INVESTIGATIONS INTO THE COORDINATION CHEMISTRY OF SUBSITUTED THIOBIURETS AND THEIR ANALOGUES WITH LANTHANIDES AND EARTH-ABUNDANT METALS

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in Partial Fulfilment of the Requirements
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By

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ABSTRACT

Rare earth elements (REE) are increasingly becoming important in modern society as those elements are widely added to novel inventions to enhance performance, such as lanthanum (La) being used to increase refraction and keep dispersion low in optical glasses or neodymium (Nd) being commercially used in permanent magnets, but our high demand for REE is not fully satisfied since it remains very difficult to separate REE from each other during hydrometallurgical processes even though the natural abundance of REE is rather high. The "rarity" of REE comes from their unique characteristics and also separation issues because of similar chemical and physical properties. Use of common extractants result in a low differentiation between different elements and low efficiency during separation is unavoidable. To result in effective separation (liquid-liquid, liquid-solid), different extractants has been designed and among those extractants, bifunctional (two donor atoms) extractants are well-developed such as diglycolamide, ethylenediaminetetraacetic acid (EDTA), beta-diketone, malonamide and succinamide. This thesis starts the idea of expanding the choice of bifunctional extractants and make exploratory attempts in the extraction or even in the separation of lanthanide elements.

The initial hypothesis for this thesis was that by varying the degree of hardness of the donor atoms on a biuret-based ligand skeleton from relatively polarizable Sulfur atoms to relatively no-polarizable O donor atoms, we could control the preference of ligands to the rare earth elements. Biuret-based ligands were chosen due to their ease of synthesis and success within the Foley group with regards to selective leaching of gold by dithiobiuret-based ligands.

The first part of the thesis explores methodologies by which substituted dithiobiurets can be selectively oxidized into their corresponding monothiobiuret or biuret derivatives with an easy control and good yield under mild conditions. Initial focus was on dithiobiurets synthesised from secondary amines, CS_2, and a carbodiimide. General procedures were established resulting in the

synthesis of several previously unreported monothiobiuret and biuret derivatives in high yields. Alternative synthetic strategies involving thiocarbomoyl isothiocynate derivatives as the starting materials were also explored however the resulting thiobiurets were found to be relatively unstable compared to those obtained via the CS_2 route.

After determining how to efficiently and selectively convert substituted dithiobiuret into their corresponding monothiobiuret or biuret derivatives, the second part of the thesis involves investigation towards the selective leaching of lanthanides. While preliminary results indicated a degree of coordination of select ligands to lanthanides, progress was complicated by insolubility issues and paramagnetism of the resulting compounds. Under the conditions evaluated, biuret-based ligands did not yield conclusive results for the selective extraction of lanthanides.

Due to the inconclusive nature of the investigation involving the selective leaching of lanthanides. The research focus shifted to the exploring the coordination chemistry of dithiobiuret, monothiobiuret and biuret-based ligands with earth-abundant metals. While previous members of the Foley group have shown the dithiobiuret ligands have high selectivity towards gold over base metal, little research have been carried to study the efficiency of the ligands in coordination to base metals or the nature of the resulting complexes that might form. To better understand the chemistry of the dithiobiuret ligands and their oxidized analogues, their coordination chemistry was investigated with earth abundant metal including Fe, Ni, Cu and Zn.

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DEDICATION

I dedicate my thesis to **Tianqi Ji**, for all her love and support. A special feeling of gratitude to her who has always been there during those difficult and trying times. I deeply appreciate all of what she has done for me since we have been in love and wish I could compensate for what I owe her in my next new life journey.

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Ning Chang

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LIST OF ABBREVIATIONS

DCC ..... Dicylcohexylcarbodiimide

DMDOHEMA..... N,N'-dimethyl-N,N'-dioctylhexylethoxymalonamide

ESI..... Electron Spray Ionization

FD ..... Field Desportion

HDEHP ..... Di(ethylhexyl)phosphoric Acid

H2EHPA ..... Di(ethylhexyl)phosphoric Acid

MS..... Mass Spectrometry

MeOD ..... Deuterated-methanol

NMR ..... Nuclear Magnetic Resonance

REE..... Rare Earth Elements

REO..... Rare Earth Oxide

R.T. ..... Room Temperature

TBP ..... Tributylphosphate

THF..... Tetrahydrofuran

K_d ..... Equilibrium Constant

D..... Distribution Coefficient

β ..... Separation Factor

CHAPTER 1
INTRODUCTION

1.1 Lanthanide Elements

Lanthanide elements are a group of 14 elements, whose atomic numbers are from 57 to 71, and when scandium and yttrium are added up together with lanthanides, they are also known as rare earth elements. Traditionally, lanthanide elements are divided into two categories, based on the size of atoms: one is light lanthanide element, from lanthanum (La) to europium (Eu), and the other is heavy lanthanide element, from gadolinium (Gd) to lutetium (Lu). The first rare earth found was Y_2O_3 and discovered in 1794 and the last one was lutetium discovered in 1907. Separation and characterization of those elements took us more than 100 years. Those elements had been omitted for a while in the history but in modern society, they are in high demand for their distinguished electrical, chemical, magnetic, and optical properties[1]. For example, Cerium (Ce) is used for polishing in glass industry; neodymium (Nd) and praseodymium (Pr) are used for making permanent magnets; samarium (Sm) is used to make optical laser or absorbing neutron in nuclear reactor. Moreover, lanthanide organic complexes are popular research area in terms of preparation of luminescent hybrid material.

The rarity comes from their unique characteristic to enhance device performance and also more from the difficulty to separate one from another. The nature abundance of lanthanides or rare earth elements are relatively high compared to the precious group metal, like gold, and even common metals, like copper. Their physical and chemical properties are so similar that the difficulty of lanthanides separation is rather great, which hugely increases the cost of using lanthanide elements. The reason for lanthanides showing similarity comes from their electron

configuration. When the electrons are filling into the 4f orbital, the outer electron configuration stays unchanged as $6s^2$ or $5d^1$,$6s^2$ and therefore the common oxidation state of lanthanide is 3+. The atomic size of 3+ lanthanide ions is decreasing along the series, though they are all having large ionic radii. In principle, larger (softer acid) lanthanide ions have a higher affinity towards the softer base ligands whereas smaller (harder) lanthanide ions have a higher affinity towards harder base ligands, which is designed by Pearson and called "hard and soft acids and bases"[2]. In fact, there is only up to 3 % difference in radius between adjacent lanthanides[3], which makes the lanthanides separation a tough commission. The reason to do the separation is that little impurity of other elements from lanthanides will compromise the electrical or optical performance based on a certain lanthanide element and adjacent lanthanide are always found staying together in minerals[4,5]. Exploring proper techniques to separate lanthanide or adjacent lanthanide has become a rewarding mission to complete, especially in an industry scale.

1.2 Natural Occurrence of Lanthanide Elements

Lanthanides, which are also called as rare earth elements, have been mined in different places since 1950s, such as South Africa, Brazil, India, America, China. More and more places have been found to reserve huge amount of rare earth mines such as Vietnam. China has become the largest producer in the world by exporting cheaper product comparing to other places and has provided more than 90% of the world's total supply. The global rare earth mine production in the past two years and reserves in 2018 are summarized below[5].

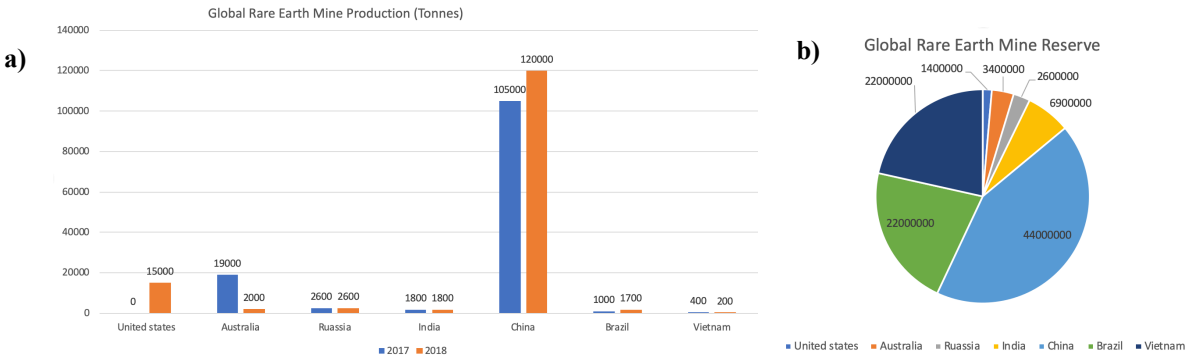


Figure 1.1[5] (a) Global rare earth mine production in 2017 and 2018 and (b) reserves in 2018.

The variety of lanthanide minerals is huge including loparite $(Ce,Na,Ca)(Ti,Nb)O_3$, ancylite $(Sr(La,Ce)(CO_3)_2OH.H_2O)$, parasite $(Ca(Ce,La)_2(CO_3)_3F_2)$, Pyrochlore $((Ca,Na,REE)_2Nb_2O_6(OH,F)$ and so on but the most famous-species are bastnesite, $(La, Ce)(CO_3)F$, monazite, $(Ce,La,Y,Th)PO_4$, and xenotime, YPO_4. The percentage of total rare earth oxide in those principal minerals is listed below[6,7].

	Bastnesite	**Monazite**	**Xenotime**
Y_2O_3	0.1	2.1	60.8
La_2O_3	32	23	0.5
CeO_2	49	45.5	5
Pr_6O_{11}	4.4	5	0.7
Nd_2O_3	13.5	18	1.1
Sm_2O_3	0.5	3.5	1.9
Eu_2O_3	0.1	0.1	0.2
Gd_2O_3	0.3	1.8	4
Tb_2O_3			1
Dy2O3			8.7
Ho_2O_3			2.1
Er_2O_3	0.1	1	5.4
Tm_2O_3			0.9
Yb_2O_3			6.2
Lu_2O_3			0.4
Total	100	100	100

Table 1.1 Preliminary estimated percentage of total rare earth oxide in principal minerals[6,7]

1.3 Brief Introduction of Lanthanide Extraction and Concentration Process

Before the separation of lanthanide elements, a concentrated lanthanides solution needs to be achieved first. After mining, comminution and flotation (or magnetic or gravity method), ore concentrates are collected and using acidic or alkaline route to extract lanthanide elements from minerals into an aqueous phase is the usual route and before that, to reduce the acid cost, roasting ore to get rid of carbonate is also necessary[7]. Among the different routes to collect the concentrate, the acidic route is the most common one, which is dominating most of extraction processes. Giving bastnesite ($(La,Ce)(CO_3)F$) as an example[8], the first step is roasting rare earth ores with concentrated sulfuric acid at around 300℃ to get rid of fluoride to make the mineral more soluble in water (Excess acid needs to be neutralized by magnesia). Lanthanides are then dissolved into water and precipitated out by adding ammonium bicarbonate or sodium hydroxide. In the end, the precipitate will be filtered and washed with hydrochloric acid to give a mixture of lanthanide chlorides. Simplified chemical equations (eqn. 1.1-1.4) of the total process are listed below.

$$(La,Ce)(CO_3)F_{(s)} \xrightarrow{\text{Roasting}} (La,Ce)OF_{(s)} + CO_{2(aq)} \quad \text{(eqn. 1.1)}$$

$$(La,Ce)OF_{(s)} + 6H_2SO_{4(l)} \rightarrow La_2(SO_4)_{3(aq)} + Ce_2(SO_4)_{3(aq)} + HF_{(g)} + H_2O_{(l)} \quad \text{(eqn. 1.2)}$$

$$La_2(SO_4)_{3(aq)} + Ce_2(SO_4)_{3(aq)} + 12NaOH \rightarrow 2La(OH)_{3(aq)} + 2Ce(OH)_{3(aq)} + 6Na_2SO_4 \quad \text{(eqn. 1.3)}$$

$$La(OH)_{3(aq)} + Ce(OH)_{3(aq)} + 6HCl_{(aq)} \rightarrow LaCl_{3(aq)} + CeCl_{3(aq)} + H_2O_{(l)} \quad \text{(eqn. 1.4)}$$

A schematic extraction and concentration process of bastnesite in Baotou (China) is listed below. Finally, lanthanide has been extracted and concentrated and further separation methods are still required, of which solvent extraction is the most common one.

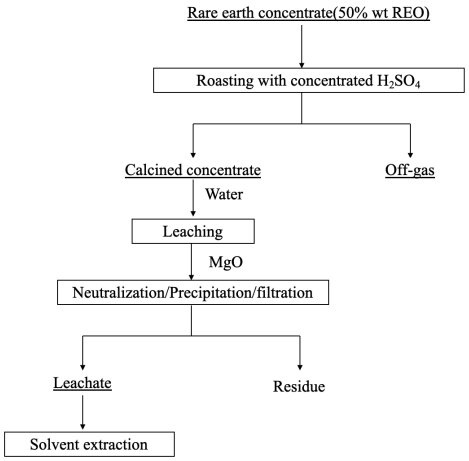


Figure 1.2[8] Flow chart of leaching process for rare earth concentrates from bastnesite ((La,Ce)(CO_3)F) (REO means rare earth oxide).

1.4 Ways to Separate Lanthanides

Ion-exchange, fractional crystallization, solvent extraction, fractional precipitation are common methods to separate lanthanides[9,10,11]. Before the introduction of solvent extraction in the 1960s, resin ion-exchange extraction was the only practical way to get individual lanthanides in high purity and large quantities. However, because of low capacity of resin, large columns and batch operations are required, which prevent the application of ion-exchange methods in commercial scales[10]. Now, the ion-exchange method is more often used to get small amounts of high-purity lanthanides for analytical or electronical applications[11].

1.4.1 Solvent Extraction of Lanthanides

"Extraction" conveys the idea of taking something from something else. Here extraction just represents a separation process, based on the different solubility in different solvents. In hydrometallurgy, solvent extraction, also known as liquid-liquid extraction is a method to extract a kind of metal from an aqueous phase into an organic phase. The selectivity of a specific metal comes from the interaction between the metal ions in the aqueous phase and the ligand in the organic phase. This method was firstly and pioneeringly used to extract Uranium from ores and

has been used for almost 80 years by analytical chemists. Flow sheets (Figure 1.3) have been designed for most of metal ions, like transition metals or rare earth metals, especially for those naturally available at low concentration or needed for high purity[12]. Organic chemists have synthesized different types of extractants to expand choices in the field of solvent extraction. Generally, there are three types of extractants for solvent reaction, whose principle is to make the metal ions more hydrophobic: (1) Make metal cations reacting with anions to form neutral complex; (2) Formation of ion pairs; (3) Replace the hydrated water molecules with organic solvating reagents. More specific explanations will be presented on Chapter **1.7**. As for lanthanides, they have been separated in industrial scale by using different types of extractants, such as tributylphosphate (TBP), or di(ethylhexyl)phosphoric acid (HDEHP), while multiple times of separation are necessary because of poor differentiation. Till now, we still do not have a full understanding of the chemistry of lanthanide solvent extraction, so trying to understand if there are any other types of extractants we could design and how to manipulate and control the separation well are the most priorities in the pressure of high demand of high purity lanthanides in modern society.

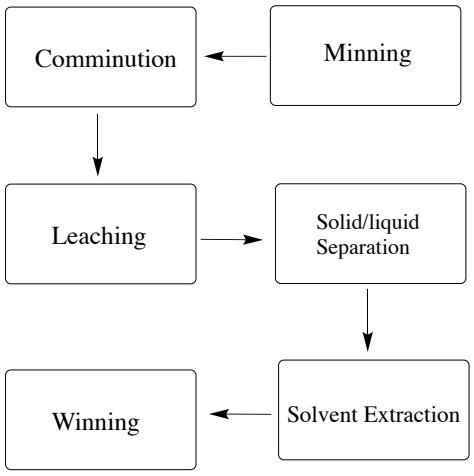


Figure 1.3[12] Flow sheet of how to deal with metal ores

1.4.2 Chemistry of Lanthanide Solvent Extraction

The elements from Ce to Lu form a class named lanthanides by the virtue of their electronic configuration. Because there is an abrupt change in energy of the 4f orbitals at atomic number 57, these orbitals are filled first after lanthanum. f orbitals penetrate the xenon core to a substantial degree and are well shielded by the filled 5s, 5p, and 6s sub-shells, which brings the result of poor interaction (weak covalent bond) between lanthanide ions and ligand orbitals[13]. In this series, there is a gradual decrease in the trivalent lanthanide ions and Table 1.2 show the exact different between each rare earth element in terms of atomic mass and ionic radius. The trivalent lanthanide ions are highly electropositive and large in size, so according to the hard-soft acid and base theory[2], they are typical hard acids and will preferentially bind with hard bases such as carbonyl groups. Soft base ligands such as thiocarbonyl group will be an alternative if there is no other had base ligand left. The coordination number of lanthanide ions could be from 6 to 12 and is capable to adapt to different coordination environments[3,13].

Element	Atomic number	Atomic mass	Ionic radius
La (Lanthanum)	57	138.9	1.061
Ce (Cerium)	58	140.1	1.034
Pr (Praesodynium)	59	140.9	1.013
Nd (Neodynium)	60	144.2	0.995
Pm (Promethiium)	61	—	0.979
Sm (Samarium)	62	150.4	0.964
Eu (Europium)	63	152.0	0.950
Gd (Gadolinium)	64	157.3	0.938
Tb (Terbium)	65	158.9	0.923
Dy (Dysprosium)	66	162.5	0.908
Ho (Holmium)	67	164.9	0.894
Er (Erbium)	68	167.3	0.881
Tm (Thulium)	69	168.9	0.869
Yb (Ytterbium)	70	173.3	0.858
Lu (Lutetium)	71	175.0	0.848
Y (Yttrium)	39	88.9	0.88

Table 1.2[13] Comparison of rare earth elements

The extraction of lanthanides is governed by composition of the aqueous phase. The extraction is affected by the nature and concentration of the metal complexes. The more stability lanthanide complexes have in the aqueous phase, the less amount of lanthanide complexes will be loading into the organic phase[14-22].

1.4.3 Extraction Equilibrium

The extraction of a metal by solvent extraction is based on the Nernst distribution law, which can be expressed as:

$$K_d = [M]_o/[M] \quad \text{(eqn. 1.5)}$$

$[M]_o$ and $[M]$ represent the concentration of metal complexes in the organic phase and aqueous phase respectively when system is at equilibrium. K_d is equilibrium constant. But sometimes the metal has different chemical forms existing in organic phase and aqueous phase, M_1, M_2, M_3, … So, the total concentration of the metal is directly determined by using atomic absorption spectroscopy or inductively coupled plasma analysis. The distribution coefficient, D, for the system is defined as:

$$D = [M]_{ot}/[M]_t \quad \text{(eqn. 1.6)}$$

$[M]_{ot}$ and $[M]_t$ are the total metal concentrations in the organic phase and aqueous phase respectively. D is determined by the nature of the extractant itself and will be constant at a certain temperature and independent of the ratio of organic phase to aqueous phase, but the ratio influences the amount of metal extracted.

1.4.4 Kinetics of Extraction

The kinetics governs the throughput of the solvent extraction processes. Commercially, the solvent extraction system should have overall extraction rates of the order of no more than a few minutes. The rate of solvent extraction is depending on the surface area, which is correlating with the extent to agitation. But too much agitation can result in an emulsion, which is undesired in the solvent extraction.

1.4.5 Separation Factor

The separation factor β reflects the selectivity of two different metals, M_a, and M_b in solvent extraction (eqn. 1.7 ,1.8 and 1.9). The selectivity is given by the ratio of the extraction equilibrium constants, k_a and k_b, or the ratio of the distribution coefficients, D_a and D_b (eqn. 1.9).

$$M_a + HL \leftrightharpoons M_aL + H^+ \text{ Equilibrium constant } K_a \quad \text{(eqn. 1.7)}$$

$$M_b + HL \leftrightharpoons M_bL + H^+ \text{ Equilibrium constant } K_b \quad \text{(eqn. 1.8)}$$

$$\beta = {}^{K_a}/_{K_b} = {}^{D_a}/_{D_b} \quad \text{(eqn. 1.9)}$$

In the analytical separations, the desired metal should have a high distribution coefficient (usually larger than 100) and high selectivity, because a single step of separation is always the first choice[12,14]. However in industry, counter current operations with multistages are needed because separation factors and distribution factors are relatively low, and moreover there are so many different metal ions in the sample that one separation step is really impractical.

1.4.6 Classes of Extractants

The classes of extractants, which have been published so far, could be divided into three catagories: cation exchangers (or acidic extractants), anion exchangers (or basic extractants), and solvation exchangers (or neutral extractants)[12,14].

1.5 Mechanisms in Solvent Extraction

Overall, there are three different mechanisms in solvent extraction[7,12,14]. A direct comparison of different extraction is listed below (Figure 1.4).

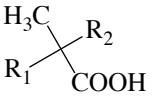
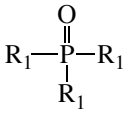
Mechanism Class	Equation	Example
Cation Exchanger	$Ln^{3+} + 3\,HA \rightleftharpoons LnA_3 + 3\,H^+$	 Verstatic 10 $R_1 + R_2 = C_7$
Anion Exchanger	$2\,RNH_2 + H_2SO_4 \rightleftharpoons (RNH_3)_2SO_4$	RNH_2 N1923 ($R = C_{19}$~C_{23})
Solvation Extractants	$Ln^{3+} + 3NO_3^- + 3\,TBP \rightleftharpoons Ln(NO_3)_3(TBP)_3$	 TBP (Tri-n-butyl-phosphate) $R_1 = CH_3(CH_2)_2CH_2O$

Figure 1.4[12] Three types of extractants in lanthanide solvent extraction

1.5.1 Cation Exchangers

A simplified expression of extraction of lanthanide elements by cation exchanger in their acidic form could be shown below:

$$Ln^{3+} + 3HA_{Org} \rightleftharpoons LnA_{3Org} + 3H^+ \quad \text{.....(eqn. 1.10)}$$

Ln^{3+} represents any lanthanide ions, and A^- represents the organic anion. Org denotes that the corresponding species are in organic phase, while other species are in aqueous phase. However, real situation is more complicated that acidic extractants are usually aggregating together to form dimers, trimers or even oligomers in non-polar organic solution[7,12,14]. A more accurate expression could be shown below (eqn 1.11). H_2A_2 represents the dimer of HA. After having a look at the equation, it is clear that if we were using acidic extractants, increasing the pH of aqueous phase

could push the equilibrium forward during solvent extraction. While if we were at the stripping process, when we need to recollect the extracted metal in aqueous phase, increasing the acidity could push the equilibrium to the reverse direction.

$$Ln^{3+} + 3H_2A_{2Org} \rightleftharpoons Ln(HA_2)_{3Org} + 3H^+ \quad \text{.....(eqn. 1.11)}$$

There are two major classes of cation exchangers commercially used: carboxylic acids and organic derivatives of phosphorous acid. Versatic acid[16] (Figure 1.5 a) was one of the most famous carboxylic acids, having been commercially used for extracting middle lanthanides. As for phosphorous acids, di(2-ethylhexyl) phosphoric acid[17], D2EHPA (Figure 1.5 b), is popularly used to extract heavy lanthanides, while it requires higher concentration of hydrofluoric acid or sulfuric acid during stripping processes.

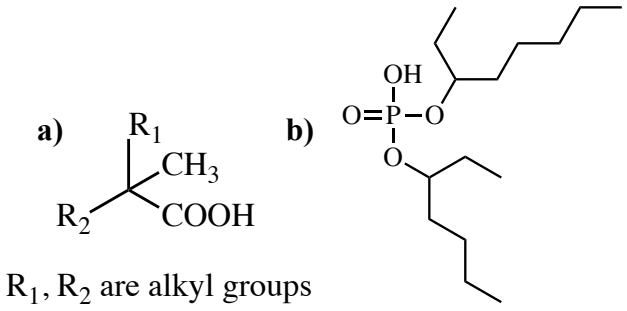


Figure 1.5 (a) Versatic acid and (b) D2EHPA

1.5.2 Anion Exchangers

Anion exchangers will form anionic complexes during extraction reaction. For example, quaternary ammonium salts, such as tri-octyl methylammonium nitrate[18,19] (Aliquat 336) (Figure 1.6) are used to selectively extract lighter lanthanides. High purity yttrium is produced through this method[20]: Yttrium performs like heavy lanthanides in nitrate media so by using an ammonium extractant and a nitrate solution, yttrium and heavy lanthanide will be left over in the solution

whereas light lanthanides are extracted. Yttrium also could perform like light lanthanide in thiocyanate solution, so yttrium could be extracted by using an ammonium extractant and a thiocyanate solution. It has been found that asymmetric amine compounds could give higher distribution coefficient. The equilibrium could be shown below (eqn. 1.12). Still Ln^{3+} represents lanthanide salts and $R_4N^+NO_3^-$ represent quaternary ammonium salts. Org denotes that the corresponding substances are in organic phase.

$$Ln^{3+} + 3NO_3^- + x(R_4N^+NO_3^-)_{Org} \rightleftharpoons [Ln(NO_3)_3 \cdot x(R_4N^+NO_3^-)]_{Org} \quad \text{.....(eqn 1.12)}$$

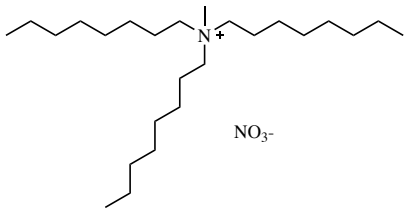


Figure 1.6: tri-octyl methylammonium nitrate (Aliquat 336)

1.5.3 Solvation Extractants

The most famous neutral extractant, which is still commercially being used, is tributyl phosphate (TBP, shown in Figure 1.7), used to select heavy lanthanide elements[21,22]. The lanthanide ions, Ln^{3+} are coordinated by phosphoryl group of TBP, in the form of neutral nitrato complexes dissolving in non-organic solvent, which could be shown as below (eqn. 1.13):

$$Ln^{3+} + 3NO_3^- + 3TBP_{Org} = [Ln(NO_3)_3 \cdot (TBP)_3]_{Org} \quad \text{.....(eqn. 1.13)}$$

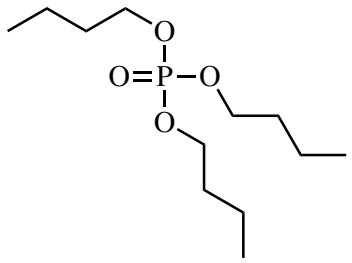


Figure 1.7: Tributyl phosphate (TBP)

1.5.4 Use of Counterions

Nitrate is usually used as counterions during industrial solvent extraction, which performs better than chloride or sulfate solutions. ClO_4^- and $CF_3SO_3^-$ is also usually used as counter ions in the laboratory scale. Those three counterions are believed to be easily pushed out by extractants when the extraction reaction is happening, whereas chloride and sulfate cannot do the same effect but still be used if necessary or for economic reasons. But sometimes, nitric solution doesn't work as expected. For example, Peppard et. al[22] found that in the situation of using TBP (tributyl phosphate), concentrated nitric acid is good at separating lanthanides lighter than Samarium but unable to separate heavier lanthanides.

The choice of counterions is usually based on experience or depending on the specific situation like what kinds of extractants are applied or what kind of lanthanide is expected to collect. About the mechanism of counter ions, Baaden et al.[23] did a computational study about how solvent and counterions effect the lanthanide cation and phosphoryl-calix[4]arene interaction by using molecular dynamics and quantum mechanical simulations. It has been found that tetra-substituted calix[4]arene will encapsulate the lanthanide cation (host-guest type) in gas phase or anhydrous solvent or as long as little other competing coordination site available. Once those competing coordination sites are available, which is happening at the organic/aqueous interface, the

lanthanide cation will move "*exo*", which contradicting with the lock-and-key metaphor. An illustration of what is happening is shown below (Figure 1.8).

