ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Synthesis and Analysis of Metal Chelating Amino and Diamine Precursors and their Complex Formation on Copper (II) using Conductivity and Spectroscopic Methods.

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ABSTRACT

The use of amphiphilic molecules as metal chelating agents have been found to gain increasing importance in both medicine and environmental chemistry. In medicine, the presence of degenerative diseases such as hepatolenticular degeneration (Wilson Disease) and heavy metal toxicity enhances the importance of using chelation therapy to overcome these problems [1,2]. In terms of our environment, heavy metal exposure is a global health concern. Metals such as lead, mercury and copper have been found to be present in landfills, rivers and seawater [3]. Hence new ways are needed to remove heavy metal toxicity. With this in mind, two amphiphilic chelating ligands derived from a β-amino alcohol and diamine have been synthesized. Their coordination and binding ability with copper (II) ions have been compared to their related intermediates. Comparisons on their binding ability have also been investigated where the effect of molecules possessing an OH moiety (amino alcohol) were compared to that of NH_2 in diamine systems. Also the effects of adding a short chained amide to increase the amphiphilic nature of the ligands as well as increasing the availability of producing more binding sites have been investigated.

Keywords: Amino alcohols, diamines, copper chelation, stoichiometry, binding strength.

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ISSN: 0975-8585

INTRODUCTION

β–Amino alcohols and di-amines are important compounds that have potential uses in the biological and environmental sector [2,4]. The study of the interaction of these compounds and their substituted derivatives, can help us to understand their coordination ability through the hydroxyl and amino groups that can chelate with heavy metal ions.

Exposure to heavy metals such as copper, lead, cadmium, mercury and arsenic have been known to be potential threats to human health. These metals can bio-accumulate in the food chain and end up in the human body and tissues, such as the brain, liver and kidneys, thereby disrupting their ability to function normally [1,5].

In this context our preliminary work has focused on synthesizing ligands derived from β-amino alcohols and di-amines to study their interaction and coordination on copper (II) ions.
Copper occurs naturally from ores (copper sulphides, oxides and carbonates) and minerals (such as chalcopyrite and bornite) and can spread into the environment through natural phenomena [6,7]. Humans widely utilize copper. Its most common use being in electrical equipment such as wiring and motors. It is also used in roofing, guttering, plumbing and in cookware and cooking utensils [3,8]. Due to its high demand, an increase in the amount of copper waste in the environment has been observed [6,8].

Copper found from wastewater sources, can originate from printed circuit board manufacturing, electronic plating, wire drawing, printing operations, paint manufacturing and anti-fouling coating operations [3]. As a result, rivers with deposited sludge on their banks tend to be contaminated with copper. Too much copper in water can be detrimental to marine life. It has been reported that a high concentration of copper in fish and aquatic invertebrates can lead to damage of their gills, through rapid binding of copper to the gill membranes, which interferes with the osmoregulatory processes causing damage [9].

In addition this can affect human health as the contaminated fish forms part of the food chain. As a result of copper toxicity, the presence of copper in the bloodstream which is bound to celluloplasmin, albumin and other smaller molecules in the blood system, would enable the free copper ions to generate reactive oxygen species such as hydroxyl radicals, hydrogen peroxides and superoxides which can damage the proteins, lipids and DNA in the body [10].

Long exposure to copper have been reported to irritate the nose, mouth and eyes as well as cause nausea, vomiting and diarrhea [11]. Copper toxicity can also lead to other health problems such as depression, chronic lung infection, insomnia, allergies and stress. Its toxicity has been shown to affect the organ systems in our body, namely the nervous system, the male and female reproductive system, the liver as well as the connective tissues such as the skin, hair and nails [11].

Reports have indicated that copper toxicity can lead to a decrease in soil fertility, resulting in a reduction of plant growth [12]. The involvement of copper in the automosomal

ISSN: 0975-8585

degenerative disease, hepatolenticular degeneration (Wilson Disease) also needs to be discussed, in which an inherited disorder of copper metabolism characterized by the deposit of copper in the liver, brain and other tissues, occurs, which can lead to cirrhosis [1]. The presence of both hepatolenticular degeneration (Wilson Disease) and heavy metal toxicity enhances the importance of using chelation therapy to overcome these problems.

