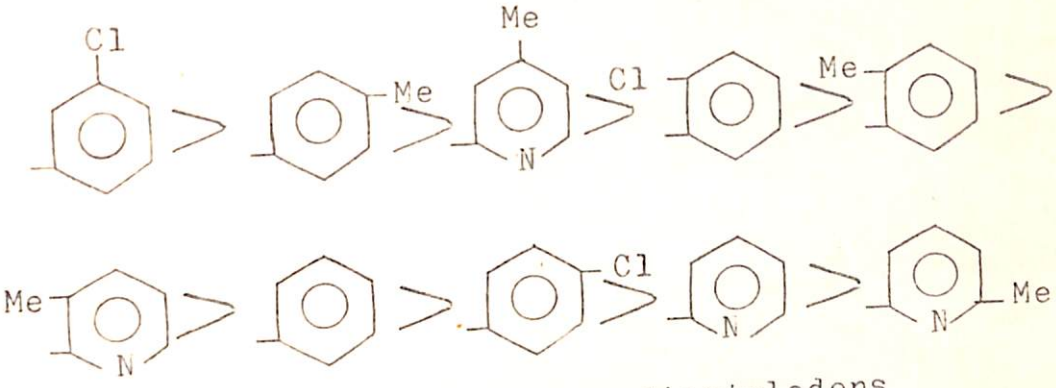
From the results obtained, the following structure activity correlations can be obtained.

C_6H_5-NH-CS-NH-R, R varies as:

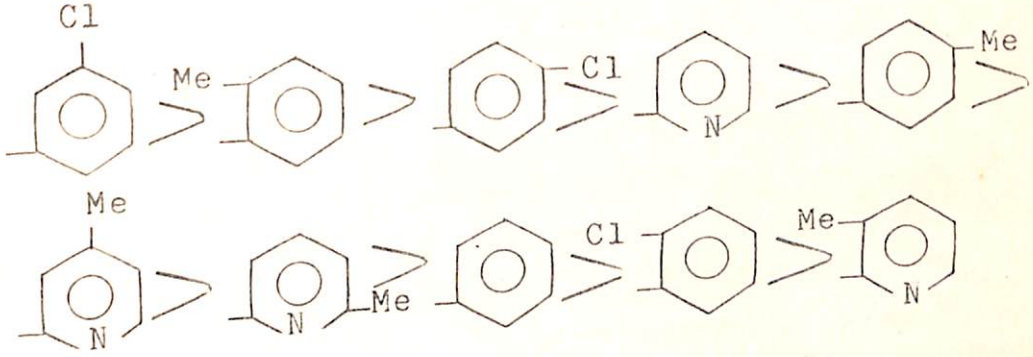
Pre-emergence activity for monocotyledon



Post-emergence activity for monocotyledons



dicotyledons



N-phenyl thiourea derivatives showed some departure in their behaviour. For the first time ortho and para substituted halo phenyl nucleus structures showed reduced herbicidal activity. However the meta isomer was still highly herbicidal.

From the above observations, the meta substituted halo phenyl nucleus has the best structural unit for herbicidal activity. In the present studies the compound is N-allyl, N'-meta chlorophenyl thiourea. Vassilev et al (1982b) in their studies with the same compound

against wheat (monocotyledons) and cucumber (Dicotyledons) found it to be very effective and selective (I.S.A. 1.0:5.4 for monocotyledon). They also showed that amongst various halo groups bromo is the most effective to enhance herbicidal activity.

Alkyl substitution on phenyl nucleus has no consistent trends to draw any conclusion. The substitution of alkyl group (viz methyl) has in most of the cases led to the reduced herbicidal activity.

N-phenyl derivatives with halogenated phenyl nucleus were again found to be very selective herbicides for dicotyledons (I.S.A. 1.0:4.0) in pre-emergence treatment, as was the case in N-methyl derivatives. Rest of the derivatives were moderately selective towards monocotyledons. (Figs 5.27 to 5.30.)

Qualitative assessment of plants does not provide any strong indications for a particular symptom, but in a few cases chlorosis was observed.

These results indicate that N, N'disubstituted thioureas are better pre-emergence treatment herbicide and thus can be assigned to soil borne herbicides. A class of substituted ureas which have produced numerous commercially established herbicides (monouron, diuron etc) have basic structural skeleton very similar to thioureas. A comparison of two leads to quite a number of similarities on being, predominantly soil borne, selective for monocotyledons and at slightly higher doses acting as non-selective herbicide. (see figs. 5.21 to 5.30 and tables in Appendix A).

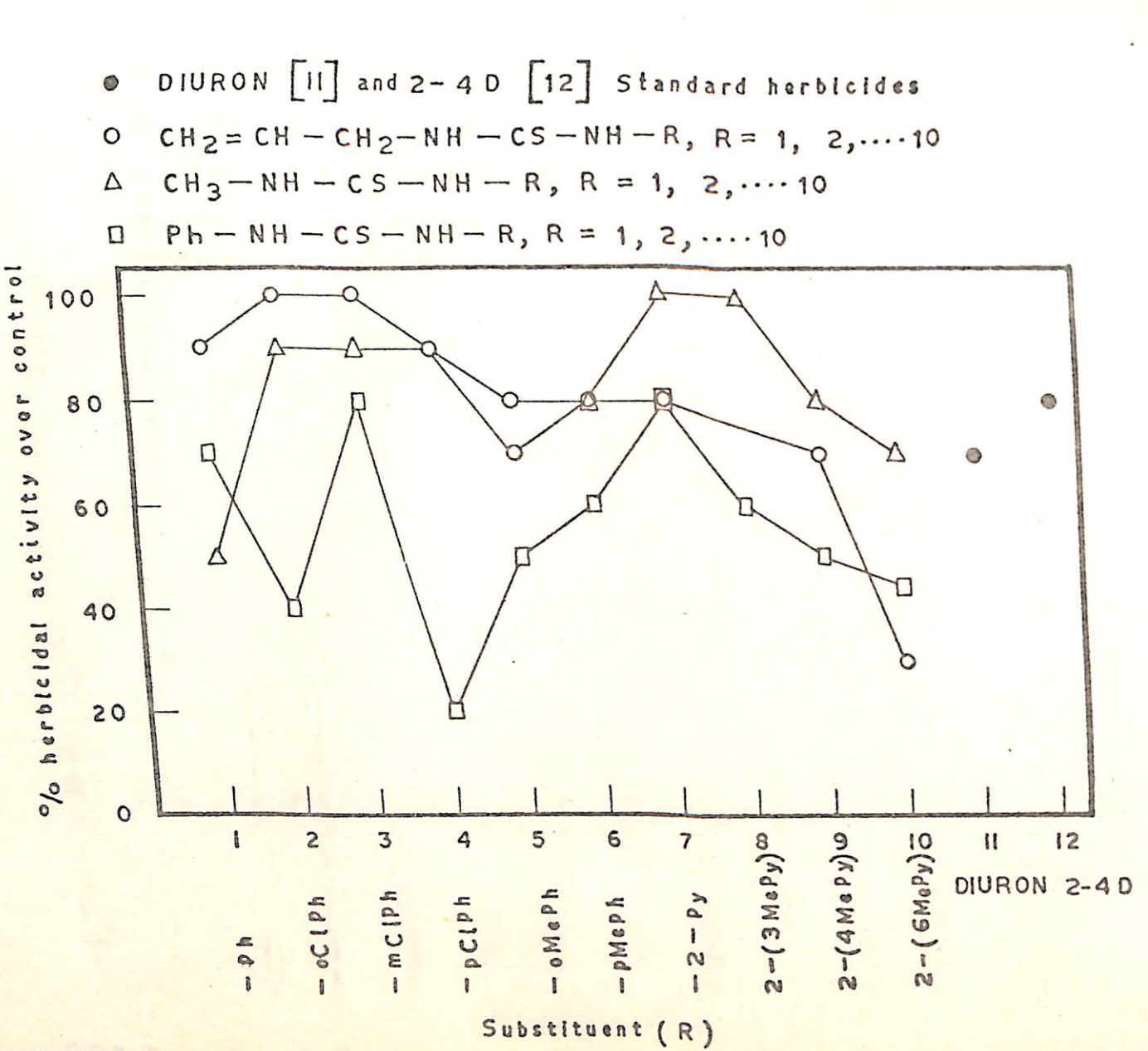


Fig.527 Trends of Pre-emergence herbicidal activity upon structural variation of substituted thioureas for Barley (Monocotyledons)