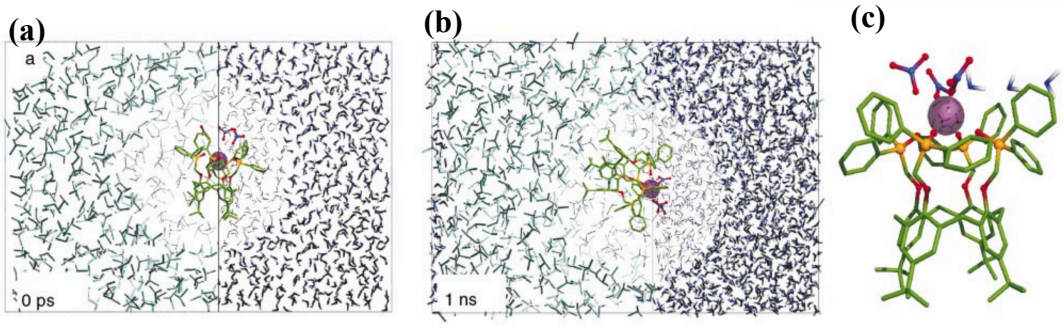


Figure 1.8[23] **(a)** The process of formation of $Eu(NO_3)_3L$ complex at chloroform/water interface; **(b) and (c)** Final complex structure showing the cation coordination sphere. (The diagram is reproduced from the work done by Baaden et al[23].)

1.5.5 Synergistic Effect During Extraction Reaction

The synergistic reaction is considered as a branch of solvent extraction, usually by combining chelating extractants and solvating extractant together to provide the extraction ability greater than the sum of the two ligands. It is a popular method used in metal separation. For example, Cyanex301 (bis(2,4,4-trimethylpentyl) dithiophosphinic acid, shown in Figure 1.9 (a)) and D2EHPA (di-(2-ethylhexyl) phosphoric acid, shown in Figure 1.9 (b)) together are found to be effective to select Gadolinium in nitrate media, whereas a single extractant system neither Cyanex301 or D2EHPA cannot finish the task. HEHEHP (2-ethylhexylphosphonic acid mono-(2-ethylhexyl) ester) combined with Cyanex272 (bis(2,4,4-trimethylpentyl)-phosphinic acid) are employed to extract Thulium (Tm), Ytterbium (Yb) and Lutetium (Lu) in chloride media, while individual extractant either has a lower loading capacity or less distribution factor[24].

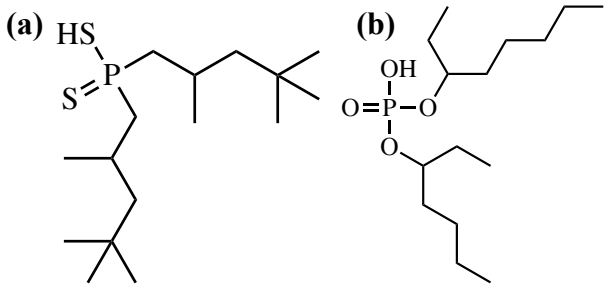


Figure 1.9. (a) Cyanex301 and **(b)** D2EHPA

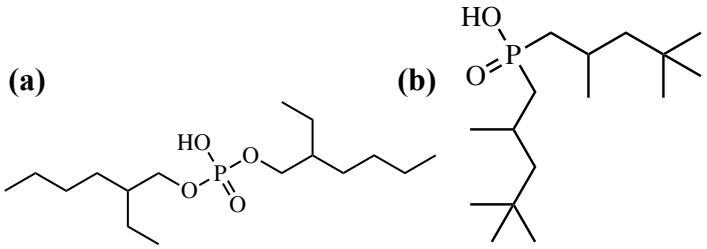


Figure 1.10. (a) HEHEHP and **(b)** Cyanex 272

The synergistic effect is a popular study area but as for the mechanism, how or why the synergistic effect contribute to the separation of lanthanide is usually omitted. There are some researches about how the synergistic influence the solvent reaction. Muller et. al[25] have studied one system using malonamide (DMDOHEMA, N,N'-dimethyl-N,N'-dioctylhexylethoxymalonamide, shown in Figure 1.11.(a)) with dialkyl phosphoric acid (D2EHPA, di-(2-ethylhexyl) phosphoric acid, shown in 1.11.(b)). They have found when they add DMDOHEMA to the Eu-D2EHPA complex, the D2EHPA will come off the Eu-D2EHPA complex to leave enough space for DMDOHEMA to form Eu-D2EHPA-DMDOHEMA complex. In the meantime, water and nitrate are replaced by the D2EHPA. This newly formed complex becomes more hydrophobic thus a better extraction ability is performed.

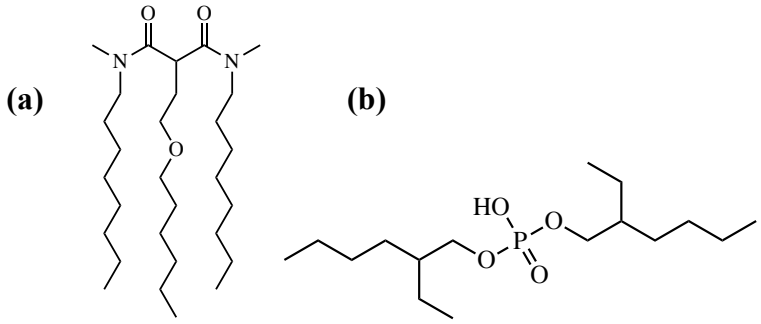


Figure 1. 11. (a) DMDOHEMA and **(b)** D2EHPA

1.6 Bi-functional Extractants

Malonamide is one kind of bi-functional extractant having been found good at separating lanthanide in lab scale since last three decades[26-31]. The structure of malonamide is listed below (Figure 1.12).

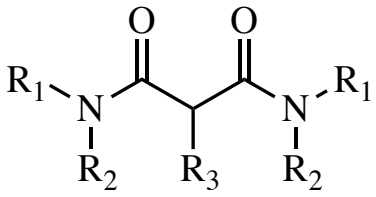


Figure 1.12 Structure of malonamide ($R_1$and R_2 is alkyl chain and R_3 could be ether or alky group).

Two carbonyl groups in the carbon structure, called a bi-functional extractant, act to coordinate with Lanthanide ions with advantages of low price, high separation factor and easy functionalization. In 1987, Musikas[26] et. al thought since N,N-dialkylamides were good extractants, beta-diamide should also perform well or even better. So N,N'-dimethyldioctylmalonamide was designed and synthesized and has showed good performance in lanthanide solvent extraction. So

substituted malonamides had become a popular research area since then and have been fully explored and studied.

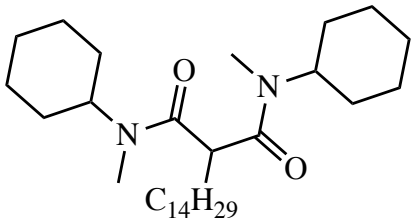


Figure 1.13 N,N'-dimethyl-N,N'-dicyclohexyltetradecyl malonamide

For example, N,N'-dimethyl-N,N'-dicyclohexyltetradecyl malonamide (Figure 1.13) were synthezied in 1997 by Spjuth et. al[27]. By introducing long tetradecyl alkyl chains at the middle methylene bridge, malonamide is easier to dissolve in non-polar organic solvent like hexane after coordination reaction with lanthanide ions, which is a great method and makes substituted malonamides potentially applied in industry. In 2009, Lisowski et. al[28] thought about the grafting malonamide on gold nanoparticles, which shows great possible application in the detection of trace number of lanthanides in aqueous solutions. In 2012, Ross J. Ellis and Mark R. Antonio[29] cooperated to study how the supramolecular architecture aggregated by N,N'-dimethyl-N,N'-dibutyltetradecylmalonamide affect the Ce(III)-malonamide solvent extraction system and proved that micellar chains are easier to aggregate when higher concentrations of nitric acid are used. Different supramolecular architectures as a factor of acid concentrations are shown in Figure 1.14. The length of alkyl side chain and the concentration of nitric acid both effect the selectivity of malonamide towards lanthanides.

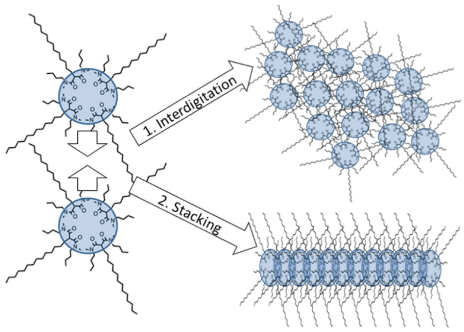


Figure 1.14 Two different supramolecular architectures aggregated by malonamides from two different concentration of nitric acid (Diagram was reproduced from the work done by Ross J. Ellis and Mark R. Antonio[29]).

1.7 Dithiobiuret Derivatives

In the Foley lab, there is a general synthesis procedure to get a series of ligands (Figure 1.15), which has already been used in biphasic extraction for different metal ions, such as gold or palladium. These dithiobiuret-based ligands start from one equiv. of a secondary amine, for example, morpholine, one equiv. of CS_2 and one equiv. of dicyclohexylcarbodiimide (DCC)[32].

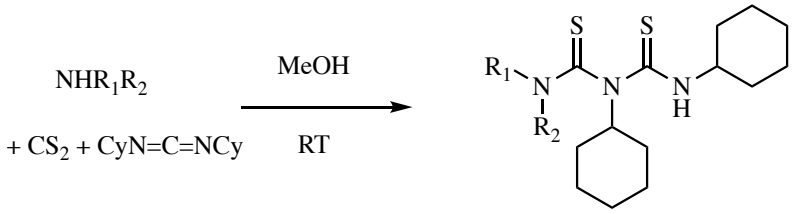


Figure 1.15[31] Schematic route to synthesis substituted dithiobiuret-based ligands

This synthesis route hasn't been proved to be applied to all secondary amines, and the successfully-made ligands are partially listed below (Figure 1.16). According to the Pearson's hard-soft acid and base theory, appropriate sulfur containing compounds are potentially good candidates for gold extraction because gold ions can be classified as soft acids and sulfur

containing compound are usually considered as soft bases. These sulfur-based ligands could provide two thiocarbonyl donor sites, which show great selectivity towards gold over other metals. Those dithiobiuret-based extractants have been explored in the area of precious group metal extraction or separation, however the exploration of oxidation reaction of those ligands and application of those oxidized products haven't been investigated yet. The oxidation chemistry of these different substituted dithiobiuret-based ligands is of interest, since oxidation can change the properties of those sulfur-based ligand to become harder bases by converting the thiocarbonyl groups into carbonyl groups, resulting in the formation of two possible distinct monothiobiurets or biuret.

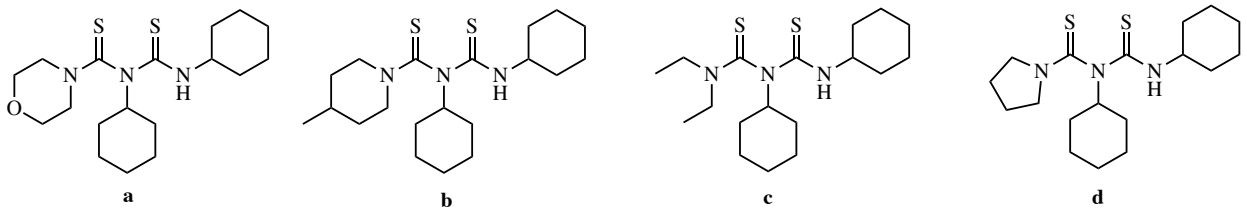
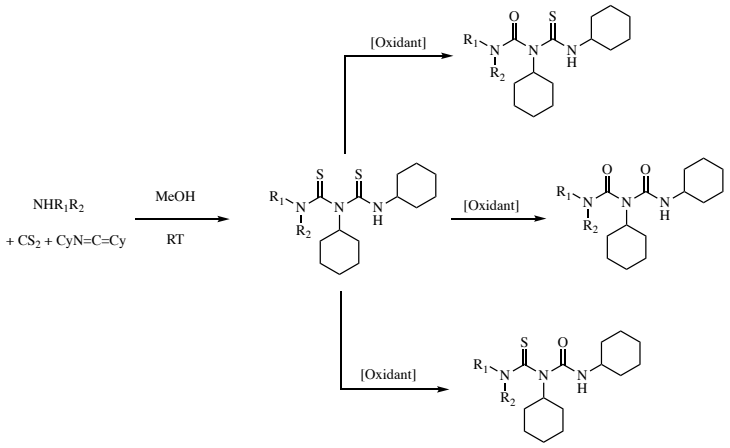


Figure 1.16 Different substituted dithiobiuret-based ligands

1.7.1 Oxidation of Dithiobiuret

A proposed oxidation route is listed below (Scheme 1.1), which would result in oxidation of one or two thiocarbonyl groups into their corresponding carbonyl groups. However, there is no researches related to the conversion of dithiobiuret-based ligands into biuret or monothiobiuret based ligands. Only reviews on oxidation of thiourea and substituted thiourea are available and served as references to propose a reasonable oxidation route.



Scheme 1.1 Route of oxidizing dithiobiuret-based ligands

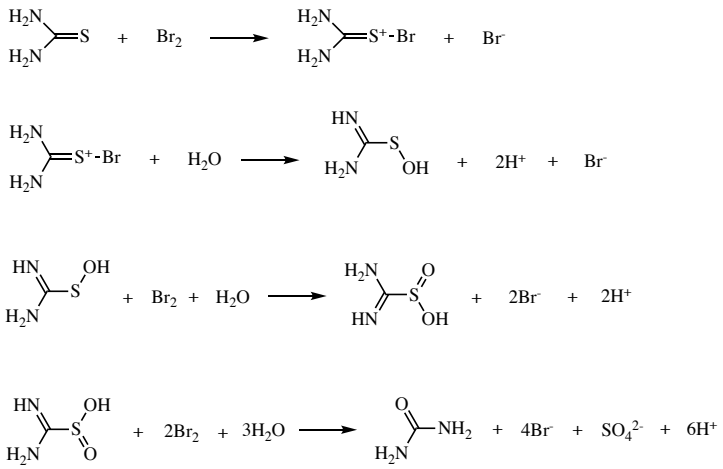
1.7.2 Oxidation of Thiourea and Substituted Thiourea

Thioureas, which contain sulfur and nitrogen atoms, are rather reactive sulfur containing compounds and could be oxidized by a large number of oxidants, yielding various products such as ureas, sulfides, oxides of sulfur, and nitrogen. The types of final products are controlled by the reaction conditions and species of oxidants[33-44]. This part will introduce some common methods, including synthetic aspects and the mechanism/schemes of the reaction.

1.7.2.1 Oxidation into Urea

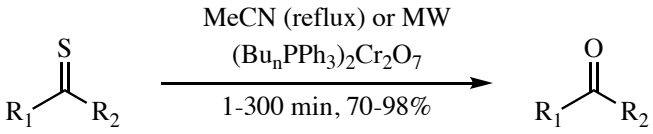
Bromine water is used to oxidize thiourea into urea within the pH range 2-4. Because of great difference between the size of carbon and sulfur, there is an incomplete pi-bond overlap of carbon-sulfur double bond, resulting in double bond becoming extremely polar. Sulfur atoms become vulnerable to electrophile attack since there is negative dipole staying on the sulfur atom. A proposed mechanism is given based on this fact (Scheme 1.2). The initial step is the rapid electrophile attack of bromine on sulfur to yield the sulfenyl bromide as the intermediate.

The second step is the hydrolysis of sulfenyl bromide to form sulfinic acid. Then bromine continues to oxidize sulfinic acid into sulfate[34].



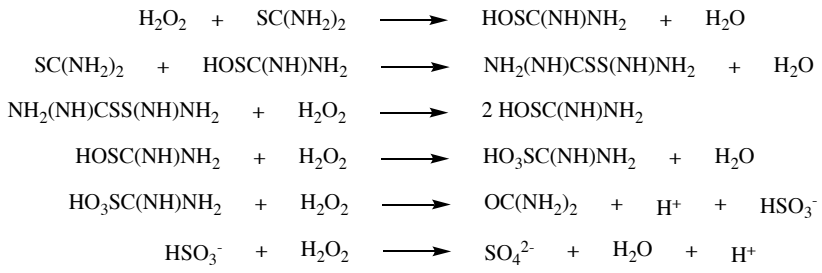
Scheme 1.2 Oxidation of thiourea by bromine water

The Cr(VI) oxidant, 1-Butyltriphenylphosphonium dichromate is used to transform thio- to their corresponding oxo- derivatives (Scheme 1.3). The oxidation reaction needs to be carried out in solution or irradiated by solid-state microwave. This reagent is commonly used for deprotection of thioamides, thioureas, thiono esters and thioketones[35].



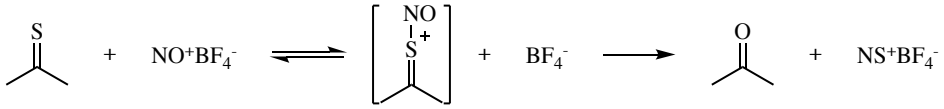
Scheme 1.3 Oxidation of thioamide, thiourea, thioester and thioketones by Cr(VI) oxidant

Hydrogen peroxide was reported to oxidize thiourea into urea stepwise (Scheme 1.4). A reversed-phase ion-pair high-performance liquid chromatography (HPLC) technique was used to monitor and elucidate what the reaction mechanism is[36].



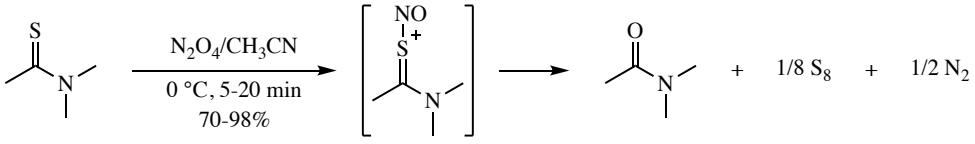
Scheme 1.4 Oxidation of thiourea by hydrogen peroxide

Olah et al. and Doyle and Hedstrand[37] proved that nitrosonium cations make the first electrophile attack to the thiocarbonyl group and fulfill the conversion of thiocarbonyl group to carbonyl group by adding nitrosomium tetrafluoroborate to thioketones, thioamides and 1,3-dithiolane-2-thiones (Scheme 1.5).



Scheme 1.5 Oxidation of thiourea by nitrosonium cations

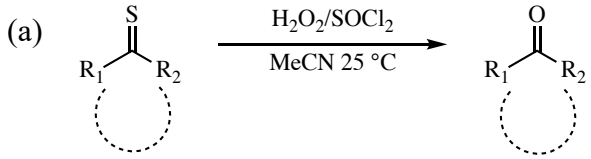
Kim[38] found that by using dinitrogen tetroxide, secondary and tertiary thioamides and thiocarbonates could be converted into corresponding oxygen analogues (Scheme 1.6).



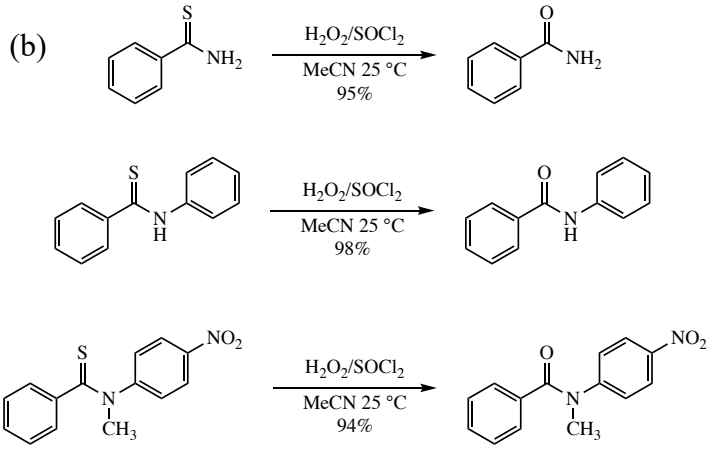
Scheme 1.6 Oxidation of thioamides by dinitrogen tetrooxide

$H_2O_2/SOCl_2$ system has been creatively found to efficiently deprotect thiocarbonyl groups into carbonyl groups[39](Scheme 1.7 (a)) Primary, secondary, and tertiary thioamides all

undergo the conversion with equal high efficiency, for example, benzamide in 95% yield, N-phenyl benzamide in 98% yield and N-methyl-4-nitro-N-phenylbenzamide in 94% yield (Scheme 1.7 (b)).



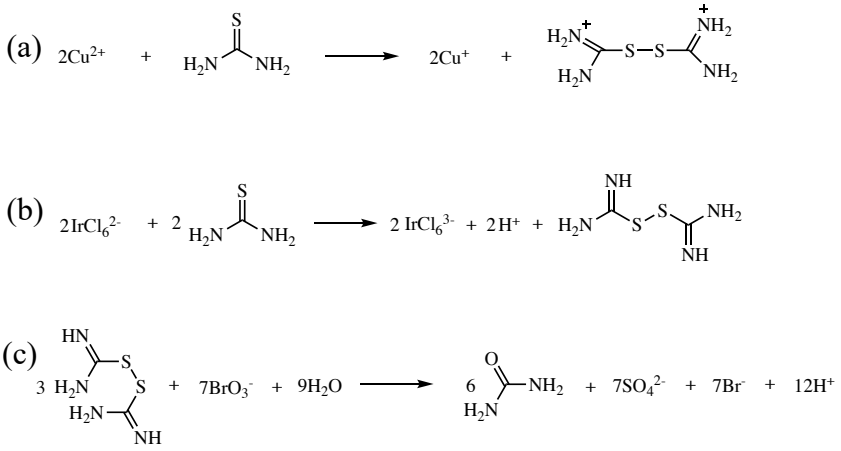
Scheme 1.7 (a) Oxidation of thiocarbonyl groups by $H_2O_2/SOCl_2$ system



Scheme 1.7 (b) Different thioamides with their corresponding percentage conversions

1.7.2.2 Oxidation into Formamidine Disulfide

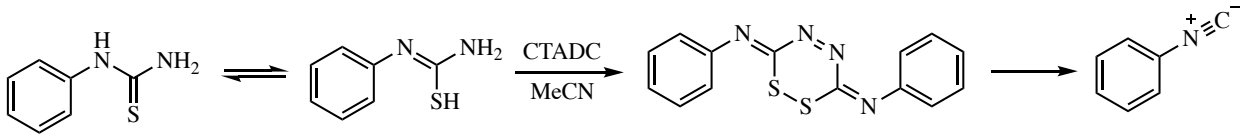
Thiourea is also possible to be oxidized into formamidine disulfide. Copper(II) perchlorate is one of effective oxidants to finish the concersion[40] (Scheme 1.8 (a)). The outer-sphere oxidant, $IrCl_6^{2-}$ could also be used to oxidize thiourea into formamidine disulfide and works out for other substituted thiourea such as N,N'-dimethylthiourea and 2-imidazolinethione to yield corresponding disulfide derivatives[41] (Scheme 1.8 (b)) and the formamidine disulfide could be further oxidized into urea, for example by bromate[42] (Scheme 1.8 (c)).



Scheme 1.8 Thiourea oxidized into formamidine disulfide by (a) Cu(II) and (b) $IrCl_6^{2-}$. (c) Oxidation of formamidine disulfide into urea by bromate.

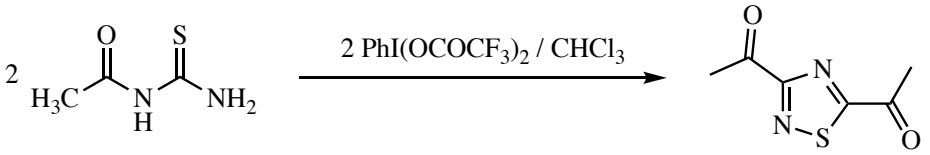
1.7.2.3 Oxidation into Other Products

Sahu et al.[43] found that not only arylthiourea could be oxidized into corresponding urea by cetyltrimethylammonium dichromate (CTADC), but also aryl isocyanide was found as main products (Scheme 1.9). A probable mechanism was proposed for the formation of corresponding isocyanide: the first step is the coupling between $-NH_2$ and -SH of one molecule with $-NH_2$ and -SH of another molecule, respectively. The removal of elemental sulfur and nitrogen and the formation of isocyanide are followed then.



Scheme 1.9 Formation of acryl isocyanide during oxidation of arylthiourea and proposed mechanism

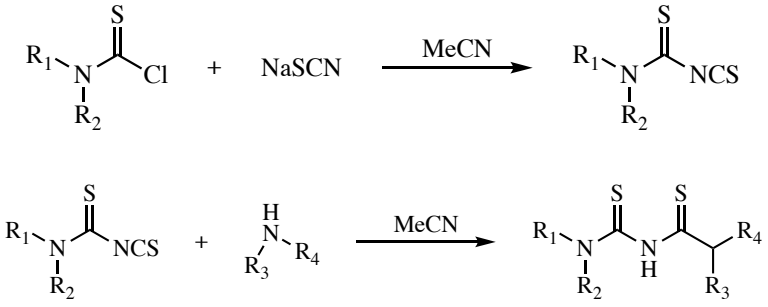
Mamaeva and Bakibaev[44] found that 1-acetylthiourea (ATU) could be oxidized by bis(trifluoroacetoxy) iodobenzene (BTI) in acetonitrile to form 3,5-diacetylamino-1,2,4-thiadiazole (Scheme 1.10).



Scheme 1.10 1-acetylthiourea oxidized into 3,5-diacetylamino-1,2,4-thiadiazole by BTI.

1.8 Alternative Ways to Synthesize Dithiobiuret-based Ligands

The first report of a series of substituted thioimidodicarbonic diamides were published on Journal of Medicinal Chemistry in 1971[45]. The application of these ligands was used as chemo sterilant for insects. These kinds of ligands were omitted for a while until they were first found to be a suitable single molecule sulfur source to synthesize ZnS or CdS thin film[46], which is popularly used in the area of solid-state cell windows, electro-optic modulators, sensors, electroluminescent and photo luminescent devices and anti-reflection coatings. The synthesis route starts from one kind of thiocarbomoyl chloride and react will sodium thiocyanate to yield thiocarbomoyl isocyanate. The thiocarbomoyl isocyanate will further react with any kind of secondary amine to yield the corresponding substituted thioimidodicarbonic diamides (or substituted dithiobiuret).



Scheme 1.11 An alternative way to synthesize dithiobiuret-based ligands

1.9 Hypothesis and Research Objectives

Dithiobiuret-based ligands have been explored well in the area of recycling precious group metals in the Foley group, however, the conversion of dithiobiuret-based ligands hasn't been explored yet. According to the Pearson's hard-soft acid and base theory[2], oxidized dithiobiuret-based ligands, monothiobiuret-based ligands or biuret-based ligands, which are becoming harder bases, are possibly used in other places. Besides, the biuret-based ligands show great similarity to substituted malonamides (Figure 1.17), which share the same central framework except that the central methylene bridge is substituted with nitrogen atoms and has great potentials in the area of lanthanide separation.