One of the criteria for a good chelating agent is to increase its lipophilic character [2]. With this view, two metal chelating surfactant precursors, one derived from ethylene diamine, compound (**1**) and the other from β-amino alcohol (**2**) were synthesized. Their chelating and binding abilities were compared to their respective analogues, ethanolamine (**4**) and phenylalaninol (**5**) as well as quoted results obtained using ethylene diamine (**3**).

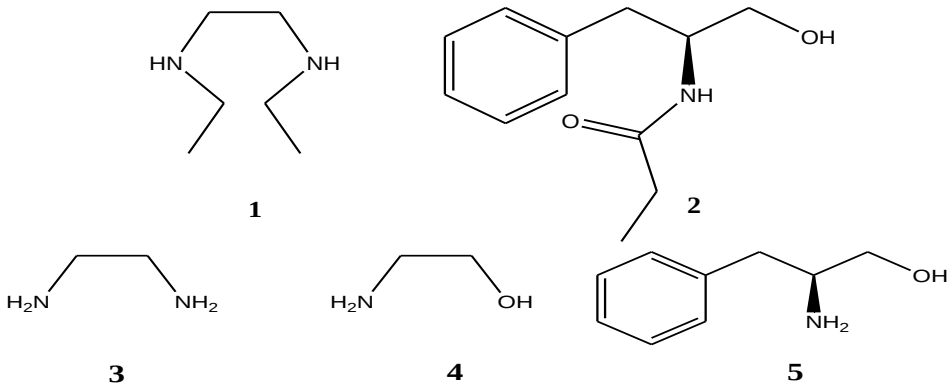

Figure 1: List of Ligands used for chelation

Diamine (**1**) was synthesized to investigate the effects of increasing the lipophilic nature of the molecule with respects to ethylene diamine, This was done by incorporating ethyl groups onto the nitrogen moiety. To better understand the binding ability of (**1**), its chelating and binding properties were compared with that of ammonia as well as quoted results obtained from ethylenediamine.

The binding ability between β-amino alcohols and diamines were also investigated where the chelating and binding effects of the molecules possessing an OH group (amino alcohol) and NH_2 group (diamine) were compared. Hence the simplest β-amino alcohol, ethanolamine was studied. Its binding strength was compared to the synthesized *L*-phenylalanine analogue *L*-phenylalaninol. This was selected since the aromatic rings in *L*-phenylalaninol can potentially induce π-π stacking with each other in order to help in chelating interaction. Incoorporation of a 3-carbon amide chain to the phenylalaninol molecule was investigated (compound **2**), with an aim to increase its chelating strength, since it was envisaged that the presence of the chain would increase the number of metal binding sites by presenting a highly basic amide oxygen donor which would make compound **2** a more strongly complexing analogue. Addition of the amide chain would also increase the lipophilicity of the molecule which is important in chelation therapy since lipophilic chelators can provide better binding onto metals and so can aid in the removal of metals from polluted waters as well as

from the body. Also lipophilic systems are able to gain access to intracellular and extracellular spaces, due to their lipophilic nature and mobilize heavy metals from tissues, as the chelating agents pass across the cell membrane, and help the metals to be excreted from the body [2].

MATERIALS AND METHODS

The chemicals and reagents used for the synthetic study were of analytical grade and were purchased from Sigma-Aldrich Co. Ltd and Acros-Fisher Scientific, UK. THF was freshly distilled and dried using molecular sieves (4Å) prior to use. Both ethyl acetate and hexane were distilled before being used. All air and moisture sensitive reactions were carried out under an inert nitrogen atmosphere.

For the analytical studies, ethylene diamine and copper (II) sulphate were purchased from BDH chemicals, ethanolamine was purchased from Scharlau chemicals and ammonia solution was purchased from alpha chemicals.