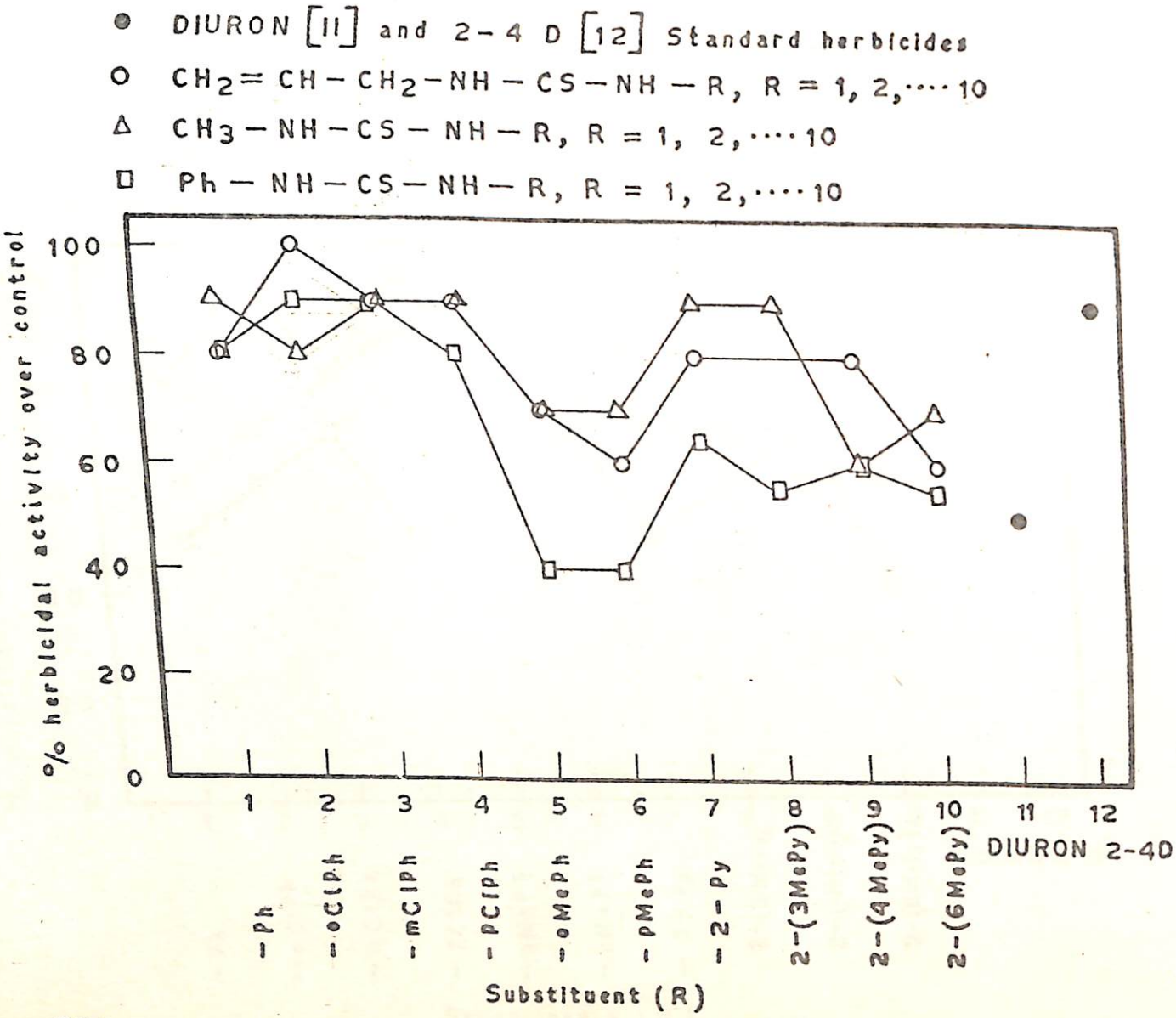


Fig. 5.28 Trends of Pre-emergence herbicidal activity upon structural variation of substituted thioureas for Mustard (Dicotyledons)

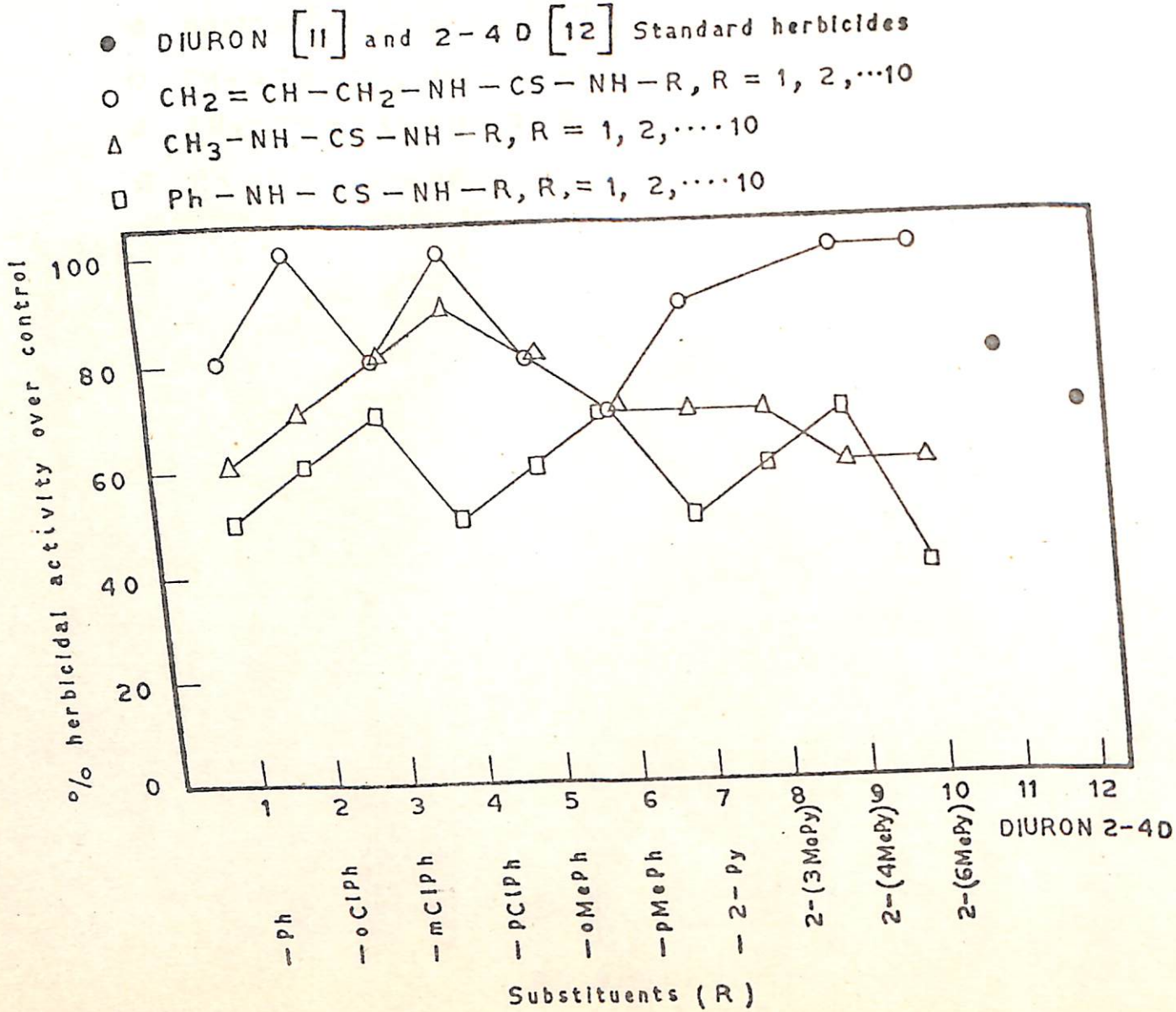


Fig.5.29 Trends of Post-emergence herbicidal activity upon structural variation of substituted thioureas for Barley (Monocotyledons)

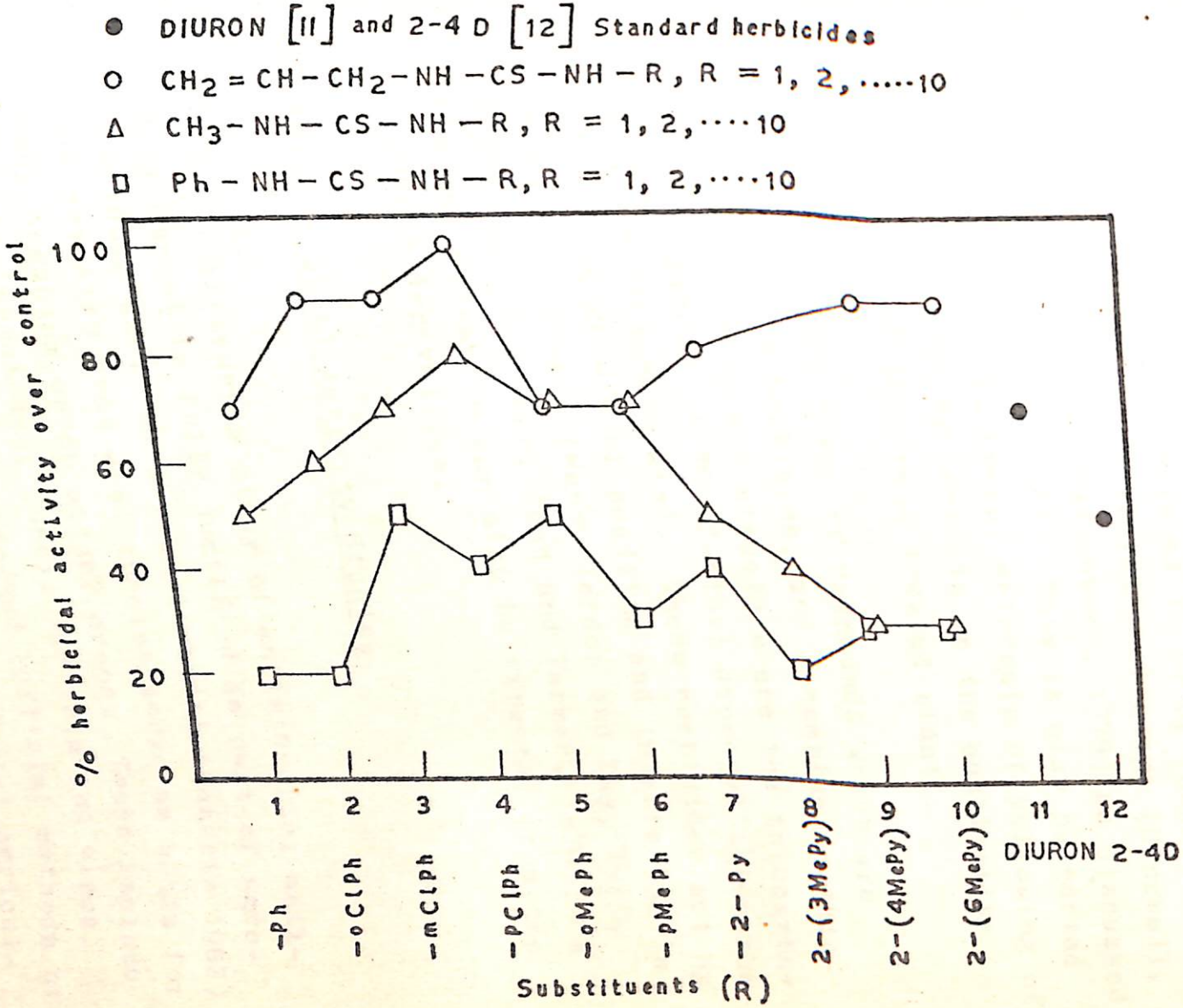


Fig.5.30 Trends of Post-emergence herbicidal activity upon structural variation of substituted thioureas for Mustard (Dicotyledons)

Thus we can also expect these thiourea herbicides to have similar mechanism for herbicidal action as substituted thioureas. The mechanism has been found and established to be by inhibition of photosynthesis at photosystem II stage (Minshall, 1957; Ashton, 1965; Radosevich, 1979) as discussed earlier (section 5.3.4). This is also supported by symptoms of paleness, chlorosis or yellowing of leaves followed by necrosis in the qualitative assessment of thioureas treated plants.

Another class of compounds which are established as herbicide, and resembles to thiourea in activity and structure are the thiocarbamates (example: EPTC (S-ethyl dipropyl thiocarbamate), benthiocarb etc). These herbicides act by inhibiting growth of seedling and interfering in protein synthesis (Mann, Jordon and Day, 1965; Mooreland, Blackman, Todd and Farmer, 1970). A similar mechanism can also be expected from the thiourea derivatives.

