UNIVERSITI PUTRA MALAYSIA

SYNTHESIS, CHARACTERISATION & BIOLOGICAL ACTIVITIES OF MIXED-LIGAND COPPER(II) COMPLEXES CONTAINING SACCHARIN

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MASTER OF SCIENCE
UNIVERSITI PUTRA MALAYSIA

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SYNTHESIS, CHARACTERISATION AND BIOLOGICAL ACTIVITIES OF MIXED-LIGAND COPPER(II) COMPLEXES CONTAINING SACCHARIN

By
THAHIRA BEGUM

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

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

SYNTHESIS, CHARACTERISATION & BIOLOGICAL ACTIVITIES OF
MIXED-LIGAND COPPER(II) COMPLEXES CONTAINING SACCHARIN AS
ONE OF THE LIGANDS

By

THAHIRA BEGUM

February 2005

Chairman: Professor Karen A.Crouse, PhD
Faculty: Science

New mixed-ligand copper(II) saccharinate complexes of HNNS Schiff bases of S-
methyldithiocarbazate, S-benzylthiocarbazate, S-2-picolylthiocarbazate and S-4-
picolylthiocarbazate were synthesized by reacting [Cu(sac)\(_2\)(H\(_2\)O)\(_4\)]\(2\)H\(_2\)O with the
appropriate Schiff bases in water-ethanol-methanol mixtures. These complexes were
characterized by elemental analysis, conductance, magnetic susceptibility, IR and
electronic spectroscopic measurements. Magnetic and spectral results for the complexes
support either a four or five-coordinate geometry in which the Schiff bases coordinate as
NNS tridentate ligands and the saccharinate anion coordinates as a unidentate N-donor
ligand. X-ray crystallographic structural analysis of the copper(II)saccharinate complex
of S-methyl-\(\beta\)-N-(6-methylpyrid-2-yl)methylenedithiocarbazate shows that the complex
has a distorted square-pyramidal structure in which the Schiff base is coordinated to the
copper ion as a tridentate NNS chelating agent via the pyridine nitrogen atom, the
azomethine nitrogen atom and the thiolate sulphur atom. The fourth and fifth
coordination positions of the five-coordinate Cu(II) ion are occupied by the imino
nitrogen of the saccharinate anion and oxygen atom of the aqua ligand. X-ray crystallographic structural analysis of the copper(II)saccharinate complex of S-benzyl-β-N-(2-acetylpyridyl)methylenedithiocarbazate shows that this complex has a distorted square-planar structure in which the Schiff base is also coordinated to the copper ion as a tridentate NNS chelating agent with the fourth coordination position of the four-coordinate Cu(II) ion being occupied by the imino nitrogen of the saccharinate anion. The complexes have been evaluated for their biological activities against seven pathogenic microbes and three cancer cell lines, HL-60 (Human myeloid leukemic cells), MCF-7 (Human breast carcinoma cells with positive estrogen receptor) and Caov-3 (Human ovarian adenocarcinoma cancer cells). Most of the complexes exhibit marked cytotoxicity against the cell lines and display moderate activity against pathogenic bacteria and fungi.
Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia bagi memenuhi keperluan Ijazah Master Sains

SINTESIS, PENCIRIAN DAN AKTIVITI BIOLOGI BAGI KOMPLEKS KUPRUM(II) BERLIGAN CAMPURAN YANG MENGANDUNGI SAKARIN SEBAGAI SALAH SATU LIGAN

Oleh:

THAHIIRA BEGUM

Februari 2005

Pengerusi: Profesor Karen A.Crouse, PhD

Fakulti: Sains

Kompleks kuprum(II) sakarinat baru yang mengandungi bes Schiff S-metilditiokarbazat, S-benzilditiokarbazat, S-2-pikolilditiokarbazat serta S-4-pikolilditiokarbazat telah disintesiskan melalui tindak balas diantara \([\text{Cu(sac)}_2(\text{H}_2\text{O})_4]\) \(2\text{H}_2\text{O}\) dengan bes Schiff yang sesuai dalam pelarut campuran air-etanol-metanol. Kompleks ini telah dicirikan melalui analisis unsur dan konduktiviti, kerentanan magnetik, pengukuran spektroskopi elektronik dan IR. Kebanyakan komplex didapati berkoordinatan empat atau lima. Ini dibuktikan melalui nilai kerentanan magnetik dan spektra yang diperolehi. Bes Schiff berkoordinat sebagai ligan tridentat NNS dan ion sakarin berkoordinat sebagai ligan N-penderma unidentat. Analisis struktur hablur sinar X menunjukkan bahawa kompleks kuprum(II) sakarinat bes Schiff S-metil-ß-N-(6-metilpirid-2-il) berstruktur piramid segiempat terherot di mana bes Schiff terkoordinat kepada ion kuprum sebagai agen kelat tridentat NNS melalui atom nitrogen piridin, atom nitrogen azometin dan atom sulfur.
tiolat. Ligan yang keempat ialah ion sakarinat yang terkoordinat melalui nitrogen imino. Manakala kompleks yang terkoordinat lima, ligan yang kelima ialah air. Analisis struktur hablur sinar X bagi kompleks kuprum(II) sakarinat bes Schiff S-benzil-β-N-(2-asetilpirid-2-il)metilinditiokarbazat menunjukkan bahawa kompleks ini mempunyai struktur segiempat planar terherot dimana bes Schiffnya juga terkoordinat kepada ion kuprum sebagai agen kelat tridentat NNS. Pengkoordinatan yang ke empat bagi ion kuprum(II) diduduki oleh nitrogen imino daripada anion sakarinat. Tujuh patogen mikrob terpilih dan tiga jenis sel kanser, [HL-60 (Sel leukemia myeloid), MCF-7 (Sel kanser payudara dengan reseptor estrogen positif) dan Caov-3 (sel kanser ovari adenocarcinoma)] telah digunakan untuk menilai keaktifan biologi. Kebanyakan kompleks tersebut menunjukkan tanda positif sitotoksik terhadap sel kanser dan menunjukkan keaktifan keatas bakteria dan fungi.
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To my family—without your support and encouragement, I would have never made it. To my father and mother, thank you for always wishing me the best and encouraging me, even when I have trouble believing in myself at times. To my sisters, Abidha – your advice and practical way of seeing things often pulled my feet back on the ground and made me realize my goals and ambitions. You’re a great source of inspiration to me. To Husna, your wackiness often kept me from going mad over the little pitfalls I had during the course of my work. To Sharifa, for being so sweet and for making me smile. To Dhekra from Yemen, thank you so much for being the best friend I ever had in Malaysia. We went through a lot together. I will never forget you. Last, but certainly not least, I would like to thank Pradeep, my best friend, for being there for me, both physically and emotionally and for encouraging me to be the best I can be, and for wishing good things for me always. It means a lot to me. Thank you.
I certify that an Examination Committee met on 25\textsuperscript{th} February 2005 to conduct the final examination of Thahira Begum on her Master of Science thesis entitled “Synthesis, characterization and biological activities of mixed-ligand Copper(II) complexes containing saccharin as one of the ligands” in accordance with Universiti Pertanian Malaysia (Higher Degree) Act 1980 and Universiti Pertanian Malaysia (Higher Degree) Regulations 1981. The Committee recommends that the candidate be awarded the relevant degree. Members of the Examination Committee are as follows:

