



UNIVERSITI PUTRA MALAYSIA

**SYNTHESIS, CHARACTERIZATION AND BIOACTIVITY OF
SUBSTITUTED DITHIOCARBAZATE SCHIFF BASES OF
ACETYLTHIOPHENYL ISOMER AND THEIR METAL COMPLEXES**

EDDY CHAN MUN HOE.

FS 2005 25



**SYNTHESIS, CHARACTERIZATION AND BIOACTIVITY OF
SUBSTITUTED DITHIOCARBAZATE SCHIFF BASES OF
ACETYLTHIOPHENYL ISOMER AND THEIR METAL COMPLEXES.**

EDDY CHAN MUN HOE

**Master of Science
Universiti Putra Malaysia
2005**



**SYNTHESIS, CHARACTERIZATION AND BIOACTIVITY OF
SUBSTITUTED DITHIOCARBAZATE SCHIFF BASES OF
ACETYLTHIOPHENYL ISOMER AND THEIR METAL COMPLEXES**

By

EDDY CHAN MUN HOE

**Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia,
in Fulfilment of the Requirements for the Degree of Master of Science**

May 2005



Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfillment of the requirements for the degree of Master of Science

**SYNTHESIS, CHARACTERIZATION AND BIOACTIVITY OF
SUBSTITUTED DITHIOCARBAZATE SCHIFF BASES OF
ACETYLTHIOPHENYL ISOMERS AND THEIR METAL COMPLEXES**

By

EDDY CHAN MUN HOE

May 2005

Chairman: Professor Karen A. Crouse, PhD

Faculty: Science

The condensation reaction between S-benzylthiocarbamate (SBTDC) and S-methylthiocarbamate (SMTDC) and acetylthiophene isomers (2-acetylthiophene and 3-acetylthiophene) to produce benzyl N-[1-(thiophen-2-yl)ethylidene] hydrazine carbodithioate (SB2ATP), benzyl N-[1-(thiophen-3-yl)ethylidene] hydrazine carbodithioate (SB3ATP), methyl N-[1-(thiophen-2-yl)ethylidene] hydrazine carbodithioate (SM2ATP) and methyl N-[1-(thiophen-3-yl)ethylidene] hydrazine carbodithioate (SM3ATP) has been carried out. Cobalt (II), nickel (II), copper (II), zinc (II) and cadmium (II) complexes of the synthesized Schiff bases were prepared. All the compounds were characterized by standard physico-chemical techniques and in addition, single crystal x-ray analyses were done where possible. Antimicrobial activity and cytotoxic assays were carried out using the synthesized Schiff bases and their metal complexes. Four target microbes and four fungi were used in the antimicrobial activity studies and five target cancer cell lines were used for the cytotoxic assays. The SB2ATP, SB3ATP, SM2ATP and SM3ATP coordinate to Co(II), Ni(II), Cu(II), Zn(II) and Cd(II) ion as uninegatively



charged bidentate ligands. All complexes are non-electrolytes in DMSO. Magnetic moments and electronic spectra show that the Cu(II) complexes are paramagnetic compounds with distorted square planar structures while the Ni(SB2ATP)₂ are diamagnetic with distorted square planar environments. The structure of SB2ATP was solved in a triclinic crystal class with a *P* -1 space group while the SM2ATP was solved in a monoclinic crystal class and with a *P* 2₁/*c* space group. The Ni(SB2ATP)₂ (monoclinic, *P* 2/*c*) contains four-coordinated nickel(II) in non-planar environment as a distorted square planar monomeric entity. The crystal system of Ni(SM2ATP)₂ is monoclinic of space group *P* 2₁/*c*. This asymmetric unit consists of 2 molecules. The two bidentate ligands are coordinated to the nickel atom through an azomethine nitrogen and thiole sulfur in a distorted tetrahedral environment around the nickel atom. In general, it is clearly seen that the thiophene Schiff bases and their metal complexes do not inhibit the growth of fungi except for SB2ATP and its Cu(II) complex, which showed antifungal activity towards *Candida lypolytica* (2075) only. With the exception of Cu(SM2ATP)₂, which is active against *Methicillin* resistant *staphylococcus* (MRSA), *Bacillus subtilis*-wild type (B29) and *S. Typhimurium* (S.T.), the thiophene Schiff bases and their metal complexes are inactive. It can be concluded that chelation of Cu(II) ion increases the antifungal activity of the Schiff bases towards the target microbes. The compounds synthesized were particularly active against human breast carcinoma with positive estrogen receptor (MCF-7). However, there was only slight activity towards the human myeloid leukemia (HL-60) cell line. The remainder of the cell lines are not responsive to the compounds.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia
sebagai memenuhi keperluan untuk ijazah Master Sains