5.4 Antimicrobial Activity Studies

5.4.1 Aim

Although a study of antimicrobial activity cannot be fully justified as part of agrochemicals use, but a recent report (Roberts 1982) has revealed that weed species serve as hosts for many organism which attack crops. These include insects, nematodes, fungi, bacteria and virus. Further it has been reported (©fficial methods of analysis of the Association of Official Agricultural Chemists, 10th Edition, 1965, Washington)

that microbes are responsible for the untimely decay of various disinfectant and agrochemicals.

Looking to these facts, it was thought worth while to assess these compounds for their antimicrobial role as well, so that they have a multiple role as agrochemicals (Tokushu and Seizo, 1981).

The present work deals with studies of antimicrobial activity of thiourea derivatives against the organism chosen to represent the class of microbes, the bacterial strains. Bacteria is the most widely found microbe and it plays an important part in all human affairs. This is also the most convenient organism to handle in laboratory.

5.4.2 Experimental

Material: Facility of aseptic microbiology laboratory for working with microbes at the institute was utilized. All innoculation and transfering of culture media into petri dishes was carried out in Laminar flow chamber (Cleanair of Atlantus(I), Applengg Ltd., New Delhi), which has facility of U.V. lamps, spirit burners, air flow through laminar filters and all equipment necessary to keep it aseptic.

BDH bacteriological grade ingredients of culture media were used.

All the glassware used was of corning. All of these were sterilized by method of hot air incubation at 160°C for 45 minutes, after packing them in kraft paper (Collins and Lyne,1976)

All cultures and solutions used were pre-sterilized in gravity displacement autoclaves (National Steel Equipment Company, Bombay) using moist heat, after they were sealed inside glass containers.

The two bacterial strains which were used for these studies are Bacillus subtilis and Escherichia coli obtained from National Chemical Laboratory, Pune.

Incubator (SEW India) maintained at 37 ± 1°C, was used to keep control and treated replicate petri dishes for growth of bacteria in the culture. The dosage of thiourea derivatives, whose sensitivity was to be tested, was soaked by 6 mm diameter Whatman paper disc (W & R Balston Ltd., London).

Methodology: When a bacterial cell is placed in a nutrient environment and is unable to multiply beyond more than a few generations it is considered to be dead. The mechanism of the lethal process may be protein denaturation, enzyme inactivation, damage to a membrane or the blocking of an essential metabolic path. Whatever may be the path the result is the same. Thus, when an organism has been subjected to the action of a chemical antibacterial agent and is unable to recover a "bactericidal" action is considered to have taken place.

This bactericidal activity of seventeen N,N'disubstituted thiourea derivatives was tested against two strains of bacteria, viz Bacillus subtilis

and Escherichia coli, which are known to belong to two classes of bacteria, the gram positive and gram negative respectively.

The method of 'Diffusion technique' described by Sykes et al (1972) using the solid culture media was adopted for these experiments.

Solutions of desired concentration (ranging from 10 to 500 ppm of thiourea derivatives in aqueous media was prepared. Due to sparingly soluble nature of these derivatives, use of 0.5% Tween 80 surfactant was done to solubilize them in aqueous media by micelle formation mechanism (Rosen, 1978). Such methods are very common and widely used (Kulcsar, 1970; Elworthy and Treon, 1967) in pharmaceutical fields.

The solid culture media for the growth of bacteria has its ingredients as 10 gm dextrose, 10 gm peptone, 3 gm meat extract and 5 gm sodium chloride for one liter bulk, which contained 2% agar solution.

The contents for each petri dish was stored in a plugged test tube, which was sterilized by moist hot air at 15 lbs pressure and 160°C for 45 minutes in autoclave. Each test tube content was brought to the molten state and then inoculated with the bacterial inoculum which was cultured on the slants of culture media. This was carried out inside the laminar flow chamber using a sterilized loop, in the vicinity of flame of a burner. Approximately 0.5 gm of inoculum was

taken for each petri dish content. This was immediately transferred into sterilized petri dishes and left for setting of media with proper cover lid. Once the culture media was ready, Whatman paper discs, pre-soaked in different thioureas solutions for nearly 25 to 30 minutes was kept in the center of the petri dish for sensitivity test of bacteria towards the chemical present. This was checked after 40 - 45 hours of growth of bacteria in these culture media, at an ambient temperature of 37°C inside the incubator. Each set was in three replicates with a separate control.

Observations: Bacterial strain sensitivity towards various thiourea derivatives was estimated by finding the zone of inhibition (shown in fig. 5.1) around the paper disc for each of the petri dishes. These observations have been presented in table 5.7.

5.4.3 Result and Discussion

A review of antibacterial activity of thiourea derivatives by Pandeya et al (1981) reveals that most of the bacterial strains, which are found to be sensitive and inhibited by thioureas belong to gram positive class. The same was found to be true by the present studies for the seventeen thioureas tested for their bactericidal activity. It was found that these could inhibit the growth of gram positive Bacillus subtilis only.

Amongst the three series of thiourea studied namely N-allyl, N-methyl and N-phenyl the

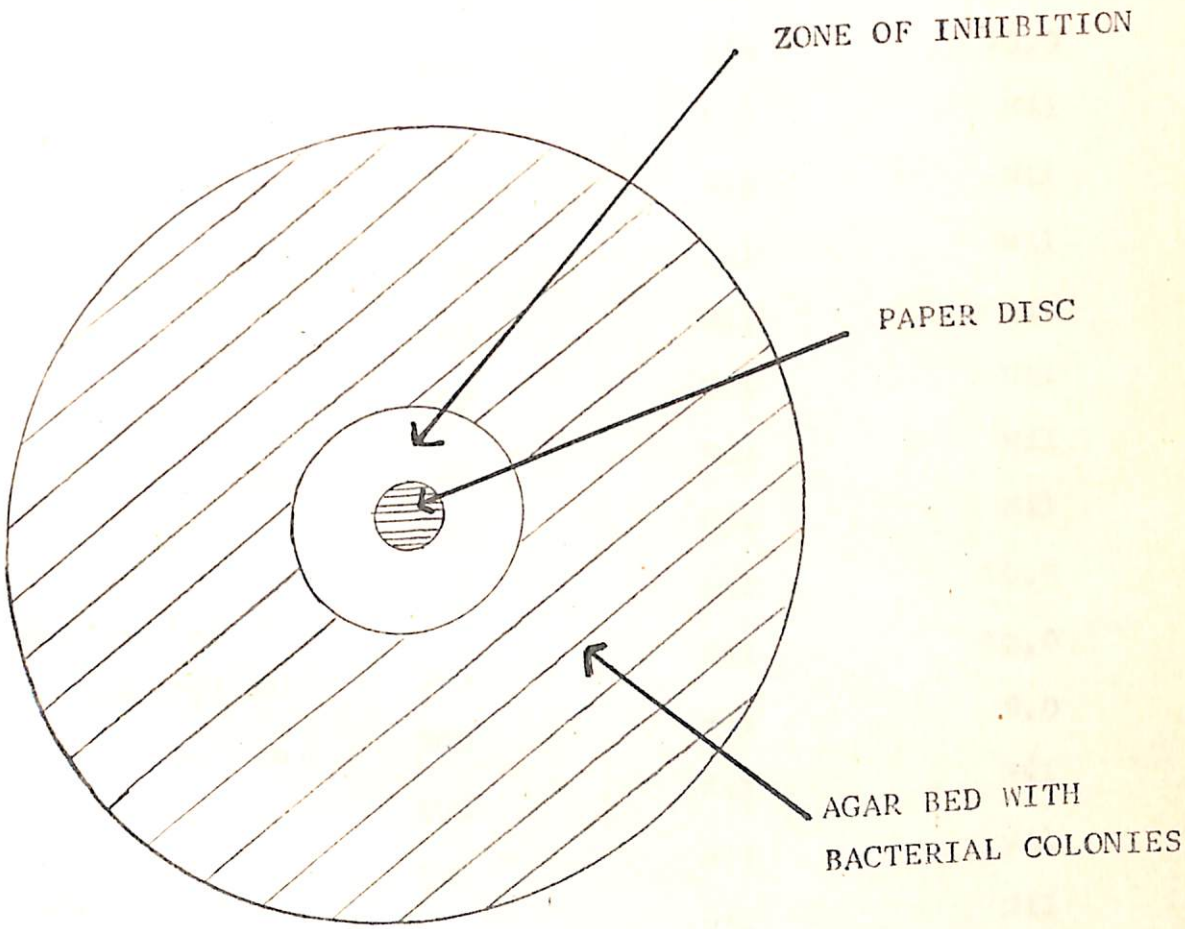


Fig 5.31 Diagram showing a petridish with zone of inhibition

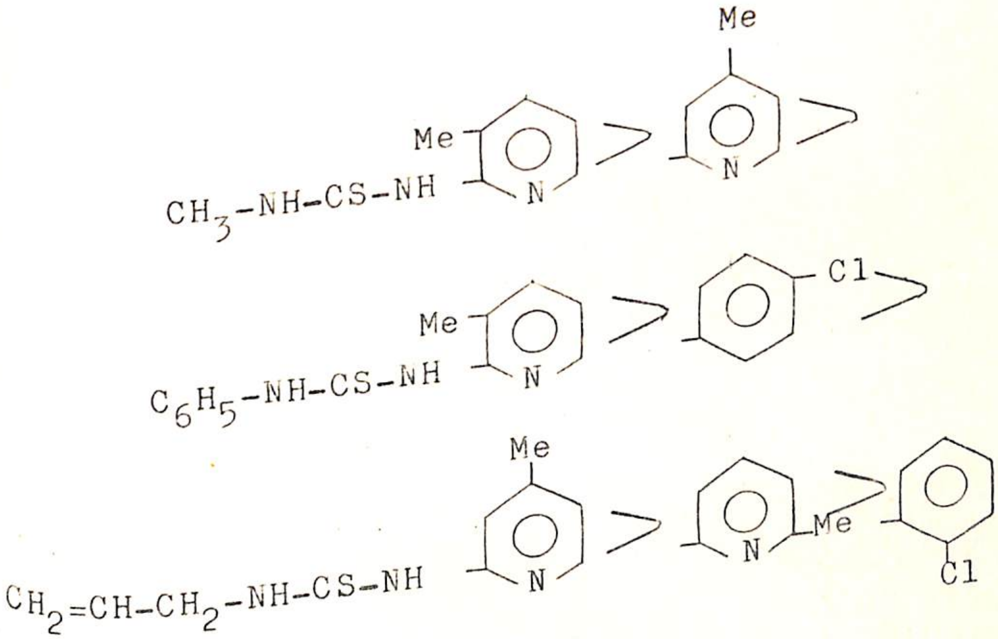
Table 5.7 Antimicrobial Activity of Thiourea Derivatives for *E. coli* and *B. subtilis*.