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Date: 19 May 2005
The thesis submitted to the Senate of Universiti Putra Malaysia has been accepted as fulfillment of the requirement for the degree of Master of Science. The members of the Supervisory Committee are as follows:

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Universiti Putra Malaysia

Date:
DECLARATION

I hereby declare that the thesis is based on my original work except for quotations and citations which have been duly acknowledged. I also declare that it has not been previously or concurrently submitted for any other degree at UPM or any other institution.

__________________
THAHIRA BEGUM

Date:
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABSTRACT</td>
<td>2</td>
</tr>
<tr>
<td>ABSTRAK</td>
<td>4</td>
</tr>
<tr>
<td>ACKNOWLEDGEMENTS</td>
<td>6</td>
</tr>
<tr>
<td>APPROVAL</td>
<td>7</td>
</tr>
<tr>
<td>DECLARATION</td>
<td>9</td>
</tr>
<tr>
<td>LIST OF ABBREVIATIONS</td>
<td>13</td>
</tr>
<tr>
<td>LIST OF TABLES</td>
<td>16</td>
</tr>
<tr>
<td>LIST OF FIGURES</td>
<td>17</td>
</tr>
<tr>
<td>EQUATIONS</td>
<td>22</td>
</tr>
</tbody>
</table>

## CHAPTER

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>I INTRODUCTION</td>
<td>23</td>
</tr>
<tr>
<td>Saccharin - Structure and Historical Background</td>
<td>23</td>
</tr>
<tr>
<td>Metal-Saccharinate Complexes - Their Biological Relevance</td>
<td>26</td>
</tr>
<tr>
<td>Properties Associated with Sulphur and Nitrogen as Donor Ligands</td>
<td>28</td>
</tr>
<tr>
<td>Cytotoxicity of Some Sulphur-Nitrogen Ligands and Their Metal Complexes</td>
<td>29</td>
</tr>
<tr>
<td>OBJECTIVES</td>
<td>32</td>
</tr>
<tr>
<td>II LITERATURE REVIEW</td>
<td>33</td>
</tr>
<tr>
<td>Coordination Chemistry of the Saccharinate Anion in Various Transition-Metal Complexes</td>
<td>33</td>
</tr>
<tr>
<td>Coordination Chemistry and Bioactivities of Tridentate NNS Schiff Bases and Their Metal Complexes</td>
<td>43</td>
</tr>
<tr>
<td>III MATERIALS AND METHODS</td>
<td>49</td>
</tr>
<tr>
<td>Chemicals</td>
<td>49</td>
</tr>
<tr>
<td>Preparation of Ligands</td>
<td></td>
</tr>
<tr>
<td>S-benzyldithiocarbazate</td>
<td>50</td>
</tr>
<tr>
<td>S-methyldithiocarbazate</td>
<td>50</td>
</tr>
<tr>
<td>S-2-picolyldithiocarbazate</td>
<td>51</td>
</tr>
<tr>
<td>S-4 - picolyldithiocarbazate</td>
<td>52</td>
</tr>
<tr>
<td>Preparation of Schiff Bases</td>
<td>53</td>
</tr>
<tr>
<td>S-R-β-N-(2-pyridyl)dithiocarbazate</td>
<td>53</td>
</tr>
<tr>
<td>(R= benzyl or methyl or S-2-picoly or S-4-picolyl)</td>
<td>53</td>
</tr>
</tbody>
</table>
S-R-β-N-(6-methylpyrid-2-yl)dithiocarbazate
(R=benzyl or methyl or S-2-picolyl or S-4-picolyl) 53

S-R-β-N-(Di-2-pyridylketone)dithiocarbazate
(R= benzyl or methyl or S-2-picolyl or S-4-picolyl) 54

S-R-β-N-(2-acetylpyridyl)dithiocarbazate
(R= benzyl or methyl or S-2-picolyl or S-4-picolyl) 54

S-R-β-N-(2-benzoylpyridyl)dithiocarbazate
(R= benzyl/methyl/S-2-picolyl/ S-4-picolyl) 55

Preparation of \([\text{Cu}(\text{sac})_2(H_2O)_4]\). 2H_2O 55

Preparation of \([\text{Cu}(\text{sac})(\text{NNS})]\) Complexes 56

General Preparation of \([\text{Cu}(\text{S2P}-2)(\text{sac})]\) and \([\text{Cu}(\text{S2P}-4)(\text{sac})]\) 56