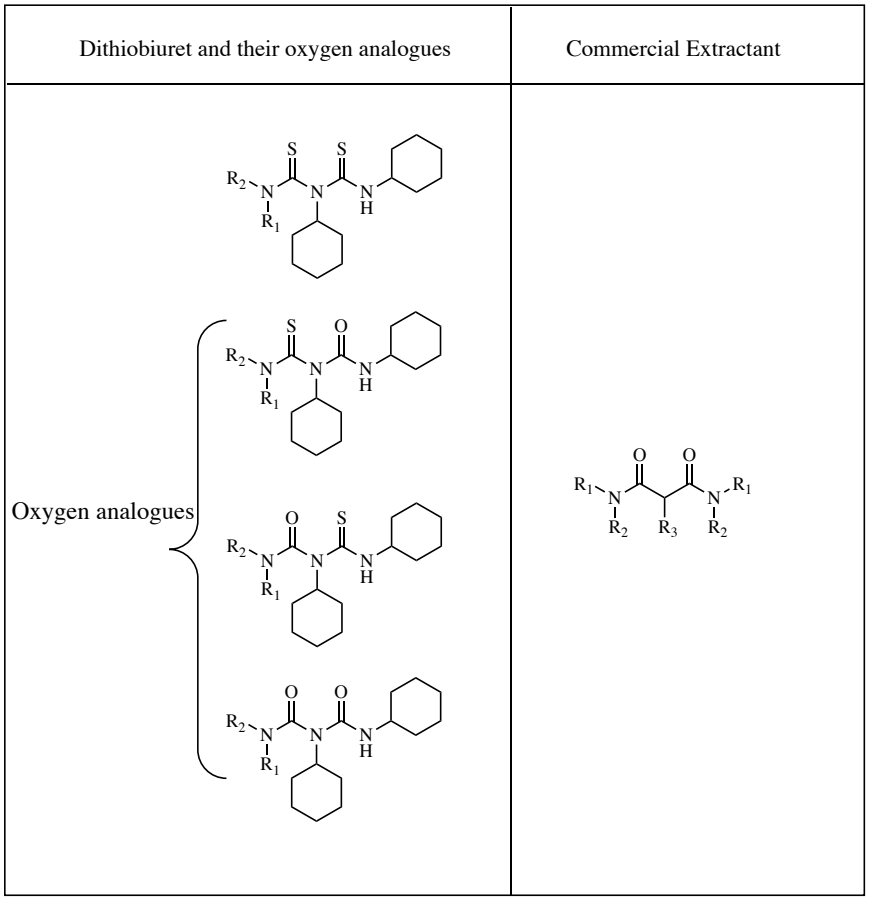


Figure 1.17 A comparison of dithiobiuret-based ligands and their oxygen analogues with malonamides

The main objective of my research was to develop a possible oxidation route to oxidize a series of dithiobiuret-based ligands into monothiobiuret-based ligands or biuret-based ligands. High oxidation state metal ions, hydrogen peroxide, and halogen gas et al[33-41]., which are introduced in the topic of oxidation of thiourea, are all worthwhile for the reagents to study.

After finding a suitable oxidation route, the exploration of these oxidized ligands in other different areas is necessary, especially in the area of lanthanide separation, since those biuret-based ligands show great similarity to substituted malonamides, which have been explored already and have shown great potential ability in lanthanide separation.

Over the course of my studies, a third objective emerged: given that these dithiobiuret ligands have been shown to be highly selective for gold over base metals, it was desirable to understand if these ligands could actually coordinate to base metals and what conditions would be required for the coordination to occur. By better understanding the requirement of the system to include (or exclude) coordination to base metals, one can better tune the ligands to achieve higher selectivities.

1.10 References

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CHAPTER 2

SYNTHESIS AND CHARACTERIZATION OF DITHIOBIURET-BASED EXTRACTANTS AND THEIR OXYGEN ANALOGUES

2.1 Introduction

Thiourea and substituted thioureas are widely applied in industry, for example gold leaching agents[1] and acid inhibitors[2]. Thiourea and substituted thioureas have been found to be susceptible to oxidation by different oxidants with varied oxidation potentials from chlorite to Co(II) octasulfophenyltertapyrazinoporphyrazine, from $KHSO_5$ to Fe(VI)[3-7]. Dithiobiuret could be consider as a condensation product of two thioureas and in principle substituted dithiobiurets could also be oxidized. Substituted dithiobiurets have been researched in the area of precious metal leaching in the Foley group, but their oxidized products have never been investigated, and the possible applications of those oxidized products still need to be determined. Therefore, an economic synthetic route to oxidize dithiobiuret-based ligands is necessary to be developed.

The oxidation of substituted dithiobiuret-based ligands was firstly found during the gold recycling process[8] where gold was suspected to be a catalyst for the formation of monothiobiurets and then interest had been drawn into how to control the oxidation process and the application of those oxidized products, which are called substituted monothiobiuret-based ligands and substituted biuret-based ligands. Initial attempt to oxidize dithiobiuret-based ligand was using hydrogen peroxide but no oxygen analogues was resulted. Then oxidant was performed to different concentrations of HCl/HNO_3 with different amounts of metallic gold or just nitric acid itself. 0.4M HNO_3/2M HCl with catalytic amount of metallic gold was firstly used to oxidize dithiobiuret and the timing of converting all or most of dithiobiuret-based ligand into monothiobiuret-based ligand

or biuret-based ligand could be controlled well. Then, the role of metallic gold and the impact of concentration of oxidant were explored by direct comparison. We found that metallic gold were oxidized first and served as catalyst to speed up the oxidation and of course, different concentrations of oxidants also have a huge impact on the rate of oxidation, and moreover, we found the choices of oxidant will affect the formation of oxidized product, which is consistent with literature. In the meantime, the stability of those oxidized products was studied and briefly discussed. Effort has been paid to understand mechanism of the oxidation process and the formation of side product. Since only limited evidence was collected, a preliminary speculation about the mechanism of side product and how to control to favor or disfavor the reaction into side product is given, which need further exploration to determine whether the speculation is correct or not. Based on the evidence we have, a future work about what we could do will be discussed.

During the exploration of the oxidation process of our dithiobiuret-based ligands, we spent some time on comparing our ligands with other previously published substituted dithiobiuret-based ligands by using dialkylthiocarbomoyl isocyanate reacting with a secondary amine. The attempts to synthesize previously published dithiobiuret-based ligand resulted in the formation of substituted 1,3,4-dithiazolium salts will be discussed.

2.2 Results and Discussion

2.2.1 Oxidation of Substituted Dithiobiuret-based Ligand

The structure of dithiobiuret-based ligands is listed below. The one-pot synthesis route is to add one equivalent of a secondary amine, one equivalent of carbon disulfide and one equivalent of dicyclohexylcarbodiimide in methanol and keep stirring up for 5 hours. White solid was precipitated and could be filtered, washed by methanol and dried with a high yield up to 90%.

During recycling gold process, we found that 2M HCl /0.4M HNO_3 with metallic gold could oxidize the dithiobiuret-based ligands into monothiobiuret or convert the dithiobiuret-based ligands into biuret by different time scales without need of further purification. Initially, this method was only applied to morpholine derivatives of dithiobiuret-based ligands (L1-1), but later we found this method also could be applied to 4-methylpiperidine (L2-1), pyrrolidine (L3-1), and diethyl amine (L-4-1) derivatives as long as stirring rate and timing could be controlled well (the corresponding exact procedure will be listed separately). The dithiobiuret ligands and their oxygen analogues we used and synthesized in this chapter are listed below (Figure 2.1).

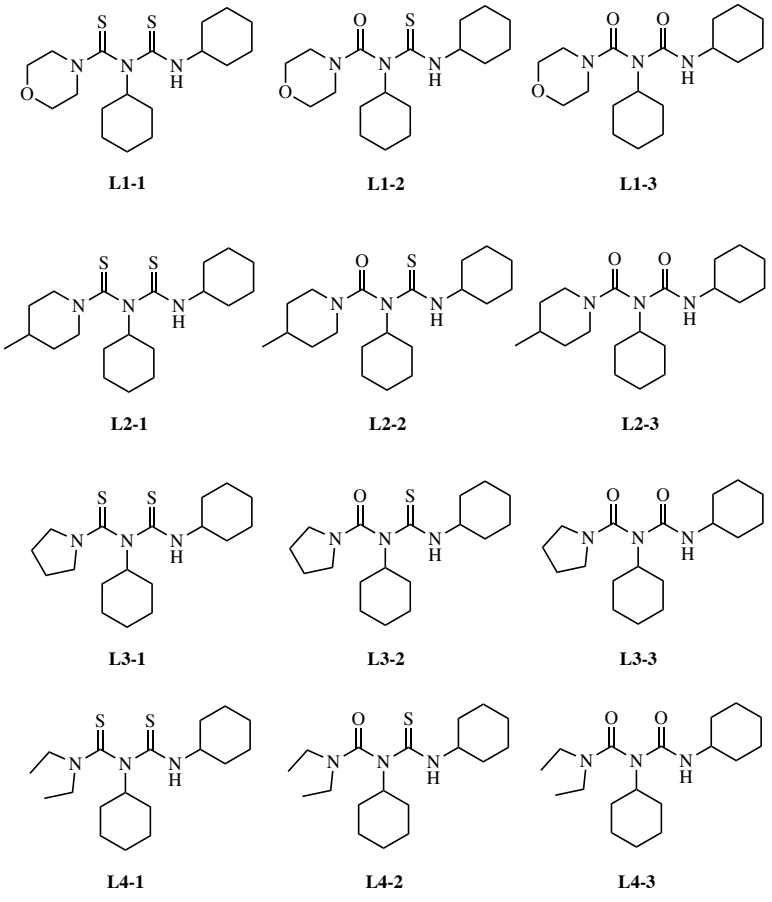
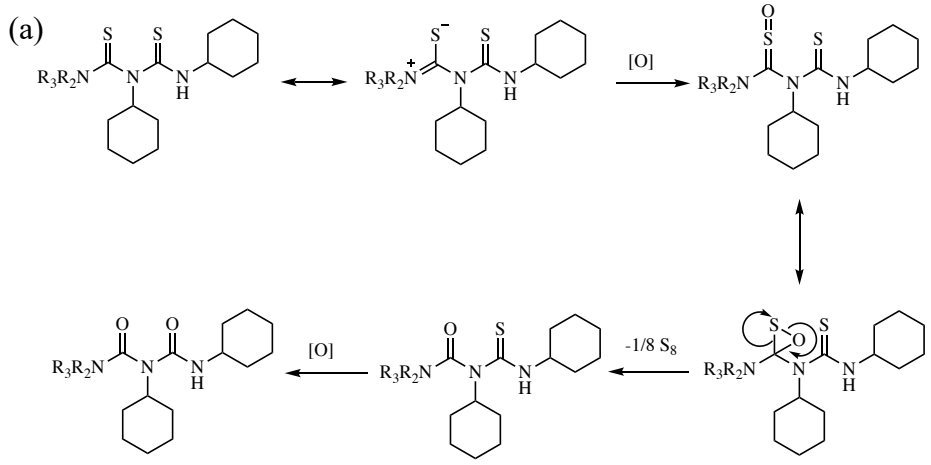
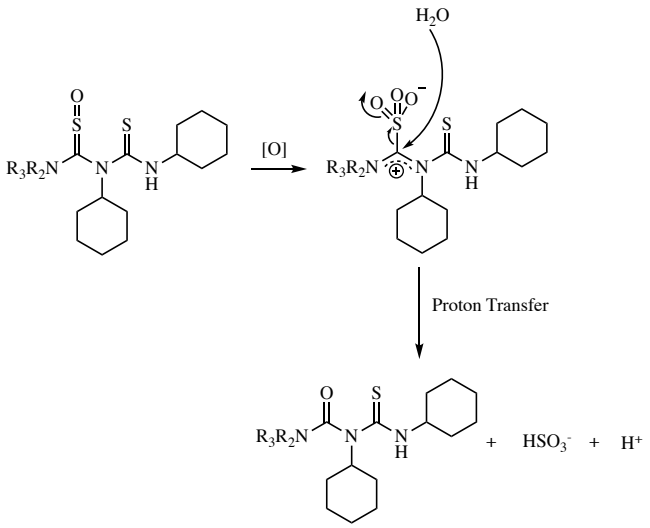


Figure 2.1 The dithiobiuret-based ligands and their oxygen analogues talked in this chapter

A general procedure is listed below. Dithiobiuret could be firstly and selectively oxidized into monothiobiuret, where the oxidation happened first on the thiocarbonyl adjacent to the secondary amine. Possible mechanisms of oxidation by nitric acid are proposed below based on the literature review[3-7]: With the help of oxidant (nitric acid in this case), thiocarbonyls will turn into sulfines (thiocarbonyl S-monoxides) or formamidinio sulfonates (thiocarbonyl S,S,S-trioxides). S-monoxides will go through a cyclic intermediate that undergoes sulfur extrusion. S,S,S-trioxides will go through a nucleophilic attack from water with an extrusion of sulfonates. Evidence for the proposed mechanism is provided by the isolation of elemental sulfur as a byproduct of the reaction. However, the mechanism still needs to be further investigated despite of all the evidences we listed. The selectivity for one carbon sulfur bond over the other is proposed: Because there is more electron donating from the secondary amine part (NR_2R_3) comparing to the cyclohexyl amine part, the thiocarbonyl closed to the secondary amine is more polarized to be influenced first, for example by nitrate ions in our experiments. Also, steric hindrance from two bulky cyclohexyl group, the sulfur closer to the secondary amine group (HNR_2R_3) is more prone to be affected by the oxidant, whereas the other sulfur is more protected, only one monothiobiuret is favored during the oxidation. More explanation and evidence for the selectivity based on the data from crystallography will be discussed on chapter 2.3.3.1.



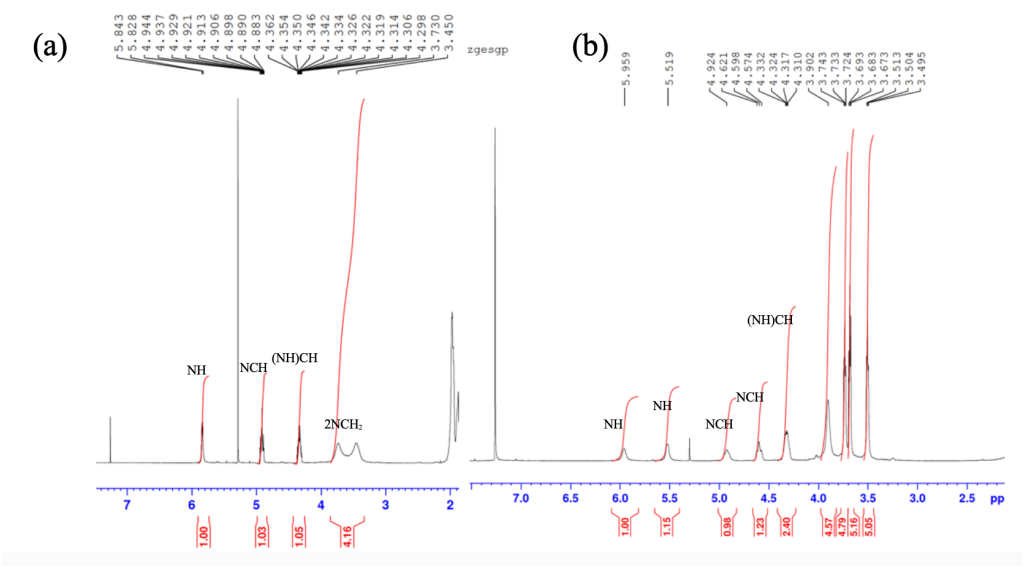
(b)



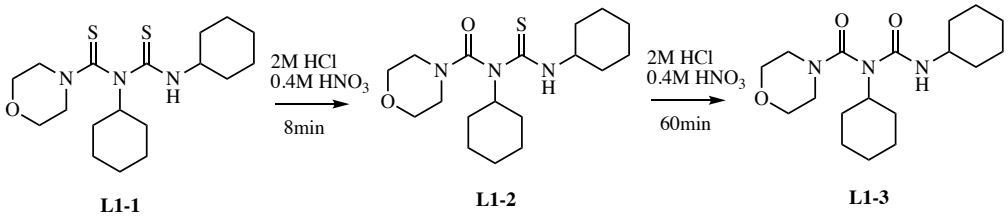
Scheme 2.1 Two possible oxidation mechanisms (a) and (b) of dithiobiuret-based ligands into monothiobiurets or biurets.

As time goes by, the monothiobiuret could be further oxidized into biuret. The structures of these series of dithiobiuret-based extractants are the same except for the choice of secondary amine. Morpholine derivatives of dithiobiuret-based ligands were the first ones explored. We found that the morpholine derivatives were easily converted from dithiobiuret to monothiobiuret or biuret and no further purification is needed. Under the condition of 2M HCl/0.4M HNO_3, dithiobiuret-based ligands remain unreacted until stirring (Figure 2.2 (a)). After stirring for 5min, morpholine derivative of dithiobiuret-based ligands was partially oxidized into monothiobiuret with a 55% conversion (corresponding ^{1}H NMR showed in Figure 2.2 (b). In the ^{1}H NMR spectrum, 5.95 ppm corresponds to the NH peak from dithiobiuret whereas 5.5 ppm corresponds to that of monothiobiuret. After 8min, dithiobiuret of morpholine derivatives are fully converted to the corresponding monothiobiuret (Figure 2.2 (c)). If we let the reaction go further, all of the monothiobiuret could be converted to the corresponding biuret after 60min (Figure 2.2 (d)). The

NH resonance moves from 5.83 ppm into 5.52 ppm after the first oxidation and finally to 4.72 ppm after the second oxidation.



(e)



L1-1 **L1-2** **L1-3**

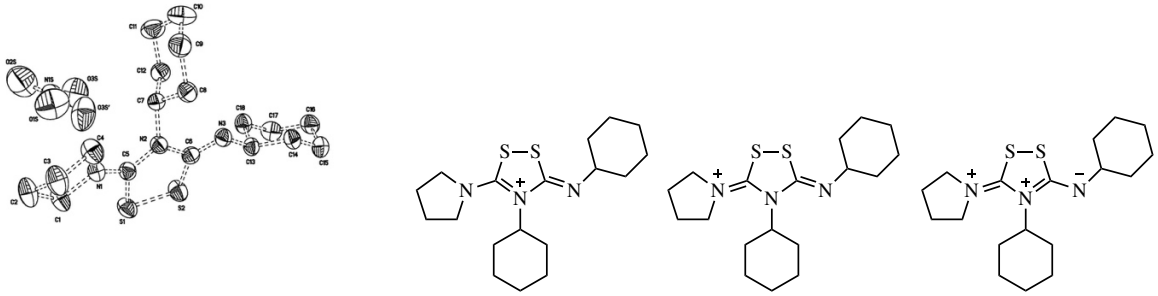
Figure 2.2 ^{1}H NMR spectrum of **(a)** free ligand of L1-1; **(b)** a mixture of L1-1 and L1-2 (ratio is around 1:1.) after 5min of oxidation; **(c)** free ligand of L1-2 after 8min of oxidation; **(d)** free ligand of L1-3 after 60 min of oxidation; **(e)** Scheme of oxidation of L1-1 into L1-2 and L1-3.

Moreover, the oxidation process could proceed with the addition of catalytic quantities of metallic gold but in a relatively quicker rate. 6 hours are needed to fully the morpholine derivatives of dithiobiuret but with the help of metallic gold, only 1 hour is enough in the meantime both yields could be reaching to around 70%. More comparison and discussion about the choice of oxidant will be listed on Chapter 2.2.2.

4-methyl piperidine, pyrrolidine and diethyl amine derivatives of dithiobiuret-based ligands also could be oxidized on the condition of 0.4M HNO_3 with 2M HCl or other conditions but have shown some complicated ^{1}H NMR spectra to different degrees after the oxidation, which is indicating that there are some other side reaction is going on or by-product is formed. So further crystallization is needed to purify those series of monothiobiuret or biuret and find out the nature of by-product if possible.

As for the purification of these oxidized product from different secondary amine derivatives, crystallization is used and worked really well. After trying different solvent to optimize the condition of crystallization, we found 9:1 ratio of methanol to DCM is the best condition we found to crystalize monothiobiuret-based ligands and 3:1 ratio of methanol to isopropanol is used to crystalize biuret-based ligands. The crystal structures of each of these monothiobiuret-based ligands and biuret-based ligands are collected except the pyrrolidine substituted ligands L3-3 and diethyl amine substituted L4-3. Crystal information is shown and compared in chapter 2.2.3.

During the attempts to crystalize of L3-3, cyclized by-product was observed (Figure 2.3 (a)). The crystal structure of cyclized by-product is provided below, and more specific descriptions and explanations will be discussed on chapter 2.2.3.3



(a) (b) (c) (d)

Figure 2.3 (a) Crystal structure of cyclized dithiobiuret of pyrrolidine derivatives; **(b)-(d)** are three possibilities for resonance structures based on the date from crystallography.

2.2.2 Choice of Oxidants

Different oxidation conditions have been applied for the series of dithiobiuret-based ligands. Initially applied oxidation condition is 0.4M HNO_3/2M HCl with metallic gold, in which it was previously[2] found morpholine substituted dithiobiuret-based ligand could be oxidized into corresponding monothiobiuret-based ligand. So, in order to understand the role of metallic gold, nitric acid and hydrochloric acid or if there is any other convenient condition to optimize the conversion of dithiobiuret to monothiobiuret and dithiobiuret to biuret, different conditions were designed and compared (Figure 2.4 (a)-(d). The moles number of starting material, stirring rate, room temperature, vails, species and volume of organic solvent and volume of aqueous phase are set constant (The set-up is shown on Figure 2.4 (e)), except that the species or concentration of oxidants varies and those all specifically listed on the experimental part.

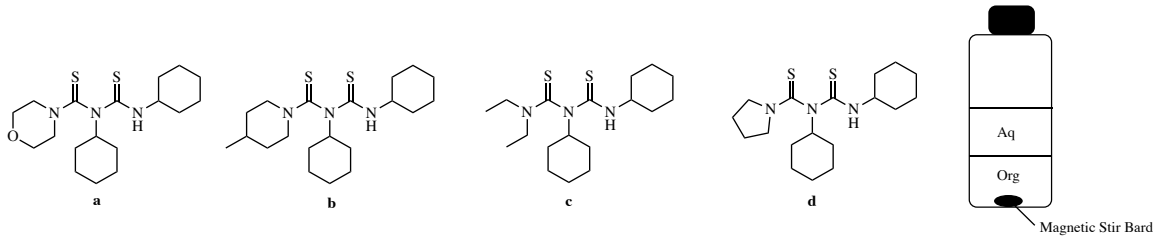


Figure 2.4 (a)-(d) are four different derivatives of dithiobiuret-based ligand used to explore oxidation reactions; **(e)** is the illustration of the set-up of the oxidation reaction.

0.4M HNO_3/2M HCl with 3% metallic gold, 0.4M HNO_3/2M HCl, 2M HNO_3, 0.4M HNO_3, 2M HNO_3, 4M HNO_3, and 25% H_2O_2/1M H_2SO_4 have been tried on the choice of oxidant to explore if 4-methylpiperidine derivatives of dithiobiuret-based ligands could be oxidized into oxygen analogues. Except for 25% H_2O_2/1M H_2SO_4, all the other oxidants could successively fulfill the commission in different time scales.

2.2.2.1 Role of Metallic Gold:

Morpholine substituted dithiobiuret based ligand L1-1 could be fully oxidized into corresponding biuret-based ligand after 1hour on the condition of 2M HCl/0.4M HNO_3 with metallic gold, whereas without metallic gold, around 6 hours was necessary to finish the full conversion (Table 2.1). We find that with the help of gold, which also need to be oxidized into gold(III) first to accelerate the reaction, the reaction will speed up while the yields of oxidized products are almost the same.

Morpholine substituted L1-1	2M HCl/0.4M HNO_3 8mg Au(0)	2M HCl/0.4M HNO_3 no Au
L1-1 to L1-2	15(±1) min	3 h
L1-1 to L1-3	60 min	6 h

Table 2.1 Different conditions to oxidize morpholine derivatives of dithiobiuret-based ligands with different time scale

2.2.2.2 Role of Nitric Acid

4-methyl piperidine substituted dithiobiuret based ligands could be fully oxidized into corresponding biuret-based ligand using 2M HNO_3 after 1 hours, whereas 4M HNO_3 only took around 30 min to finish the conversion. However, at least 48 hours are needed on the condition of 0.4M HNO_3. Nitric acid is served as oxidant to finish the conversion and the concentration of nitric acid has a huge impact on the rate of oxidation, which also match with Nernst Equation. Biuret-based ligands are stable in 2M HNO_3 and won't go further reaction even kept stirring for 3 days. Figure 2.5 (b) is the ^{13}C NMR spectrum of the crude sample stirred for 72 hours in 2M HNO_3, showing the biuret ligands still intact. But after it was kept stirring for 7 days in 2M HNO_3, biuret decomposition was observed.

	0.4M HNO_3	2M HNO_3	4M HNO_3
4-methyl piperidine substituted L2-1	L2-1 to L2-2: 10 h	L2-1 to L2-2: 18(±2) min	L2-1 to L2-2: 7(±1) min
	L2-1 to L2-3: 48 h	L2-1 to L2-3: 1 h	L2-1 to L2-3: 30 min

Table 2.2 Different concentration of nitric acid to oxidize 4-methyl piperidine derivatives of dithiobiuret-based ligand with different time scale

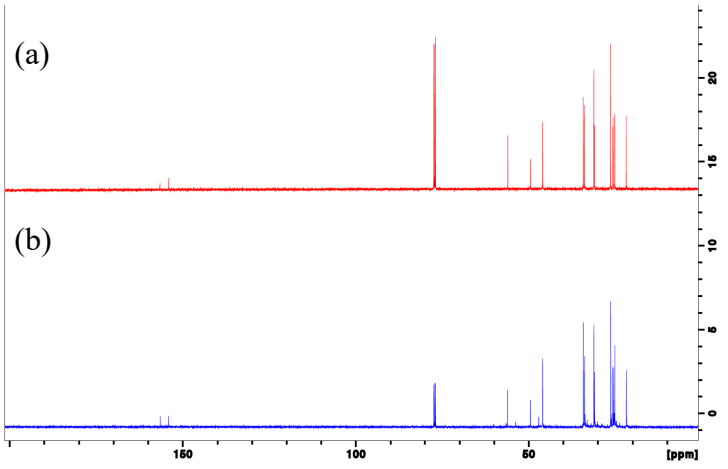


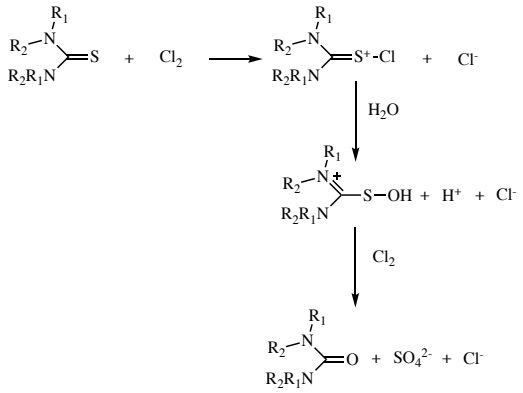
Figure 2.5 ^{1}H NMR spectrum of **(a)** free ligand of L2-3 and **(b)** crude sample of L2-1 stirred in 2M HNO_3 for 3 days and still intact.

2.2.2.3 Role of Hydrochloric Acid

The role of hydrochloric acid is preliminary explored. By comparison, we found that hydrochloric acid won't oxidized dithiobiuret-based ligand by itself but could cooperate with nitric acid to speed up the oxidation reaction all most the same as free nitric acid itself (Table 2.3). We postulate the formation of chlorine could be favored when nitric acid is combined with hydrochloric acid and chlorine also participate in the oxidation reaction by forming sulfenyl chloride intermediate and further converted into carbonyl. Proposed mechanism is given below (Scheme 2.2).

	2M HNO_3/2M HCl	**2M HNO_3**	**4M HNO_3**	**2M HCl**
4methyl piperidine L2-1	L2-1 to L2-2: 5(±1) min	L2-1 to L2-2: 18(±2) min	L2-1 to L2-2: 7(±1) min	No Reaction
	L2-1 to L2-3: 30 min	L2-1 to L2-3: 1 h	L2-1 to L2-3: 30 min	No Reaction

Table 2.3 Different concentration of hydrochloric acid with nitric acid to oxidize 4-methyl piperidine L2-1 (DTB) into corresponding monothiobiuret or biuret with different time scale.