Infrared spectra (IR) were recorded on an Avalar 320 FTIR spectrometer in the range of 4000 to 500 cm^{-1}. ^{1}H NMR and ^{13}C NMR spectra were recorded in 5 mm outer diameter tubes in $CDCl_3$, or D_2O as solvent at room temperature using a FT Brucker 250 MHz spectrometer. The chemical shift (δ) of each peak was assigned relative to tetramethylsilane (TMS). Elemental analysis was obtained using a LECO 932 CHNS Mattson 1000 Spectrophotometer. Melting point analysis was carried out using an Electrothermal melting point apparatus and the value was quoted uncorrected to the nearest 0°C. Optical rotations were determined using a Billingham-Stanley Model D optical activity polarimeter.

Chromatography refers to using a “flash column” technique over silica gel (70-230 mesh). Thin layer chromatography (TLC) was performed on a glass backed or on plates precoated with silica. Visualisation was achieved by exposure to an iodine atmosphere or with ultraviolet light (254 nm).

The conductivity measurements were made using a Jenway 4510 conductivity meter. The binding studies were carried out using UV analysis on a Biochrom Libra S22 spectrophotometer, where quartz cells, 1cm wide were used.

N, N’- Diethylethane-1, 2-diamine (1)

Ethane-1,2-diamine (5 ml, 72.2 mmol) was dissolved in THF (100ml) at 80^{o}C for 30 minutes. Triethylamine (10ml, 72.2 mmol) was slowly added and the reaction mixture was left to stir for two hours. Bromoethane (8.00ml, 106.8 mmol) was subsequently added dropwise over a period of 15 minutes. The reaction was left to stir at 80^{o}C for 24 hours. A white precipitate was produced in the solution, which was filtered off and washed with ethyl acetate (50ml). The solid product was dried via vacuum suction to yield the title compound as a white solid (1.9g, 23 %). ν_{Max}/cm^{-1}: 3527, 3271, 1820, 1702. ^{1}H NMR ($CDCl_3$) δ (ppm): 1.10 (6H, t, *J* 5.5 Hz); 2.0 (2H, s, N-H): 3.02-3.15 (8H, m). ^{13}C NMR ($CDCl_3$) δ (ppm): 11.0, 48.0, 49.5.

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Propanoyl chloride (6)

Thionyl chloride (40 ml, 536 mmol) was added dropwise to propanoic acid (40 ml, 402 mmol) at room temperature. The reaction mixture was refluxed for 3 hours under inert atmosphere.

The resulting solution was then distilled to obtain the title compound as a colourless solution (6.2 g, 85%). ν_{Max}/cm^{-1} (KBr): 2989, 1788.^{1}H NMR ($CDCl_3$) δ (ppm): 1.15 (3H, t, *J* 7.3 Hz), 2.87 (2H, q, *J* 7.5 Hz). ^{13}C NMR ($CDCl_3$) δ (ppm): 9.7, 41.1, 174.9.

***L*-Phenylalaninol (5)**

The reaction was carried out under an inert nitrogen atmosphere. Sodium borohydride (1.14g, 30.3mmol) was dissolved in 40ml THF (freshly distilled and predried over sodium). *L*-Phenylalanine (2.01g, 12.11 mmol) was added in small portions. The mixture was cooled to 0°C. A solution of iodine (2.9g, 27.35mmol dissolved in 20ml THF) was added slowly over 30min resulting in vigorous evolution of hydrogen. After addition of iodine, the mixture was heated to reflux for 22 hours and then cooled to room temperature. Methanol was added until a clear mixture was obtained. The resulting mixture was left to stir for 30 min and the solvent was removed in *vacuo* leaving a white paste that was dissolved in 30ml of 20% KOH. The solution was stirred for 4 hours and extracted with 4 × 25 ml of dichloromethane (DCM). The organic extracts were dried over anhydrous sodium sulphate, filtered and concentrated in *vacuo* to give a crude solid (1.270g, 8.41mmol) which was recrystallised from toluene (10ml) to yield the title compound as white crystals (1.20g, 60%). M.pt 89-90 ^{o}C.ν_{Max}/cm^{-1}: 3438, 3355, 2938, 1633, 1579, 1454, 753. ^{1}H NMR ($CDCl_3$) δ (ppm): 2.28 (3H, br, s); 2.52 (1H, dd, *J 5.25,* 8.75 Hz); 2.74 (1H, dd, *J* 5.25, 8.75 Hz); 3.09 (1H, m); 3.40 (1H, dd, *J* 3.75*,* 7.25 Hz); 3.61 (1H, dd, *J* 3.75, 7.25 Hz); 7.17 -7.25 (5H, m).