Physical Measurements and Elemental Analyses 57

Melting Points 57

CHNS Analyses 57

Determination of Metal Content 57

Conductivity Measurements 58

Magnetic Susceptibility Measurements 58

Ultraviolet/ Visible(UV/Vis) Spectra 58

Fourier Transform-Infrared (FT-IR) Spectra 59

Single Crystal Structure Determination 59

Determination of Biological Activity 60

Qualitative Antimicrobial Assay 60

Quantitative Antimicrobial Assay 61

Culture of Cells and Cytotoxic Assay 61

IV RESULTS AND DISCUSSION 62

Microanalytical Data for the Copper(II) Saccharinate Complexes 64

Molar Conductance and Magnetic Data for the
Copper(II) Saccharinate Complexes 66

Electronic Spectral Data for the HNNS Schiff Bases
and Their Copper(II) Saccharinate Complexes 70

Fourier-Transform Infrared Data for the HNNS Schiff Bases
and Their Copper(II) Saccharinate Complexes 77

X ray Crystallographic Analysis of \([\text{Cu}(\text{SM}-2)(\text{sac})(\text{H}_2\text{O})]\)
and \([\text{Cu}(\text{SB}-4)(\text{sac})]\) 87

X-ray Crystal Structure of the \([\text{Cu}(\text{SM}-2)(\text{sac})(\text{H}_2\text{O})]\)
Complex 87

X-ray Crystal Structure of the \([\text{Cu}(\text{SB}-4)(\text{sac})]\) Complex 92

Biological Activities 99

Qualitative Antimicrobial Activities of the HNNS Schiff
Bases and Their Copper(II) Saccharinate Complexes 99

Quantitative Antimicrobial Activities of the HNNS Schiff
Bases and Their Copper(II) Saccharinate Complexes 108

Cytotoxic Activities of the HNNS Schiff Bases and
Their Copper(II) Saccharinate Complexes 110
V CONCLUSION
BIBLIOGRAPHY
APPENDICES
BIODATA OF THE AUTHOR
116
118
125
162
LIST OF ABBREVIATIONS

sac  Saccharinate anion
1D  One-dimensional
FT-IR  Fourier-transform Infrared
B.M  Bohr magneton
LMCT  Ligand to metal charge transfer
MLCT  Metal to ligand charge transfer
DMSO  Dimethylsulphoxide
CD50  Cytotoxic Dose at 50%
DNA  Deoxyribonucleic acid
HL-60  Human myeloid leukemic cells
MCF-7  Human breast carcinoma cells with positive estrogen receptor
Caov-3  Human ovarian adenocarcinoma cancer cells
CHNS  Carbon, Hydrogen, Nitrogen & Sulphur
NNS  Nitrogen-nitrogen-sulphur
UV/Vis  Ultraviolet/Visible Spectroscopy
L  Ligand
Bpy  Bipyridine
PPh3  Triphenylphosphine
Ap-SBz  2-acetylpyridine Schiff base of S-benzylthiocarbazate
HSB-1  S-benzyl-β-N-(pyridine-2-yl)methylenethiocarbazate.
HSB-2  S-benzyl-β-N-(6-methylpyrid-2-yl)methylenethiocarbazate.
HSB-3  S-benzyl-β-N-(di-2-pyridylketone)methylenethiocarbazate.
HSB-4  S-benzyl-β-N-(2-acetylpyridyl)methylenethiocarbazate.
HSB-5  S-benzyl-β-N-(2-benzoylpyridyl)methylenethiocarbazate.
HSM-2  S-methyl-β-N-(6-methylpyrid-2-yl)methylenethiocarbazate.
HSM-3  S-methyl-β-N-(di-2-pyridylketone)methylenethiocarbazate.
HSM-4  S-methyl-β-N-(2-acetylpyridyl)methylenethiocarbazate.
HSM-5  S-methyl-β-N-(2-benzoylpyridyl)methylenethiocarbazate.
HS2P-1  S-2-picoyl-β-N-(pyridine-2-yl)methylenethiocarbazate.
HS2P-3  S-2-picoyl-β-N-(di-2-pyridylketone)methylenethiocarbazate.
HS2P-5  S-2-picoyl-β-N-(2-benzoylpyridyl)methylenethiocarbazate.
HS4P-1  S-4-picoyl-β-N-(pyridine-2-yl)methylenethiocarbazate.
HS4P-2  S-4-picoyl-β-N-(6-methylpyrid-2-yl)methylenethiocarbazate.
HS4P-3  S-4-picoyl-β-N-(Di-2-pyridylketone)methylenethiocarbazate.
HS4P-4  S-4-picoyl-β-N-(2-acetylpyridyl)methylenethiocarbazate.
HS4P-5  S-4-picoyl-β-N-(2-benzoylpyridyl)methylenethiocarbazate.

[Cu(SB-1)(sac)]  Copper(II) Saccharinate Complex of S-benzyl-β-N-(pyridine-2-yl)methylenethiocarbazate

[Cu(SB-2)(sac)]  Copper(II) Saccharinate Complex of S-benzyl-β-N-(6-methylpyrid-2-yl)methylenethiocarbazate

[Cu(SB-3)(sac)]  Copper(II) Saccharinate Complex of S-benzyl-β-N-(di-2-pyridylketone) methylenethiocarbazate

[Cu(SB-4)(sac)]  Copper(II) Saccharinate Complex of S-benzyl-β-N-(2-acetylpyridyl) methylenethiocarbazate

[Cu(SB-5)(sac)]  Copper(II) Saccharinate Complex of S-benzyl-β-N-(2-benzoylpyridyl)methylenethiocarbazate
[Cu(SM-2)(sac)] Copper(II) Saccharinate Complex of S-methyl-β-N-(6-methylpyrid-2-yl)methyleneedithiocarbazate

[Cu(SM-3)(sac)] Copper(II) Saccharinate Complex of S-methyl-β-N-(di-2-pyridylketone)methyleneedithiocarbazate

[Cu(SM-4)(sac)] Copper(II) Saccharinate Complex of S-methyl-β-N-(2-acetylpyridyl)methyleneedithiocarbazate

[Cu(SM-5)(sac)] Copper(II) Saccharinate Complex of S-methyl-β-N-(2-benzoylpyridyl)methyleneedithiocarbazate