Scheme 2.2 Proposal mechanism of hydrochloric acid cooperating with nitric acid to produce chlorine to speed up the reaction similar to the proposal made by Simoyi et al[3].

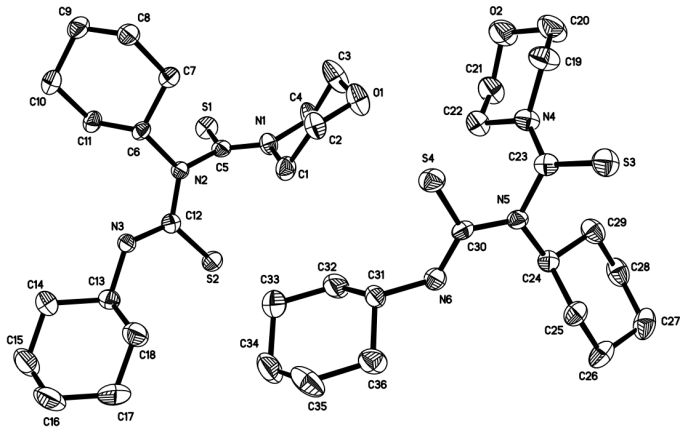
2.2.2.4 Role of 25% H_2O_2/ 1M H_2SO_4:

25% H_2O_2/ 1M H_2SO_4 was used to oxidize L2-1 but failed to make L2-2 monothiobiuret or L2-3 biuret product. The starting material L2-1 did not show up in the final product. The resulting decomposition products were not determined.

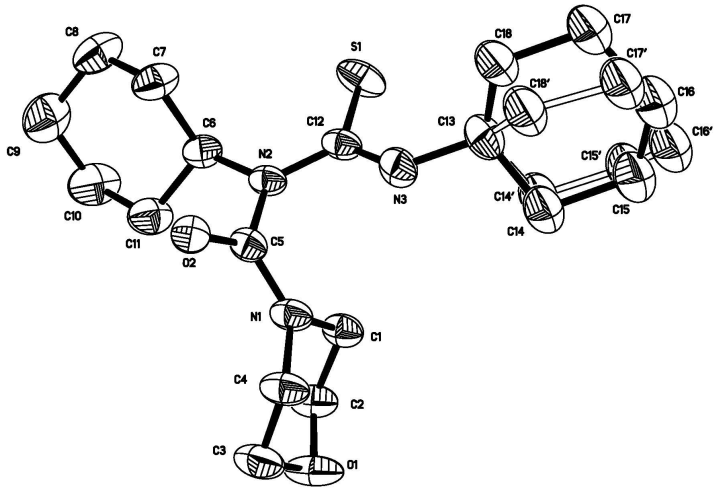
2.2.3 Crystallography

2.2.3.1 Comparison and Analysis of Morpholine Derivatives of Dithiobiuret, Monothiobiuret, and Biuret-based Ligands

(a)



(b)



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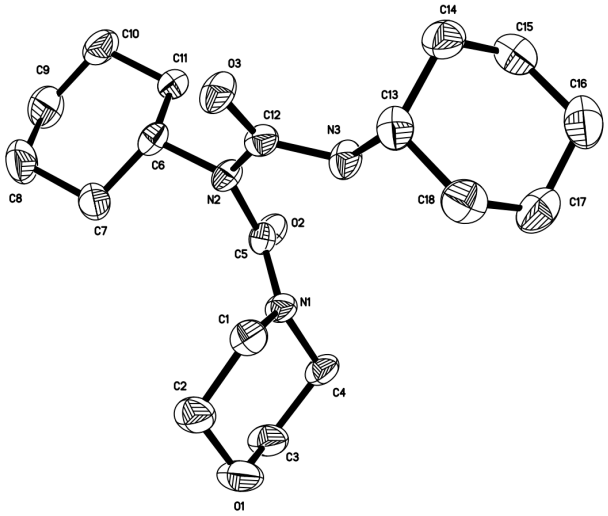


(d)

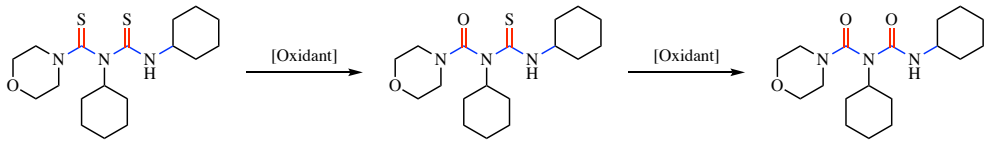


Figure 2.6 Crystal structures of **(a)** morpholine subsituted dithiobiuret L1-1 (Hydrogen atoms are omitted for clarity. Selected bond lengths [Å] and bond angles for the crystal: S(1)-C(5)=1.669(4); S(2)-C(12)=1.686(4); N(1)-C(5)=1.332(4); N(2)-C(5) =1.452(4); N(3)-C(12)=1.347(4); N(3)-C(13)=1.455(4); C(12)-N(2)-C(5)=117.7(3); N(2)-C(12)-S(2)=121.0(3); N(2)-C(5)-S(1)=120.0(3) **(b)** monothiobiuret L1-2 (Hydrogen atoms are omitted for clarity. Selected bond lengths [Å] and bond angles for the crystal: S(1)-C(12)=1.683(2); O(2)-C(5)=1.242(3); N(1)-C(5)=1.343(3); N(2)-C(12)=1.376(3); N(2)-C(5)=1.441(3); N(3)-C(12)=1.335(3). S(1)-C(12)-N(2)=121.66(19); C(12)-N(2)-C(5)=121.44(19); O(2)-C(5)-N(2)=119.6(2)) and **(c)** biuret-based ligand L1-3 (Hydrogen atoms are omitted for clarity. Selected bond lengths [Å] and bond angles for the crystal: O(2)-C(5)=1.236(2); O(3)-C(12)=1.220(2); N(1)-C(5)=1.350(2); N(2)-C(5)=1.411(2); N(2)-C(12)=1.404(2); N(3)-C(12)=1.357(3).); C(5)-N(2)-C(12)=123.97(16); O(3)-C(12)-N(2)=120.93(18) O(2)-C(5)-N(2)=120.61(16) (d) colored bonds are targets to discuss.

Crystal data and structure refinement of morpholine derivatives series of ligands are listed (Figure 2.6 (a)-(c) and Table 2.6-2.8). The total oxidation process is that dithiobiuret is firstly oxidized into monothiobiuret and then converted to fully oxidized biuret. By controlling the reaction time well, each oxidized product could be separated easily by re-crystallization. Attention is paid to the two carbon-sulfur double bonds and four carbon-nitrogen single bonds from

thioamide groups. Bond lengths [Å] of two thiocarbonyl group marked in red color: S(1)-C(5) is 1.669(4) and S(2)-C(12) is 1.686(4). In the first step of oxidation, S(1)-C(12) has almost no change and O(2)-C(5) is 1.242(3). After full oxidation, O(2)-C(5) changes from 1.242(3) to 1.236(2) and O(3)-C(12) changes from 1.683 to1.220(2) (Table 2.4). The lengths of O(2)-C(5) and O(3)-C(12) show more double bond character whereas S(1)-C(12) and S(2)-C(5) shows an almost halfway between a single and a double bond. The bond lengths [Å] of four carbon-nitrogen single bonds (N(1)-C(5)-N(2)-C(12)-N(3)) starts from 1.332(4), 1.452(4) 1.361(4) and 1.347(4). In the first step of oxidation, those four bonds changes to 1.343(3), 1,441(3), 1.376(3) and 1.335(3) respectively. After full oxidation, they are then into 1.350(2), 1.411(2), 1.404(2) and 1.357(2) (Table 2.5). As the oxidation goes, the lengths of carbon-nitrogen bonds are usually slightly changed because of increase in delocalization. The length of carbon-sulfur or carbon-oxygen "double" bonds are longer than typical double length (1.56 for C=S and and 1.16 for C=O) but the carbon-sulfur bond shows more single bond character whereas the carbon-oxygen bond shows more double character, which also matches with the increased delocalization along the backbone. Carbon-nitrogen single bonds are shorter than typical single bonds (1.48 for C-N). Based on the bond lengths we just listed, proposed resonance structures are given below (Figure 2.7), and the mechanism of selectively is discussed here: Because the length of N(1)-C(5) in Figure 2.8 (a) is the shortest one among the four C-N bonds, we speculate that in ligand L1-1, the C(5)-S(1) carbon sulfur bond shows more electron density localized on S(1) compared to that of C(12)-S(2). Thus C(5)-S(1) is more prone to be attacked by nucleophile (NO_3^- in our cases) and only one monothiobiuret is favored during the oxidation. 4-methyl piperidine, pyrrolidine and dimethyl amine all provide similar electron donating capability as morpholine, so we assume the same explanation also could be applied for the oxidation of L1-1, L2-1, L3-1, and L4-1dithiobiuret ligands.

	Dithiobiuret	Monothiobiuret	Biuret
S(1)/O(2)-C(5)	1.669(4)	1.242(3)	1.236(2)
S(2)/O(3)-C(12)	1.686(4)	1.683(2)	1.220(2)

Table 2.4 Comparison of bond length of carbon-sulfur and carbon-oxygen double bonds in morpholine substituted dithiobiuret (L1-1), monothiobiuret (L1-2) and biuret-based ligands (L1-3).

	Dithiobiuret	Monothiobiuret	Biuret
N(1)-C(5)	1.332(4)	1.343(3)	1.350(2)
N(2)-C(5)	1.452(4)	1.441(3)	1.411(2)
N(2)-C(12)	1.361(4)	1.376(3)	1.404(2)
N(3)-C(12)	1.347(4)	1.335(3)	1.357(3)

Table 2.5 Comparison of bond length of carbon-sulfur and carbon-oxygen double bonds in morpholine substituted dithiobiuret (L1-1), monothiobiuret (L1-2) and biuret-based ligands (L1-3).

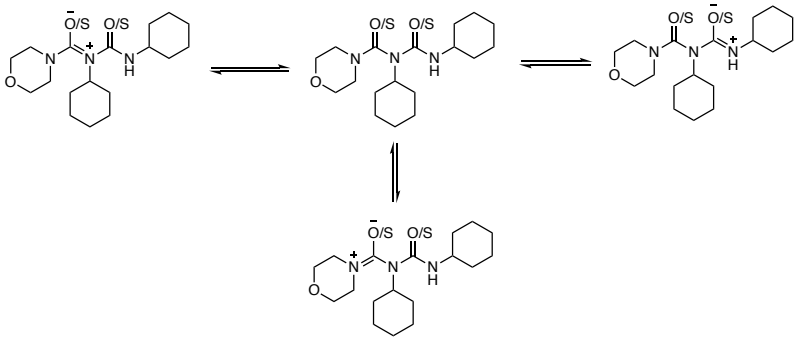


Figure 2.7 Proposed resonance structures of L1 ligands

Empirical formula	C18 H31 N3 O S2 (Dithiobiuret)	
Formula weight	369.58	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 10.8680(9) Å	α= 70.779(4)°.
	b = 12.2553(10) Å	β= 79.054(4)°.
	c = 17.2084(15) Å	γ = 66.029(4)°.
Volume	1973.4(3) $Å^3$	
Z	4	
Density (calculated)	1.244 Mg/m^3	
Absorption coefficient	0.280 mm-1	
F(000)	800	
Crystal size	0.270 x 0.040 x 0.020 mm^3	
Theta range for data collection	2.220 to 27.712°.	
Index ranges	-14<=h<=14, -15<=k<=15, -22<=l<=22	
Reflections collected	29516	
Independent reflections	8847 [R(int) = 0.1455]	
Completeness to theta = 25.242°	97.7 %	
Absorption correction	Multi-scan	
Refinement method	Full-matrix least-squares on F2	
Data / restraints / parameters	8847 / 0 / 433	
Goodness-of-fit on F_2	0.955	
Final R indices [I>2sigma(I)]	R1 = 0.0675, wR2 = 0.1090	
R indices (all data)	R1 = 0.1808, wR2 = 0.1435	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.350 and -0.348 $e.Å^{-3}$	

Table 2.6 Crystal data and structure refinement for Morpholine substituted dithiobiuret-based ligand (L1-1)

Empirical formula	C18H31N3O2S (Monothiobiuret)
Formula weight	353.52
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Trigonal

Space group	R-3	
Unit cell dimensions	a = 33.2806(8) Å	α= 90°.
	b = 33.2806(8) Å	β= 90°.
	c = 10.4254(3) Å	γ = 120°.
Volume	10000.1(6) $Å^3$	
Z	18	
Density (calculated)	1.057 Mg/m^3	
Absorption coefficient	0.159 mm^{-1}	
F(000)	3456	
Crystal size	0.250 x 0.190 x 0.170 mm^3	
Theta range for data collection	1.224 to 27.535°.	
Index ranges	-41<=h<=43, -43<=k<=43, -13<=l<=13	
Reflections collected	54979	
Independent reflections	5131 [R(int) = 0.0349]	
Completeness to theta = 25.242°	99.8 %	
Absorption correction	Multi-scan	
Refinement method	Full-matrix least-squares on F2	
Data / restraints / parameters	5131 / 216 / 263	
Goodness-of-fit on F_2	1.079	
Final R indices [I>2sigma(I)]	R1 = 0.0697, wR2 = 0.2185	
R indices (all data)	R1 = 0.1011, wR2 = 0.2586	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.600 and -0.602 e.$Å^{-3}$	

Table 2.7 Crystal data and structure refinement for Morpholine substituted monothiobiruet-based ligand (L1-2)

Empirical formula	C18 H31 N3 O3 (Biuret)	
Formula weight	337.46	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C2/c	
Unit cell dimensions	a = 24.7836(7) Å	α= 90°.
	b = 10.1752(4) Å	β= 123.257(2)°.
	c = 17.2563(5) Å	γ = 90°.
Volume	3638.9(2) Å3	

Z	8
Density (calculated)	1.232 Mg/m3
Absorption coefficient	0.084 mm-1
F(000)	1472
Crystal size	0.220 x 0.130 x 0.100 mm3
Theta range for data collection	2.333 to 27.605°.
Index ranges	-31<=h<=32, -9<=k<=13, -22<=l<=22
Reflections collected	25807
Independent reflections	4097 [R(int) = 0.0510]
Completeness to theta = 25.242°	97.6 %
Absorption correction	Multi-scan
Refinement method	Full-matrix least-squares on F2
Data / restraints / parameters	4097 / 0 / 218
Goodness-of-fit on F_2	1.009
Final R indices [I>2sigma(I)]	R1 = 0.0541, wR2 = 0.1054
R indices (all data)	R1 = 0.1159, wR2 = 0.1299
Extinction coefficient	0.0008(2)
Largest diff. peak and hole	0.231 and -0.207 e.Å-3

Table 2.8 Crystal data and structure refinement for Morpholine substituted biruet-based ligand (L1-3)

2.2.3.2 Different Secondary Amine Substituted Monothiobiuret and Biuret-based Ligand

The crystals of L-2-2 (Figure 2.9), L-2-3 (Figure 2.10) and L-3-2 (Figure 2.8) are also collected by using similar methods. As for pyrrolidine substituted biuret (L3-3) and diethyl amine substituted biuret (L4-3), those crystal structures are not collected because crystals were poorly grown.

By direct comparison of length of carbon-sulfur/oxygen from 6 different ligands we collected, those bonds are not affected by the nature of used secondary amine. The lengths of carbon-sulfur bonds stay around 1.68 Å and the lengths of carbon-oxygen bonds keep around

1.23 Å. As for the length of carbon-nitrogen bonds, those bonds are not affected by the nature of secondary amine but were changed because of enhanced resonance.

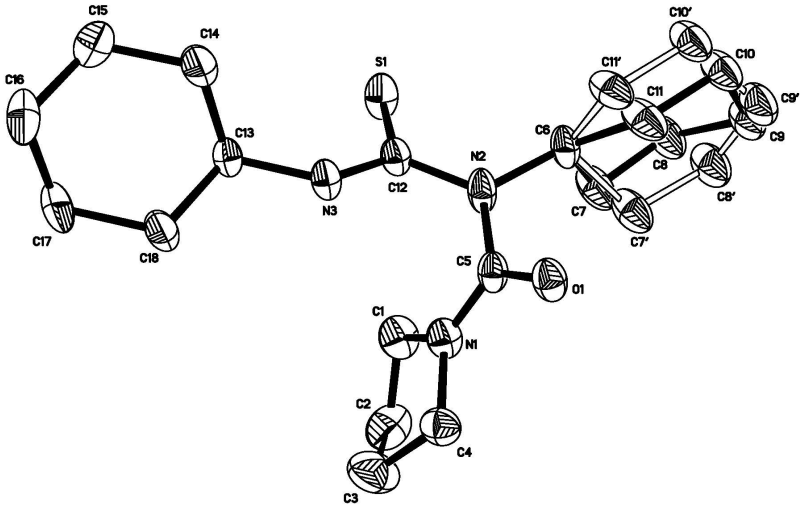


Figure 2.8 Crystal structures of pyrrolidine substituted monothiobiuret L3-2 with thermal ellipsoids at the 50% probability level (Hydrogen atoms are omitted for clarity. Selected bond lengths [Å] and bond angles for the crystal: S(1)-C(12)=1.6756(17); O(1)-C(5)=1.240(2); N(1)-C(5)=1.335(2); N(2)-C(12)=1.393(2); N(2)-C(5)=1.433(2); N(3)-C(12)=1.334(2).)

Empirical formula	C18H31N3OS	
Formula weight	337.52	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P21/c	
Unit cell dimensions	a = 10.4861(3) Å	α= 90°.
	b = 16.4057(4) Å	β= 93.4870(10)°.
	c = 10.9868(3) Å	γ = 90°.
Volume	1886.58(9) Å3	
Z	4	

Density (calculated)	1.188 Mg/m3
Absorption coefficient	0.180 mm-1
F(000)	736
Crystal size	0.370 x 0.250 x 0.190 mm3
Theta range for data collection	2.888 to 27.519°.
Index ranges	-12<=h<=13, -21<=k<=14, -12<=l<=14
Reflections collected	18401
Independent reflections	4287 [R(int) = 0.0232]
Completeness to theta = 25.242°	99.9 %
Absorption correction	Multi-scan
Refinement method	Full-matrix least-squares on F2
Data / restraints / parameters	4287 / 158 / 254
Goodness-of-fit on F_2	1.029
Final R indices [I>2sigma(I)]	R1 = 0.0512, wR2 = 0.1261
R indices (all data)	R1 = 0.0644, wR2 = 0.1349
Extinction coefficient	n/a
Largest diff. peak and hole	0.564 and -0.506 e.Å-3

Table 2.9 Crystal data and structure refinement for Pyrrolidine substituted monothiobiuret-based ligand

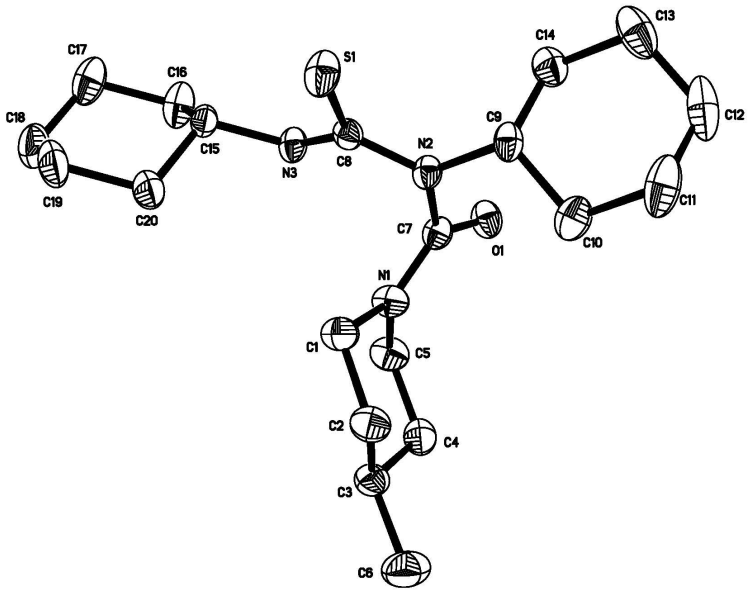


Figure 2.9 Crystal structures of 4-methyl piperidine substituted monothiobiuret L2-2 (Hydrogen atoms are omitted for clarity. Selected bond lengths [Å] and bond angles for the crystal: S(1)-C(8)=1.6773(15); O(1)-C(7)=1.2313(18); N(1)-C(7)=1.343(2); N(2)-C(8)=1.3808(18); N(2)-C(7)=1.4405(19); N(3)-C(8)=1.3389(19).)

Empirical formula	C20 H35 N3 O S	
Formula weight	365.57	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	Pbca	
Unit cell dimensions	a = 20.0762(4) Å	α= 90°.
	b = 9.4828(2) Å	β= 90°.
	c = 21.8599(4) Å	γ = 90°.
Volume	4161.66(14) Å3	
Z	8	
Density (calculated)	1.167 Mg/m3	
Absorption coefficient	0.168 mm-1	
F(000)	1600	
Crystal size	0.380 x 0.280 x 0.220 mm3	
Theta range for data collection	2.552 to 27.551°.	
Index ranges	-25<=h<=26, -12<=k<=10, -26<=l<=28	
Reflections collected 37670		
Independent reflections	4793 [R(int) = 0.0477]	
Completeness to theta = 25.242°	99.9 %	
Absorption correction	Multi-scan	
Refinement method	Full-matrix least-squares on F2	
Data / restraints / parameters	4793 / 0 / 227	
Goodness-of-fit on F_2	1.058	
Final R indices [I>2sigma(I)]	R1 = 0.0447, wR2 = 0.1150	
R indices (all data)	R1 = 0.0605, wR2 = 0.1226	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.334 and -0.279 e.Å-3	

Table 2.10 Crystal data and structure refinement for 4-methyl piperidine substituted monothiobiuret-based ligand (L2-2)

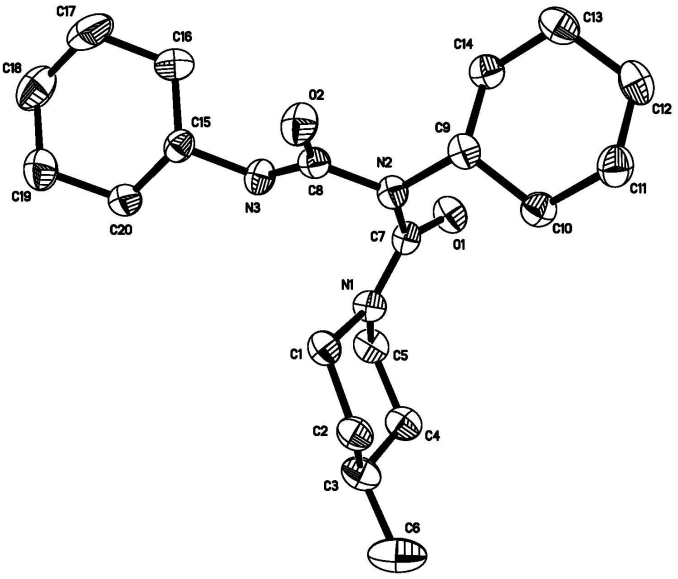


Figure 2.10 Crystal structures of 4-methyl piperidine substituted biuret (L2-3) (Hydrogen atoms are omitted for clarity. Selected bond lengths [Å] and bond angles for the crystal: O(1)-C(7)=1.234(2); O(2)-C(8)=1.222(2); N(1)-C(7)=1.343(3); N(2)-C(8)=1.411(2); N(2)-C(7)=1.420(2); N(3)-C(8)=1.348(2).)

Empirical formula	C20H35N3O2	
Formula weight	349.51	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	Pbca	
Unit cell dimensions	a = 17.0396(8) Å	α= 90°.
	b = 10.6091(5) Å	β= 90°.
	c = 22.7664(10) Å	γ = 90°.
Volume	4115.6(3) Å3	
Z	8	
Density (calculated)	1.128 Mg/m3	
Absorption coefficient	0.073 mm-1	
F(000)	1536	
Crystal size	0.300 x 0.240 x 0.150 mm3	
Theta range for data collection	2.152 to 27.524°.	

Index ranges	-21<=h<=22, -13<=k<=9, -29<=l<=28
Reflections collected	26889
Independent reflections	4701 [R(int) = 0.0556]
Completeness to theta = 25.242°	99.8 %
Absorption correction	Multi-scan
Refinement method	Full-matrix least-squares on F2
Data / restraints / parameters	4701 / 0 / 227
Goodness-of-fit on F2	1.056
Final R indices [I>2sigma(I)]	R1 = 0.0583, wR2 = 0.1320
R indices (all data)	R1 = 0.0998, wR2 = 0.1509
Extinction coefficient	n/a
Largest diff. peak and hole	0.303 and -0.273 e.Å-3

Table 2.11 Crystal data and structure refinement for 4-methyl piperidine substituted biuret-based ligand (L2-3)

2.2.3.3 Cyclization of Dithiobiuret-based Ligands

Cyclized dithiobiuret is found during the oxidation of pyrrolidine substituted dithiobiuret-based ligands (L3-3). The cyclized product could also be called pyrrolidine substituted 1,2,4-dithiazolium salts, which was founded as white crystal when we were trying to crystalize the oxidized product of pyrrolidine substituted dithiobiuret on the condition of 2M HCl/0.4M HNO_3. The characterization and synthesis route of the cyclized salt is incomplete because of little knowledge of cyclization reaction, except for the crystallography information (Figure 2.11). The presence of cyclized dithiobiuret was attributed to the oxidation by nitric acid through direct electron transfer. Similar ligands such as dithiomalonamides were found going through similar cyclization reaction in the presence of oxidants, like Pd(II)[3]. However, it was not always found in the final crude product and how to favor the oxidation reaction towards cyclized product over oxygen analogues is thus still unknown and but worthy being studied and determined. The crystal structure and structure refinement are listed below.

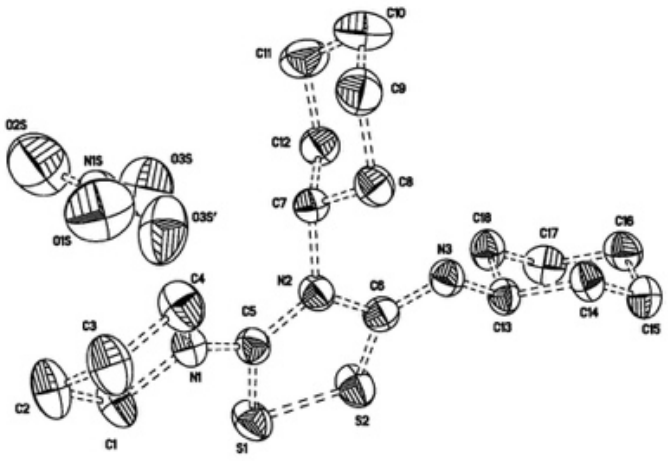


Figure 2.11 Crystal structures of pyrrolidine substituted 1,2,4-dithiazolium nitrate (Hydrogen atoms are omitted for clarity. Selected bond lengths [Å] and bond angles for the crystal: S(1)-C(5)=1.744(3); S(1)-S(2) 2.0447(11); S(2)-C(6)=1.774(3); N(1)-C(5)=1.305(3); N(2)-C(5)=1.349(3); N(2)-C(6)=1.420(3); N(3)-C(6)=1.260(3); N(3)-C(13)=1.461(3); C(5)-S(1)-S(2)=94.81(10); C(6)-S(2)-S(1)=95.13(10); C(5)-N(2)-C(6)=116.7(2); N(2)-C(5)-S(1)=117.7(2); N(2)-C(5)-S(1)=117.7(2); N(1)-C(5)-N(2)=126.0(2); N(2)-C(6)-S(2)=113.5(2); N(2)-C(6)-N(3)=120.8(2); N(3)-C(6)-S(2)=125.6(2).