**SINTESIS, PENCIRIAN DAN KAJIAN BIOAKTIVITI TERHADAP BES
SCHIFF DITIOKARBAZAT TERTUKARGANTI YANG MENGANDUNGI
ISOMER- ISOMER ASETILTIOFENIL SERTA KOMPLEKS LOGAM
MASING-MASING.**

Oleh

EDDY CHAN MUN HOE

Mei 2005

Pengerusi: Professor Karen A. Crouse, Ph.D.

Fakulti: Sains

Tindak balas kondensasi di antara S-benzilditiokarbazat (SBDTC) dan S-metilditiokarbazat (SMDTC) dengan isomer-isomer asetiltiofin (2-asetiltiofin dan 3-asetiltiofin) menghasilkan benzil N-[1-(tiofin-2-il)etilidin] hidrazin karboditiozato (SB2ATP), benzil N-[1-(tiofin-3-il)etilidin] hidrazin karboditiozato (SB3ATP), metil N-[1-(tiofin-2-il)etilidin] hidrazin karboditiozato (SM2ATP) dan metil N-[1-(tiofin-3-il)etilidin] hidrazin karboditiozato (SM3ATP) telah dilakukan. Kompleks kobalt (II), nikel(II), kuprum(II), zink(II) dan kadmium(II) dengan bes Schiff tersebut telah disintesis. Semua sampel yang disediakan dicirikan dengan menggunakan teknik-teknik analisis kimia-fizik piawai dan apabila terdapat hablur tunggal yang sesuai, analisis sinar-X hablur tunggal juga dijalankan. Aktiviti antimikrob dan ujian sitotoksik telah dijalankan terhadap bes Schiff dan kompleks-kompleksnya. Empat jenis mikrob dan empat jenis kulat telah digunakan dalam kajian antimikrob dan lima jenis sel barah digunakan dalam kajian sitotoksik. SB2ATP, SB3ATP, SM2ATP dan SM3ATP terkoordinat kepada ion Co(II), Ni(II), Cu(II), Zn(II)

dan Cd(II) sebagai ligan-ligan bidentat yang bercas negatif tunggal. Semua kompleks bukan elektrolit dalam larutan DMSO. Kerentanan magnet dan spektra elektronik menunjukkan bahawa kompleks-kompleks Cu(II) adalah paramagnetik dengan struktur satah segiempat yang terherot manakala kompleks Ni(SB2ATP)₂ adalah dimagnetik dengan struktur satah segiempat yang terherot. Struktur SB2ATP diselesaikan dalam kelas hablur triklinik dengan kumpulan aturan $P-1$ manakala SM2ATP diselesaikan dalam kelas hablur monoklinik dengan kumpulan aturan $P 2_1/c$. Ni(SB2ATP)₂ (monoclinic, $P 2_1/c$) mengandungi nikel(II) berkoordinat empat di dalam satah satah segiempat yang terherot. Sistem hablur Ni(SM2ATP)₂ ialah monoklinik dengan kumpulan aturan $P 2_1/c$. Unit asimetrik ini mengandungi dua molekul. Dua ligan bidentat ini terkoordinat kepada atom nikel melalui nitrogen azometin dan sulfur tiolo dalam aturan tetrahedral tak sempurna. Secara umum, bes Schiff tiofin dan kompleks-kompleks logamnya tidak merencatkan pertumbuhan kulat kecuali SB2ATP dan kompleks Cu(II) yang menunjukkan aktiviti antikulat terhadap *Candida lypolytica* (2075) sahaja. Hanya Cu(SM2ATP)₂ aktif terhadap Methicillin resistant *staphylococcus* (MRSA), *Bacillus subtilis*-wild type (B29) dan *S. Typhimurium* (S.T.), bes Schiff tiofen dan kompleks-kompleksnya tidak aktif. Kesimpulannya, pengkelatan kepada ion Cu(II) boleh meninggikan aktiviti antikulat bes Schiff. Bahan-bahan yang disintesis adalah aktif terutama terhadap barah payu dara dengan reseptor estrogen positif (MCF-7). Manakala, hanya terdapat sedikit aktiviti sahaja terhadap sel leukemia myeloid manusia (HL-60). Bahan-bahan yang lain tidak memberikan sebarang aktiviti terhadap sel barah yang lain yang diuji.