Thiourea derivative	Conc. ppm	Zone of inhibition (dia. in mm) *E. coli*	*B. subtilis*
N-Me-N'-2-(3Me Py) tu	10	Nil	Nil
N-Me-N'-2-(3Me Py) tu	100	Nil	7.0
N-Me-N'-2-(3Me Py) tu	500	Nil	12.0
N-Me-N'-2-(4Me Py) tu	500	Nil	10.0
N-Me-N'-oMe Ph tu	500	Nil	Nil
N-Me-N'-oCl Ph tu	500	Nil	Nil
N-Me-N'-mCl Ph tu	500	Nil	Nil
N-Me-N'-pCl Ph tu	500	Nil	Nil
N-Me-N'-Ph tu	500	Nil	Nil
N-Ph-N'-2-(3Me Py) tu	10	Nil	Nil
N-Ph-N'-2-(3Me Py) tu	100	Nil	Nil
N-Ph-N'-2-(3Me Py) tu	500	Nil	10.0
N-Al-N'-2-(4Me Py) tu	500	Nil	10.0
N-Al-N'-2-(6Me Py) tu	500	Nil	8.0
N-Al-N'-o-Me Ph tu	500	Nil	Nil
N-Al-N'-p-Me Ph tu	500	Nil	Nil
N-Al-N'-oCl Ph tu	500	Nil	Nil
N-Al-N'-mCl Ph tu	500	Nil	8.0
N-Al-N'-pCl Ph tu	500	Nil	9.0
N-Al-N'-Ph tu	500	Nil	Nil

N-methyl substituted derivatives were most effective example N-methyl, N'-2-(3methyl pyridyl) was found to be antibacterial at 100 and 500 ppm concentration (table 5.7). These studies show that a substitution only at meta position enhances the antibacterial activity of these compounds. Mackay (1959) also reported similar findings.

Lastly it was found that there is significant antimicrobial activity exhibition by thioureas in which heterocyclic moeity was incorporated, as has also been reported by Devani et al (1976), Crank et al (1973) and Stewart et al (1973).

The order of antimicrobial activity shown by various thioureas against <u>Bascillus subtilis</u> is as follows:



SUMMARY

The thesis concerns itself with the spectroscopic and agrochemical studies on substituted thiourea and their metal complexes.

The aspects which have been selected for detailed study are:

a) Synthesis and characterization of some new substituted thiourea derivatives.

b) Metal complexation study with Co(II), Ni(II), Cd(II) and Zn(II) transition metals.

c) Conformation study of thiourea derivative by I.R. and N.M.R.

d) Agrochemical studies of thiourea derivatives
   i) Seed treatment and growth regulatory activity.
   ii) Pre and post-emergence herbicidal activity.
   iii) Antimicrobial activity.

The work is presented in five Chapters. A brief introduction to the sulphur donor ligands and their complexes, along with the survey of biological activity shown by thiourea derivative forms the first Chapter.

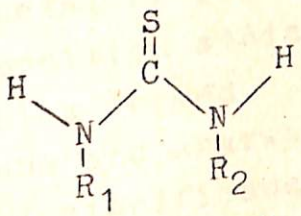
...r deals with the synthesis of ... derivatives.

substituents and their isomers, so as to study the effect of structural changes on their biological activity. This is part of a plan to obtain a theoritical framework for their activity.

These compounds were characterized using information obtained from U.V., I.R. and elemental studies. The m.p. and other physical parameters have also been determined and reported. ^{1}H-N.M.R. studies, aimed towards conformational studies conform with the structure of these derivatives.

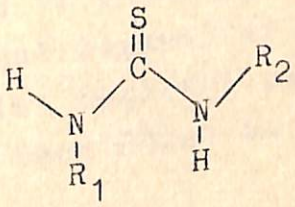
The purity of these substituted thiourea derivatives is very important for an accurate evaluation of their biological activity. The studies revealed that the compounds were 95 - 98% pure.

In Chapter III, a detailed discussion on the ^{1}H-N.M.R. spectras of these thiourea derivatives, which along with I.R. spectra leads to the conformational structure to these derivatives, which can be represented as (I, II, III and IV)



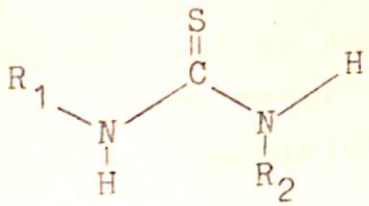
cis-cis

I

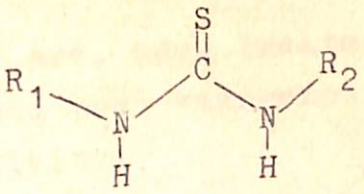


cis-trans

II



trans-cis
III



trans-trans
IV

The cis-cis conformation was found to be preferred in derivatives with bulkier R_1 and R_2 substituents. This has been explained as being due to steric hinderance of sulphur atom upon C-N bond free rotation. These results agree with similar finding by other workers (Vassilev, Koleva, Ilieva and Galabov, 1982; Burman and Sathyanarayana, 1982)

Chapter IV discusses the spectrophotometric studies on metal complex formation behaviour by various thiourea derivatives in solution phase. Limiting logarithmic method (Moore and Anderson, 1945) taking ratio of the slopes obtained by plot of optical density against varying concentration of metal or ligand was adopted to find out the composition stoichiometry (metal:ligand) of the complex formed. Similar studies reported recently (Sinha and Agarwal, 1983) has been found to be of great significance.

The last Chapter deals with the most important aspect for which these studies were undertaken and forms the bulk of the work presented. It deals with testing of these substituted thiourea derivatives as potent-agrochemicals.

The activities screened for are, seed treatment and growth promoting, pre and post-emergence herbicidal and antimicrobial activity.

The seed treatment and growth promoting agents, are usually applied for enhancing the germination and initial growth of the plant, to effectively promote multiple cropping. Some very interesting results have been obtained. It has been found that a lower concentration of thioureas is more effective and efficient.

The herbicidal activity of these compounds have also been studied. Some very interesting results like the selective and specific action towards some of the monocotyledons were observed.

Pre-emergence herbicidal activity was screened by a new technique using solidified agar bed in aqueous media, incorporated with dispersed or miscible solution of thioureas. This method was found to be more quicker and convenient with equally reproducible results as compared to older methods.

N-allyl series of substituted thiourea derivatives were found to be most potent and lethal.

The post-emergence herbicidal activity have been tested by a variant of conventional green house pot method.

An attempt to correlate the structure with their herbicidal activity has also been made.

The test plant chosen for present studies are Barley K-125 (Hordeum vulgare L.) representing monocotyledons and mustard 'varuna' (Brassica compestris L.) representing the dicotyledons.

Some antimicrobial studies of these derivatives against two strains of bacteria belonging to gram positive (Bacillus subtilis) and gram negative (Escherchia coli) class were made. It was found that only Bacillus subtilis strain was sensitive and its growth was inhibited by thiourea derivatives.

Each Chapter gives a brief introduction of its relevance, giving the material and methods used and discusses the results obtained.

A consolidated bibliography has been presented at the end of the thesis.

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APPENDICES

Appendix A : Growth regulatory and herbicidal activity tables.

Appendix B : Computer program listings
PROG 1 : Regression analysis
PROG 2 : Duncans multiple range test
PROG 3 : Bibliography sorting.

APPENDIX A

TABLES SHOWING THE GROWTH REGULATORY AND HERBICIDAL ACTIVITY OF SUBSTITUTED THIOUREAS

THIOUREA DERIVATIVES CODES

DERIVATIVES	CODES
CONTROL	Ü
N-ALLYL,N'-PHENYL THIOUREA	A-i
N-ALLYL,N'-ortho CHLORO PHENYL THIOUREA	A-Z
N-ALLYL,N'-meta CHLORO PHENYL THIOUREA	A-3
N-ALLYL,N'-para CHLORO PHENYL THIOUREA	A-4
N-ALLYL,N'-ortho METHYL PHENYL THIOUREA	A-5
N-ALLYL,N'-para METHYL PHENYL THIOUREA	A-6
N-ALLYL,N'-Z PYRIDYL THIOUREA	A-7
N-ALLYL,N'-Z-(3 METHYL PYRIDYL) THIOUREA	A-8
N-ALLYL,N'-Z-(4 METHYL PYRIDYL) THIOUREA	A-9
N-ALLYL,N'-Z-(6 METHYL PYRIDYL) THIOUREA	A-iÜ
N-METHYL,N'-PHENYL THIOUREA	M-i
N-METHYL,N'- ortho CHLORO PHENYL THIOUREA	M-Z
N-METHYL,N'- meta CHLORO PHENYL THIOUREA	M-3
N-METHYL,N'- para CHLORO PHENYL THIOUREA	M-4
N-METHYL,N'- ortho METHYL PHENYL THIOUREA	M-5
N-METHYL, N'-para METHYL PHENYL THIOUREA	M-6
N-METHYL,N'-Z PYRIDYL THIOUREA	M-7
N-METHYL,N'-Z-(3 METHYL PYRIDYL) THIOUREA	M-8
N-METHYL,N'-Z-(4 METHYL PYRIDYL) THIOUREA	M-9
N-METHYL,N'-Z-(6 METHYL PYRIDYL) THIOUREA	M-iÜ
N-PHENYL,N'-PHENYL THIOUREA	P-i
N-PHENYL,N'-ortho CHLORO PHENYL THIOUREA	P-Z
N-PHENYL,N'-meta CHLORO PHENYL THIOUREA	P-3
N-PHENYL,N'-para CHLORO PHENYL THIOUREA	P-4
N-PHENYL,N'-ortho METHYL PHENYL THIOUREA	P-5
N-PHENYL,N'-para METHYL PHENYL THIOUREA	P-6
N-PHENYL,N'-Z PYRIDYL THIOUREA	P-7
N-PHENYL,N'-Z-(3 METHYL PYRIDYL) THIOUREA	P-8
N-PHENYL,N'-Z-(4 METHYL PYRIDYL) THIOUREA	P-9
N-PHENYL,N'-Z-(6 METHYL PYRIDYL) THIOUREA	P-iÜ
DIURON	ii
Z,4-D	iZ

RESULTS ARE EXPRESSED AS $\bar{x}$ + S.D.