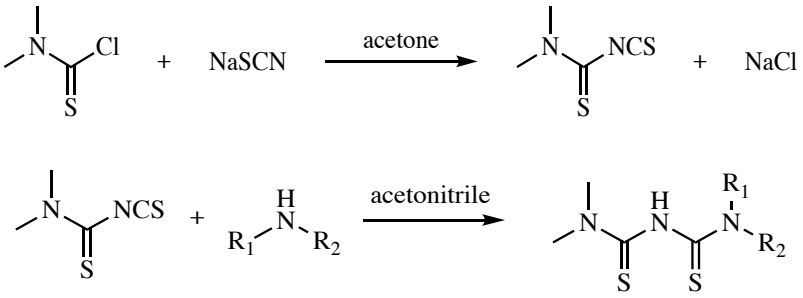
Empirical formula	C18 H30 N4 O3 S2	
Formula weight	414.58	
Temperature	293(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P21/n	
Unit cell dimensions	a = 6.8336(3) Å	α= 90°.
	b = 24.3112(13) Å	β= 98.092(3)°.
	c = 12.7240(7) Å	γ = 90°.
Volume	2092.83(19) Å3	
Z	4	
Density (calculated)	1.316 Mg/m3	
Absorption coefficient	0.280 mm-1	
F(000)	888	

Crystal size	0.240 x 0.210 x 0.060 mm3
Theta range for data collection	2.989 to 27.516°.
Index ranges	-8<=h<=8, -31<=k<=20, -16<=l<=16
Reflections collected	14610
Independent reflections	4785 [R(int) = 0.0700]
Completeness to theta = 25.242°	99.9 %
Absorption correction	Multi-scan
Refinement method	Full-matrix least-squares on F2
Data / restraints / parameters	4785 / 0 / 255
Goodness-of-fit on F_2	1.002
Final R indices [I>2sigma(I)]	R1 = 0.0563, wR2 = 0.1063
R indices (all data)	R1 = 0.1358, wR2 = 0.1344
Extinction coefficient	0.0026(7)
Largest diff. peak and hole	0.416 and -0.308 e.Å-3

Table 2.12 Crystal data and structure refinement at room temperature for pyrrolidine substituted 1,2,4-dithiazolium nitrate

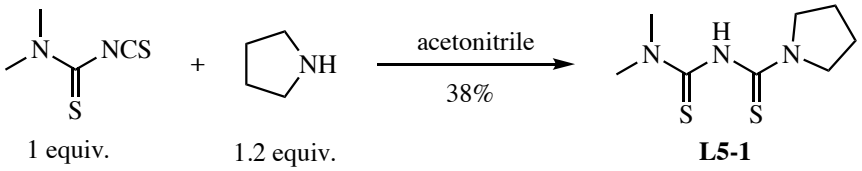
2.3 Alternative Routes to Synthesize Dithiobiuret-based Extractants

An alternative way to synthesize dithiobiuret-based extractants was also explored. Based on previous literature[9,10], we started from dimethylcarbomoyl chloride reacting with sodium thiocyanate to yield dimethylcarbomoyl thiocyanate, which was reorganized into dimethylcarbomoyl isocyanate. Addition of a secondary amine was reported to result in a dithiobiuret-based ligand which could be collected with a yield up to 60%. A scheme of the reaction is listed below.



Scheme 2.3 An alternative route to synthesize dithiobiuret-based ligands

Dimethyl amine, diethyl amine, morpholine, pyrrolidine, 4-methyl piperidine were all studied to synthesize corresponding dithiobiuret-based ligand and make a comparison of which secondary amine is more suitable to do the synthesis. We found that pyrrolidine could react will dimethyl isothiocyanate to yield orange yellow precipitate out of acetonitrile (Scheme 2.5), which we thought was our desired product. Initially, we thought pyrrolidine might be the best choice and characterization of that was followed.



Scheme 2.4 Attempted synthesis route of pyrrolidine substituted dithiobiuret L5-1 used in the lab

The orange yellow precipitate was firstly found soluble in MeOH and MeOD was used as deuterated solvent to run ^{1}H NMR (Figure 2.12). In figure 2.12, two triplets around 3.9ppm and 3.6ppm correspond to two NCH_2 and 2 singlets around 3.3ppm and 3.5ppm correspond to two dimethyl group. And two quartets around 2.2ppm and 2.1ppm correspond to one CH_2CH_2, except that NH of L5-1 is missing.

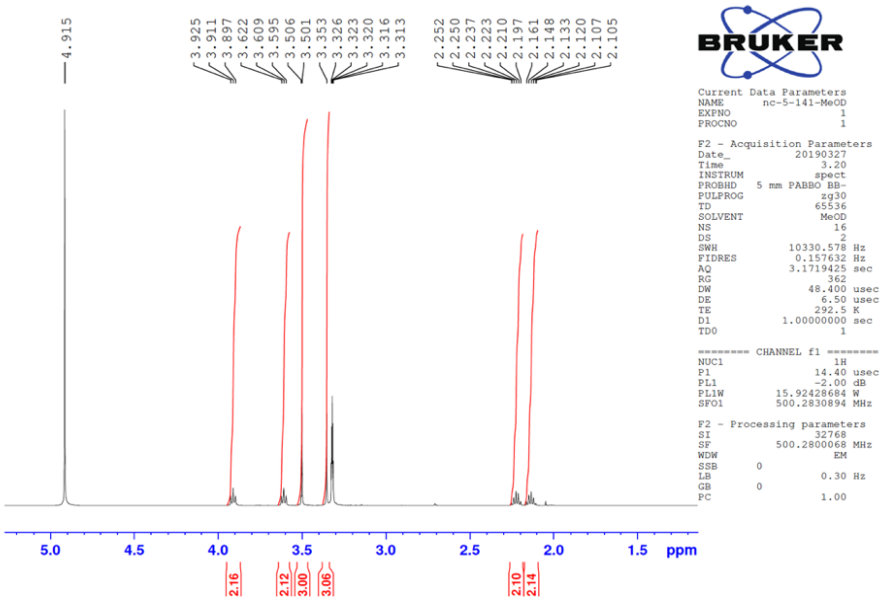


Figure 2.12 The ^{1}H NMR Spectrum of orange precipitate (synthesized through scheme 2.4) in deuterated-methanol showing cyclized dithiobiuret formed.

Other common solvents, like DCM, benzene, and chloroform are explored but none could dissolve the orange yellow precipitate, which contradicts our expectation. Finally, water was picked up and found out it did dissolve the product completely, which make us question the structure. Electrospray ionization (ESI) mass spectrometry was employed. Instead of observing 218 m/z, which should come from $[L+H^{+}]$, 216 m/z was collected as the main peak, which should come from $[L-H]^{+}$. Field desorption (FD) ionization method was also applied, and it showed identical as what we saw in ESI method. There were a few attempts to crystalize the orange precipitates but failed to grow suitable size of crystal and thus no crystallography information was collected. Based on the result of solubility tests, $^{1}H/^{13}C$ NMR and ESI-MS all showing expected dithiobiuret structure L5-1 wasn't successfully synthesized, and an alternative proposal of the structure was given. The conclusion is that the expected dithiobiuret-based structure L5-1 transformed into a cyclized dithiazolium under ambient conditions, where the possible oxidizing source is oxygen. However, in principle, the cyclization of dithiobiuret-based ligand will happen

in the presence of direct oxidants like metal ions (Co^{3+}) with high oxidation states, hydrogen peroxide or perchlorate. This cyclizing situation has been discussed by Pellacani[9]. et al in dithiomalonamide systems and Kohler. et al[10] observed the same for dithiazolium tetrachloronicolate. We are assuming a similar reaction for the this morpholine substituted dithiobiuret-based ligands and the proposed transformation is illustrated below (Figure 2.13 (a) and (b)).

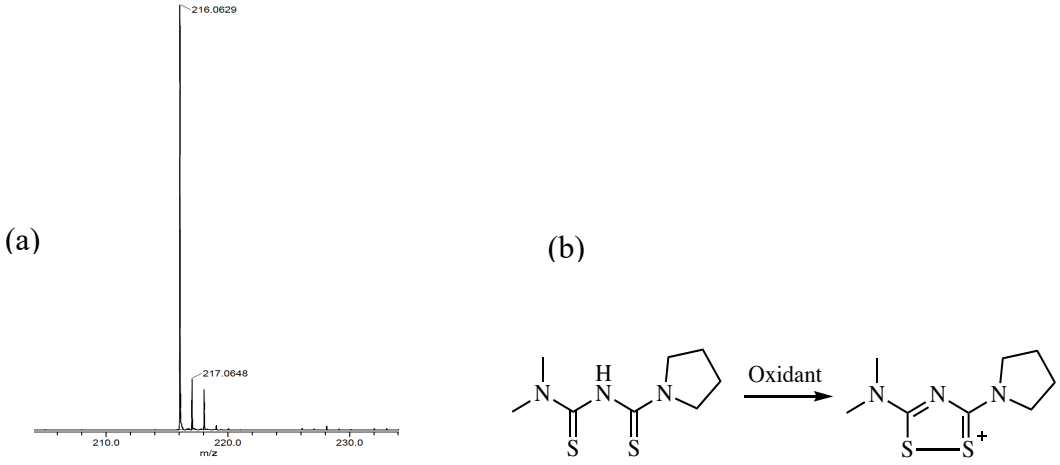


Figure 2.13 (a) m/z 216.0629 amu found correlated with dithiazolium salts and **(b)** proposal of possible transformation

2.4 Experimental

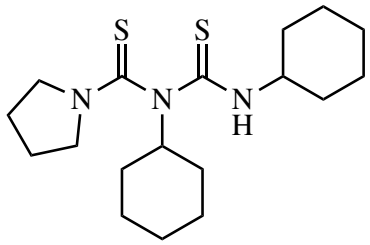
2.4.1 Material and Methods

Pyrrolidine, morpholine, 4-methyl piperidine, diethyl amine, dicyclohexycarbodiimide, carbon disulfide, dimethylcarbamoyl chloride, and sodium thiocyanate were directly purchased from Sigma Aldrich. Hydrochloric acid 37%, nitric acid 69.5%, hydrogen peroxide 30%, sulfuric acid 98% and all organic solvents including, methanol, ethanol, acetonitrile, acetone, tetrahydrofuran, dichloromethane were purchased from Fisher Scientific and used as received. Mass spectral data were obtained from a QSTAR XL MS/MS System operated by the Saskatchewan Structural

Sciences Centre at the University of Saskatchewan. $^{1}H/^{13}C$ NMR spectra were recorded with a Bruker spectrometer at 500 MHz. Single crystals were coated with Paratone-N oil, mounted using a micromount (MiTeGen-Microtechnologies for Structural Genomics), and frozen in the cold stream of an Oxford Cryojet attached to the diffractometer. Crystal data were collected on a Bruker APEX II diffractometer at −100 °C using monochromated Mo Kα radiation (λ = 0.71073 Å). An initial orientation matrix and cell was determined by ω scans, and the X-ray data were measured using ϕ and ω scans[13]. Frames were integrated with the Bruker SAINT software package[14] and data reduction was performed with the APEX2 software package[13]. Multiscan absorption corrections (SADABS) were applied[15]. The structures were solved by the Intrinsic Phasing method implemented with SHELXT and refined using the Bruker SHELXTL software package.

2.4.2 Dithiobiuret Synthesis

2.4.2.1 Pyrrolidine Derivatives of Dithiobiuret L3-1

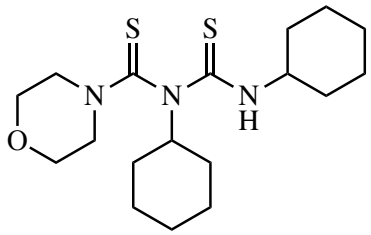


1.425 g pyrrolidine (20.05 mmol) was added in small portions to a mixture of 1.825 g CS_2 (23.97 mmol) and 4.125 g dicyclohexylcarbodiimide (19.99 mmol) in 50.0 ml methanol at room temperature. The reaction mixture was stirred for 5 hours, and then the resulting white precipitate was filtered and separated from the solution. Then, it was washed with methanol, and finally dried under vacuum, resulting in 6.223 g final product (17.62 mmol, yield = 88%), which was then analyzed by ^{1}H NMR, ^{13}C NMR. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.14 (m, 4H, $2CH_2$), 1.38 (m, 4H, $2CH_2$), 1.58 (m, 4H, $2CH_2$), 1.78 (m, 4H, $2CH_2$), 1.88 (m, 2H,

CH_2), 1.97 (m, 6H, $3CH_2$), 3.46 (br, 2H, CH_2), 3.75 (br, 2H, CH_2), 4.34 (m, 1H, CH), 4.92 (m, 1H, CH), 5.85 (d, *J*=6.9Hz, 1H, NH).

^{13}CNMR (500 MHz, $CDCl_3$): δ (ppm) 24.5 (CH_2), 24.9 (CH_2), 25.4 (CH_2), 25.5 (CH_2), 25.9(CH_2), 30.4 (CH_2), 32.5 (CH_2), 33.0 (CH_2), 53.2 (NHCH), 60.5 (NCH), 178.4 (C=S), 181.6 (C=S)

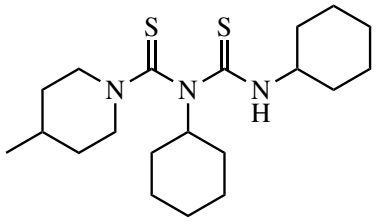
2.4.2.2 Morpholine Derivatives of Dithiobiuret L1-1



1.745 g morpholine (20.04 mmol) was added in small portions to a mixture of 1.825 g CS_2 (23.97 mmol) and 4.125 g dicyclohexylcarbodiimide (19.99 mmol) in 50.0 ml methanol at room temperature. The reaction mixture was stirred for 5 hours and then the resulting white precipitate was filtered and separated from the solution. Then, it was washed with methanol, and finally dried resulting in 6.710 g final product (18.2 mmol, yield = 91%). The product was recrystallized by using 9:1 ratio of DCM to methanol in the fridge after two days. The crystal was then analyzed by ^{1}H NMR, ^{13}C NMR and Crystallography. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.09-1.21 (m, 4H, $2CH_2$), 1.24-1.41 (m, 4H, $2CH_2$), 1.72-1.81 (m, 4H, $2CH_2$), 1.78 (m, 4H, $2CH_2$), 1.90 (d, *J*=8.5Hz 2H, CH_2), 1.99-2.03 (m, 2H, CH_2), 3.73 (m, 4H, NCH_2), 3.90 (br, 4H, OCH_2), 4.29-4.39 (m,1H, (NH)CH), 4.97 (tt, J=3.5Hz, 12Hz, 1H, NCH), 5.93 (d, *J*= 7.5, 1H, NH).

^{13}CNMR (500 MHz, $CDCl_3$): δ (ppm) 25.1 ($2CH_2$), 25.9 (CH_2), 26.0 (CH_2), 26.5 ($2CH_2$), 30.9 ($2CH_2$), 33.3 ($2CH_2$), 50.7 (NCH_2), 50.9 (NHCH), 61.1 (NCH), 66.6 (OCH_2), 179.3 (C=S), 184.7(C=S).

2.4.2.3 4-methyl piperidine Derivatives of Dithiobiuret L2-1

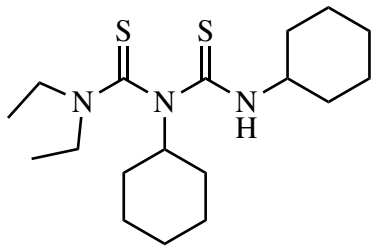


1.983 g 4-methyl piperidine (19.99 mmol) was added in small portions to a mixture of 1.825 g CS_2 (23.97 mmol) and 4.125 g dicyclohexylcarbodiimide (19.99 mmol) in 50.0 ml methanol at room temperature. The reaction mixture was stirred for 5 hours and then the resulting white precipitate was filtered and separated from the solution. Then, it was washed with methanol, and finally dried under vacuum, resulting in 6.856 g final product (17.98 mmol, yield = 90%), which was then analyzed by ^{1}H NMR and ^{13}C NMR.

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 0.97 (d, *J*=6.45Hz, 3H, CH_3), 1.05-1.46 (m, 10H, CH_2), 1.53-1.83 (m, 11H, $5CH_2$+CH), 1.85-1.95 (br, 2H, CH_2), 1.99 (d, *J*=9.15Hz, 2H, CH_2), 2.99 (tr, *J*=12.0Hz, 2H, NCH_2), 4.32 (m, 1H, (NH)CH), 4.43-5.10 (br, 2H, NCH_2), 4.97 (trtr, J=3.6Hz, 11.9Hz, 1H, NCH)

^{13}CNMR (500 MHz, $CDCl_3$): δ (ppm) 21.6 (CH_3), 25.0 (CH_2), 25.9 (CH_2), 26.0 (CH_2), 26.4 (CH_2), 30.7 (CH_2), 31.0 (CH_2), 33.2 (CH_2), 34.2 (CH), 51.1 (NHCH), 53.7 (NCH_2), 61.0 (NCH), 179.1 (C=S), 183.5 (C=S).

2.4.2.4 Diethyl amine Derivatives of Dithiobiuret L4-1



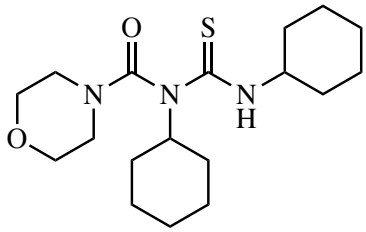
1.463 g diethylamine (20.02 mmol) was added in small portions to a mixture of 1.825 g CS_2 (23.97 mmol) and 4.125 g dicyclohexylcarbodiimide (19.99 mmol) in 50.0 ml methanol at room temperature. The reaction mixture was stirred for 5 hours and then left in the fridge to yield pale yellow crystal. Pale yellow crystal was filtered and separated from the solution, collecting in 4.125 g final product (11.61 mmol, 58%), which was then analyzed by ^{1}H NMR and ^{13}C NMR.

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.05-1.45 (m, 14H, CH_2), 1.53-1.82 (m, 6H, CH_3), 1.82-2.08 (m, 6H, CH_2), 3.76 (br, 4H, NCH_2), 4.23-4.32 (m, 1H, (NH)CH), 4.92 (trtr, *J*=3.55Hz, 11.8Hz, 1H, NCH), 6.16 (d, *J*=7.4Hz, 1H, NH).

^{13}CNMR (500 MHz, $CDCl_3$): δ (ppm) 24.6 (CH_3), 25.4 (CH_2), 25.5 (CH_2), 25.9 (CH_2), 32.6 (CH_2), 33.2 (CH_2), 33.3 (CH_2), 46.4 (NCH_2), 53.4 (NHCH), 60.8 (NCH), 179.1 (C=S), 183.7 (C=S).

2.4.3 Monothiobiuret Synthesis

2.4.3.1 Morpholine Derivatives of Monothiobiuret L1-2



100mg (0.271mmol) of morpholine derivatives dithiobiuret was added to 8ml DCM and 8ml of 2M HCl/0.4M HNO_3 was added as oxidant. We kept the stirring rate as 700 r.p.m. and after 8min we isolated the organic phase, evaporated the DCM and collect

83mg (0.24mmol, 87%) of light yellow solid as a crude product. The crude product could be re-dissolved in methanol/DCM (10:1) and go further recrystallization in freezer and after two days white clear crystal block could be found at the bottom of solution (41mg, 0.12mmol, 44%), which was then analyzed by ^{1}H NMR, ^{13}C NMR, Mass Spectrometry and Crystallography.

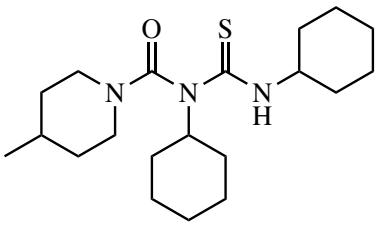
^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.07-1.22 (m, 4H, $2CH_2$), 1.28-1.45 (m, 4H, $2H_2$), 1.58-1.70 (m, 4H, $2CH_2$), 1.72-1.81 (m, 4H, $2CH_2$), 1.93 (d, *J*=11.3Hz, 2H, CH_2), 2.08 (dd, *J*=3.3Hz, 12.3Hz, 2H, CH_2), 3.50 (tr, *J*=4.6Hz, 4H, $2NCH_2$), 3.68(tr, *J*=5.1Hz, 4H, $2OCH_2$), 4.28-4.37 (m, 1H, (NH)CH), 4.60(tt, *J*=3.4Hz, 14.2Hz, 1H, NCH), 5.51 (d, *J*=7.4Hz, 1H, NH)

^{13}C NMR (500 MHz, $CDCl_3$): δ (ppm) 25.0 (CH_2), 25.4 (CH_2), 25.6 (CH_2), 26.0 (CH_2), 30.8 (CH_2), 33.1 (CH_2), 45.5 (NCH_2), 54.0 (NHCH), 59.5 (OCH_2), 66.7 (NCH), 155.1 (C=O), 179.6 (C=S)

FD-MS(+): Found: m/z 353.21474 amu Calculated: 353.21371 amu

CH&N elemental analysis (%) Calculated for $C_{18}H_{31}O_2N_3S{\cdot}0.95S$: C 56.30 H 8.13 N 10.94; Found: C 56.37 H 7.77 N 10.89

2.4.3.2 4-methyl piperidine Derivatives of Monothiobiuret L2-2



103mg (0.271 mmol) of 4-methyl piperidine derivatives dithiobiuret was added to 8ml DCM and 8ml of 2M HCl/0.4M HNO_3 was added as oxidant. We kept the stirring rate as 700 r.p.m. and after 5min we isolated the organic phase, evaporate the DCM and collect 89mg of light yellow solid as a crude product. The crude product could be re-dissolved in methanol/DCM (10:1) and go further recrystallization in freezer and after two days

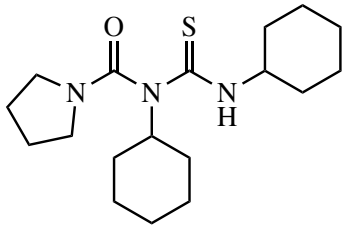
white clear crystal block could be found at the bottom of solution (53mg, 0.15mmol, 55%), which was then analyzed by ^{1}H NMR, ^{13}C NMR, Mass Spectrometry and Crystallography.

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 0.9623 (d, *J*=6.55Hz, 3H, CH_3), 1.04-2.10 (m, 25H, Cy), 1.04-1.21 (m, 6H, $3CH_2$), 1.30-1.42 (m, 4H, $2CH_2$), 1.46-1.74 (m, 9H, $4CH_2$ and 1CH), 1.75-1.82 (m, 1H, CH), 1.94 (d, *J*=11Hz, CH_2), 2.06 (dd, *J*=3.1Hz, 12.0Hz, 2H, CH_2), 2.82 (td, *J*= 2.6Hz, 13.0Hz, 2H, NCH_2), 4.07 (br, 4H, NCH_2), 4.29-4.37 (m, 1H, NCH), 4.75 (tt, *J*=3.4Hz, 11.9Hz, 1H, NCH), 5.50 (d, *J*=7.4Hz, 1H, NH)

^{13}C NMR (500 MHz, $CDCl_3$): δ (ppm) 21.6 (CH_3), 24.8 (CH_2), 25.4 (CH_2), 25.5 (CH_2), 25.9 (CH_2), 26.2 (CH_2), 30.6 (CH_2), 30.7 (CH_2), 32.9 (CH_2), 34.0 (CH_2), 34.1 (CH), 45.4 (NCH_2), 53.7 (NHCH), 59.4 (NCH), 154.6 (C=O), 179.2 (C=S)

FD-MS(+): Found: m/z 365.2510 amu; Calculated m/z 365.2501 amu

2.4.3.3 Pyrrolidine Derivatives of Monothiobiuret L3-2



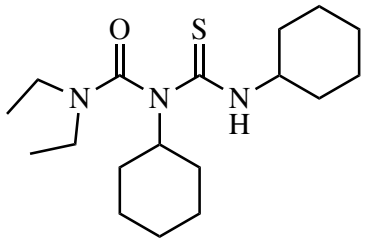
96mg (0.271mmol) of pyrrolidine derivatives dithiobiuret was added to 8ml DCM and 8ml of 2M HCl/0.4M HNO_3 was added as oxidant. Stirring rate was 700 r.p.m. and after 5min we isolated the organic phase, evaporate the DCM and collect 65mg of light yellow solid as a crude product. The crude product could be re-dissolved in methanol/DCM(10:1) and go further recrystallization in freezer and after two days white clear crystal could be found at the bottom of solution(40mg, 0.11mol, 41%), which was then analyzed by ^{1}H NMR, ^{13}C NMR, Mass Spectrometry and Crystallography.

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.03-2.08 (m, 24H, Cy), 3.41 (br, 4H, NCH_2), 4.31-4.39 (m, 1H, NCH), 4.62 (tt, *J*=3.6Hz, 12.0Hz, 1H, NCH), 5.51 (d, *J*=6.9Hz, 1H, NH)

^{13}C NMR (500 MHz, $CDCl_3$): δ (ppm) 24.8 (CH_2), 25.3 (CH_2), 25.5 (CH_2), 25.9 (CH_2), 30.6 (CH_2), 32.9 (CH_2), 53.4 (NCH_2), 53.6 (NHCH), 59.2 (NCH), 154.3 (C=O), 179.0 (C=S)

FD-MS(+): Found: m/z 337.2187 amu; Calculated m/z 337.2188 amu

2.4.3.4 Diethyl amine Derivatives of Monothiobiuret L4-2



96mg(0.271mmol) of diethyl amine derivatives dithiobiuret was added to 8ml DCM and 8ml of 2M HCl/0.4MHNO_3 was added as oxidant. Stirring rate was 700r.p.m and after 5min we isolated the organic phase, evaporate the DCM and collect 68mg of light yellow solid as crude product. The crude product could be re-dissolved in methanol/DCM (10:1) and go further crystallization in freezer and after two days white clear crystal could be found at the bottom of solution (40mg, 0.117mmol, 43%), which was then analyzed by ^{1}H NMR, ^{13}C NMR, Mass Spectrometry and Crystallography.

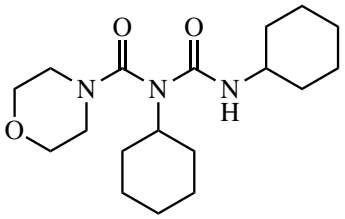
^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.02-2.11 (m, 20H, Cy), 1.17 (tr, *J*=7.1Hz, 6H, $2CH_3$), 3.21-3.40 (m, 4H, NCH_2), 4.26-4.35 (m, 1H, NCH), 4.73 (tt, J=3.6Hz, 11.9Hz, 1H, NCH), 5.51 (d, *J*=7.5Hz 1H, NH)

^{13}C NMR (500 MHz, $CDCl_3$): δ (ppm) 13.1 (CH_3), 25.0 (CH_2), 25.6 (CH_2), 25.7 (CH_2), 26.1 (CH_2), 30.7 (CH_2), 33.0 (NCH_2), 53.9 (NHCH), 59.8 (NCH), 155.6 (C=O), 180.0 (C=S)

FD-MS(+): Found: m/z 339.2336 amu; Calculated m/z 339.2344 amu

2.4.4 Biuret Synthesis

2.4.4.1 Morpholine Derivatives of Biuret L1-3



300 mg (0.812 mmol) of morpholine derivatives of dithiobiruet was added to the solvent of dichloromethane (10 ml), with metallic Au (10mg, 0.051mmol). 10 ml aqueous solution of 0.4M HNO_3, 2M HCl was poured into. The biphasic system was stirred for 1 hour. After washed by water, the organic phase was further purified by stirring with 10ml of 2M H_2SO_4 thiourea(200 mg) aqueous solution. The organic phase was evaporated in the fume hood and 191 mg (0.568 mmol, 70%) of morpholine substituted biuret is collected,

100mg(0.271mmol) of morpholine derivatives dithiobiuret was added to 8ml DCM and 8ml of 2M HCl/0.4M HNO_3 was added as oxidant. We kept the stirring rate as 700 r.p.m. and after 60min we isolated the organic phase, evaporated the DCM and collect 74mg of lightyellow solid as a crude product. The crude product could be re-dissolved in isopropanol/DCM (1:5) and slowly evaporate in fume hood and after three days white clear crystal chip could be found (38mg, 0.12mmol, 44%), which was then analyzed by ^{1}H NMR, ^{13}C NMR, Mass Spectrometry and Crystallography.