ACKNOWLEDGEMENT

First of all, I would like to extend my sincere gratitude to my fellow supervisors Professor Dr. Karen A. Crouse and Dr. Mohamed Ibrahim Mohamed Tahir for their guidance and support throughout the duration of my studies. This thesis could not have been completed without their supervision, constructive comments, encouragements and suggestions.

I would like to express my appreciation to Prof. Dr. Bohari M. Yamin from Universiti Kebangsaan Malaysia and Dr. Andrew R. Cowley from University of Oxford for their contribution to the single crystal X-ray analyses, Dr. Rozita Rosli and Mr. Nasir Umar Tsafe from Clinical Genetics Unit, Department of Human Growth and Development, Faculty of Medicine and Health Science for their help in the cytotoxicity studies. My appreciation also goes to all the laboratory technicians at the Chemistry Department of Universiti Putra Malaysia for their help.

I thank the Department of Chemistry, Faculty of Science, Clinical Genetics Unit, Department of Human Growth and Development, Faculty of Medicine and Health Sciences and the Laboratory of Molecular and Cell Biology, Institute of Biosciences, Universiti Putra Malaysia for the provision of laboratory facilities. I would like to thank the Ministry of Science, Technology and Innovation of Malaysia for the funding of this project under the

Intensification of Research in Priority Areas Scheme (IRPA grant no: 09-02-040755-EA001 and 09-02-04-0296).

I would also like to send many thanks and love to my fellow laboratory mates at BSF116; Teng Jin, Kar Beng, Yean Kee, Thahira Begum, Md. Uwaisulqarni, Norazlinaliza Salim and Fiona How for their help, support guidance and laughter through my stay there.

I would like to send my gratitude and appreciation to my parents, Joseph Chan and Lam Yuen Yee, and my brother, Eric Chan, for their patience, guidance and love. Lastly, I would like to send my love to Christina Chung for her patience, love, guidance and support.

APPROVAL

This thesis submitted to the Senate of Universiti Putra Malaysia and has been accepted as fulfilment of the requirement for the degree of Master of Science. The members of the Supervisory Committee are as follows:

Main Supervisor, Ph.D.
Professor Dr. Karen Ann Crouse
Faculty of Science
Universiti Putra Malaysia
(Chairperson)

Co-Supervisor, Ph.D.
Dr. Mohamed Ibrahim Mohamed Tahir
Faculty of Science
Universiti Putra Malaysia
(Member)



TABLE OF CONTENTS

	Page
ABSTRACT	ii
ABSTRAK	iv
ACKNOWLEDGEMENTS	vi
APPROVAL	viii
DECLARATION	x
LIST OF TABLES	xiii
LIST OF FIGURES	xv
LIST OF ABBREVIATIONS	xvi
CHAPTER	
I INTRODUCTION	1
Objectives	5
II LITERATURE REVIEW	6
III METHODOLOGY	11
Preparation of Substituted Dithiocarbazate Compounds	11
S-benzylidithiocarbazate (SBDTC)	11
S-methyldithiocarbazate (SMDTC)	12
Preparation of Schiff Bases	13
Benzyl N-[1-(thiophen-2-yl)ethylidene] hydrazine carbodithioate (SB2ATP) and Benzyl N-[1-(thiophen-3-yl)ethylidene] hydrazine carbodithioate (SB3ATP)	13
Methyl N-[1-(thiophen-2-yl)ethylidene] hydrazine carbodithioate (SM2ATP) and Methyl N-[1-(thiophen-3-yl)ethylidene] hydrazine carbodithioate (SM3ATP)	13
Preparation of Metal Complexes	14
Preparation of Metal Complexes of SB2ATP, SB3ATP, SM2ATP and SM3ATP	14
Physico-Chemical Analyses	15
Fourier Transform-Infrared (FT-IR) Spectroscopy	15
Carbon, Hydrogen, Nitrogen and Sulfur (CHNS) Analyses	15
Melting Point Determination	15
Nuclear Magnetic Resonance (^1H and ^{13}C NMR) Spectroscopy	15
Inductively Coupled Plasma – Atomic Emission Spectroscopy (ICP-AES)	16
Molar Conductivity Measurements	16
Ultraviolet/Visible (UV-Vis) Spectroscopy	16
Magnetic Susceptibility Measurements	16
Single Crystal X-Ray Diffraction	17
Determination of Biological Activity	18