^{13}C NMR ($CDCl_3$) δ (ppm): 39.8, 53.1, 65.2, 125.4, 127.5, 128.3, 137.7. Anal. calc. for $C_9H_{13}ON$: C, 71.5; H, 8.6; N, 9.26; found C, 70.92; H, 5.75; N, 9.24 %. $[\alpha]_D$ = -24.6° (c=1, 1M HCl).

***N*-Propanoyl Phenylalaninol (2)**

L-Phenylalaninol (0.69 g, 4.63 mmol) was dissolved in THF (60 ml) at room temperature followed by the addition of triethylamine (0.9 ml, 6.5 mmol). The solution was left to stir for about 1 hour. Propanoyl chloride (0.4 ml, 4.32 mmol) was slowly added over a period of 15 minutes. A catalytic amount of DMAP (4-Dimethylaminopyridine) was added to the mixture and the reaction heated to reflux at 70ºC for 3 hours.

The reaction mixture was quenched with water (100 ml) and the aqueous and organic layers were separated. The aqueous layer was washed with ethyl acetate (4 x 25 ml) and the combined organic extracts were washed with sodium hydrogen carbonate (5%, 25 ml). The organic layer was dried over anhydrous magnesium sulphate and concentrated under reduced

pressure. The crude material was then purified via flash chromatography (ethyl acetate:hexane, 1:1) to yield the title compound as a yellow oil (0.66 g, 68%).

ν_{Max}/cm^{-1}: 3085, 2972, 1736, 1648, 701.^{1}H NMR ($CDCl_3$) δ (ppm): 0.99 (3H, t, *J* 7.9 Hz); 2.10 (2H, q, *J* 7.5 Hz); 2.79 (2H, m); 3.53 (2H, dd, *J* 5.0, 12.8 Hz); 4.10 (1H, m, 2-H); 6.13 (1H, m, N-H); 7.21 (5H, m).^{13}C NMR ($CDCl_3$) δ (ppm): 12.2, 32.1, 39.4, 55.0, 65.9, 128.9, 130.8, 131.6, 140.3, 177.2. $[\alpha]_D$ = -28.0º (c=1, $CHCl_3$).

Conductivity measurements to determine stoichiometry:

The analysed ligand (**1**), (**2**), (**4**), (**5**) or NH_3 (50mL, 0.01M) was titrated against copper (II) sulphate solution (50mL, 0.0025M) with continuous stirring to ensure proper distribution of the mixture.

Conductivity measurements were taken using a platinum probe after each 0.5ml addition of the ligand. A graph showing the volume of ligands added against conductivity was plotted. The resulting lines obtained were solved through simultaneous equations where Y represents the conductivity of copper ions recorded and X represents the volume of ligand added to give the ratio of the number of ligands binding to metal ions.

Determination of Binding Strengths using UV methods.

Deionized doubly distilled water was used throughout the experiment. Copper (II) sulphate (MW 160) solutions (7.5 x 10^{-3}M), (3.5 x 10^{-4}M), (1 x 10^{-4}M) and (1 x 10^{-5}M) respectively were prepared by dissolving copper (II) sulfate in distilled water. Ligand solutions (7.5 x 10^{-3}M) of NH_3, (3.5 x 10^{-4} M) of (**4**), (1 x 10^{-4}M) of (**2**) and (**5**) and (1 x 10^{-5}M) of (**1**) was freshly prepared in methanol.