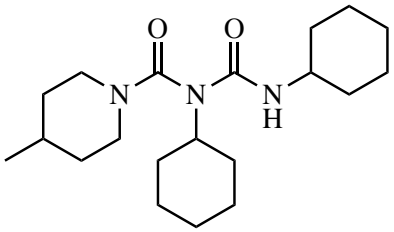
^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.03-1.16 (m, 4H, $2CH_2$),1.26-1.38 (m, 4H, $2CH_2$), 1.60(sdd, *J*=2.8Hz, 9.4Hz, 2H, CH_2), 1.66-1.73(m, $2CH_2$, 4H), 1.73-1.81(m, $2CH_2$, 4H), 1.92(dd, *J*=3.5Hz, 12.2Hz, 2H, CH_2), 3.50 (tr, *J*=5.1Hz, 4H, NCH_2), 3.59-3.64(m, 1H, (NH)CH), 3.67(tr, *J*=4.6Hz, 4H, OCH_2), 3.90 (tt, *J*=3.7Hz, 11.7 Hz, 1H, NCH), 4.69(d, *J*=7.2Hz, 1H, NH)

^{13}C NMR (500 MHz, $CDCl_3$): δ (ppm) 25.1 (CH_2), 25.6 (CH_2), 25.7 (CH_2), 26.3 (CH_2), 31.3 (CH_2), 33.9 (CH_2), 46.0 (NCH_2), 49.7 (OCH_2), 56.5 (NHCH), 66.8 (NCH), 154.0 (C=O), 156.8(C=O)

ESI-MS: Found: m/z 338.2451 amu; Calculated $[L+H]^+$ m/z 338.2444 amu

CH&N elemental analysis (%) Cal for $C_{18}H_{31}O_3N_3 \cdot 0.73S$: C 59.91 H 8.66 N 11.64; Found: C 59.82 H 9.07 N 11.50

2.4.4.2 4-methyl Piperidine Derivatives of Biuret L2-3



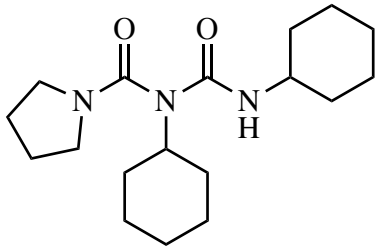
103mg (0.271mmol) dithiobiuret 4methylpiperidine was added to 8ml DCM and 8ml of 2MHCl/0.4MHNO_3 was added as oxidant. We kept the stirring rate as 700 r.p.m. and after 60 min we isolated the organic phase, evaporate the DCM and collect 77mg of light-yellow solid as a crude product. The crude product could be re-dissolved in isopropanol/dichloromethane (1:5) and slowly evaporate in fume hood and after 3 days white clear crystal chip could be found (44mg, 0.13mmol, 48%), which was then analyzed by ^{1}H NMR, ^{13}C NMR, Mass Spectrometry and Crystallography.

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 0.95 (d, *J*=6.6Hz, 3H, CH_3), 1.01-1.08 (m, 6H, $3CH_2$), 1.22-1.40 (m, 4H, $2CH_2$), 1.53-1.82 (m, 13H, $6CH_2$, $1NCH(CH_2)_2$), 1.92 (sdd, *J*=3.2Hz, 12.3Hz, 2H, CH_2), 2.81 (tr, *J*=12.2Hz, 2H, NCH_2), 3.63 (m, 1H, NCH), 3.94 (tt, *J*=3.4Hz, 11.7Hz, 1H, NCH), 4.08(d, *J*=13.1Hz, 2H, NCH_2), 4.69 (d, *J*=7.5Hz, 1H, NH)

^{13}C NMR (500 MHz, $CDCl_3$): δ (ppm) 21.8 (CH_3), 25 (CH_2), 25.6 (CH_2), 25.7 (CH_2), 26.3 (CH_2), 31.0 (CH_2), 31.2 (CH_2), 33.9 (CH_2), 34.3 (CH_2), 46.0 (NCH_2), 49.5 (NHCH), 56.1 (NCH), 154.1 (C=O), 156.6 (C=O)

ESI-MS: Found: m/z 338.2451 amu; Calculated $[L+H]^+$ m/z 338.2444 amu

2.4.4.3 Pyrrolidine Derivatives of Biuret L3-3



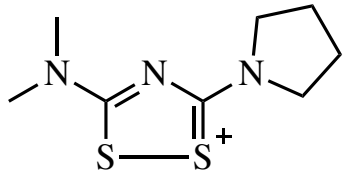
96mg (0.271mmol) dithiobiuret pyrrolidine derivatives was added to 8ml DCM and 8ml of $2MHCl/0.4MHNO_3$ was added as oxidant. We kept the stirring rate as 700 r.p.m and after 40 min we isolated the organic phase, evaporate the DCM and collect 80mg of yellow solid. The crude solid was re-dissolved in methanol and left in fume hood for 2 days. White needle crystal could be found (20mg, 0.062mmol, 23%), which was then analyzed by ^{1}H NMR, ^{13}C NMR, Mass Spectrometry.

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.02-1.41 (m, 10H, $5CH_2$), 1.55-1.63 (m, 2H, CH_2), 1.63-1.72 (m, 2H, CH_2), 3.43 (tr, *J*=6.8Hz, 4H, NCH_2), 3.65 (br, 1H, NCH), 3.83 (m, 1H, NCH), 4.91 (br, 1H, NH)

^{13}C NMR (500 MHz, $CDCl_3$): δ (ppm) 25.1 (CH_2), 25.4 (CH_2), 25.7 (CH_2), 26.4 (CH_2), 31.3 (CH_2), 38.9 (CH_2), 47.5 (NCH_2), 49.5 (NHCH), 56.7 (NCH), 154.1 (C=O), 156.6 (C=O)

FD-MS(+): Found: m/z 321.2423 amu Calculated: m/z 321.2416 amu

2.4.5 Pyrrolidine Substituted 1,3,4-dithiazolium



Dimethylthiocarbamoylchloride (0.123g, 1.0 mmol) and sodium thiocyante (0.081 g, 1.0 mmol) were added to 20 mL of acetonitrile, heated to reflux temperature, maintained for 1 h, and cooled to room temperature. Filtered NaCl formed as side product. To the filtrate, 0.085 g (1.2 mmol) of pyrrolidine was added and stirred for 5 hours at room temperature. Orange precipitate were collected and dried (0.082g, 0.38mmol, 38%) after filtration and washed by DCM.

^{1}H NMR (500 MHz, MeOD): δ (ppm) 2.09-2.26 (m, 4H, $2CH_2$), 3.35 (s, 3H, NCH_3), 3.50 (s, 3H, NCH_3, 3.60 (tr, *J*=6.95Hz, NCH_2), 3.91 (tr, *J*=6.98, NCH_2)

^{13}C NMR (500 MHz, MeOD): δ (ppm) 24.9 (CH_2), 25.6 (CH_2), 40.7 (NCH_2), 41.8 (NCH_2), 50.6 (CH_3), 53.3 (CH_3)

FD-MS(+): Found: m/z 216.0630 amu Calculated: m/z 216.0629 amu

2.5 Conclusions

The oxidation of dithiobiuret-based ligands has never been investigated in the Foley group. In this chapter, 4 kinds of dithiobiuret-based ligands and their oxygen analogues are successfully synthesized under mild condition with a good yield of up to 70%. Methods to synthesize and

recrystalize those 4 series of ligands and the crystal structure of different derivatives are listed and compared. The choice of secondary amine doesn't have a great impact on the bond length of C-N and C=S (or C=O). However, the bond length of C-N and C=S (or C=O) have been significantly affected through the oxidation process. By the oxidation of dithiobiuret to biuret, there is an increased delocalization along the backbone which makes the carbonyl have more double bond character compared to the thiocarbonyl, which shows more single bond character. The roles of gold, nitric acid, hydrochloric acid and hydrogen peroxide were tested and explored and discussion of stability of dithiobiuret-based ligands and their oxygen analogues in each reaction condition were followed. Metallic gold could be used to speed up the reaction but is not necessary. Nitric acid is the key oxidant to fulfill the conversion and hydrochloric acid could somehow help to speed up the oxidation. The mechanism of how nitric acid and hydrochloric acid contribute to the oxidation process is proposed but still needs to be explored and confirmed. Generally, the dithiobiuret and monothiobiuret are oxidized in nitric acid and the oxidation rate will increase under higher concentration of nitric acids conditions. The oxidized product biuret is relatively stable in nitric acid but still could decompose if it was left for a longer time. Finally, an alternative method following previous research method to synthesize similar dithiobiuret-based ligand was tried and discussed. However, the expected structure did not show up whereas we conclude that the cyclized pyrrolidine substituted 1,3,4-dithiazolium salt was formed.

2.6 References

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CHAPTER 3

INVESTIGATION INTO SELECTIVE SOLVENT EXTRACTION OF LANTHANIDES USING BIURET-BASED COUMPOUND

3.1 Introduction

Lanthanide elements are a group of 14 elements, whose numbers are from 57 to 71 in the periodic table and they are also usually called rare earth elements including yttrium because of difficulty to separate them from each other, even though the natural deposit is rather high. This series of elements has been in higher demand in the last 20 years and the research related to lanthanide separation with focus on a simple and efficient process have been a popular area ever since. However, the separation of lanthanide elements is hard to achieve because of the slight difference in size between two adjacent lanthanide ions.

The techniques to separate lanthanide have been explored a lot: ion-exchange, fractional crystallization, solvent extraction, fractional precipitation and so on. Among those techniques, solvent extraction is the most convenient and commercial one with a long history up to 70 years[1-7]. Solvent extraction, also known as liquid-liquid extraction, is the method to extract one kind of metal from an aqueous phase into an organic phase and the selectivity comes from the interaction between the extractants and desired extracted metal ions. Over the past 60 years, different extractants have been invented and applied to separate lanthanides, such as tributylphosphate, or di(ethylhexyl)phosphoric acid (HDEHP)[8-11]. However, those extractants usually have a poor differentiation and multiple times of solvent extraction are always necessary, which also brings the problems of environmental and energy issues. Designing new extractants with a better selectivity is still worthwhile and necessary, such as substituted diglycolamides[12], beta-diketones[13],

or substituted malonamides[14]. After the route of conversion of different substituted dithiobiuret-based ligands to biuret-based ligands is clear (Chapter 2), the exploration of those series of ligands in the lanthanide separation is followed. In this chapter, all the dithiobiuret-based ligands and their oxygen analogues are all using the morpholine derivatives (Figure 3.1) unless stated otherwise. The experiments are divided into two parts: one is to test if there is any direct reaction between biuret-based, monothiobiuret-based or dithiobiuret-based ligands with lanthanide ions. The second part is to test how well those series ligands could perform in the lanthanide solvent extraction and try to find an optimized condition.

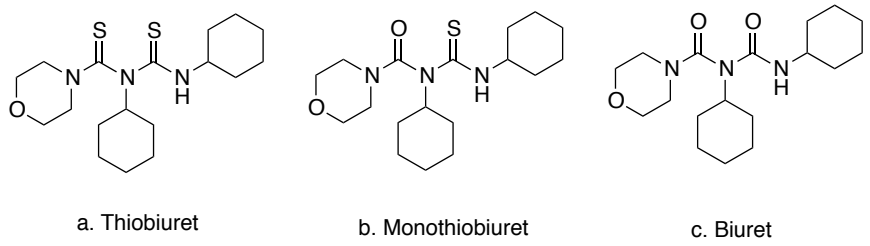


Figure 3.1 Morpholine substituted dithiobiuret-based ligands and its oxygen analogues used in chapter 3

3.2 Result and Discussion

3.2.1 Direct Reaction

Before doing tests of those series of ligands on lanthanide separation, doing direct reaction tests between a ligand and a lanthanide ion allows us to have a preliminary picture of if and how those series of ligands could coordinate with lanthanide salts.

The first part of a direct reaction was to find a suitable solvent for the direct reaction. The choice of solvents is important, since the competition between the solvent and the ligands determine the success of the direct reaction. Generally speaking, acetonitrile, methanol (or ethanol), tetrahydrofuran, DCM, water, kerosene (or long chain alkane, like n-dodecane) or any combined

mixture solvents just mentioned are previously used[1-6] in lanthanide solvent extraction and used to study the coordination chemistry between the Ln(III) and the ligands, since they won't show great coordination ability with lanthanides and also are rather achievable common solvents in the lab. The solubility of lanthanide salts, dithiobiuret-based ligands, monothiobiuret-based ligands and biuret-based ligands, solubility test results are listed and compared below (Table 3.1). Since the good performance of ethanol, methanol and tetrahydrofuran dissolving those series of ligands and lanthanide salts at the same time, those three major solvents were picked up for the direct reaction tests. As for poor solubility of dithiobiuret-based ligands in methanol and ethanol, dichloromethane could be used to dissolve dithiobiuret-based ligands first and mix them with lanthanide solution in methanol (Methanol could be replaced by isopropanol or ethanol).

	Hexane	Dichloromethane	Acetonitrile	Tetrahydrofuran	Methanol	Isopropanol	Ethanol (95%)
Lanthanide salts	Small	Small	Small	Medium	Large	Medium	Large
Dithiobiuret-based	Small	Large	Medium	Large	Small	Small	Small
Monothiobiuret-based	Small	Large	Medium	Large	Medium	Medium	Medium
Biuret-based	Small	Large	Large	Medium	Large	Medium	Large

Table 3.1 Solubility test of dithiobiuret, monothiobiuret, biuret-based ligands and lanthanide salts *All in room temperature. Small, medium, and large are used to qualitatively describe the solubility of lanthanide salts, dithiobiuret, monothiobiuret, and biuret in different organic solvents. Small means almost no solubility, medium means around 20mg could be dissolved in 10ml solvent. Large means at least 100mg could be dissolved in 10ml solvent.

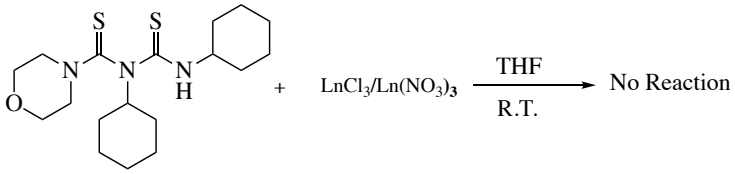
About the choice of lanthanide salts: chloride and nitrate salts were chosen, since chloride and nitrate are the usual counter ions during commercial separations. But there is a slight difference between chloride and nitrate salts: nitrate ions are bigger ions comparing to the chloride salts, they are easier to dissociate from lanthanide ions during direct reaction, which means usage of nitrate salts is a slightly better choice in this chapter[7-13].

After determining what the best solvent condition is, the following main effort was to make a homogenous solution of different ligands and different lanthanides and try to understand the basic chemistry of the interaction between those series of ligands and different lanthanides. By

using ^{1}H and ^{13}C NMR, crystallography, mass spectrometry, infrared spectroscopy and ultraviolet-visible spectroscopy, we should have a whole picture of how those ligands coordinate with lanthanides. However, the experiments didn't go as well as we expected.

3.2.1.1 Dithiobiuret-based Ligands in Direct Reaction

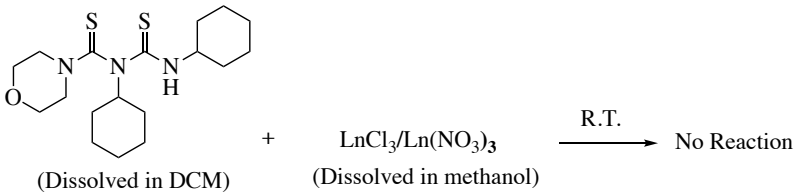
Morpholine derivatives of dithiobiuret-based ligands were firstly tested and the solvent first used was tetrahydrofuran (Scheme 3.1). Different ratios of 1:4, 1:2, 1:1, 2:1 and 4:1 have been tried and try to shift the equilibrium to the right (eqn. 1.11 or 1.13). Tetrahydrofuran could fully dissolve dithiobiuret-based ligands, however there are always a visible amount of lanthanide salt found. We chose to collect the clear solution and do crystallization but only crystals of morpholine derivatives of dithiobiuret-based ligands were observed. The clear solution part is pipetted out, vacuumed and then re-dissolved in $CDCl_3$. Attention was drawn on the change of protons nearby the thiocarbonyl, which should show obvious chemical shift as long as lanthanide complex is formed. However, no change has been observed on the ^{1}H NMR, which is indicating there was no interaction happening in the tetrahydrofuran system.



Scheme 3.1 First attempts to do direct reaction in tetrahydrofuran (THF) but failed to find any reaction. Lanthanide salts didn't fully dissolve in THF and a homogeneous solution wasn't achieved.

Failure might be from solubility issues. An alternative method was tried (Scheme 3.2). We firstly dissolved lanthanide salts fully in ethanol or methanol, and dissolved morpholine derivatives of dithiobiuret-based ligands in dichloromethane. Then those two homogeneous solutions were completely mixed up. Finally, a homogeneous solution of dithiobiuret-based ligands with

lanthanide salts was achieved. Crystallization method was tried again, however only crystal of dithiobiuret-based ligands were collected and no complex has been found. Also, we pipetted out the homogeneous solution out, vacuumed the solvent and re-dissolved the solid in $CDCl_3$ (There were undissolved solid found, soluble in water. We assume that is only free lanthanide salts precipitating out during vacuum). As for lanthanum(III) chloride, lanthanum(III) nitrate, yttrium(III) chloride, there are only peaks from free ligands found available (Figure 3.1 (a)). As for cerium(III) nitrate, cerium(III) chloride, samarium(III) nitrate, gadolinium(III) nitrate, erbium(III) nitrate, and ytterbium(III) nitrate, only free ligand with broadening peaks were found, which might be because of trace of paramagnetic lanthanide salts going to $CDCl_3$(Figure 3.2 (b)). All in all, no obvious chemical shifts were found on the ^1H NMR.



Scheme 3.2 Homogeneous solution could be achieved by mixing dithiobiuret-based ligand dissolving in dichloromethane (DCM) and lanthanide salts dissolving in methanol or ethanol.

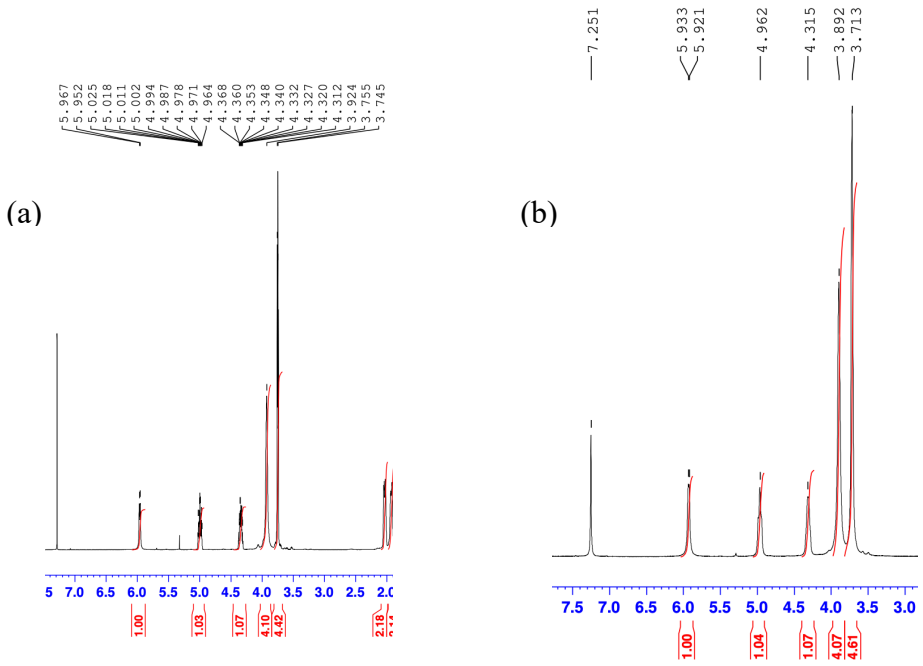


Figure 3.2 Example of **(a)** direct reaction between dithiobiuret and $LaCl_3$ showing ^1H NMR of the free ligand and **(b)** direct reaction between dithiobiuret and $CeCl_3$, showing ^1H NMR of the free ligand with resolution lost.

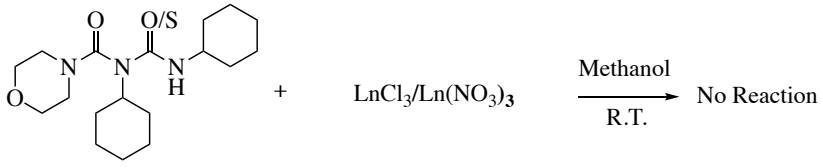
The summary of dithiobiuret with lanthanide salts in a direct reaction method is listed below (Table 3.2).

	$La(NO_3)_3$ $LaCl_3$	**$Ce(NO_3)_3$ $CeCl_3$**	**$Sm(NO_3)_3$**	**$Gd(NO_3)_3$**	**$Er(NO_3)_3$**	**$Yb(NO_3)_3$**	**YCl_3**
Morpholine Dithiobiuret	No Complex No Reaction found on NMR	No Complex No Reaction found on NMR (with broader peak)	No Complex No Reaction found on NMR (with broader peak)	No Complex No Reaction found on NMR (with broader peak)	No Complex No Reaction found on NMR (with broader peak)	No Complex No Reaction found on NMR (with broader peak)	No Complex No Reaction found on NMR

Table 3.2 Direct reactions have been done between dithiobiuret-based ligand and lanthanide salts. Four different ratios have been tried: 1:4, 1:2, 1:1, 2:1, 4:1. Yttrium(III) was also studied because of similarity with lanthanide(III).

3.2.1.2 Monothiobiuret-based and Biuret-based Ligands in Direct Reaction

Oxygen analogues are discussed together here. Methanol and ethanol could dissolve monothiobiuret-based (or biuret-based ligands) and lanthanide salts at the same time so the solubility issue no longer exists (Scheme 3.3). Different ratios of 1:4, 1:2, 1:1, 2:1 and 4:1 are applied again. No obvious change was found after mixing up and no crystal of complex was found. Only free ligand was observed.



Scheme 3.3 A homogeneous direct reaction between biuret or monothiobiuret and lanthanide salts in methanol (Methanol could be replaced with ethanol).

As for lanthanum chloride, lanthanum nitrate and yttrium chloride, the homogeneous solution was pipetted out and re-dissolved in deuterated chloroform. Attention was still put on the change of protons nearby the thiocarbonyl or carbonyl groups. However, no change was found on the ^1H NMR. As for other paramagnetic lanthanide salts, there were still only broader peaks of the

free ligands (Also ethanol or methanol were usually observed in the ^{1}H NMR, which helped lanthanide salts remain soluble in $CDCl_3$ and introduced paramagnetism issues).

The summary of monothiobiuret and biuret with lanthanide salts in a direct reaction method is listed below (Table 3.3).

	$La(NO_3)_3$ $LaCl_3$ YCl_3	$CeCl_3$	$Sm(NO_3)_3$	$GdCl_3$	$Er(NO_3)_3$	$YbCl_3$
Morpholine Monothiobiuret	No complex found so far; No reaction found on NMR	No Lanthanide complexes found so far; No Reaction found on NMR (with broadening peak).				
Morpholine biuret						

Table 3.3 Direct reactions have been done between dithiobiuret-based ligand and lanthanide salts. Four different ratios have been tried: 1:4, 1:2, 1:1, 2:1, 4:1. Yttrium(III) was also studied because of similarity with lanthanide(III).

Biuret-based ligands with $LaCl_3$ (or $CeCl_3$) were also chosen to do a preliminary study by Electrospray ionization mass spectrometry (ESI-MS). Spectra were collected in positive-ion mode through a QSTAR XL MS/MS System. Two homogeneous liquid samples were prepared by mixing morpholine substituted biuret with $LnCl_3$ ($LaCl_3$ or $CeCl_3$) in methanol in 1:2 ratio. 338, coming from $[biuret+H]^+$ both showing up at two experiments as expected. The expected possible lanthanide complexes were guessed as $[LnCl_nL_m(H_2O)_z(MeOH)_k]^{3-n}$ or $[LnCl_3H_nL_m(H_2O)_z(MeOH)_k]^n$ (n,m,z should be integer). However, no such peaks were found. So, we are assuming no complex formed here.

3.2.2 Liquid-liquid Reaction

As we have mentioned the chemistry of liquid-liquid reaction in the first chapter, as for different kinds of extractants, different mechanisms can be applied. As for neutral extractants, after coordinating with metal ions, counter ions are needed to form a neutral complex, and then the formed complex will be extracted into organic phase (eqn. 1.13). Higher concentration of counterions or acid concentrations, more extractants or metal ions could favor the formation of lanthanide complexes. Since the result of direct reactions didn't meet our expectation, the reaction

between our ligands and lanthanide(III) could be acid-dependent and liquid-liquid reactions were followed.

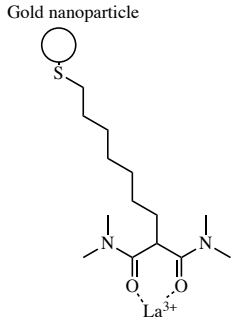
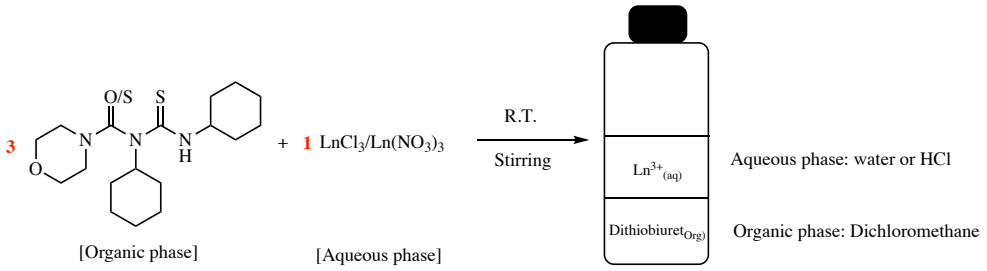


Figure 3.3 Example of the grafted malonamide coordinating with La^{3+}

The study of malonamide is a good example[20-24] that we could follow. The example of how the malonamide coordinate with lanthanide(III) is listed above in Figure 3.3. Contrary to the long alkyl chain substituted malonamide, dithiobiuret and its oxygen analogues are not soluble in alkane solvents, so dichloromethane is still used during the study. The focus in our investigation has been put on the effect of acid concentration counterions and the corresponding coordination ability of dithiobiuret and its oxygen analogues to lanthanide (III) in each condition. Based on the introduction in chapter 1 and chapter 2[7-19], different conditions of biphasic reactions are designed try to find if there is new complex formed in the biphasic reaction. The proof of coordination between dithiobiuret (or its oxygen analogues) with lanthanide(III) depends on the change of chemical shift on ^{1}H NMR experiments. The color change of system and the formation of complex crystals were also used as extra evidences to indicate if any coordination reaction happens. The study of malonamide is not only a good example to follow but also it helps us to investigate of the bridged nitrogen could play a role in the coordination chemistry.