Means OF REPLICATES WITH SAME LETTER (a,b,....) WITHIN A COLUMN ARE NOT SIGNIFICANTLY DIFFERENT AT THE 5 % LEVEL BASED ON DUNCANS MULTIPLE RANGE TEST

TABLE 1 GROWTH REGULATORY ACTIVITY OF THIOUREAS

DERIVATIVE	CONC. PPM	% OF CONTROL		
		GERMINATION	ELONGATION OF SHOOT	ELONGATION OF ROOT
A	B	C	D	E
A1 thiourea	10	134+10a	89.1+9.1c	92.9+12.3bc
	100	97 + 8 cd	110.4+9.2a	102.5+7.2
	500	56+ 5	56.9+ 6.1	59.5+ 8.1
A-1	10	126+11 a	128.3+7.1 a	142.1+ 9.4
	100	115+10 ab	105.3+10.3ab	98.7+10.1
	500	115+12 ab	94.4+8.4 b	83.7+ 6.2
A-5	10	81+ 9 d	81.5+10.1c	85.8+ 8.6
	100	95+ 3 cd	87.8+ 9.5c	80.5+12.1
	500	81+ 4 d	35.5+ 6.6	49.2+10.2
A-6	10	105+15 bc	113.2+11.3a	103.7+12.1
	100	100+10 c	77.2+13.2c	74.1+ 9.1
	500	96+ 8cd	77.5+ 9.1c	72.5+11.2
U	Nil	100	100.0	100.0

TABLE 2 GROWTH REGULATORY ACTIVITY

A	B	C	D	E
M-7	10	117± 8	90.8± 9.10	104.0±10.3
	100	143 ±7	81.2± 8.3 bc	82.2± 7.5c
M-8	10	102±11 a	109.7± 9.6 a	119.6±9.6 a
	100	100± 9 a	74.9± 7.8 c	95.3± 8.3 b
	500	89± 7 b	68.9± 5.4 c	68.3± 5.2 d
M-9	10	105±12 a	90.9± 9.2 b	80.4± 4.6 c
	100	91± 5 b	95.6± 8.2 ab	83.5± 4.7 c
	500	85± 6 b	51.0± 6.3 d	63.5± 5.2 d
M-10	10	95± 5 ab	132.5±11.7	165.5± 9.6
	100	100± 8 a	151.2±10.6	123.2±10.2 a
	500	97± 7 ab	111.9± 9.8 a	117.3±10.9 a
0	-	100	100.0	100.0

TABLE 3 GROWTH REGULATORY ACTIVITY

DERIVATIVE AT 10 PPM	% OF CONTROL					
	GERMINATION		ELONGATION OF SHOOT		ELONGATION OF ROOT	
	Monocot	Dicot	Monocot	Dicot	Monocot	Dicot
A	B	C	D	E	F	G
0	100	100	100.0	100.0	100.0	100.0
M-1	123±6a	125±5a	123.6±14.3a	127.4±8.6b	121.5±6.2a	120.3±13.8b
M-2	107±3b	105±7b	125.6±11.2a	113.5±11.3c	122.3±7.8a	103.6±9.8a
M-3	100±2bc	106±8b	108.9±9.2b	109.5±10.3c	100.2±6.8c	111.4±9.2c
M-4	98±6c	91±5c	95.6±8.5c	107.7±9.3c	90.4±7.2c	100.2±8.6d
M-5	100±5bc	92±9c	110.6±8.6b	121.3±10.6b	109.2±8.9b	115.4±10..c
M-6	105±1b	99±6c	118.7±9.6ab	145.6±11.4a	120.3±10.3a	140.3±11.0a
M-7	101±4bc	85±10c	100.6±7.5c	98.8±8.4d	98.7±8.9c	109.3±9.8cd
M-8	106±3b	102±5bc	112.6±9.1b	130.6±8.9b	100.3±9.2c	121.6±10.7b
M-9	140±2	123±11a	115.9±10.0b	152.6±9.9a	108.4±8.6b	141.3±11.6a
M-10	130±1a	140±12	153.4±12.1	142.4±10.3a	136.7±10.1	125.6±10.9b

A	B	C	D	E	F	G
0	100	100	100.0	100.0	100.0	100.0
0	110+5a	130+11a	101.3+6.3ab	121.0+4.3b	98.4+9.2b	113.0+12.1c
A-2	109+3a	122+9a	111.3+7.2a	122.4+6.2b	106.8.3a	124.0+15.3b
A-3	98+2b	110+7a	98.6+9.2b	110.3+11.3c	102.5+8.3a	117.3+12.0b
A-4	95+4b	98+5c	88.6+5.1	109.5+13.5c	92.5+6.1b	98.3+8.8d
A-5	99+1b	96+6c	99.2+4.3b	125.3+15.7b	92.3+6.2b	122.6+16.5cd
A-6	103+5ab	101+5bc	105.6+6.8a	145.3+8.3a	104.2+10.9a	130.8+9.9a
A-7	97+5b	92+4c	95.6+5.4b	101.1+8.3cd	84.0+6.5	115.3+15.3c
A-9	104+4ab	86+5c	105.2+9.6a	90.6+13.2d	100.3+9.6ab	110.4+8.2c
A-10	110+3a	102+7bc	109.4+8.7a	142.7+15.7a	110.2+10.4a	135.3+9.3a

TABLE 5 GROWTH REGULATORY ACTIVITY

A	B	C	D	E	F	G
0	100	100	100.0	100.0	100.0	100.0
1	110+5bc	121+6b	131.5+14.3b	122.6+9.2b	125.6+9.2	112.6+8.1c
2	105+6d	109+9d	132.6+13.1b	135.6+8.2a	130.2+8.1b	130.2+13.0b
3	107+4cd	106+7cd	130.8+14.8b	126.7+9.1b	132.1+4.9ab	120.3+9.5b
4	108+4cd	102+5d	112.4+14.2	101.3+9.8d	100.3+7.3	112.4+8.1c
5	115+5b	120+9b	142.3+15.0	132.3+8.9a	125.6+8.9b	125.6+14.2
6	130+6a	128+8a	155.6+9.6a	143.6+8.6	141.3+12.2a	144.6+13.9a
7	115+6b	110+10c	122.3+10.3b	112.6+9.1c	105.6+8.7c	105.3+8.0c
8	120+7b	125+8b	133.7+12.3b	113.0+9.5c	122.9+8.2b	109.0+8.0c
9	130+6a	132+9a	155.6+15.3a	133.6+14.3a	140.2+8.2a	123.5+9.8b
10	135+7a	140+11a	163.2+14.2a	155.6+15.2	140.3+8.9a	142.0+9.8a

TABLES SHOWING HERBICIDAL ACTIVITY OF THIOUREA DERIVATIVES

TABLE i Pre-Emergence Herbicidal activity of DIURON in agar and soil

GROWTH MEDIA	CONCENTRATION OF DIURON in PPM	% OF CONTROL			
		ELONGATION OF SHOOT		ELONGATION OF ROOT	
		Monocot	Dicot	Monocot	Dicot
A	B	C	D	E	F
CONTROL	Nil	100.0	100.0	100.0	100.0
AGAR	10	96.7±5.4ab	159.3±8.3	78.6±4.2a	163.2±5.8
	100	74.8±5.1c	51.8±4.0c	12.5±2.2c	20.5±2.2
	200	48.7±2.8	47.7±2.7c	6.1±1.3d	8.4±1.7c
	500	66.5±4.8c	47.3±5.2c	9.2±1.3cd	11.7±1.8c
SOIL	10	93.0±5.3b	78.5±4.2a	117.0±6.7	78.1±6.0a
	100	93.0±5.3b	74.0±5.7a	89.0±5.8a	51.9±4.2b
	150	90.1±6.2b	54.7±5.8c	80.5±6.8a	78.7±6.2a
	200	103.1±9.1a	62.0±5.6b	74.4±6.1ab	49.6±4.9b
	500	100.3±5.9a	64.7±4.2b	61.7±4.5b	18.8±2.1

TABLE 2 Pre-Emergence Herbicidal activity of 2,4-D in agar and soil

	B	C	D	E	F
ONTROL	Nil	100.0	100.0	100.0	100.0
AR	10	47.2±3.4	17.4±1.6a	10.2±1.3a	8.1±1.2a
	100	27.8±2.3a	20.0±2.0a	6.8±0.8ab	9.1±0.9a
	200	23.3±1.3ab	12.4±1.8b	4.5±0.6b	4.1±0.3b
	500	00.0±0.0	8.2±0.3bc	00.0±0.0	2.3±0.2b
OIL	10	61.1±4.8	12.5±1.3b	27.7±1.7	9.1±0.9a
	100	31.4±1.9a	6.9±0.3c	4.5±0.5b	4.6±0.1b
	150	26.6±1.6a	5.7±0.9c	3.7±0.1b	3.1±0.1b
	200	9.3±0.9	00.0±0.0	4.7±0.5b	00.0±0.0
	500	19.2±1.1b	00.0±0.0	3.0±0.1b	00.0±0.0

DOSE RESPONSE STUDIES

TABLE 1 Pre-Emergence Herbicidal activity

DERIVATIVE	B.	C	D	E	F.
Ü	–	100.0	100.0	100.0	100.0
A-1	10	80.6+6.3	82.3+6.1	72.3+5.6a	81.4+6.8
	100	91.5+9.2a	65.3+5.3a	81.2+6.3a	60.0+5.3a
	500	41.3+4.5b	46.3+4.8	45.4+4.9b	35.2+3.8
	1000	20.2+2.1c	21.4+3.1	22.6+4.6c	20.3+3.2
A-7	10	60.3+5.6	65.3+6.2a	59.2+4.2b	60.3+4.9a
	100	43.3+4.1b	59.8+3.9a	32.6+3.2c	50.8+5.2a
	500	21.2+3.2c	11.2+1.4	16.3+3.1	9.6+1.5
	1000	10.4+1.5	00.0+0.0	11.5+1.6	00.0+0.0

TABLE 2 Pre-Emergence Herbicidal activity

A	B	C	D	E	F
Ü	–	100.0	100.0	100.0	100.0
A-1	10	80.5+6.5a	113.6+9.3a	72.6+5.6a	100.2+5.6a
	100	35.3+4.2b	69.7+7.3b	30.4+3.5c	80.6+6.1
	500	41.2+3.8b	25.6+2.1c	43.2+3.5b	20.3+1.9b
	1000	22.6+1.9	12.3+1.3d	25.4+2.1c	10.6+0.9
A-7	10	72.3+5.3a	102.3+6.8a	70.1+5.3a	99.2+6.2a
	100	44.6+3.9b	88.4+5.9b	42.2+3.7bc	82.6+6.3
	500	10.3+1.5	21.3+1.6c	12.1+1.1	20.4+1.2b
	1000	00.0+0.0	13.6+0.9dc	00.0+0.0	12.3+1.5