The Job's method of continuous variations [13] (Likussar and Boltz 1971), was carried out using UV methods to determine the binding strengths (formation constant K_f) between the coordinated tested ligands and the copper ions. For this purpose, different volumes (0, 0.2, 0.4, 0.6, 0.8, 1.0, 1.2, 1.4, 1.6, 1.8, and 2.0 mL) of a specific concentration of copper (II) sulfate solution were mixed with different volumes (2.0, 1.8, 1.6, 1.4, 1.2, 1.0, 0.8, 0.6, 0.4, 0.2, and 0 mL) of the analysed ligand of the same concentration and diluted with ethanol in a 10-mL standard volumetric flask.

The absorbance was recorded at wavelengths specific to the ligand complexing with copper (II) ion, [460nm for NH_3 according to literature [14], 550 nm for ethanolamine (4) according to literature [15], 550 nm for *L*-Phenylalaninol (5) and for N-propanoyl phenylalaninol (2). Their wavelength was selected in comparison to the wavelength used for the complexation of (4), the simplest □-amino alcohol. The absorbance was plotted against the mole fraction of copper (II). The K_f value was calculated using the expression shown in equation (**i**).

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RESULTS AND DISCUSSION

Synthesis of a diamine analogue

Since ethylenediamine is known to be a good chelator with copper (II) ions, it was envisaged to use this backbone to making a ligand with increased chelating ability and ampiphilic nature [2]. Hence compound (**1**) was synthesized. This was done by incorporating the ethyl chains onto the nitrogen centres of the diamine, making the centres more electron rich to facilitate binding with the copper ion. Ethylene diamine was thus reacted with ethyl bromide using 1 equivalence of triethylamine in THF to give compound (**1**) in 23% yield. This was confirmed by ^{1}H NMR and ^{13}C NMR analysis which showed that the 2 ethyl groups had attached to the diamine according to the structure shown in figure 2.

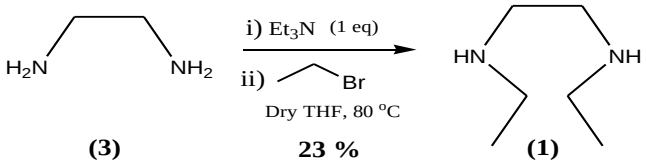

Figure 2: Synthesis of (1)

The stoichiometry and chelation binding was compared with its related analogues ethylenediamine and ethanolamine as well as ammonia. This would enable us to validate the effects of whether β-amino alcohol systems would provide better chelation compared to diamine systems.

Synthesis of L-Phenylalanine analogues

L-phenylalanine analogues (**5**) and (**2**) were selected since it was postulated that the presence of the aromatic ring would result in π-π stacking between the rings as well as exposing the different binding sites to the copper ion. It was envisaged that a combination of these factors would help increase the binding ability of the ligand.

L-phenylalaninol (**5**) was therefore synthesized as a direct comparison with ethanolamine (the simplest β-amino alcohol). *L*-phenylalanine was subsequently reduced using sodium borohydride and iodine in dry THF to yield (**5**) in 60 % yield.

Since it has been reported that amide systems can help facilitate metal chelation as its structure provides extra binding sites on the nitrogen and oxygen atoms of the amide molecule [16], we decided to incorporate a propanoyl chloride chain onto the *L*-phenylalaninol structure. This would also help improve the ampiphilic nature of the molecule which would aid metal chelation.

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The propanoyl chloride chain was synthesized by acylating propanoic acid using thionyl chloride to give (**6**) in 85% yield. *L*-phenylalaninol (**5**) was subsequently reacted with the acyl chloride using triethylamine base (1.5 equivalence) and a catalytic amount of DMAP in THF solvent to give compound (**2**) exclusively in 68% yield.