[Cu(S2P-1)(sac)] Copper(II) Saccharinate Complex of S-2-picolyl-β-N-(pyridine-2-yl)methyleneedithiocarbazate

[Cu(S2P-2)(sac)] Copper(II) Saccharinate Complex of S-2-picolyl-β-N-(6-methylpyrid-2-yl)methyleneedithiocarbazate

[Cu(S2P-3)(sac)] Copper(II) Saccharinate Complex of S-2-picolyl-β-N-(di-2-pyridylketone)methyleneedithiocarbazate

[Cu(S2P-4)(sac)] Copper(II) Saccharinate Complex of S-2-picolyl-β-N-(2-acetylpyridyl)methyleneedithiocarbazate

[Cu(S2P-5)(sac)] Copper(II) Saccharinate Complex of S-2-picolyl-β-N-(2-benzoylpyridyl)methyleneedithiocarbazate

[Cu(S4P-1)(sac)] Copper(II) Saccharinate Complex of S-4-picolyl-β-N-(pyridine-2-yl)methyleneedithiocarbazate

[Cu(S4P-2)(sac)] Copper(II) Saccharinate Complex of S-4-picolyl-β-N-(6-methylpyrid-2-yl)methyleneedithiocarbazate

[Cu(S4P-3)(sac)] Copper(II) Saccharinate Complex of S-4-picolyl-β-N-(di-2-pyridylketone)methyleneedithiocarbazate

[Cu(S4P-4)(sac)] Copper(II) Saccharinate Complex of S-4-picolyl-β-N-(2-acetylpyridyl)methyleneedithiocarbazate

[Cu(S4P-5)(sac)] Copper(II) Saccharinate Complex of S-4-picolyl-β-N-(2-benzoylpyridyl)methyleneedithiocarbazate

[Cu(sac)₂(OH₂)₄].₂H₂O Copper(II) Saccharinate
## LIST OF TABLES

<table>
<thead>
<tr>
<th>Table</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Microanalytical Data for the Copper(II) Saccharinate Complexes</td>
</tr>
<tr>
<td>2</td>
<td>Molar Conductance and Magnetic Data of the Copper(II) Saccharinate Complexes</td>
</tr>
<tr>
<td>3</td>
<td>Electronic Spectral Data for the HNNS Schiff Bases and Their Copper(II) Saccharinate Complexes</td>
</tr>
<tr>
<td>4</td>
<td>FT-IR Data for the HNNS Schiff Bases and their Copper(II) Saccharinate Complexes</td>
</tr>
<tr>
<td>5</td>
<td>Crystallographic Data and Structure Refinement Details for [Cu(SM-2)(sac)(H₂O)]</td>
</tr>
<tr>
<td>6</td>
<td>Selected Bond Lengths (Å) and Bond Angles for Cu(SM-2)(sac)(H₂O)]</td>
</tr>
<tr>
<td>7</td>
<td>Crystallographic Data and Structure Refinement Details for [Cu(SB-4)(sac)]</td>
</tr>
<tr>
<td>8</td>
<td>Selected Bond Lengths (Å) and Bond Angles for [Cu(SB-4)(sac)]</td>
</tr>
<tr>
<td>9</td>
<td>Comparison of Bond Lengths in Some Copper(II) Saccharinate Complexes</td>
</tr>
<tr>
<td>10</td>
<td>Qualitative Antimicrobial Assay</td>
</tr>
<tr>
<td>11</td>
<td>Quantitative Antimicrobial Assay (MIC value, µg ml⁻³)</td>
</tr>
<tr>
<td>12</td>
<td>Cytotoxic Activities of the Schiff Bases and Their Copper(II) Saccharinate Complexes</td>
</tr>
</tbody>
</table>
### LIST OF FIGURES

<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Structure of Saccharin</td>
<td>23</td>
</tr>
<tr>
<td>2</td>
<td>Structure of Pyridine-2-carboxaldehyde Thiosemicarbazone</td>
<td>29</td>
</tr>
<tr>
<td>3</td>
<td>Structure of Kethoxal(bis)thiosemicarbazone</td>
<td>30</td>
</tr>
<tr>
<td>4</td>
<td>Structure of the Saccharinate Anion</td>
<td>33</td>
</tr>
<tr>
<td>5</td>
<td>Structure of [Cu( C_{5}H_{4}NO_{3}S)<em>{2}(H</em>{2}O)_{4}]</td>
<td>34</td>
</tr>
<tr>
<td>6</td>
<td>Reaction Scheme of the Copper(II) Complexes with Saccharin and the Auxiliary Ligands H_{2}O, PPh_{3} and NH_{3}</td>
<td>36</td>
</tr>
<tr>
<td>7</td>
<td>ORTEP Diagram of [CuL(sac)(H_{2}O)].0.5 H_{2}O</td>
<td>38</td>
</tr>
<tr>
<td>8</td>
<td>ORTEP Diagram of <a href="sac">CuL(bpy)</a>.2H_{2}O</td>
<td>38</td>
</tr>
<tr>
<td>9</td>
<td>General Structure of the Pyridine-2-carboxaldehyde Schiff Base of S-Methyldithiocarbazate and 6-Methyl-2-pyridinecarbaldehyde thiosemicarbazone</td>
<td>39</td>
</tr>
<tr>
<td>10</td>
<td>Thioketo Form of Pyridine-2-carboxaldehyde Schiff Base of SBDTC</td>
<td>43</td>
</tr>
<tr>
<td>11</td>
<td>Thiol Form of Pyridine-2-carboxaldehyde Schiff Base of SBDTC</td>
<td>43</td>
</tr>
<tr>
<td>12</td>
<td>ORTEP Diagram of [Cu(Ap-SBz)(NO_{3})]</td>
<td>45</td>
</tr>
<tr>
<td>13</td>
<td>ORTEP Diagram of [Cu(NNS)_{2}]</td>
<td>47</td>
</tr>
<tr>
<td>14</td>
<td>Thione-Thiol Tautomerism of the HNNS Schiff Bases</td>
<td>63</td>
</tr>
<tr>
<td>15</td>
<td>Expected Structures for the Copper(II) Saccharinate Complexes</td>
<td>63</td>
</tr>
<tr>
<td>16</td>
<td>Structure of the Copper(II) Saccharinate Complex of Nicotinamide</td>
<td>68</td>
</tr>
<tr>
<td>17</td>
<td>Electronic Spectrum of HSB-4</td>
<td>75</td>
</tr>
<tr>
<td>18</td>
<td>Electronic Spectrum of [Cu(SB-4)(sac)]</td>
<td>75</td>
</tr>
<tr>
<td>19</td>
<td>d-d Transition of [Cu(SB-4)(sac)]</td>
<td>75</td>
</tr>
<tr>
<td>20</td>
<td>Electronic Spectrum of HSM-2</td>
<td>76</td>
</tr>
<tr>
<td>21</td>
<td>Electronic Spectrum of[Cu(SM-2)(sac)(H_{2}O)]</td>
<td>76</td>
</tr>
<tr>
<td>22</td>
<td>d-d Transition of [Cu(SM-2)(sac)(H_{2}O)]</td>
<td>76</td>
</tr>
<tr>
<td>23</td>
<td>Coordination Sites of the HNNS Schiff Bases</td>
<td>77</td>
</tr>
<tr>
<td>24</td>
<td>FT-IR Spectrum of HSB-4</td>
<td>85</td>
</tr>
</tbody>
</table>
25 FT-IR Spectrum of [Cu(SB-4)(sac)]