TABLE 3 Pre-Emergence Herbicidal activity

A	B	C	D	E	F
Ù	–	100.0	100.0	100.0	100.0
F-1	10	115.3+7.2	125.6+6.5	110.2+5.8a	120.2+6.9
	100	98.3+5.8a	66.3+4.6b	90.2+4.2a	62.8+4.1b
	500	35.6+5.2b	21.2+3.2c	30.2+1.9b	20.6+2.1c
	1000	29.2+2.6b	19.4+1.3c	20.4+1.6c	21.6+1.8c
F-7	10	92.3+7.5a	95.6+8.1a	90.4+7.1a	90.2+6.9a
	100	55.3+4.3	72.5+5.2b	51.3+4.8	65.4+5.1b
	500	32.5+2.8b	32.1+2.1	35.0+2.8b	9.2+0.9
	1000	31.2+1.8b	11.6+1.2	26.5+2.3bc	30.5+1.9

TABLE 4 Post-Emergence Herbicidal activity

A	B	C	D	E	F
Ù	–	100.0	100.0	100.0	100.0
-1	10	92.6+8.6a	90.1+8.5a	85.8+7.5a	88.6+7.2a
	100	73.2+6.3b	71.3+6.9b	70.2+7.2ab	68.3+6.1
	500	31.5+4.1c	41.6+5.2	25.6+3.1c	38.3+3.0b
	1000	22.3+2.6c	20.6+1.9c	20.5+1.8c	18.6+1.2
A-7	10	81.6+7.2b	88.6+7.1b	78.6+6.8a	80.1+7.5a
	100	62.6+5.8	70.8+6.8a	60.6+5.9b	73.8+6.9a
	500	34.1+2.9c	30.9+3.1c	31.2+2.6c	29.2+2.5b
	1000	10.9+1.2	00.0+0.0	9.3+1.0	00.0+0.0

TABLE 5 Post-Emergence Herbicidal activity

A	B	C	D	E	F
ü	–	iüü.ü	iüü.ü	iüü.ü	iüü.ü
ñ-i	iü	95.ó+8.óa	ii5.3+iü.Z	9ü.Z+9.ia	iüZ.ó+ii.5a
	iüü	55.3+5.ib	88.4+7.3	5ü.Z+4.8	8ó.Z+9.Z
	5üü	35.i+Z.5c	5i.Z+3.8b	3Z.ó+Z.8b	5ü.4+4.3b
	iüüü	ZZ.ó+Z.ic	3ü.ó+Z.Zc	Zü.i+Z.ü	3i.Z+i.9c
ñ-7	iü	8ó.Z+7.3	iü9.Z+9.8a	8Z.4+7.ó	iüó.3+iü.ia
	iüü	ó4.4+5.3b	ó0.4+ó.3b	ó0.8+5.9	óZ.4+ó.ób
	5üü	3i.Z+3.ic	4i.ó+4.0c	33.4+3.ü0	4Z.i+4.üc
	iüüü	üü.ü+ü.ü	30.Z+Z.8c	üü.ü+ü.ü	Z9.ó+8.Zc

TABLE ó Post-Emergence Herbicidal activity

A	B	C	D	E	F
ü	–	iüü.ü	iüü.ü	iüü.ü	iüü.ü
-i	iü	iiZ.ó+iZ.3	i23.3+ii.8	iüó.ó+iü.8	iZi.ó+i3.ü
	iüü	75.Z+8.3b	83.ó+9.Zb	7Z.3+7.8b	8ü.7+7.Zb
	5üü	4i.3+3.8c	7Z.4+ó.Zb	4ü.5+3.Zd	73.Z+ó.3b
	iüüü	3ü.ó+Z.9c	33.ó+Z.Zc	Z9.Z+Z.id	3Z.9+Z.5c
ñ-7	iü	iü5.Z+iü.3a	98.ó+9.ia	iüü.ó+ii.üa	9ó.7+8.3a
	iüü	88.3+7.5b	7Z.3+ó.8b	8ü.7+7.9b	74.3+ó.8b
	5üü	5ó.3+4.8	54.5+5.Z	5i.3+4.8c	5ü.ó+4.Z
	iüüü	35.3+3.ic	4i.Z+3.ócc	3Z.ó+3.üd	4ü.Z+3.ic

HERBICIDAL ACTIVITY OF SUBSTITUTED THIOUREA DERIVATIVES

PRE-EMERGENCE HERBICIDAL ACTIVITY

BLE i

RIVATIVE AT ÜÜ PPM	% OF CONTRÜL				S.A.I. (Selective activity index)
	SHÜÜT ELÜNGATIÜN		RÜÜT ELÜNGATIÜN		
	Monocot	Dicot	Monocot	Dicot	
Á	B	C	D	E	F
Ü	iÜÜ.Ü	iÜÜ.Ü	iÜÜ.Ü	iÜÜ.Ü	—
i	9.6±8.ic	ZZ.3±i.8b	iÜ.Z±Ü.8ab	ZÜ.Z±i.6b	i.Ü ¦ Z.Ü
Z	ÜÜ.Ü±Ü.Ü	ÜÜ.Ü±Ü.Ü	ÜÜ.Ü±Ü.Ü	ÜÜ.Ü±Ü.Ü	—
3	ÜÜ.Ü±Ü.Ü	3.Z±Ü.9c	ÜÜ.Ü±Ü.Ü	Z.i±Ü.6c	—
4	7.Z±i.6c	7.Z±i.Üc	7.5±Ü.7b	4.7±Ü.9c	i.6 ¦ i.Ü
5	ZZ.Z±Z.6b	3Z.i±Z.3ab	ZÜ.4±i.8a	3Z.6±i.8a	i.Ü ¦ i.6
6	ZÜ.Z±i.8b	4Z.3±3.8a	Zi.4±Z.Üa	4Ü.9±Z.3a	i.Ü ¦ i.9
7	Z5.5±i.7b	ZZ.7±i.6b	ZÜ.Ü±i.8a	iÜ.i±i.Üb	Z.Ü ¦ i.Ü
8	45.5±3.ia	3Z.4±i.3ab	i4.8±i.Zab	iZ.4±i.ib	i.Z ¦ i.Ü
9	63.4±4.6	67.8±4.9	74.Z±4.Z	33.6±Z.6a	Z.Z ¦ i.Ü
iÜ	45.6±3.8a	5Ü.Z±4.Za	7.Ü±i.Üb	iZ.i±i.3b	i.Ü ¦ i.7
	Zi.Z±i.9b	ZÜ.4±Z.ib	3.Ü±Ü.8	5.Z±Ü.8c	i.Ü ¦ i.7

TABLE 2

A	B	C	D	E	F
0	100.0	100.0	100.0	100.0	—
M-1	45.6±2.6a	19.4±1.2b	59.2±4.8	11.4±1.3b	5.1 ; 1.0
M-2	14.1±1.2	20.7±1.1b	8.0±0.9b	2.4±1.2c	3.3 ; 1.0
M-3	2.3±0.8c	3.7±0.9d	7.8±0.8b	2.1±1.0c	3.7 ; 1.0
M-4	4.7±0.9c	6.9±0.8d	4.9±1.5c	2.0±1.3c	2.6 ; 1.0
M-5	29.8±2.3ab	30.2±1.6a	31.2±1.3a	31.3±2.3a	1.0 ; 1.0
M-6	19.6±1.6b	31.3±1.8	22.3±1.6a	30.4±1.9a	1.0 ; 1.4
M-7	00.0±0.0	10.8±1.0cd	00.0±0.0	2.8±0.6	—
M-8	00.0±0.0	12.4±0.8c	00.0±0.0	6.4±0.6c	—
M-9	21.0±3.1b	40.2±3.2a	8.1±0.5b	6.5±0.4c	1.2 ; 1.0
M-10	31.0±3.2b	32.9±2.2a	9.9±0.9b	10.9±1.0b	1.0 ; 1.1
11	45.2±3.6a	46.9±2.8a	6.9±1.0bc	8.7±0.8 bc	1.0 ; 1.3
12	25.2±2.1b	12.5±1.0c	4.9±0.3c	4.3±0.4c	1.1 ; 1.0

TABLE 3

A	B	C	D	E	F
0	100.0	100.0	100.0	100.0	-
P-1	34.9+4.2b	22.5+3.6c	30.7+4.7b	14.1+3.0	2.1 ; 1.0
P-2	64.5+5.3a	19.1+2.1c	55.4+6.2a	14.0+2.5c	4.0 ; 1.0
P-3	30.6+7.8b	11.9+3.2d	10.0+4.0	9.6+3.0c	1.0 ; 1.0
P-4	82.8+8.8	20.0+3.0c	89.8+9.1	22.0+3.9b	4.0 ; 1.0
P-5	51.2+5.3a	62.3+5.2a	50.3+4.8a	60.1+5.2a	1.0 ; 1.2
P-6	41.6+5.4b	61.3+4.8a	40.0+5.5b	60.3+5.2a	1.0 ; 1.5
P-7	20.2+4.3c	33.6+3.2c	19.5+5.1	34.9+3.8b	1.0 ; 1.8
P-8	40.3+5.7b	55.2+4.2a	39.2+4.2b	57.7+4.8a	1.0 ; 1.5
P-9	50.6+4.5a	60.9+5.1a	51.2+4.9a	61.3+5.3a	1.0 ; 1.2
P-10	45.6+5.3b	55.8+4.2a	46.6+5.9ab	56.8+4.5a	1.0 ; 1.2
11	48.7+3.2ab	47.7+5.0b	6.1+3.5c	8.4+2.8c	1.0 ; 1.4
12	23.3+3.0c	12.4+4.2d	4.5+3.0c	4.1+2.0	1.1 ; 1.0