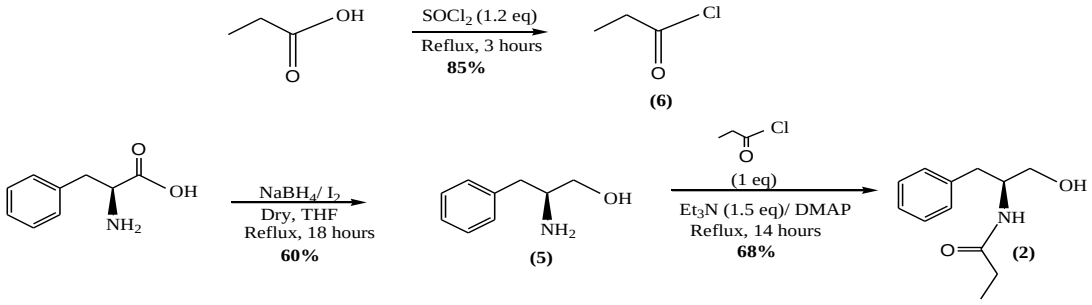

Figure 3: Synthesis of (2)

Stoichiometric and Binding studies

Using the wavelengths specified in section 1.2.6, upon addition of the tested ligands [(1), (2), (4), (5) and NH_3] with copper (II) ions, a shift in the wavelength was observed confirming that complexation between the ligand and copper (II) ions was occurring. A summary of the stoichiometric and binding study results can be shown in table 1

Table 1: Summary of Stoichiometric and Binding studies of tested ligands

Ligand	Stoichiometric Ratio with Cu (II)	K_f Value
NH_3	4:1	1.07×10^{13}
1	2:1	7.11×10^{11}
2	3:1	1.44×10^{15}
4	2:1	7×10^{8}
5	5:1	9×10^{9}

Copper chelation with NH_3 was first carried out as a comparative analysis with our synthesized compounds as well as confirming the validity of using the Job's method in order to determine the binding strength (K_f) of our tested ligands with copper (II). The K_f value was calculated using the following expressions [17]:

$$K_f = \frac{(A_{obs} / A_{extrp})\bar{C}}{[C_M - (A_{obs} / A_{extrp})\bar{C}]\,[C_L - n(A_{obs} / A_{extrp})\bar{C}]^n} \qquad \textbf{Equation 1}$$

where A_{obs} and A_{extrp} are observed and extrapolated absorbance values of the complex. C_M and C_L are initial concentrations of copper (II) and the ligand used in moles per litre,

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respectively, $\bar{C}$ is the limiting concentration and n is the number of ligands coordinating with the copper (II) ions, which is determined by the stoichiometric ratio.

From the Job's plot shown in figure 4, a stoichiometric ratio of 4:1 between ammonia and the copper (II) ion was obtained as indicated in figure 5. The K_f was found to be 1.07×10^{13} which was in good accordance with the literature [14] value (1.20×10^{13}) and also confirmed the validity of using the Job's method to determine the K_f values for the rest of the ligands synthesized.

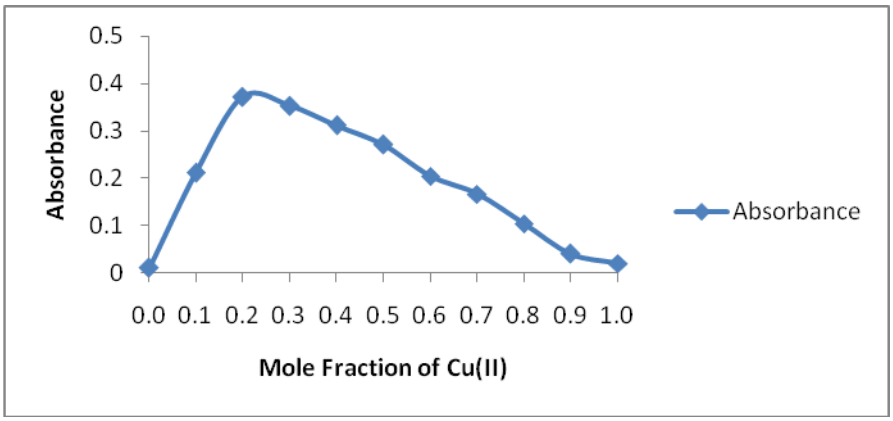

Figure 4: Job's plot for Cu(II)-NH_3 complex

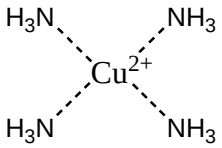

Figure 5: Possible interaction between ammonia and Copper (II)

When using ethanolamine (**4**), the stoichiometry of the copper (II) complex was found to be 2:1 which was confirmed by both the Job's plot and conductivity measurements (figure 6 and 7).