26 FT-IR Spectrum of HSM-2

27 FT-IR Spectrum of [Cu(SM-2)(sac)(H₂O)]

28 ORTEP Diagram of C₁₆H₁₄N₄S₃O₄Cu
   (with 50% probability displacement ellipsoids)
   with atomic numbering scheme.

29 ORTEP Diagram of C₂₂H₁₈CuN₄O₃S₃
   (with 50% probability displacement ellipsoids)
   with atomic numbering scheme.
<table>
<thead>
<tr>
<th>Appendix A</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1 Electronic Spectrum of HSB-1</td>
<td>125</td>
</tr>
<tr>
<td>A2 Electronic Spectrum of ([\text{Cu}(\text{SB}-1)(\text{sac})])</td>
<td>125</td>
</tr>
<tr>
<td>A3 View of d-d Transition of ([\text{Cu}(\text{SB}-1)(\text{sac})])</td>
<td>126</td>
</tr>
<tr>
<td>A4 Electronic Spectrum of HSB-2</td>
<td>127</td>
</tr>
<tr>
<td>A5 Electronic Spectrum of ([\text{Cu}(\text{SB}-2)(\text{sac})])</td>
<td>127</td>
</tr>
<tr>
<td>A6 View of d-d transition of ([\text{Cu}(\text{SB}-2)(\text{sac})])</td>
<td>127</td>
</tr>
<tr>
<td>A7 Electronic Spectrum of HSB-3</td>
<td>128</td>
</tr>
<tr>
<td>A8 Electronic Spectrum of ([\text{Cu}(\text{SB}-3)(\text{sac})])</td>
<td>128</td>
</tr>
<tr>
<td>A9 View of d-d Transition of ([\text{Cu}(\text{SB}-3)(\text{sac})])</td>
<td>128</td>
</tr>
<tr>
<td>A10 Electronic Spectrum of HSB-4</td>
<td>129</td>
</tr>
<tr>
<td>A11 Electronic Spectrum of ([\text{Cu}(\text{SB}-4)(\text{sac})])</td>
<td>129</td>
</tr>
<tr>
<td>A12 View of d-d Transition of ([\text{Cu}(\text{SB}-4)(\text{sac})])</td>
<td>129</td>
</tr>
<tr>
<td>A13 Electronic Spectrum of HSB-5</td>
<td>130</td>
</tr>
<tr>
<td>A14 Electronic Spectrum of ([\text{Cu}(\text{SB}-5)(\text{sac})])</td>
<td>130</td>
</tr>
<tr>
<td>A15 View of d-d Transition of ([\text{Cu}(\text{SB}-5)(\text{sac})])</td>
<td>130</td>
</tr>
<tr>
<td>A16 Electronic Spectrum of HSM-2</td>
<td>131</td>
</tr>
<tr>
<td>A17 Electronic Spectrum of ([\text{Cu}(\text{SM}-2)(\text{sac})])</td>
<td>131</td>
</tr>
<tr>
<td>A18 View of d-d Transition of ([\text{Cu}(\text{SM}-2)(\text{sac})])</td>
<td>131</td>
</tr>
<tr>
<td>A19 Electronic Spectrum of HSM-3</td>
<td>132</td>
</tr>
<tr>
<td>A20 Electronic Spectrum of ([\text{Cu}(\text{SM}-3)(\text{sac})])</td>
<td>132</td>
</tr>
<tr>
<td>A21 View of d-d Transition of ([\text{Cu}(\text{SM}-3)(\text{sac})])</td>
<td>132</td>
</tr>
<tr>
<td>A22 Electronic Spectrum of HSM-4</td>
<td>133</td>
</tr>
<tr>
<td>A23 Electronic Spectrum of ([\text{Cu}(\text{SM}-4)(\text{sac})])</td>
<td>133</td>
</tr>
<tr>
<td>A24 View of d-d Transition of ([\text{Cu}(\text{SM}-4)(\text{sac})])</td>
<td>133</td>
</tr>
<tr>
<td>A25 Electronic Spectrum of HSM-5</td>
<td>134</td>
</tr>
<tr>
<td>A26 Electronic Spectrum of ([\text{Cu}(\text{SM}-5)(\text{sac})])</td>
<td>134</td>
</tr>
<tr>
<td>A27 View of d-d Transition of ([\text{Cu}(\text{SM}-5)(\text{sac})])</td>
<td>134</td>
</tr>
<tr>
<td>A28 Electronic Spectrum of HS2P-1</td>
<td>135</td>
</tr>
</tbody>
</table>
A29  Electronic Spectrum of [Cu(S2P-1)(sac)]  135
A30  Electronic Spectrum of [Cu(S2P-2)(sac)]  136
A31  Electronic Spectrum of HS2P-3  137
A32  Electronic Spectrum of [Cu(S2P-3)(sac)]  137
A33  View of d-d Transition of [Cu(S2P-3)(sac)]  137
A34  Electronic Spectrum of [Cu(S2P-4)(sac)]  136
A35  Electronic Spectrum of HS2P-5  138
A36  Electronic Spectrum of [Cu(S2P-5)(sac)]  138
A37  View of d-d Transition of [Cu(S2P-5)(sac)]  138
A38  Electronic Spectrum of HS4P-1  139
A39  Electronic Spectrum of [Cu(S4P-1)(sac)]  139
A40  Electronic Spectrum of HS4P-2  140
A41  Electronic Spectrum of [Cu(S4P-2)(sac)]  140
A42  View of d-d Transition of [Cu(S4P-2)(sac)]  140
A43  Electronic Spectrum of HS4P-3  141
A44  Electronic Spectrum of [Cu(S4P-3)(sac)]  141
A45  Electronic Spectrum of HS4P-4  142
A46  Electronic Spectrum of [Cu(S4P-4)(sac)]  142
A47  Electronic Spectrum of HS4P-5  143
A48  Electronic Spectrum of [Cu(S4P-5)(sac)]  143
A49  View of d-d Transition of [Cu(S4P-5)(sac)]  143