	Cytotoxic Assay	18
	Cell Culture	18
	Treatments and Sample Dilutions	19
	MTT Assay	20
	Antimicrobial Assay	21
	Qualitative	21
	Quantitative	22
IV	RESULTS AND DISCUSSION	23
	SB2ATP, SB3ATP and Their Metal Complexes	23
	SM2ATP, SM3ATP and Their Metal Complexes	49
V	CONCLUSIONS	74
	REFERENCES	78
	APPENDICES	87
	BIODATA OF THE AUTHOR	126



LIST OF TABLES

Table	Page
1. Cancer cell lines and inoculation densities used in screening.	18
2. Yield, colour and melting point of synthesized compounds.	26
3. Elemental analyses of synthesized compounds.	27
4. Significant IR bands of the Schiff bases and their metal complexes.	28
5. Molar conductivity and magnetic susceptibility measurements of the metal complexes.	30
6. Electronic spectral data for synthesized compounds.	32
7. Summary of crystal data and structure refinement parameters for SB2ATP.	35
8. Selected bond lengths (Å) and bond angles (°) for SB2ATP.	36
9. Hydrogen-bonding geometry (Å, °).	36
10. Summary of crystal data and structure refinement parameters for Ni(SB2ATP) ₂ .	40
11. Selected bond lengths (Å) and bond angles (°) for Ni(SB2ATP) ₂ .	41
12. Qualitative antimicrobial assay results.	46
13. Cytotoxic activity.	47
14. Yield, colour and melting point of synthesized compounds.	50
15. Elemental analyses of synthesized compounds.	51
16. Significant IR bands of the Schiff bases and their metal complexes.	52
17. Molar conductivity and magnetic susceptibility measurements of the metal complexes.	53
18. Electronic spectral data for synthesized compounds.	55
19. Summary of crystal data and structure refinement parameters for SM2ATP.	59



20. Selected bond lengths (Å) and bond angles (°) for SM2ATP.	60
21. Summary of crystal data and structure refinement parameters for Ni(SM2ATP) ₂ .	66
22. Selected bond lengths (Å) for Ni(SM2ATP) ₂ .	67
23. Selected bond angles (°) for Ni(SM2ATP) ₂ .	67
24. Qualitative antimicrobial assay results.	71
25. Cytotoxic activity.	72



LIST OF FIGURES

Figure		Page
1.	The thione and thiol tautomeric isomers of SB2ATP (a, b) and SB3ATP (c, d).	25
2.	NS bonded dialkylthiocarbazate (I), SS bonded dialkylthiocarbazate (II), dialkyldithiocarbamates (III) and dialkyldithiophosphates (IV).	25
3.	Molecular structure of SB2ATP, with 50% probability displacement ellipsoids. Intramolecular hydrogen bonds are shown as dashed lines.	33
4.	Packing diagram of SB2ATP, viewed down the c axis. Dashed lines denote the N-H...S hydrogen bonds.	34
5.	Molecular structure of Ni(SB2ATP) ₂ with 50% probability displacement ellipsoids.	38
6.	Packing arrangement of Ni(SB2ATP) ₂ , viewed along axis-b.	39
7.	The thione and thiol tautomeric isomers of SM2ATP (e, f) and SM3ATP (g, h).	48
8.	Molecular structure of SM2ATP with 50% probability displacement ellipsoids.	57
9.	Packing arrangement of SM2ATP, viewed along axis-a.	58
10.	Molecular structure of Ni(SM2ATP) ₂ with 50% probability displacement ellipsoids.	62
11.	Packing arrangement of Ni(SM2ATP) ₂ , viewed along axis-c.	63