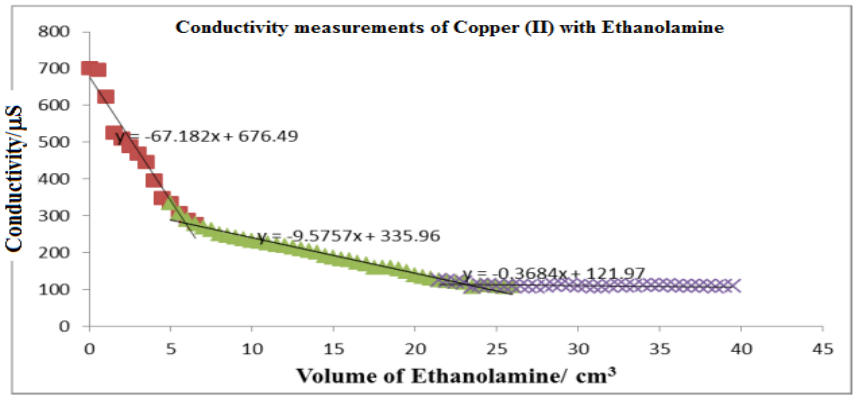

Figure 6: Conductivity measurements for ethanolamine

ISSN: 0975-8585

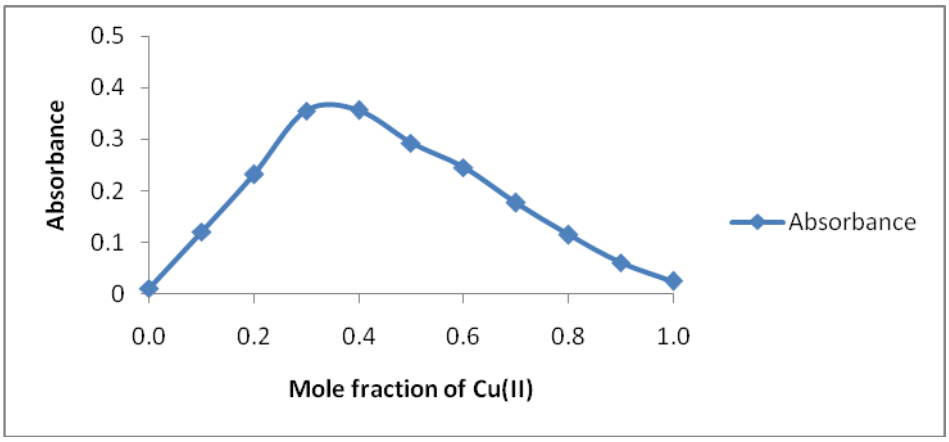

Figure 7: Job's Plot for Cu(II)-Ethanolamine Complex

This stoichiometry reveals that they act as bidentate ligands coordinating to the copper ions, as indicated in figure 8. Figure 9 shows the shift in the UV spectra from 550 nm to about 680 nm signifying that coordination is taking place.

We have represented a possible structure showing that the coordination between the ethanolamine ligands and Cu^{2+} ions maybe of a square planar form similar to the type of coordination reported between copper (II) ions and ethylenediamine. It was reported that an extreme Jahn-Teller distortion was found in these complexes preventing the copper (II) ions to form six-coordinated complexes [18].