APPENDIX B

B1  FT-IR Spectrum of HSB-1  144
B2  FT-IR Spectrum of [Cu(SB-1)(sac)]  144
B3  FT-IR Spectrum of HSB-2  145
B4  FT-IR Spectrum of [Cu(SB-2)(sac)]  145
B5  FT-IR Spectrum of HSB-3  146
B6  FT-IR Spectrum of [Cu(SB-3)(sac)]  146
<table>
<thead>
<tr>
<th>Page</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>B7</td>
<td>FT-IR Spectrum of HSB-4</td>
</tr>
<tr>
<td>B8</td>
<td>FT-IR Spectrum of [Cu(SB-4)(sac)]</td>
</tr>
<tr>
<td>B9</td>
<td>FT-IR Spectrum of HSB-5</td>
</tr>
<tr>
<td>B10</td>
<td>FT-IR Spectrum of [Cu(SB-5)(sac)]</td>
</tr>
<tr>
<td>B11</td>
<td>FT-IR Spectrum of HSB-5</td>
</tr>
<tr>
<td>B12</td>
<td>FT-IR Spectrum of [Cu(SB-5)(sac)]</td>
</tr>
<tr>
<td>B13</td>
<td>FT-IR Spectrum of HSB-6</td>
</tr>
<tr>
<td>B14</td>
<td>FT-IR Spectrum of [Cu(SB-6)(sac)]</td>
</tr>
<tr>
<td>B15</td>
<td>FT-IR Spectrum of HSB-7</td>
</tr>
<tr>
<td>B16</td>
<td>FT-IR Spectrum of [Cu(SB-7)(sac)]</td>
</tr>
<tr>
<td>B17</td>
<td>FT-IR Spectrum of HSB-8</td>
</tr>
<tr>
<td>B18</td>
<td>FT-IR Spectrum of [Cu(SB-8)(sac)]</td>
</tr>
<tr>
<td>B19</td>
<td>FT-IR Spectrum of HSB-9</td>
</tr>
<tr>
<td>B20</td>
<td>FT-IR Spectrum of [Cu(SB-9)(sac)]</td>
</tr>
<tr>
<td>B21</td>
<td>FT-IR Spectrum of HSB-10</td>
</tr>
<tr>
<td>B22</td>
<td>FT-IR Spectrum of [Cu(SB-10)(sac)]</td>
</tr>
<tr>
<td>B23</td>
<td>FT-IR Spectrum of HSB-11</td>
</tr>
<tr>
<td>B24</td>
<td>FT-IR Spectrum of [Cu(SB-11)(sac)]</td>
</tr>
<tr>
<td>B25</td>
<td>FT-IR Spectrum of HSB-12</td>
</tr>
<tr>
<td>B26</td>
<td>FT-IR Spectrum of [Cu(SB-12)(sac)]</td>
</tr>
<tr>
<td>B27</td>
<td>FT-IR Spectrum of HSB-13</td>
</tr>
<tr>
<td>B28</td>
<td>FT-IR Spectrum of [Cu(SB-13)(sac)]</td>
</tr>
<tr>
<td>B29</td>
<td>FT-IR Spectrum of HSB-14</td>
</tr>
<tr>
<td>B30</td>
<td>FT-IR Spectrum of [Cu(SB-14)(sac)]</td>
</tr>
<tr>
<td>B31</td>
<td>FT-IR Spectrum of HSB-15</td>
</tr>
<tr>
<td>B32</td>
<td>FT-IR Spectrum of [Cu(SB-15)(sac)]</td>
</tr>
<tr>
<td>B33</td>
<td>FT-IR Spectrum of HSB-16</td>
</tr>
<tr>
<td>B34</td>
<td>FT-IR Spectrum of [Cu(SB-16)(sac)]</td>
</tr>
<tr>
<td>B35</td>
<td>FT-IR Spectrum of HSB-17</td>
</tr>
<tr>
<td>B36</td>
<td>FT-IR Spectrum of [Cu(SB-17)(sac)]</td>
</tr>
</tbody>
</table>
### EQUATIONS

<table>
<thead>
<tr>
<th>No.</th>
<th>Reaction</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>$[ML,\text{Cl}] + \text{DMSO} \rightarrow [ML\text{(DMSO)}]^+ + \text{Cl}^-$</td>
<td>48</td>
</tr>
<tr>
<td></td>
<td>$[M= \text{Ni(II), Cu(II), Zn(II) and Sn(II)}, \text{L= NNS}]$</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>$[M'(\text{NNS})\text{Cl}_2\cdot\text{H}_2\text{O}] + 3\text{DMSO} \rightarrow [M'(\text{NNS})(\text{DMSO})_3]^{2+} + 2 \text{Cl}^- + \text{H}_2\text{O}$</td>
<td>48</td>
</tr>
<tr>
<td></td>
<td>$[M' = \text{Cr(III), Sb(III)}]$</td>
<td></td>
</tr>
</tbody>
</table>
CHAPTER I

INTRODUCTION

Saccharin – Structure and Historical Background

The structure of saccharin (sac), 1,2-benzisothiazoline-3-(2H)one 1,1-dioxide or o-sulphobenzoimide is shown in Figure 1.