POST-EMERGENCE HERBICIDAL ACTIVITY

TABLE 4

A	B	C	D	E	F
0	100.0	100.0	100.0	100.0	—
A-1	19.6+1.30	31.3+2.0a	21.2+1.2	29.6+2.1ab	1.0 ; 1.6
A-2	00.0+0.0	12.3+1.1b	00.0+0.0	9.6+0.8	—
A-3	21.2+1.8b	11.5+1.0b	20.6+1.8b	10.6+1.0	1.8 ; 1.0
A-4	00.0+0.0	00.0+0.0	00.0+0.0	00.0+0.0	—
A-5	19.4+1.3b	30.9+2.8	23.6+1.3ab	31.2+2.3a	1.0 ; 1.6
A-6	30.2+2.6a	29.6+1.1a	31.0+2.4a	31.2+1.7a	1.0 ; 1.0
A-7	10.0+1.3	22.4+2.0	12.2+1.6	21.0+1.9b	1.0 ; 2.2
A-9	00.0+0.0	11.2+1.1b	00.0+0.0	9.6+0.9c	—
A-10	00.0+0.0	10.9+1.2b	00.0+0.0	8.4+0.8c	—
11	28.5+1.8a	36.8+2.6a	21.5+1.8b	32.3+2.7a	1.0 ; 1.3
12	51.2+4.2	38.6+2.0a	52.6+4.2	30.6+2.6a	1.3 ; 1.0

TABLE 5

A	B	C	D	E	F
0	100.0	100.0	100.0	100.0	—
M-1	39.8+2.8a	51.7+4.7b	40.2+3.2a	49.9+3.9b	1.0 ; 1.3
M-2	28.3+2.1b	46.6+4.1b	29.2+2.8bc	50.1+4.9b	1.0 ; 1.7
M-3	20.6+1.9c	30.2+3.2c	19.2+1.8c	31.3+2.8c	1.0 ; 1.5
M-4	11.2+1.0	18.6+2.8	10.6+1.0	20.1+2.3	1.0 ; 1.7
M-5	21.2+1.3c	30.6+3.7c	19.6+1.9c	29.9+2.0c	1.0 ; 1.4
M-6	29.9+1.8b	31.5+2.9c	31.2+1.1b	30.7+2.4c	1.0 ; 1.1
M-7	25.6+2.1bc	49.7+3.9b	28.3+2.2bc	48.8+3.2b	1.0 ; 1.9
M-8	28.9+2.4b	58.9+4.7ab	32.2+2.6b	60.1+5.8a	1.0 ; 2.0
M-9	40.1+3.4a	65.6+5.3a	38.8+2.3a	69.2+5.0a	1.0 ; 1.6
M-10	41.3+3.9a	69.3+7.0a	40.7+3.7a	69.9+5.3a	1.0 ; 1.7
1	24.2+2.6c	35.8+5.0c	21.1+1.5c	29.2+4.0c	1.0 ; 1.4
2	31.2+2.5a	37.5+3.5c	59.8+4.5	29.4+3.6c	1.4 ; 1.0

TABLE 6

A	B	C	D	E	F
0	100.0	100.0	100.0	100.0	10
P-1	49.7+4.50	75.2+6.90	51.3+5.80a0	79.9+6.80	1.0 ¦ 1.5
P-2	39.3+4.30	80.2+6.30	40.7+3.70c0	79.6+5.30	1.0 ¦ 2.0
P-3	30.8+3.20	50.3+4.50	29.9+3.00	51.2+3.80	1.0 ¦ 1.6
P-4	51.2+4.30	59.4+5.10c0	48.2+3.90	60.3+6.00	1.0 ¦ 1.2
P-5	40.3+4.70	53.3+5.30	39.8+3.20	50.9+4.70	1.0 ¦ 1.3
P-6	29.9+3.00	69.7+6.30	31.2+2.90	71.2+6.90	1.0 ¦ 2.3
P-7	50.6+4.30	59.8+4.80c0	48.9+5.20	60.2+5.10	1.0 ¦ 1.2
P-8	60.3+5.70	71.2+7.10	61.2+6.90	70.6+7.20	1.0 ¦ 1.2
P-9	30.2+2.80	70.4+6.10	33.4+3.20	69.2+5.80a0	1.0 ¦ 2.3
P-10	61.2+4.80	72.3+6.80	60.4+7.10	70.8+6.20	1.0 ¦ 1.2
11	23.4+2.80	35.6+3.10	19.0+2.1	30.1+2.30	1.0 ¦ 1.5
12	50.4+3.20	35.6+4.30	60.5+4.80	28.0+2.90	1.4 ¦ 1.0

ACTIVITY SCORES OF SUBSTTUTED THIOUREAS FOR THEIR PRE AND POST-EMERGENCE HERBICIDAL ACTIVITY

DERIVATIVE AT 300 ppm	ACTIVITY SCORE *			
	Pre-emergence		Post-emergence	
	Monocot	Dicot	Monocot	Dicot
A-1	9	8	8	7
A-2	10	10	10	9
A-3	10	9	8	9
A-4	9	9	10	10
A-5	8	7	8	7
A-6	8	6	7	7
A-7	8	8	9	8
A-8	8	8	10	9
A-9	7	6	10	9
A-10	3			
M-1	5	9	6	5
M-2	9	8	7	6
M-3	9	9	8	7
M-4	9	9	9	8
M-5	7	7	8	7
M-6	8	7	7	7
M-7	10	9	7	5
M-8	10	9	7	4
M-9	8	6	6	3
M-10	7	7	6	3
P-1	7	8	5	2
P-2	4	9	6	2
P-3	8	9	7	5
P-4	2	8	5	4
P-5	3	4	6	5
P-6	6	4	7	3
P-7	8	6.5	5	4
P-8	6	4.5	6	2
P-9	3	4	7	3
P-10	5.5	4.5	4	3
11	8	9	7	5
12	7	5	8	7

ACTIVITY SCORE 10 FOR 100 % KILL AND 0 FOR NO HERBICIDAL ACTIVITY

APPENDIX B

ROG 1. REGRESSION ANALYSIS
GE 1 K.S UPPAL

UCB T KS UPPAL 80RM2108

DRIVE CART SPEC CART AVAIL PHY DRIVE
000 010A 010A 0001

M01 ACTUAL 16K CONFIG 16K

FOR
ST SOURCE PROGRAM
E WORD INTEGERS
```
      SUBROUTINE MAXIV (A,M,N,INDEX)
       DIMENSION A(6,6),B(6)
      INDEX=0
      M1=M-1
      N1=N-1
      DO 7 L=1,M
      IF(A(1,1))9,8,9
    9 B(N)=1.0/A(1,1)
      DO 5 K=1,N1
    5 B(K)=A(1,K+1)*B(N)
      DO 6 I=1,M1
      A(I,N)=-B(N)*A(I+1,1)
      DO 6 J=1,N1
    6 A(I,J)=A(I+1,J+1)+B(J)*A(I+1,1)
      DO 7 J=1,N
    7 A(M,J)=B(J)
      GO TO 11
    8 WRITE(6,12) L
   12 FORMAT(31H DENOMINATOR ZERO AT ITERATION=I2/)
      INDEX=1
   11 RETURN
      END
```

URES SUPPORTED
WORD INTEGERS

REQUIREMENTS FOR MAXIV 22 PROGRAM 280
MON 0 VARIABLES

IVE ENTRY POINT ADDRESS IS 002F (HEX)