3.2.2.1 Dithiobiuret-based Ligands and Monothiobiuret-based Ligands in Liquid-liquid Extraction

Dithiobiuret-based ligands and monothiobiuret-based ligands can to be oxidized by nitric acid. So only hydrochloric acid was tested in this case. Different conditions of acids (water, 0.1M HCl, 1M HCl, 2M HCl, 4M HCl) were applied and we kept using dichloromethane as organic phase. The ratio of lanthanide salts to dithiobiuret or monothiobiuret was kept as 1:3. When we were using nitrate salts under acid conditions, dithiobiuret showed some degree of oxidation into monothiobiuret and monothiobiuret to biuret. Under these conditions, the formation of lanthanide complexes was not observed.



Scheme 3.4 Biphaisc reaction of dithiobiuret (or monothiobiuret) reacting with lanthanide salts in a ratio of 3:1.

Reaction time was usually for at least 5 hours. Attention was firstly paid on the obvious color change. During stirring or after stirring, there was no obvious color change neither in the organic phase nor in the aqueous phase. The organic phase stayed as the original yellow color when using dithiobiuret-based ligands, whereas it showed the light-yellow color when monothiobiuret-based ligands were used. As for the aqueous phase, $Sm(III)_{(aq)}$ has a color of pale yellow, $Er(III)_{(aq)}$ has a color of pink and all the other lanthanides$(III)_{(aq)}$ including yttrium(III) we bought are colorless. However, the color of aqueous phase stayed as what it was before starting the reaction.

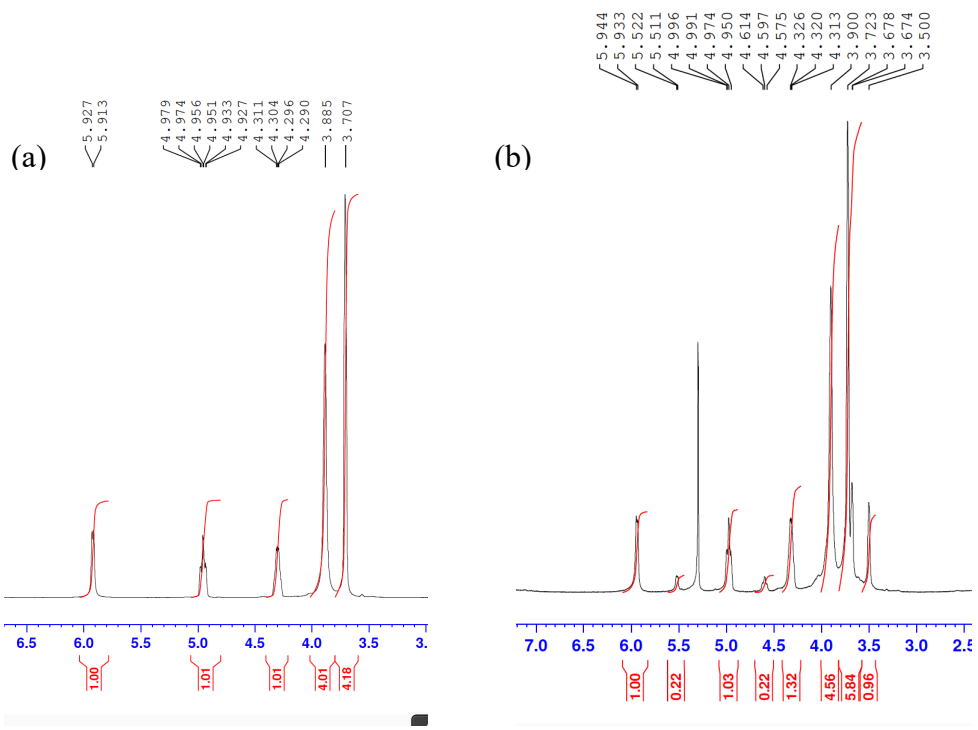


Figure 3.5 Example of (a) ^{1}H NMR spectrum of free ligand of dithiobiuret and (b) biphasic reaction between dithiobiuret-based ligands and cerium(III) nitrate salts in 1M HCl showing some degree of oxidation and resolution lost.

To check any shift from ^{1}H NMR, the organic phase was isolated and added $CDCl_3$. Lanthanum(III) and Yttrium(III) are the only two diamagnetic samples and the corresponding results of ^{1}H NMR are the free ligands of morpholine derivatives of the dithiobiuret (or the monothiobiuret) itself. As for Cerium(III), Samarium(III), Gadoliniu(III), Erbium(III) and Ytterbium(III), they are paramagnetic materials. If lanthanide complexes are formed, we will observe broadening and shifted ^{1}H NMR spectrum. There was a blank experiment done to make a comparison to see if the broadening ^{1}H NMR spectrum was from paramagnetic lanthanide(III) complex or just trace of lanthanide(III) salts presenting in $CDCl_3$. It is found that trace of Lanthanide(III) could dissolve in dichloromethane with the help of acids to result in broadening and we are assuming the broadening ^{1}H NMR spectra were at least because of that. For example

(Figure 3.5 (b)), we only observed dithiobiuret ligand and their oxygen analogues with resolution lost a little bit from the biphasic reaction between dithiobiuret and cerium nitrate in 1M HCl. The oxygen analogues were assumed because of oxidation by nitrate during the biphasic reaction.

We cannot conclude that any complexes were formed and extracted into the organic phase. Crystallization was also conducted, however only the crystals of the corresponding free ligands were yielded. The summary of dithiobiuret and monothiobiuret biphasic reactions with lanthanide salts is listed below (Table 3.4).

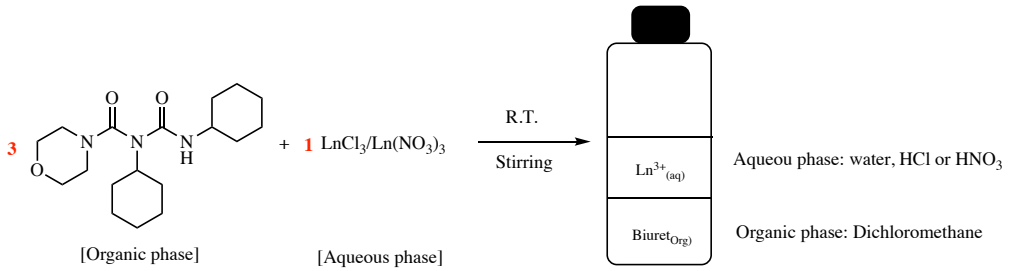
	YCl_3 $LaCl_3$	**$YbCl_3$ $GdCl_3$ $CeCl_3$**	**$Sm(NO_3)_3$**	**$Er(NO_3)_3$**	**$La(NO_3)_3$**
Water	Only free ligand found on ^{1}H NMR; No chemical shift found on ^{1}H NMR; No Obvious Color Change; Colorless aqueous phase; Yellow organic phase No complex crystal found.	Only free ligand found on ^{1}H NMR; No chemical shift found on ^{1}H NMR; No obvious color changed; Colorless aqueous phase; Yellow organic phase No complex crystal found.	Only free ligand found in ^{1}H NMR; No chemical shift found on ^{1}H NMR; No obvious color change; Pale yellow aqueous phase; Yellow organic phase; No complex crystal found.	Only free ligand found in ^{1}H NMR; No chemical shift found on ^{1}H NMR; No obvious color change; Pale pink aqueous phase; Yellow organic phase; No complex crystal found.	Only free ligand found in ^{1}H NMR; No chemical shift found on ^{1}H NMR; No obvious Color Change; Colorless aqueous phase; Yellow organic phase; No complex crystal found.
0.1M-4M HCl	Only free ligand found on ^{1}H NMR; No chemical shift found on ^{1}H NMR; No Obvious Color Change; Colorless aqueous phase; Yellow organic phase No complex crystal found.	Only free ligand found on ^{1}H NMR; No chemical shift found on ^{1}H NMR; No obvious color changed; Colorless aqueous phase; Yellow organic phase No complex crystal found.	Oxidation of dithiobiuret observed No obvious color change; Pale yellow aqueous phase; Yellow organic phase; No complex crystal found.	Oxidation of dithiobiuret observed No obvious color change; Pale pink aqueous phase; Yellow organic phase; No complex crystal found.	Oxidation of dithiobiuret observed No chemical shift found on ^{1}H NMR; No Obvious Color Change; Colorless aqueous phase; Yellow organic phase; No complex crystal found.

Table 3.4 Result of Biphasic reaction between dithiobiuret with different lanthanide salts on the condition of water and 0.1M-4M HCl.

3.2.2.2 Biuret-based Ligands in Liquid-liquid Extraction

Biuret-based ligands are not susceptible to oxidation, so hydrochloric acid and nitric acid are both used in this part. Different concentration of acids (water, 0.1M HCl, 1M HCl, 2M HCl, 4M HCl, 1M HNO_3, 2M HNO_3, 3M HNO_3, 4M HNO_3) were applied and dichloromethane was still served as organic solvent. The ratio of the extractant to the lanthanide salts started from 3:1,

but no further reaction was observed in terms of color change, NMR shift, or formation of the complex crystals (Scheme 3.5).



Scheme 3.5 Biphaisc reaction of biuret reacting with lanthanide salts in a ratio of 3:1

Reaction time was usually for at least 5 hours. Attention was still firstly paid to any obvious color change. During or after stirring, there was no obvious color change neither in the organic phase nor in the aqueous phase. The organic phase stayed pale yellow, the color of biuret-based ligands in dichloromethane. As for aqueous phase, $Sm(III)_{(aq)}$ has a color of pale yellow, $Er(III)_{(aq)}$ has a color of pink and all the other $lanthanides(III)_{(aq)}$ including yttrium(III) bought in the lab are colorless. However, the color of aqueous phase stayed as the original color. As for the condition of other different concentrations of nitric acid and hydrochloric acid, no change was observed either.

To check any shift from ^1H NMR, the organic phase was dried and added $CDCl_3$. Lanthanum(III) and yttrium(III) chloride showed results of free ligand of biuret. As for cerium(III) chloride, samarium(III) nitrate, gadolinium(III) chloride, erbium(III) nitrate and ytterbium(III) chloride salts, broadening peaks were observed and assumed at least because of trace of paramagnetic lanthanides present in dichloromethane during biphasic reaction. As for chemical shift change, no peak shift was observed.

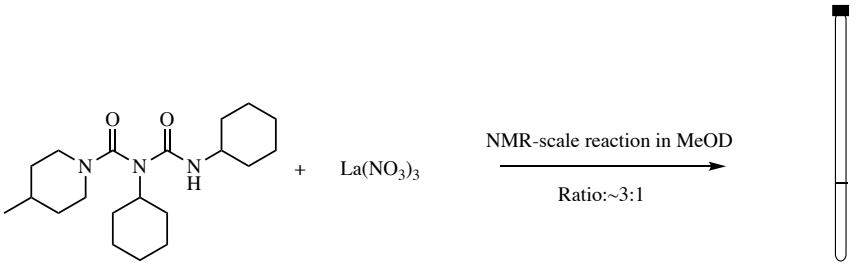
The organic phase was also used for crystallization to check any complex formed but only crystals of free ligands were yielded. The results of biphasic reaction between morpholine substituted biuret and different lanthanides are summarized below (Table 3.5).

	$La(NO_3)_3$ $GdCl_3$ YCl_3 $YbCl_3$ $CeCl_3$ $LaCl_3$	**$Sm(NO_3)_3$**	**$Er(NO_3)_3$**
Water	No Obvious Color Change; Colorless aqueous phase; Yellow organic phase No ^{1}H NMR shifted. No complex crystal found. .	No chemical shift found on ^{1}H NMR; No obvious color change; Pale yellow aqueous phase; Yellow organic phase; No complex crystal found.	No chemical shift found on ^{1}H NMR; No obvious color change; Pale pink aqueous phase; Yellow organic phase; No complex crystal found.
0.1-4M HCl			
0.1-4M HNO_3			

Table 3.5 The results of biphasic reaction between biuret and different lanthanide salts on the condition of water, 0.1-4M HCl and 0.1-4M HNO_3

3.2.3 NMR-Scale Reaction

There was a final exploration of the interaction between the lanthanide(III) and biuret-based ligands. This time, 4-methyl piperidine-derivatives of biuret-based ligand was chosen to react with lanthanum(III) nitrate in a NMR-scale reaction. The ratio was tried to keep as around 3:1 (Scheme 3.6). After sonicating for about 1 min, biuret with lanthanum(III) nitrate could both fully dissolve in deuterated-methanol to form a homogeneous solution. The reaction was observed by ^{1}H NMR and compared with the ^{1}H NMR of free 4-methyl piperidine biuret-based ligands.



Scheme 3.6 A homogeneous NMR-scale direct reaction between 4-methylpiperidine biuret-based ligand and lanthanum(III) nitrate in MeOD in a ratio of around 3:1.

The comparison between the initial ^{1}H NMR spectrum of free ligand and final ^{1}H NMR spectrum after direct reaction is listed below (Figure 3.6). Attention has been paid to protons nearby the two carbonyl groups. The direct comparison is illustrated below: the red is from the free ligand and the blue is from the direct reaction. The doublet and triplet doublet are from $CH_2NC(O)$ and two triplet triplets are from CHNC(O). However, no change was observed.

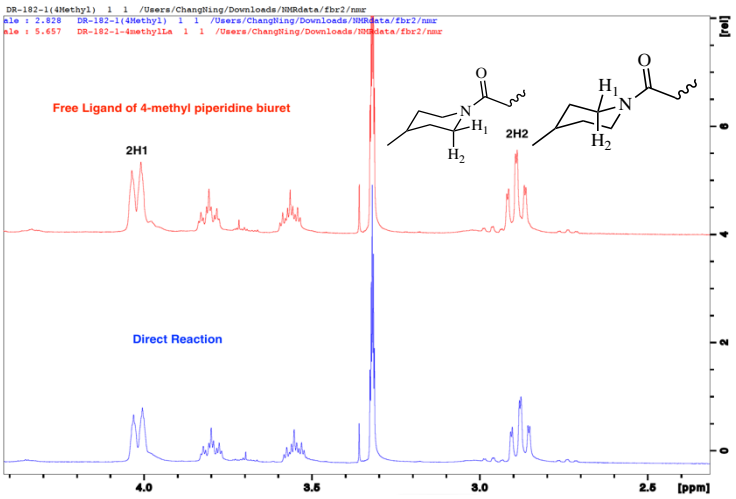


Figure 3.6 Comparison between 4-methyl piperidine substituted biuret free ligand (in red) and the result of direct NMR-scale reaction (in blue).

3.3 Discussion

The results of direct reaction and liquid-liquid reaction show no signs of interaction between dithiobiuret-based ligands (or its oxygen analogues) and lanthanide(III). The choices of solvents, the basicity of ligands in terms of the hard-soft acid and base theory, and the acid concentrations didn't become the key factors that could determine whether the complexations happen. Thus, some reasonable speculations about why the reactions didn't happen were followed.

The first possible reason is that the protonation of ligands (Figure 3.7 a) under acid condition inhibit a further coordination reaction[25], which is one of the factors that influence the neutral extractants coordination reaction with lanthanide(III). One of the future works on the

redesign of the ligands could be substituted with alkyl chain (Figure 3.7 b) to redesign the ligands with less protonation ability.

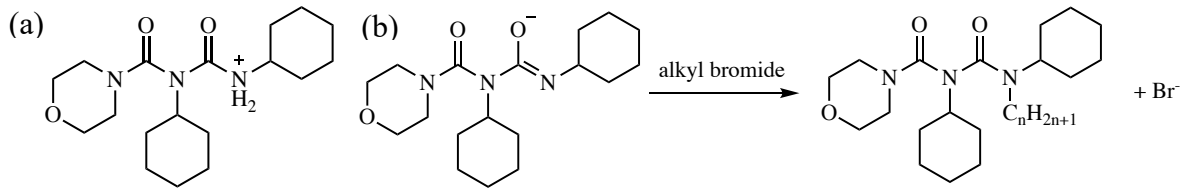


Figure 3.7 (a) Possible protonation site on the biuret ligands, which may inhibit a further coordination reaction with lanthanide(III); (b) One possible deprotonation and substitution method to redesign the ligands with less protonation ability

The second possible reason is that the symmetry of the ligand is not high enough, which strengthens the hinderance between each ligand during coordination process and the total process is less thermodynamically favored and hence the distribution ratio of lanthanide(III) will be decreased[26-27]. The future work could be focus on another biuret ligands with a higher symmetry[30] (Figure 3.8)

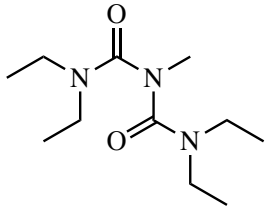


Figure 3.8 N,N,N',N'-tetramethyl-2-methyl dimidodicarbonic diamide with a higher symmetry

If all the future work still shows no sign of interaction between the biuret ligands and lanthanide(III), the third reason could be given that the bridged nitrogen did a negative impact on the coordination ability of the ligands with lanthanide(III) compared to the methylene bridged malonamide and the basicity of the biuret based ligand doesn't match with the acidity of lanthanide

in terms of the hard-soft acid and base theory. More efforts could be paid on computational studies to investigate how the bridged nitrogen could influence the energy level of dithiobiuret based (or its oxygen analogues) ligands and negatively affect the interaction between the ligands and lanthanide(III).

3.4 Conclusions

Direct reactions of dithiobiurets or any of the oxidized analogues with lanthanide salts didn't show any indication of the formation of lanthanide complexes. Solvent screening starts from common choices previously used in other labs, such as acetonitrile, tetrahydrofuran, methanol and so on and solubility issues made us set up different conditions to do the direct reactions. As for the morpholine derivatives of dithiobiuret-based ligands, a homogenous direct reaction needs dissolving dithiobiuret ligands into dichloromethane and dissolving lanthanide salts into methanol first and mix up two individual homogeneous solutions completely. Three major methods were used to verify the direct reactions, including direct observations from color change, crystallization and ^{1}H NMR experiments. As for the morpholine derivatives of monothiobiuret-based or biuret-based ligands, the solubility issue could be solved by using methanol or ethanol to dissolve different ratios of ligands to lanthanide salts at the same time to get a homogeneous solution. Major effort was paid on changing chemical shift from ^{1}H NMR tests. Also, color changes during the reactions and the formation of complex crystals also served as extra indications of complexation reactions. Till now, no sign of reaction showed. As for the morpholine substituted biuret ligands, there were mass spectrometry experiments done to explore if any lanthanide complexes formed in the direct reaction, but no reasonable peaks corresponding to the possible complexes were found.

Later, liquid-liquid reaction, where dithiobiuret ligands or their oxygen analogues in organic phase reacts with lanthanide in aqueous phase, was followed, not only mimicking the real process of metal separation, but also testing if the reaction is acid-dependent and how to optimize

the conditions. Different concentrations of hydrochloric acid and nitric acid were applied, however, no ^{1}H NMR chemical shifts were found.

The results of direct reactions and liquid-liquid reactions all show no sign of coordination reaction between dithiobiuret based ligands (or its oxygen analogues) and lanthanide(III). After all of these different preliminary tests in direct reaction and liquid-liquid reactions, no positive results were found and thus a discussion about why the dithiobiuret-based ligand and its oxygen analogues didn't work in the lanthanide extraction. Three possible reasons are given (recommendation to fix the problem are followed) : (1) the protonation of biuret-based ligands inhibit the further coordination ability with lanthanide(III); (2) the symmetry of biuret ligands we used in the research isn't high enough, which enhance the hindrance between ligands during complexation; (3) the basicity of the biuret-based ligands doesn't match with the acidity of lanthanide(III) in terms of the hard-soft acid and base theory.

3.5 Experimental

3.5.1 Materials and Methods

$La(NO_3)_3$ hydrate,$LaCl_3$ hydrate, $CeCl_3$ hydrate, $Sm(NO_3)_3$ hydrate, $GdCl_3$ hydrate, $Er(NO_3)_3$ hydrate, $YbCl_3$ hydrate, YCl_3 hydrate were purchased from Sigma Aldrich as at least 99.9% purity and used without further purification. Morpholine substituted dithiobiuret-based ligands and their oxygen analogues were synthesized according to Chapter 2.5 Experimental part. Hydrochloric acid 37%, nitric acid 69.5% and all organic solvents including, methanol, ethanol, dichloromethane were purchased from Fisher Scientific and used as received. Mass spectral data were obtained from a QSTAR XL MS/MS System operated by the Saskatchewan Structural Sciences Centre at the University of Saskatchewan. Solution. $^{1}H/^{13}C$ NMR spectra were recorded with a Bruker spectrometer at 500 MHz.

3.5.2 Direct Reaction

3.5.2.1 Dithiobiuret-based Ligands with Lanthanide(III) Salts

37 mg (0.10 mmol) morpholine substituted dithiobiuret-based ligand was firstly dissolving in 4 ml dichloromethane and 1 equivalent of lanthanum nitrate hydrate (43 mg, 0.10 mmol) was then dissolved in 4 ml methanol. After that, two solvents were mixed up to achieve a homogeneous solution and kept stirring for 1 hours. 0.40mmol to 0.10 mmol, 0.20 mmol to 0.10 mmol, 0.10 mmol to 0.20 mmol, and 0.10 mmol to 0.40 mmol of morpholine substituted dithiobiuret-based ligands to different lanthanide(III) salts ($LaCl_3$ hydrate, $CeCl_3$ hydrate, $Sm(NO_3)_3$ hydrate, $GdCl_3$ hydrate, $Er(NO_3)_3$ hydrate, $YbCl_3$ hydrate and YCl_3 hydrate) were also tried in the same way we listed. 1 ml of the homogeneous solution was pipetted out in a small vial, dried and further analyzed by ^1H NMR in deuterated chloroform ($CDCl_3$). The rest of solution was left capped loosely for crystallization. Crystals found in the vail was sent to detect the size of crystal unit cell and compared with the corresponding free ligands (Methods was the same as what we used in the chapter 2.). Crystals were determined to be the corresponding free ligands and no complex crystals with different size of unit cell were observed.

3.5.2.1 Dithiobiuret-based or Monothiobiuret-based ligands with Lanthanide(III) salts

34 mg (0.10 mmol) morpholine substituted dithiobiuret-based ligand and 1 equivalent of lanthanum nitrate hydrate (43 mg, 0.10 mmol) were added to 8 ml of methanol and kept stirring for 2 hours. 1 ml of the homogeneous solvent was pipette out and dried and analyzed by ^1H NMR in deuterated chloroform ($CDCl_3$). The left solution was sitting in the fume hood, loosely capped for crystallization. The crystals found in the vial were sent to detect the size of unit cell and compared with the corresponding free ligand. Crystals were determined to be the corresponding free ligands and no complex crystals with different size of unit cell were

observed. 0.2 mmol to 0.05 mmol, 0.2 mmol to 0.1 mmol, 0.1mmol to 0.2mmol, 0.1mmol to 0.4 mmol of biuret-based (or monothiobiuret) to different lanthanide(III) salts salts ($LaCl_3$ hydrate, $CeCl_3$ hydrate, $Sm(NO_3)_3$ hydrate, $GdCl_3$ hydrate, $Er(NO_3)_3$ hydrate, $YbCl_3$ hydrate and YCl_3 hydrate) were also tried in the same procedure and analyzed in the same method.

3.5.3 Biphasic Reaction

3.5.3.1 Dithiobiuret-based or Monothiobiuret-based ligands with lanthanide(III) salts

Different concentrations of hydrochloric acid were prepared first including 0M, 0.1M, 1M, 2M and 4M. 0.30 mmol (102 mg) morpholine substituted dithiobiuret-based ligands was first dissolved in 8 ml of dichloromethane and 0.10 mmol (35 mg) lanthanum chloride hydrate was added in 8 ml of 0.1 M HCl. Those two solutions were combined together in a 32ml vial kept stirring for 2~5 hours. The organic phase was pipetted out for ^{1}H NMR analysis and crystallization. No interactions or complex crystals were observed. Dithiobiuret could be replaced with monothiobiuret and lanthanum(III) chloride could be switched to other lanthanide salts. However, no change was observed.

3.5.3.2 Biuret-based Ligands with Lanthanide(III) Salts

Different concentrations of hydrochloric acid and nitric acid were prepared first including 0M, 0.1M, 1M, 2M and 4M. 0.15 mmol (51 mg) morpholine substituted biuret-based ligand was firstly dissolving in 8 ml of dichloromethane and 0.050 mmol (18 mg) lanthanum chloride hydrate was added in 0.1M HNO_3. Those two solutions were combined together and kept stirring for 2-5 hours. The organic solution was pipetted out for ^{1}H NMR analysis and crystallization. No interactions or complex crystals were observed. Dithiobiuret could be replaced with monothiobiuret and lanthanum(III) chloride could be switched to other lanthanide salts. 0.1M HNO_3 was changed to different concentrations of HCl and HNO_3 as listed. However, no change was observed.

3.5.4 NMR-Scale Reaction

3 equivlent of 4-methyl piperidine substituted biuret-based ligand (around 6 mg) and 1 equivalent of lanthanum(III) nitrate hydrate (around 3 mg) were added to the NMR tube. Then 2ml of deuterated methanol were added and checked any change compared with spectrum of free biuret ligands on ^{1}H NMR. No reaction was observed.

3.6 References

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CHAPTER 4

COORDINATION CHEMISTRY STUDY OF DITHIOBIURET-BASED LIGANDS WITH FIRST ROW TRANSITION METALS

4.1 Introduction

In the Foley group, different dithiobiuret-based ligands (Type 1, Figure 4.1 (a)) were explored in the area of extraction of precious group metal such as gold and palladium[1]. The selectivity of gold over other base metals was observed during gold extraction. However, the coordination chemistry between the dithiobiuret-based ligands with those base metals hasn't been investigated. Before this research, there are several examples we used as reference to give us an expectation how the dithiobiuret-based ligands could coordinate with the base metals. There are the dithiobiuret-based ligands (Type 2, Figure 4.1 (b)) starting from dialkylcarbamoyl or dialkylthiocarbomoyl isocyanate reacting with secondary amine were studied as chemo-sterilant[2] and also explored and studied as acid corrosion inhibitors[3]. Since 2009, these dithiobiurets or thiobiurets starting from dialkylthiocarbamoyl have been found as good single molecular sulfur sources to synthesize different transition metal sulfide (such as ZnS, CoS, NiS, CdS, FeS, and CuS) thin films and nanoparticles[4-6], which are popularly used in solar cell, sensors, and photo luminescent devices. There is another example to be compared with dithiobiuret-based ligands used in the Foley group, which is called dithiomalonamide (Figure 4.1 (c)). However, the study of substituted dithiomalonamide is limited in terms of paper and content and most of research were about simple transition metal or precious metal complexes[7-9] (with palladium, silver, copper, zinc or nickel) synthesis without detailed characterization and further exploration of their application.

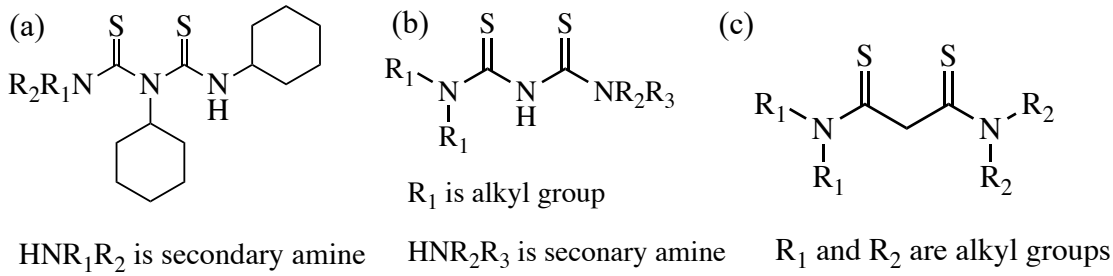


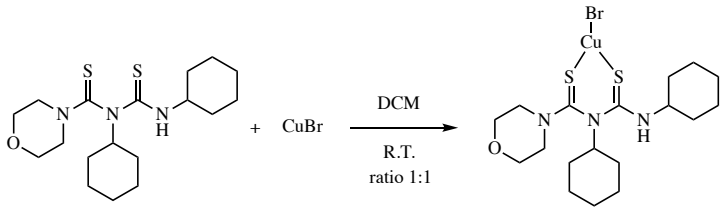
Figure 4.1 (a) Dithiobiuret (Type 1) used and studied in the Foley group; **(b)** Dithiobiuret (Type 2) used and applied in metal sulfide and nanoparticles; **(c)** Dimalonamide with limited exploration and study in the transition metal complex.