![Figure 1: Structure of Saccharin](image)

Saccharin is the world’s oldest low-calorie sweetener and is 500 times as sweet as sugar. It was discovered in 1879 by researchers led by Prof. Ira Remsen at John Hopkins University. Initially, consumption of saccharin was primarily confined to diabetics who could then enjoy sweetened foods without the extra calories, or glucose reaction associated with many sweeteners (Watkins(a), 2004). Subsequently, because of sugar rationing during the World Wars, a strong need for a sugar substitute both in the U.S and Europe developed and this need was met by saccharin. Even after World War II, saccharin continued to be used as a popular alternative to sugar, as people’s interest in weight control developed. Its usefulness remained significant until the 1970s. Due to the
synergistic and functional properties of saccharin, and its low cost, it remains a valuable low-calorie sweetener today. Saccharin continues to be important for a wide range of low-calorie and sugar-free food and beverage applications (Watkins(a), 2004).

Saccharin has been the subject of extensive scientific research. It is one of the most studied food ingredients. Although evidence indicates that saccharin is safe for human consumption, there has been controversy over its safety. The basis for the controversy was the indication of the development of bladder tumors in male rats fed high doses of sodium saccharinate. Consequently, a ban was imposed on saccharin and its usage, although the male rats used in the study were fed the human equivalent of the sodium saccharinate in hundreds of cans of diet soft drink a day for a lifetime (Watkins(b), 2004). However, extensive research on human populations has established no association between saccharin and cancer even at consumption levels above that of the average user of less than one ounce of the sweetener each year (Watkins(c), 2004).

The scientific data supporting safety of saccharin include the following:

1. Extensive research on human populations has established no association between saccharin and cancer. More than 30 human studies have been completed and indicate saccharin’s safety at human levels of consumption.

2. In fourteen single-general animal studies involving several species of animals, saccharin was not shown to induce cancer in any organ, even at exceptionally high doses.
3. Saccharin is not metabolized and does not react with DNA, meaning that saccharin lacks two of the major characteristics of a classical carcinogen (Stolberg, 1997).

4. Other research indicates that the bladder tumors developed by male rats fed high doses of sodium saccharinate are related to very high doses of the sodium salt and not saccharin per se. Sodium ascorbate (vitamin C) and sodium citrate, found in many foods and beverages, demonstrate similar effects (Stolberg, 1997).

5. Research showed that the sodium form of saccharin combines with rat urine to create crystal-like stones in the bladder of the animal. Those stones, in turn, lead to cellular changes that cause cancer. However this seems to be a rat-specific phenomenon (Stolberg, 1997) as human urine is vastly different from rat urine and does not react with saccharin in the same way (Stolberg, 1997).

In 1991, the American Food and Drug Administration (FDA) withdrew its 1977 proposal to ban the use of saccharin (Watkins(b), 2004). In July 1997, the National Institute of Health announced that its National Toxicology Program (NTP) was reviewing data that could delist saccharin from FDA’s list of carcinogens. In this announcement, NTP noted that saccharin was never listed as a known carcinogen and human studies had showed no link between saccharin and bladder cancer. The lack of effect of sodium saccharinate in mice and in monkeys further supported these findings.

In May 2000, the NTP released the 9th edition of its report on carcinogens and announced that saccharin had been delisted. The NTP report was submitted to the American Congress, and in December 2000, U.S President, Bill Clinton signed a bill that removed
the warning label that had been required on saccharin-sweetened products since 1977 (Watkins(b), 2004).

Despite the controversy, saccharin continued to be a major part of the non-nutritive sweetener market worldwide. In 2001, a report from a market research firm, Frost and Sullivan showed that the US food additive market was worth US $3000 million in 1999 and was predicted to rise to over US $5000 million by 2006. It was estimated that the non-nutritive sweetener segment of this market is worth about US $498 million of which saccharin accounts for about 45%.

Metal-Saccharinate Complexes - Their Biological Relevance

Studies revolving around saccharin and its metal complexes have been carried out to investigate the effect of saccharin consumption on humans and also living systems in general. Reports on the ability of saccharin to act as an inhibitor for certain enzyme reactions have been published (Supuran and Banciu, 1991). Carbonic anhydrase is a zinc-containing enzyme that converts carbon dioxide to soluble hydrogen carbonate in living systems. Complex-type inhibitors of this enzyme containing zinc were reported [Supuran et al. 1993(a)] and their mechanism of action investigated (Luca et al., 1991). These complexes have been found to contain aromatic or heterocyclic sulphonamides and a divalent or trivalent cation, a structure similar to that found for the metal complexes of saccharin. Such complexes are stronger inhibitors than the unsubstituted sulfonamides
due to their mechanism of action and interference with both steps of carbonic anhydrase catalytic turnover (Silverman and Lindskog, 1988).

Saccharin complexes have also been reported to have superoxide dismutase (SOD)-like behaviour. Copper-zinc superoxide dismutase, a metalloprotein found in living systems, was first found to contain copper by Mann and Keilin (1938). The presence of zinc in this protein was established later. Since the discovery of the copper-zinc enzyme (McCord and Fridovich, 1973), systems containing manganese and iron as the active metal centre have been isolated (Keele et al., 1970, DaSilva and William, 1991). The superoxide anion, produced in cells as a by-product of aerobic metabolism, is toxic to living systems. These enzymes protect the living systems by catalyzing the dismutation of the superoxide anion to generate oxygen.