LIST OF ABBREVIATIONS

CD ₅₀	Cytotoxic dose at 50%
Cd(SB2ATP) ₂	Bis{benzyl N-[1-(thiophen-2-yl)ethylidene] hydrazine carbodithioate}cadmium(II)
Cd(SB3ATP) ₂	Bis{benzyl N-[1-(thiophen-3-yl)ethylidene] hydrazine carbodithioate}cadmium(II)
Cd(SM2ATP) ₂	Bis{methyl N-[1-(thiophen-2-yl)ethylidene] hydrazine carbodithioate}cadmium(II)
Cd(SM3ATP) ₂	Bis{methyl N-[1-(thiophen-3-yl)ethylidene] hydrazine carbodithioate}cadmium(II)
CFU	Colony forming units
Co(SB2ATP) ₂	Bis{benzyl N-[1-(thiophen-2-yl)ethylidene] hydrazine carbodithioate}cobalt(II)
Co(SB3ATP) ₂	Bis{benzyl N-[1-(thiophen-3-yl)ethylidene] hydrazine carbodithioate}cobalt(II)
Co(SM2ATP) ₂	Bis{methyl N-[1-(thiophen-2-yl)ethylidene] hydrazine carbodithioate}cobalt(II)
Co(SM3ATP) ₂	Bis{methyl N-[1-(thiophen-3-yl)ethylidene] hydrazine carbodithioate}cobalt(II)
Cu(SB2ATP) ₂	Bis{benzyl N-[1-(thiophen-2-yl)ethylidene] hydrazine carbodithioate}copper(II)
Cu(SB3ATP) ₂	Bis{benzyl N-[1-(thiophen-3-yl)ethylidene] hydrazine carbodithioate}copper(II)

Cu(SM2ATP) ₂	Bis{methyl N-[1-(thiophen-2-yl)ethylidene] hydrazine carbodithioate}copper(II)
Cu(SM3ATP) ₂	Bis{methyl N-[1-(thiophen-3-yl)ethylidene] hydrazine carbodithioate}copper(II)
MIC	Minimum inhibitory concentration
MTT	3-[4,5-dimethylthiazo-2-yl]-2,5-diphenyltetrazolium bromide
NA	Nutrient agar
Ni(SB2ATP) ₂	Bis{benzyl N-[1-(thiophen-2-yl)ethylidene] hydrazine carbodithioate}nickel(II)
Ni(SB3ATP) ₂	Bis{benzyl N-[1-(thiophen-3-yl)ethylidene] hydrazine carbodithioate}nickel(II)
Ni(SM2ATP) ₂	Bis{methyl N-[1-(thiophen-2-yl)ethylidene] hydrazine carbodithioate}nickel(II)
Ni(SM3ATP) ₂	Bis{methyl N-[1-(thiophen-3-yl)ethylidene] hydrazine carbodithioate}nickel(II)
NNS	Nitrogen-nitrogen-sulfur
NS	Nitrogen-sulfur
ONS	Oxygen-nitrogen-sulfur
PDA	Potato dextrose agar
R	Residual factor
R _w	Weighted residual factor
SB2ATP	Benzyl N-[1-(thiophene-2-yl)ethylidene] hydrazine carbodithioate

SB3ATP	Benzyl N-[1-(thiophene-3-yl)ethylidene] hydrazine carbodithioate
SBDC	S-benzylthiocarbamate
SMDTC	S-methylthiocarbamate
SM2ATP	Methyl N-[1-(thiophene-2-yl)ethylidene] hydrazine carbodithioate
SM3ATP	Methyl N-[1-(thiophene-3-yl)ethylidene] hydrazine carbodithioate
SS	Sulfur-sulfur
Zn(SB2ATP) ₂	Bis{benzyl N-[1-(thiophen-2-yl)ethylidene] hydrazine carbodithioate}zinc(II)
Zn(SB3ATP) ₂	Bis{benzyl N-[1-(thiophen-3-yl)ethylidene] hydrazine carbodithioate}zinc(II)
Zn(SM2ATP) ₂	Bis{methyl N-[1-(thiophen-2-yl)ethylidene] hydrazine carbodithioate}zinc(II)
Zn(SM3ATP) ₂	Bis{methyl N-[1-(thiophen-3-yl)ethylidene] hydrazine carbodithioate}zinc(II)

CHAPTER I

INTRODUCTION

Coordination compounds have always been a challenge to inorganic chemists. In the early days of chemistry they seemed unusual (hence the name 'complex' ions) since they seemed to defy the usual rules of valence. Today one of the very active fields of study in the large body of inorganic research is the preparation and characterization of complexes containing nitrogen-sulfur donor ligands.