OF COMPILATION

UP

RE WS UA MAXIV DB CNT 0013
ID 010A DB ADDR 40E6

```
// FOR
* ONE WORD INTEGERS
* LIST SOURCE PROGRAM
* IOCS(2501READER,1403PRINTER)
C************N  IS NUMBER OF VARIABLES  AND  M IS NO. OF OBSERVATIONS
      DIMENSION X(110,6),H(6,6),SUM(6),AVG(6),YD(110),XD(110,6),
     1XY(6),B(6),YOB(110),YCAL(110),CC(6),C(6,6),TITLE(72)
    5 READ(8,211) (TITLE(I),I=1,72)
      WRITE(5,222) (TITLE(I),I=1,72)
      READ(8,1) N,M
      IF(N) 180,180,300
  300 CONTINUE
      DO  10 J=1,N
   10 READ(8,2) (X(I,J),I=1,M)
      WRITE(5,3)
      DO 20 I=1,M
   20 WRITE(5,4) (X(I,J),J=1,N)



      DO 30 I=1,N
      SUM(I)=0.0
      DO 30 J=1,M
   30 SUM(I)=SUM(I)+X(J,I)
      DO 40 I=1,N
   40 AVG(I)=SUM(I)/M
      WRITE(5,155)
      WRITE(5,4) (AVG(I),I=1,N)
      DO 50 I=1,N
      DO 50 J=1,M
   50 XD(J,I)=X(J,I)-AVG(I)
      L=N-1
   55 DO 60 I=1,L
      DO 60 J=1,L
      H(I,J)=0.0
      DO 60 K=1,M
   60 H(I,J)=H(I,J)+XD(K,I)*XD(K,J)
      WRITE(5,6)
      DO 25 I=1,L
   25 WRITE(5,6) (H(I,J),J=1,L)
      DO 80 J=1,M
   80 YD(J)=XD(J,N)
      DO 90 I=1,L
      XY(I)=0.0
      DO 90 J=1,M
      XY(I)=XY(I)+XD(J,I)*YD(J)
```

```
      GO TO 95
   92 CALL MAXIV (H,L,L,INDEX)
      IF(INDEX) 180,93,180
   93 DO 95 I=1,L
      DO 95 J=1,L
   95 C(I,J)=H(I,J)
   96 WRITE(5,7)
      DO 35 I=1,L
   35 WRITE(5,4) (C(I,J),J=1,L)
      DO 100 I=1,L
      B(I)=0.0
      DO 100 J=1,L
  100 B(I)=B(I)+C(I,J)*XY(J)
      WRITE(5,8)
      WRITE(5,4) (B(I),I=1,L)
      ADD=0.0
      DO 200 J=1,L
  200 ADD=ADD+AVG(J)*B(J)
      CONS=AVG(N)-ADD
      WRITE(5,220) CONS
      DO 110 I=1,M
      YCAL(I)=0.0
      DO 110 J=1,L
  110 YCAL(I)=YCAL(I)+B(J)*XD(I,J)
      DO 120 I=1,M
  120 YCAL(I)=YCAL(I)+AVG(N)
      WRITE(5,9)
      WRITE(5,4) (YCAL(I),I=1,M)
      DO 130 I=1,M
  130 YOB(I)=X(I,N)
      SAM=0.0
      DO 140 I=1,M
  140 SAM=SAM+(YOB(I)-YCAL(I))**2
      K=M-L-1
      SD=SQRT(SAM/K)
      DO 150 I=1,L
  150 CC(I)=SD*C(I,I)**0.5


      SUM1=0.0
      DO 160 I=1,L
  160 SUM1=SUM1+B(I)*XY(I)
      SUM2=0.0
      DO 170 J=1,M
  170 SUM2=SUM2+YD(J)**2
      COR=SQRT(SUM1/SUM2)
      F1=K*COR**2
      F2=L*(1.-COR**2)
      F=F1/F2
      WRITE(5,11) SD,COR,L,K,F
      WRITE(5,12)
      WRITE(5,4) (CC(I),I=1,L)
      L=L-1
      WRITE(5,14) L
      IF(L) 180,5,5
```

```
  1 FORMAT(2I5)
  2  FORMAT (10 F8.5)
  3 FORMAT(/28H SAMPLE=LAST COLUMN DEPENDENT VARIABLE/)
  4 FORMAT(10F12.5)
  6 FORMAT(/14H MATRIX H(I,J)/)
  7 FORMAT(/15H INVERSE MATRIX/)
  8 FORMAT(/24H REGRESSION COEFFICIENTS/)
  9 FORMAT (/18H CALCULATED VALUES/)
 11 FORMAT (/20H STANDARD DEVIATION=F9.4,4X,11H COR COEFT=F9.4,4X,
   12HF(I2,',',I2,2H)=F9.4/)
 12 FORMAT(/25H CONFIDENCE INTERVAL=CC*I/)
 14 FORMAT(//23H INDEPENDENT VARIABLE =I2//)
135 FORMAT(/8H AVERAGE/)
211 FORMAT(72A1)
220 FORMAT (/10H CONSTANT=F12.5/)
222 FORMAT (1H1,2X,72A1)
180 CALL EXIT
    END
```

```
0048  5000  FORMAT(///,15X,'VALUE OF N=',I3)
0049        TERM1=((SIGMA)**2)/N
0050        NUMB=N-ROW
0051        GSS=SUMSQ-TERM1
0052        SSA=(TOTSQ/COL)-TERM1
0053        SSE=GSS-SSA
0054        MSE=SSE/NUMB
0055        SYI=SQRT(MSE/ROW)
0056        WRITE(6,1234)SYI
0057  1234  FORMAT(/,15X,'VALUE OF SYI=',F8.3)
0058        DO 25 I=1,ROW
0059        Y(I,1)=Y(I,1)/ROW
0060        Y(I,2)=I
0061  25    CONTINUE
0062  30    COUNT=0
0063        I=1
0064  35    IF(Y(I,1).LE.Y(I+1,1))GOTO 40
0065        TEMP=Y(I,1)
0066        Y(I,1)=Y(I+1,1)
0067        Y(I+1,1)=TEMP
0068        TEMP2=Y(1,2)
0069        Y(I,2)=Y(I+1,2)
0070        Y(I+1,2)=TEMP2
0071        COUNT=COUNT+1
0072  40    I=I+1
0073        IF(I.LT.ROW)GOTO 35
0074        IF(COUNT.NE.0)GOTO 30
0075        CALL OPEN(DCB,IERR,INAM)
0076        IF(IERR.LT.0)WRITE(1,110)IERR
0077  110   FORMAT(//,15X,'ERROR IN OPENING DATA FILE:',I3)
0078        NUM=NUMB-10
0079        IF(NUMB.EQ.30)NUM=11
0080        IF(NUMB.EQ.40)NUM=12
0081        IF(NUM.GT.12)GOTO 111
0082        WRITE(6,300)NUM
0083  300   FORMAT(/,15X,'THE RECORD BEING ACCESSED FROM THE DATA FILE IS:
0084       1I3)
0085        IL=15
0086        CALL READF(DCB,IERR,BUFF,IL,LEN,NUM)
0087        IF(IERR.LT.0)WRITE(1,115)IERR
0088  115   FORMAT(//,15X,'ERROR IN READING DATA FILE',I3)
0089        NO=ROW-1
0090        DO 45 I=1,NO
0091        R(I)=BUFF(I)*SYI
0092  45    CONTINUE
0093        GOTO 48
0094  111   WRITE(1,1003)NUM
0095  1003  FORMAT(//,15X,'NO SUCH RECORD EXISTS',I3)
```

```
0096            GOTO 127
0097   48       WRITE(6,4500)
0098   4500     FORMAT(//,15X,'RESULTS OF THE COMPUTATION'//,15X,26('=')
0099            J=ROW
0100   49       I=1
0101            IJ=NO
0102   50       IF(I.EQ.J)GOTO 55
0103            DISP=Y(J,1)-Y(I,1)
0104            IF(DISP.GT.R(IJ))GOTO 7000
0105            WRITE(6,125)Y(J,2),Y(I,2),DISP,R(IJ)
0106   125      FORMAT(/,15X,F3.0,1X,'Vs',1X,F3.0,2X,F6.2,1X,'(',F6.2,3X
0107           1,'NO SIGNIFICANT DIFFERENCE')
0108            GOTO 7001
0109   7000     WRITE(6,120)Y(J,2),Y(I,2),DISP,R(IJ)
0110   120      FORMAT(/,15X,F3.0,1X,'Vs',1X,F3.0,2X,F6.2,1X,')',F6.2)
0111   7001     IJ=IJ-1
0112            I=I+1
0113            IF(I.LT.ROW)GOTO 50
0114   55       J=J-1
0115            NO=NO-1
0116            IF(J.GT.1)GOTO 49
0117   60       CONTINUE
0118   127      CALL CLOSE(DCB)
0119            WRITE(1,130)
0120   130      FORMAT(///,20X,'END OF COMPUTATION')
0121            WRITE(6,135)
0122   135      FORMAT(//,80('-'))
0123            END
0124            END$
```

```
·&CRET  T=00004 IS ON CR00013 USING 00002 BLKS R=0000
0001   FTN4,L
0002            PROGRAM CFLE
0003            DIMENSION BUFF(15),DCB(144),NAM(3),ISIZE(2)
0004            DATA NAM/2HDA,2HTA,2HF /
0005            ISIZE(1)=2
0006            ISIZE(2)=15
0007            CALL CREAT(DCB,IERR,NAM,ISIZE,2,2HUP)
0008            IF(IERR.LT.0)WRITE(1,1)IERR
0009   1        FORMAT(//,15X,'ERROR IN CREATING',I3)
0010            CALL OPEN(DCB,IERR,NAM,0,2HUP)
0011            IF(IERR.LT.0)WRITE(1,2)IERR
0012   2        FORMAT(//,15X,'ERROR IN OPENING',I3)
0013            DO 10 I=1,12
0014            WRITE(1,3)I
0015   3        FORMAT(/,40X,'RECORD NO.=',I3)
0016            READ(1,4)(BUFF(J),J=1,12)
0017   4        FORMAT(12F4.2)
0018            CALL WRITF(DCB,IERR,BUFF,12,I)
0019            IF(IERR.LT.0)WRITE(1,5)IERR
0020   5        FORMAT(//,15X,'ERROR IN WRITING',I3)
0021   10       CONTINUE
0022            CALL CLOSE(DCB)
0023            WRITE(1,6)
0024   6        FORMAT(///,20X,'END OF INPUT')
0025            END
0026            END$
```

PROG 3. BIBLIOGRAPHY SORTING

```
PAGE    1     KS UPPAL

// JOB T                                                    KS UPPAL

LOG DRIVE   CART SPEC   CART AVAIL   PHY DRIVE
  0000        010A        010A         0001

V2 M01   ACTUAL 16K  CONFIG 16K

// FOR
* LIST SOURCE PROGRAM
* ONE WORD INTEGERS
C       THIS PROGRAM WILL ARRANGE THE WORDS IN THE DICTIONARY ORDE
        FUNCTION COMPR (J1,J2)
        COMMON NAME(10,500) , IB(500)
C       FUNCTION COMPARES TWO ARRAYS OF ALPHABETS
        DO 10 I=1,10
          IF(NAME(I,J1)-NAME(I,J2))11,10,12
10      CONTINUE
        COMPR=0.
        RETURN
11      COMPR=-1.
        RETURN
12      COMPR=1.
        RETURN
        END

FEATURES SUPPORTED
 ONE WORD INTEGERS

CORE REQUIREMENTS FOR COMPR
 COMMON   5500  VARIABLES        6  PROGRAM      78

RELATIVE ENTRY POINT ADDRESS IS 000C (HEX)

END OF COMPILATION

// DUP

*STORE       WS  UA  COMPR
CART ID 010A   DB ADDR  4155   DB CNT   0006

// FOR
* LIST SOURCE PROGRAM
* ONE WORD INTEGERS
        SUBROUTINE SWAP(J1,J2)
C       SUBROUTINE EXCHANGES THE ELEMENTS OF TWO ARRAYS .
        COMMON NAME(10,500) , IB(500)
        DO 10 I=1,10
        TEMP=NAME(I,J1)
        NAME(I,J1)=NAME(I,J2)
        NAME(I,J2)= TEMP
10      CONTINUE
          TEMP= IB(J1)
        IB(J1)= IB(J2)
        IB(J2)= TEMP
        RETURN
        END

FEATURES SUPPORTED
 ONE WORD INTEGERS

CORE REQUIREMENTS FOR SWAP
 COMMON   5500  VARIABLES        8  PROGRAM      86

RELATIVE ENTRY POINT ADDRESS IS 000A (HEX)

END OF COMPILATION

// DUP

*STORE       WS  UA  SWAP
CART ID 010A   DB ADDR  415B   DB CNT   0007
```

```
// FOR
* LIST SOURCE PROGRAM
* ONE WORD INTEGERS
* IOCS(2501 READER, 1403 PRINTER)
      COMMON NAME(10,500), IB(500)
C     PROGRAM TO ARRANGE WORDS IN DICTIONARY ORDER
      READ (8,1) K
1     FORMAT (I3)
C     READ THE LIST OF NAMES
      READ (8,2) ((NAME(L,M),L=1,10),IB(M),M=1,K)
2     FORMAT (6(10A1,I3))
      NP=K
14    IPOS=1
      DO 12 J=2,NP
      IF (COMPR(IPOS,J)) 11,12,12
11    IPOS=J
12    CONTINUE


PAGE  2     KS UPPAL
      CALL SWAP(IPOS,NP)
      NP=NP-1
      IF (NP-1)13,13,14
13    WRITE(3,3) (M,(NAME(L,M),L=1,10),IB(M),M=1,K)
3     FORMAT (1H1,(5X,I3,5X,10A1,5X,I3//))
      CALL EXIT
      END

FEATURES SUPPORTED
 ONE WORD INTEGERS
 IOCS

CORE REQUIREMENTS FOR
 COMMON   4500  VARIABLES     8  PROGRAM    192

END OF COMPILATION

// XEQ
```