The superoxide dismutase activity of the saccharinate complexes of manganese, iron, cobalt, nickel, copper and zinc has been investigated (Apella et al., 1993). The results were compared with those for the native superoxide dismutase. The copper saccharinate complex was found to have the highest SOD-like activity, with a value almost double that of the nickel, cobalt and zinc complexes, and very much higher than the values for the iron and the manganese complexes (Apella et al., 1993).
Properties Associated with Sulphur and Nitrogen as Donor Ligands

Ali and Livingstone (1974) have summarized the characteristics of ligands with sulphur as donor atoms as follows:

1. The permanent dipole moment and coordinating ability normally decreases in the order: $\text{H}_2\text{O} \succ \text{ROH} \succ \text{R}_2\text{O}$, but the reverse order holds for sulphur, i.e. $\text{H}_2\text{S} \prec \text{RSH} \prec \text{R}_2\text{S}$.

2. The strength of bonding to a metal (considering both electrostatic and covalent models) is in the following order: $\text{RO}^- \succ \text{RS}^- \succ \text{R}_2\text{O} \succ \text{R}_2\text{S}$. However, sulphur has vacant d orbitals that can be used for $\text{d}_\pi - \text{d}_\pi$ bonding with the later transition metals and the early transition metals in unusually low oxidation states.

3. The polarisabilities of sulphur donors and the number of lone pairs decrease in the order $\text{S}^{2-} \succ \text{RS}^- \succ \text{R}_2\text{S}$. Consequently, thiolo ligands are more polarisable but not as effective $\text{d}_\pi$ electron acceptors as thioethers, which is why most dithiocarbazate Schiff bases coordinate in their thiolate forms.

4. Sulphur donors bind more strongly to (b) class metals than do oxygen donors. [Class (a) metals ions are small, not very easily polarized and have a greater affinity for $\text{F}^-$ than for $\text{I}^-$. Class (b) metal ions are essentially opposite in character].

5. Sulphur ligands occupy a late position in the nephalauxetic series (a measure of the degree of covalent bonding between metal and ligand). The series of donor atoms is: $\text{F}^- < \text{O}^- < \text{N} < \text{Cl} < \text{Br} < \text{S} \approx \text{I} < \text{Se}$.

6. Sulphur atoms in heterocyclic rings have very poor coordinating ability due to the pseudo-aromatic nature of the ring, which has the two-fold effect of causing the lone pairs on the sulphur atom to be less available for donation and the $\pi$ -orbitals to be less capable of accepting electrons from the metal (Ali and Livingstone, 1974).

The properties of sulphur ligands also apply to sulphur-nitrogen chelating ligands. In general, sulphur-nitrogen ligands appear to give rise to a smaller reduction in the interelectronic repulsion energy than sulphur-sulphur ligands. The presence of nitrogen tends to lower the solubility of complexes in non-polar solvents. This causes the
complexes of nitrogen-sulphur ligands to be either sparingly soluble or completely insoluble in non-polar solvents (Ali and Livingstone, 1974).

Cytotoxicity of Some Sulphur-Nitrogen Ligands and Their Metal Complexes

The following criteria can be used to evaluate whether a metal complex is carcinostatically active:

1. The complex should be reasonably labile
2. The metal chelate should have reasonably high thermodynamic stability
3. The metal should be a class (b) metal.
4. Ligands with sulphur donors are most likely to be effective, since they allow for lipid solubility of the metal complex and form stable complexes with class (b) and borderline metals (Ali and Livingstone, 1974).

In 1956, it was reported that pyridine-2-carboxaldehyde thiosemicarbazone (Fig 2) exhibited carcinostatic activity in the lymphoid leukemia-1210 test.

![Figure 2: Structure of Pyridine-2-carboxaldehyde Thiosemicarbazone](image)

Kethoxal bis(thiosemicarbazone) (Fig 3) was also reported to exhibit carcinostatic action, and its cytotoxicity was enhanced by the presence of copper and zinc ions (Ali and Livingstone, 1974).
Cytotoxic and antimicrobial tests were carried out on metal complexes of ligands derived from dithiocarbazic acid and most have been found to be biologically active. For example, Hossain *et al.* (1996) carried out biological tests on the copper(II) complexes of the 2-acetylpyridine Schiff base of S-benzyldithiocarbazate on different types of fungi and bacteria and observed that in general, chelation of the Schiff base to the copper(II) complex enhanced its antifungal activities and the activities approached that of commercially available antibiotics. Biological tests carried out on dithiocarbazate Schiff bases and their metal complexes are discussed in more detail in Chapter II.

Due to the controversy surrounding saccharin and the various biological studies carried out on it throughout the years, and the strong antibacterial and antifungal activities shown by nitrogen-sulphur complexes, this work strives to produce complexes that are biologically relevant and may have potential use as antifungal/antibacterial/anticancer agents. Copper(II) was chosen as the transition metal due to its importance in biological systems, and its presence in many enzymes, which are essential to life.

Hence, as part of the ongoing study of metal complexes of dithiocarbazate derivatives, the synthesis, characterization and bioactivity of some mixed-ligand ternary Cu(II)
complexes of some NNS donor ligands formed by condensation of several dithiocarbazate Schiff bases with the saccharinate anion and water as co-ligands (in some cases) are reported. Since very little work has been reported on metal-saccharinate complexes, the present work is expected to shed some light on the coordination biological activities of this industrially important sweetener.
OBJECTIVES

The objectives of this project were:

- To synthesize copper (II) complexes of saccharin of the type \([\text{Cu}(\text{NNS})(\text{sac})]^{-}\), where NNS is a uninegatively charged tridentate sulphur-nitrogen chelating agent and sac is the saccharinate anion.

- To characterize the new complexes by various physico-chemical techniques, including partial elemental analysis, magnetic susceptibility, molar conductance and spectroscopic techniques and X-ray diffraction analysis where possible.

- To study the antimicrobial and cytotoxic activities of the metal complexes.
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