Dithiocarbazic acid derivatives and the Schiff bases synthesized from them form interesting series of compounds [1-32]. The study of these nitrogen-sulfur donor ligands continues to be of great interest to researchers since the properties of these ligands can be modified through the introduction of different organic substituents. The number of ligands synthesized continues to increase because of the fascinating property that different ligands may show different crystal morphologies and biological properties although they may differ only slightly in their molecular structures. For example, the Schiff base of 2-benzoylpyridine with S-methyldithiocarbazate inhibits the growth of bacteria *E. coli* and *S. aureus* while the S-benzylidithiocarbazate analog shows no effect at all on the mentioned bacteria [22]. Ali *et al.* [33] found that their synthesized metal complexes showed higher antifungal activity against *A. alternata*, *F. moniliforme* and *D. oryzae* than the free ligands. Their copper(II) complexes displayed better antifungal properties than nickel(II)



complexes. Hossain et al. [34] also reported that chelation of the ligand to the metal ions increased the bioactivity of some of the compounds. Results for copper(II) complexes of the 2-acetylpyridine Schiff base of SBDTC indicated that the chelation of the ligand with metal ion enhanced its activity. The fungitoxicity of the copper(II) complex was comparable to that of nystatin(standard drug), whereas the Schiff base of the S-methyldithiocarbazate was more fungitoxic than nystatin.

However, it has also been reported that chelation with metal reduces the activity of some Schiff bases. Hossain *et al.* [22] found that copper(II) complexes containing 2-benzoylpyridine Schiff base of S-methyldithiocarbazate and S-benzyldithiocarbazate were less fungitoxic towards *A. solani*, *F. equiseti* and *M. phaseolina* than either the free ligands or the commercially available antifungal drug, nystatin. These results indicated that chelation with metal ions could either increase or decrease the activity of the ligands towards target microbes.

To date no solid pattern has emerged to enable the activity to be predicted on the basis of structure or substituents although the bioactivities of the dithiocarbazate derivative ligands and their metal complexes have been widely studied. The mode of interaction of these compounds with the cancer cells and microbes at cellular level is yet to be fully investigated.

In recent years, a vast area of research has been developed on multidentate S-benzyldithiocarbazate (SBDTC) and S-methyldithiocarbazate (SMDTC)

coordination ligands [24-26, 33, 35-40]. The condensation of SBDTC with glyoxal was reported to form a quadridentate ligand with nickel(II), copper(II), zinc(II) and cadmium(II) complexes [33]. A tridentate ligand with oxygen-nitrogen-sulfur (ONS) donor sequence was synthesized by Ali *et al.* [41] in 1999. Nickel(II) complexes were prepared from the methylpyruvate Schiff bases of S-methyldithiocarbamate and S-benzylthiocarbamate. A quadridentate Schiff base was obtained by Zhu *et al.* [25] through the condensation of SBDTC with 1,4-bis(2'-formylphenyl)-1,4-dioxabutane.

Viruses are widely believed to be the cause of a number of cancers. This means that an anticancer drug may actually be an antiviral agent. The alteration of the virus by metal chelation so that the viral activity will be lessened is the aim of metallotherapeutic designer. This is because the protein and nucleic acid portions of the viruses are effective chelating agents. Moderately stable metal chelates are necessary so that the metal ion will not be so weakly bound as to be free enough to be complexed by non-viral chelating agents such as amino acids and enzymes present in the body. The chelating agent should be able to be displaced by the virus as well. The metal ion has to be selective in regard to benign and malignant viruses [7].

Cancer cells growth depends very much on the proliferation of the malignant cells having a kinetic advantage over the body's defense mechanism. The kinetic consideration is of greater importance compared to the thermodynamic stability of the metal chelates. Therefore, a metal complex has to be labile enough to outpace cancer cell growth. The following criteria

are important in determining whether a metal complex will have carcinostatic activity [7]:

- i. The complex should be reasonably labile.
- ii. The metal chelate should have reasonably high thermodynamic stability.
- iii. Ligands with sulfur donors are likely to be most effective. They usually confer lipid solubility on the metal complex and they form stable complexes with metals.

The focus of this project is to synthesize novel bidentate (NS) acetylthiophenyl Schiff bases produced using dithiocarbazate derivatives and their metal complexes. It is worthwhile to carry out the study of new isomeric dithiocarbazates and their metal complexes to supplement available information with a view to contributing to the effort to elucidate the selectivity pattern of this class of compounds since many NS-substituted dithiocarbazate esters and their metal complexes have been found to be biologically active and their activity depends strongly on the substituents and on the metals. In this thesis, cobalt(II), nickel(II), copper(II), zinc(II) and cadmium(II) were used because of their lability and inertness. Shriver and Atkins [42], stated that across the first *d* series, complexes of the *d*-block M(II) ions are moderately labile, with distorted Cu(II) complexes among the most labile and complexes of low oxidation number d^{10} ions (Zn^{2+} and Cd^{2+}) are highly labile.