Those three different ligands((a)-(c)) are similar in structure except that the nature of the bridging group between the two thiocarbonyl groups varies from methylene to substituted nitrogen. With increasing attention paid on the ligand (b) since last decade, we have become more interested in the coordination chemistry between our dithiobiuret-based ligands (a) with transition metals like copper and its possible application. Then a direct comparison among those three different ligands could be followed and difference/similarity should be explained as well.

So a series of direct reactions between the morpholine substituted ligand (a) and their oxygen analogues with different transition metals including Cu(II), Cu(I), Ni(II), Fe(II), Fe(III), Zn(II) in the ratio of 2:1 or 1:1 were designed and conducted.

4.2 Result and Discussion

4.2.1 Dithiobiuret-based Ligands and Their Oxygen Analogues with CuBr (Copper(I) Bromide)



Scheme 4.1 1:1 ratio of dithiobiuret and CuBr reaction

Morpholine substituted L1-1 were firstly chosen to react with CuBr in dichloromethane in the ratio of 1:1 (Scheme 4.1). Reaction went smoothly with a homogeneous dark yellow solution formed. ^{1}H NMR results show distinct peaks from that of dithiobiuret free ligand (Figure 4.2 (a)), indicating new complex formed in this ratio (Figure 4.2 (b)). Solution was left for crystallization in the fridge. Yellow crystals were found at the bottom of solution.

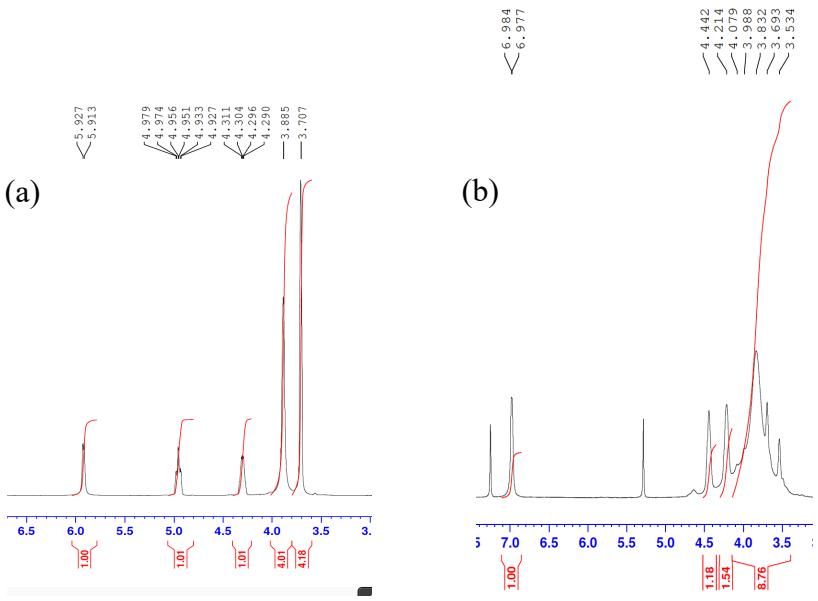


Figure 4.2 Partial comparison of ^{1}H NMR of (a) the free dithiobiuret ligand and (b) reaction of dithiobiruet and CuBr in 1:1 ratio.

The crystal structure and refinement data are listed below (Figure 4.3 and Table 4.3). The dithiobiuret ligand is chelating to Cu(I) to form one six membered rings (NC_2S_2-Cu), with Cu-S bond distances ranging from 2.2346(5) to 2.2673(5) Å. The length of N(1)-C(5) (1.324(2) Å) and N(2)-C(12) (1.366(2) Å) is relatively consistent with double bond character, whereas C(5)-N(2) (1.4423(19) Å), is relative single bond characters, indicating a delocalization along the N(1)-C(5)-N(2)-C(12)-N(3) backbone (Table 4.1 and Table 4.2), however the delocalization hasn't changed much compared to the free ligand of dithiobiuret in terms of change of bond length. As for the length of C(5)-S(1) (1.6942(17) Å) and C(12)-S(2) (1.7216(17), they are lengthened a little bit, compared to the carbon sulfur bond in the corresponding free ligand (C(5)-S(1) (1.669(4) Å) and C(12)-S(2) (1.686(4) Å), and those two carbon-sulfur bonds in the complex are more consistent with single bond character, whereas they are showing more like double bonds in the free ligands. Overall, upon coordination, a lengthening of the C-S bonds is observed, corresponding with a decrease in the length of C-N bonds along the N(1)-C(5)-C(12)-N(3) backbone.

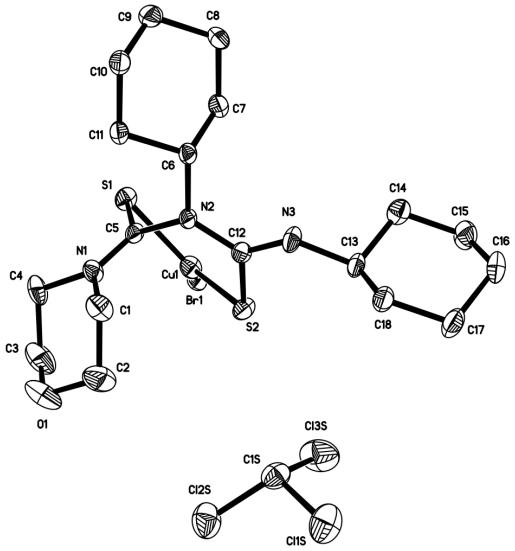


Figure 4.3 Crystal structures of CuBr-dithiobiuret complex (Hydrogen atoms are omitted for clarity. Selected bond lengths [Å] and bond angles for the crystal: Cu(1)-S(1)=2.2673(5); Cu(1)-S(2)=2.2346(5); Cu(1)-Br(1)=2.3325(3); S(1)-C(5)=1.6942(17); S(2)-C(12)=1.7216(17); N(1)-C(5)=1.324(2); N(2)-C(5)=1.4423(19); N(2)-C(12)=1.366(2); N(3)-C(12)=1.328(2); N(3)-C(13)=1.474(2); S(2)-Cu(1)-S(1)=111.452(18); S(2)-Cu(1)-Br(1)=130.081(16); S(1)-Cu(1)-Br(1)=118.402(14); C(5)-N(2)-C(12)=119.18(13); S(1)-N(2)-C(12)-S(2)=121.22(12).

	Dithiobiuret	**Dithiobiuret CuBr Complex**
S(1)-C(5)	1.669(4)	1.6942(17)
S(2)-C(12)	1.686(4)	1.7216(17)

Table 4.1 Comparison of the carbon-sulfur bond length in the dithiobiuret free ligands and dithiobiuret CuBr complex in 1:1 ratio

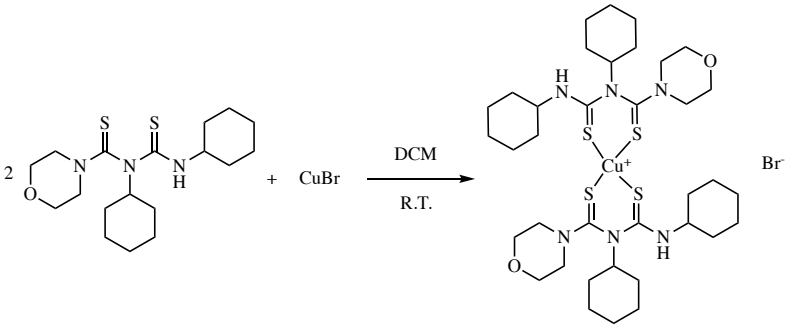
	Dithiobiuret	**Dithiobiuret CuBr Complex**
N(1)-C(5)	1.332(4)	1.324(2)
N(2)-C(5)	1.452(4)	1.4423(19)
N(2)-C(12)	1.361(4)	1.366(2)
N(3)-C(12)	1.347(4)	1.328(2)

Table 4.2 Comparison of the carbon-nitrogen bond length in the dithiobiuret free ligands and dithiobiuret CuBr complex in 1:1 ratio

Empirical formula	C19 H32 Br Cl3 Cu N3 O S2	
Formula weight	632.39	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P21/n	
Unit cell dimensions	a = 11.6002(3) Å	α= 90°.

	b = 15.1749(4) Å	β= 106.6060(10)°.
	c = 15.2959(4) Å	γ = 90°.
Volume	2580.27(12) Å3	
Z	4	
Density (calculated)	1.628 Mg/m3	
Absorption coefficient	2.885 mm-1	
F(000)	1288	
Crystal size	0.330 x 0.300 x 0.280 mm3	
Theta range for data collection	2.923 to 27.494°.	
Index ranges	-13<=h<=15, -16<=k<=19, -19<=l<=16	
Reflections collected	40817	
Independent reflections	5895 [R(int) = 0.0249]	
Completeness to theta = 25.242°	99.8 %	
Absorption correction	Multi-scan	
Refinement method	Full-matrix least-squares on F2	
Data / restraints / parameters	5895 / 0 / 271	
Goodness-of-fit on F2	1.066	
Final R indices [I>2sigma(I)]	R1 = 0.0233, wR2 = 0.0572	
R indices (all data)	R1 = 0.0297, wR2 = 0.0591	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.799 and -0.548 e.Å-3	

Table 4.3 Crystal data and structure refinement at room temperature for pyrrolidine substituted 1,2,4-dithiazolium nitrate



Scheme 4.2 2:1 ratio of dithiobiuret and CuBr reaction and proposed complex in 2:1 ratio

Morpholine substituted L1-1 were then chosen to react with CuBr in dichloromethane in the ratio of 2:1 (Scheme 4.2). The reaction went smoothly with a homogeneous dark yellow

solution formed. The ^{1}H NMR results show distinct peaks (Figure 4.3 (b)) from that of dithiobiuret free ligand (Figure 4.2 (a) and 1:1 ratio CuBr-dithiobiuret complex (Figure 4.2 (b)), indicating another new complex formed in this ratio. Solution was then going further crystallization in the fridge. Yellow crystals were found at the bottom of solution. However, that crystallography study of the yellow crystal was solved as the 1:1 ratio complex. We tried to switch to other solvents, like toluene, acetonitrile, to crystallize the possible 2:1 ratio complex, however, all the efforts failed to crystalize the 2:1 ratio complex but the 1:1 ratio complex.

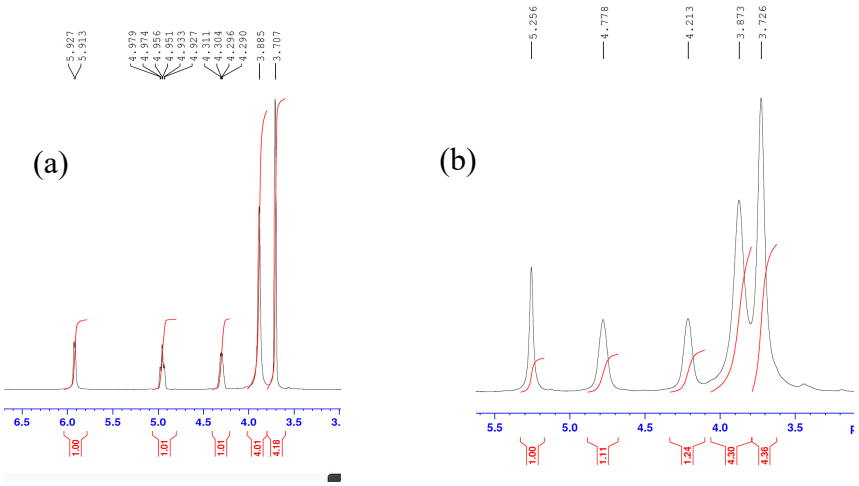
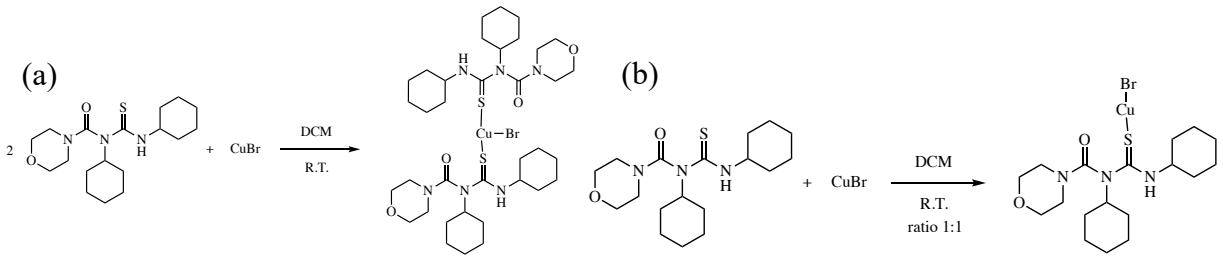


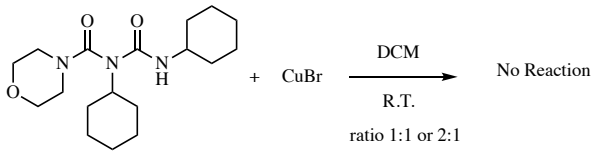
Figure 4.3 Partial ^{1}H NMR spectrum of (a) Free dithiobiuret ligand and (b) reaction of dithiobiruet and CuBr in 2:1 ratio.

Oxygen analogues are also explored during that time. 1:1 ratio and 2:1 ratio of monothiobiuret with CuBr showed distinctive peaks from each other and also from monothiobiuret free ligands (Scheme 4.3 (a) and (b)). However, inconsistency results from ^{1}H NMR spectra and no crystals of those two possible complexes having been found prevented us from understanding the reactions. Future works are needed and optimized.



Scheme 4.3 (a) 2:1 ratio of monothiobiuret and CuBr reaction and proposed corresponding complex; **(b)** 1:1 ratio of monothiobiuret and CuBr reaction and proposed corresponding complex.

As for the biuret (Scheme 4.4), after keeping stirred for several days, not only most of CuBr wouldn't dissolve, but also the ^{1}H NMR shows the free ligands of biuret. Different solvent conditions, like acetonitrile or tetrahydrofuran, were also tried. However, no positive results were observed so far. We are assuming there should be no interaction between the biuret ligands and CuBr.



Scheme 4.4 Direct reaction between biuret and CuBr in 2:1 or 1:1 ratio.

4.2.2 Dithiobiuret-based Ligands with $Zn(OAc)_2$ (Zinc(II) Acetate), $NiBr_2$ (Nickel(II) Bromide), $FeBr_2$ (Iron(II) Bromide), $FeBr_3$ (Iron(III) Bromide) and $CuBr_2$ (Copper(II) Bromide)

Morpholine substituted dithiobiutet-based ligands were also chosen to react with Zinc(II) acetate, Nickel(II) bromide, Iron(II) bromide, Iron(III) bromide or Copper(II) bromide in dichloromethane in the ratio of 1:1 or 2:1. As for Copper(II) bromide and Iron(III) bromide , reaction went smoothly with a homogeneous solution formed (dark green and dark red,

respectively) . ^{1}H NMR results failed to indicate any reaction happening in the solution because of paramagnetism issues so crystallization method was employed however, no crystals related to the possible complexes have been found so far. Infrared spectrometry was used to detect any coordination chemistry happening in the solution, but no obvious absorption peaks found could firmly prove how those dithiobiuret ligands reacting with $CuBr_2$ or $FeBr_3$.As for Zinc(II) acetate, Nickel(II) bromide and Iron(II) bromide, most of the salts were still presenting in the solution or sticking to the side of vials after the reaction was stirred for more than one day, even though different solvent conditions were applied such as acetonitrile or tetrahydrofuran. We are assuming the interaction between the dithiobiuret ligands with Zinc(II) acetate, Nickel(II) bromide or Iron(II) bromide are too weak to react with those salts and form a complex.

4.3 Conclusion

The morpholine substituted dithiobiuret and their oxygen analogues have potential to be good ligands with transition metal salts to be used in different areas such as metal sulfide thin films or nanoparticles as described in previously published work employing similar ligands but turned out to be totally different. A series of coordination experiments was performed between the dithiobiuret ligands and their oxygen analogues (from Chapter 2) with 6 different transition metal salts (CuBr, $CuBr_2$, $NiBr_2$, $Zn(OAC)_2$, $FeBr_2$, $FeBr_3$). Among those 6 metals salts, dithiobiuret-based ligand reacted with CuBr in 1:1 ratio to form a three-coordinate (dithioburet)Cu(I) bromide complex. This has been the only definitively characterized species till now. The monothiobiuret could form a complex (observed by NMR spectroscopy), however we were unable to isolate and fully characterize those species. The fully oxidized biuret showed no coordination chemistry with any of the first row transition metals studied. Since dithiobiuret-based ligands show no coordination chemistry with the studied base metals except Cu(I), a

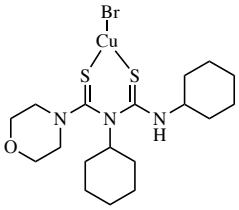
possible application of the dithiobiuret-based ligands could be a good extractant for Cu(I) minerals.

4.4 Experimental

4.4.1 Materials and Methods

Copper(II) bromide , Zinc(II) acetate, Copper(I) Bromide were purchased from Sigma Aldrich Nickel(II) bromide, Iron(II) bromide, and Iron(III) bromide were purchased from Alfa Aesar. Organic solvents were directly used as received. Refinement of crystal structure was using the same method we talked before in Chapter 2. Direct reaction of dithiobiuret-ligands and their oxygen analogues with different metal salts were carried out under ambient conditions.

4.4.2 Synthesis of (dithioburet)Cu(I) Bromide



0.501 (185 mg) mmol of morpholine dithiobiuret-based ligand and 0.50 mmol (72 mg) CuBr were added to dichloromethane and stirred for 2 hours to form a homogeneous solution. The solution was concentrated and product precipitated from the solution as small yellow crystals after 2 days at 10 °C (0.17mmol, 87mg, 34%).

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.04~2.17 (m, 20H, 2Cy), 3.37~4.52 (br, 8H, 2NCH_2 and 2OCH_2), 4.22 (br, 1H, (NH)CH)), 4.43 (br, 1H, NCH), 6.97 (dd, *J*=6.35Hz, NH)

^{13}C NMR (500 MHz, $CDCl_3$): δ (ppm) 25.3 (CH_2), 25.6 (CH_2), 30.5 (CH_2), 32.6 (CH_2), 51.5 (NHCH), 56.6 (NCH), 60.2 (NCH_2), 66.0 (OCH_2), 176.1 (C=S)

4.4.3 Monothiobiuret-based Ligands with CuBr

0.27 mmol (96 mg) of morpholine monothiobiuret-based ligands and 0.27 mmol (38 mg) CuBr were added to dichloromethane and kept stirred for 5 hours to form a homogeneous solution. Part of solution was pipetted out and analyzed by $^{1}H/^{13}C$ NMR in $CDCl_3$. However, the results of $^{1}H/^{13}C$ were inconsistent. The other part of solution was going for crystallization but failed to find complex crystals.

4.4.4 Biuret-based Ligands with CuBr

0.20 mmol (67 mg) of morpholine biuret-based ligands and 0.20 mmol (28 mg) CuBr were added to dichloromethane and kept stirred for 5 hours. A heterogeneous solution was yielded. Part of aqeous phase was pipetted our and analyzed by ^{1}H NMR in $CDCl_3$. No reaction was observed.

4.5 References

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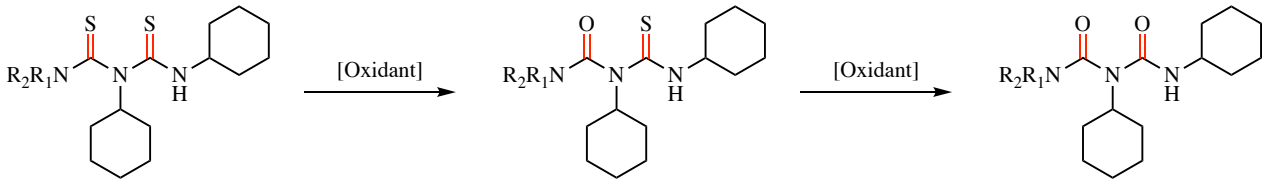
CHAPTER 5
CONCLUSIONS

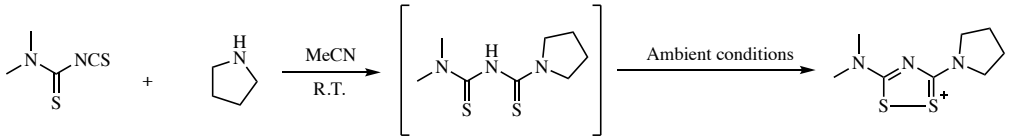
5.1 Conclusion and Summary

More and more new high-tech development leads to an increased demand for lanthanides with . Liquid-liquid extraction has been widely used in modern society to extract and separate large quantities of lanthanides. The commercially available extractants such tributylphosphate (TBP) has been used for decades but few new extractants have been designed and applied in the hydrometallurgical processes. There are lots of factors constraining the development of solvent extraction, such as solvent waste, reagent stability, reagent recyclability and lower differentiation factor between metals. In the meantime, new methods with more green chemistry have been designed to replace the industrial solvent extraction, such as grafted nanoparticles, functionalized mesoporous materials or metal organic frameworks. Most of the novel products work well for small quantities of lanthanide separation, however it still might take decades to apply these in an industrial scale because of economic reasons. Liquid-liquid extractions therefore are still dominating the entire industrial separation process for different metals and designing new potential extractants for lanthanide separation is still a rewarding commission to be solved.



Scheme 5.1 Oxidation process from dithiobiuret-based ligand (Type 1) to selective oxidized monothiobiuret ligand and fully oxidized biuret.

In the Foley group, different derivatives of dithiobiuret-based ligands (Type 1) have been investigated in gold extraction, for example from electronic wastes, and work well. The distinctive selectivity of dithiobiuret-based ligands (Type 1, Figure 5.1 (a)) for precious metals comes from the two thiocarbonyl groups, which make us question if we could use proper oxidants to tailor the basicity of these dithiobiuret-based ligands (Type 1) by converting them into monothiobiuret or biuret derivatives. The first objective of my research is brought in this context (Scheme 5.1). In the second chapter, the conversion of different derivatives of dithiobiuret-based ligands (Type 1) into corresponding monothiobiuret with good selectivity and dithiobiuret into biuret worked well by using diluted hydrochloric acid mixed with dilute nitric acid under ambient conditions. Different conditions of nitric acid with hydrochloric acid were also investigated to have a better understanding of these oxidation reactions in terms of mechanism, side reactions and stability of these ligands. A reasonable oxidation mechanism was also proposed yet still needs further confirmation. The dithiobiuret used in the lab (Type I, Figure 5.1 (a)) was compared with the previously published dithiobiuret (Type II, Figure 5.1 (b)) and we hoped to make a conversion of dithiobiuret (Type II) into their oxygen analogues by using HCl/HNO_3 and explore their application. However, attempts to synthesize Type II dithiobiurets did not proceed as expected. We were unable to isolate the dithiobiuret as it rapidly cyclized to form the corresponding 1,3,4-dithioazolium salt (Scheme 5.2). Thus, the Type I dithiobiurets proved to be considerably more stable than Type II.



Scheme 5.2 Dithiobiuret (Type II) was not found as the major product as it rapidly transformed into cyclized 1,3,4-dithiazolium salts

After we successively converted the dithiobiuret into monothiobiuret or biuret, we were trying to explore their application in different areas. My focus was drawn on the lanthanide separation, which brought the content of the third chapter. Malonamides, which are potential great extractants for lanthanide separation, have a similar backbone with biuret structures where the middle bridge is not methylene but nitrogen, which in principle could provide more electron density on the adjacent carbonyl groups and thus increase the electrostatic interaction or covalent bonding with lanthanide(III). Good selectivity for one kind of lanthanide(III) was expected to be achievable. Moreover, by oxidizing the type 1 dithiobiuret-based ligand, a series of ligands with totally different hardness are collected and could be used to select different metals with different acidity according to the Pearson's hard-soft acid and base theory. The study of the type 1 dithiobiuret-based ligands and their oxygen analogues starts from direct reaction to explore how they react with lanthanides(III). Direct reaction of morpholine substituted dithiobiuret-based (or their oxygen analogues) with different lanthanide chlorides (or lanthanide nitrates) has been tried, however there were no interactions found during the reactions in different ratios and solvent conditions by focusing on the change of chemical shift from ^{1}H NMR tests before and after the direct reactions. The poor interactions between the type 1 dithiobiuret (or its oxygen analogues) and lanthanides(III) showed in direct reaction made us question if the reactions are acid-dependent. Biphasic reactions were followed and tested in different concentrations of hydrochloric acid or nitric acid as aqueous phase. No lanthanide complexes were found in the biphasic reactions, but only the oxidation of dithiobiuret or monothiobiuret ligands.

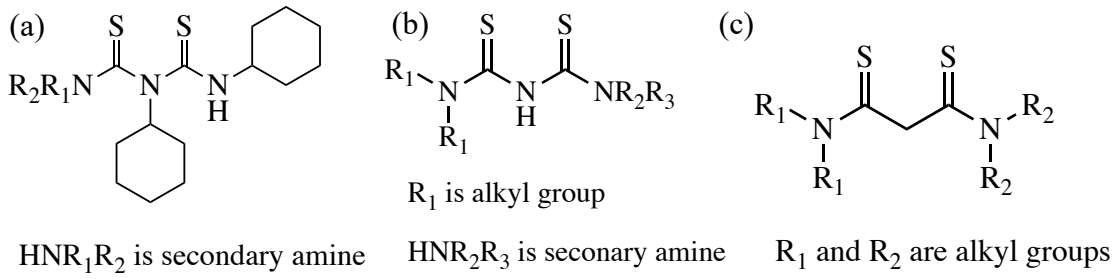
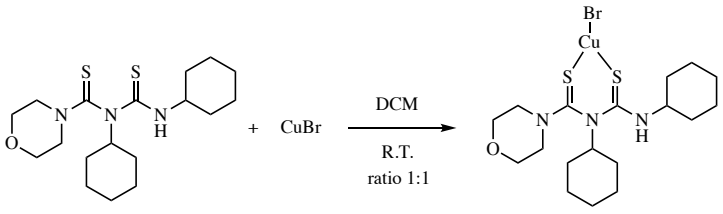


Figure 5.1 (a) Dithiobiuret-based ligands (Type 1) used in the Foley group; **(b)** Dithiobiuret-based ligands (Type 2); **(c)** Dithiomalonamide

In the fourth chapter, since the interactions between the dithiobiuret-based ligand (or its oxygen analogues) and lanthanides(III) were not observed, the coordination chemistry between the dithiobiuret-base ligands (Type 1, Figure 5.3 (a)) and different first row transition metals are explored to explain the reason why the dithiobiuret-based ligands (Type 1) shows a good selectivity toward gold over other base metals, which also give us some ideas why the efforts in the third chapter failed. The dithiobiuret-based ligands and their oxygen analogues were reacted with different transition metal salts ($NiBr_2$, $FeBr_2$, $FeBr_3$, $Zn(OAc)_2$, $CuBr_2$, CuBr), however only the 1:1 ratio of dithiobiuret-based ligands to CuBr complex was successfully characterized (Scheme 5.3). The fully oxidized biuret showed no coordination chemistry with any of the first-row transition metals studied. A reasonable application is proposed to extracted Cu(I) from minerals but still need to be designed and explored in the future work.



Scheme 5.3 1:1 ratio of dithiobiuret and CuBr reaction