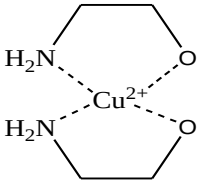

Figure 8: Possible interaction between Ethanolamine and copper (II) ions

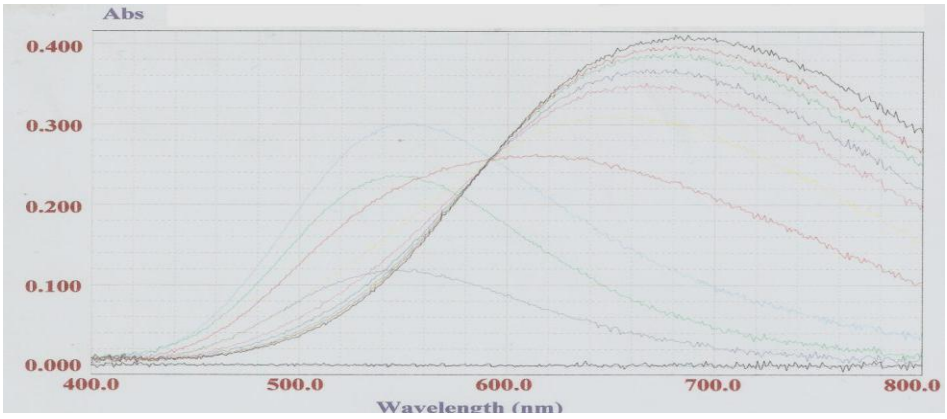

Figure 9: Absorbance showing the interaction between Copper (II) ions and ethanolamine

ISSN: 0975-8585

From the job's plot and using equation 1, the K_f for ethanolamine (**4**) was found to be 7 x 10^8. To date, limited work has been attempted on metal chelation with □-amino alcohol systems [15, 19]. However some excellent work by Djurdjevic and Bjerrum [15] showed that ethanolamine chelating with copper (II) ions gave a K_f value of 7.8 x 10^8 using potentiometric analysis, which is in line with our experimental data. To our surprise however, very few reports have carried out a comparative study on the effects of functional group variation on metal chelation. Our results clearly indicate values much lower than that reported [18] on ethylenediamine systems (Log K = 20.03, (1.07 x 10^{20}) which was not surprising since the increasing electronegativity of the oxygen moiety on □-amino alcohol systems may prevent it from readily donating its lone pair to the copper (II) ion compared to the less electronegative nitrogen in diamine systems. Despite this the K_f value of 7 x 10^8 indicates that □-amino alcohol systems can be useful ligands in chelating metals. It is with this basis that we set out synthesizing and testing *L*-phenylalaninol (**5**) as a metal chelating ligand. Incoorporating an aromatic phenyl group to the amino alcohol to give (**5**) resulted in an increase in the K_f value (9 x 10^9). The stoichiometric ratio between Copper (II) and (**5**) was found to be 2:1 when both the Job's method and conductivity methods were used.

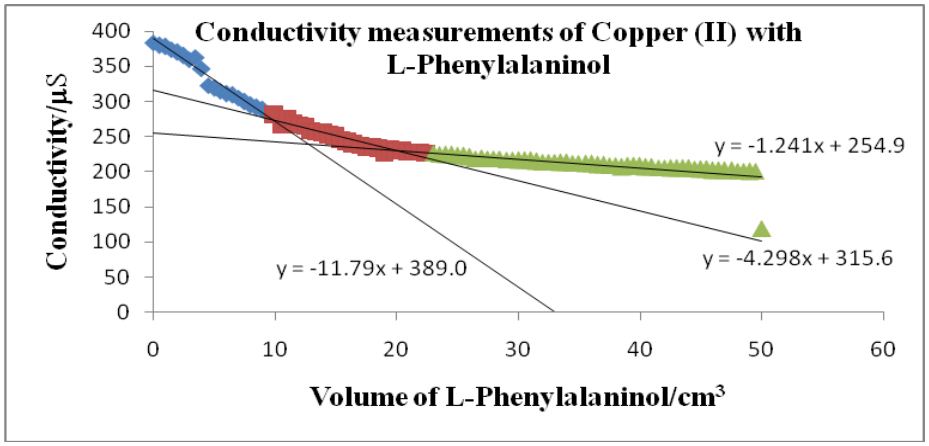

Figure 10: Conductivity measurements for L-phenylalaninol

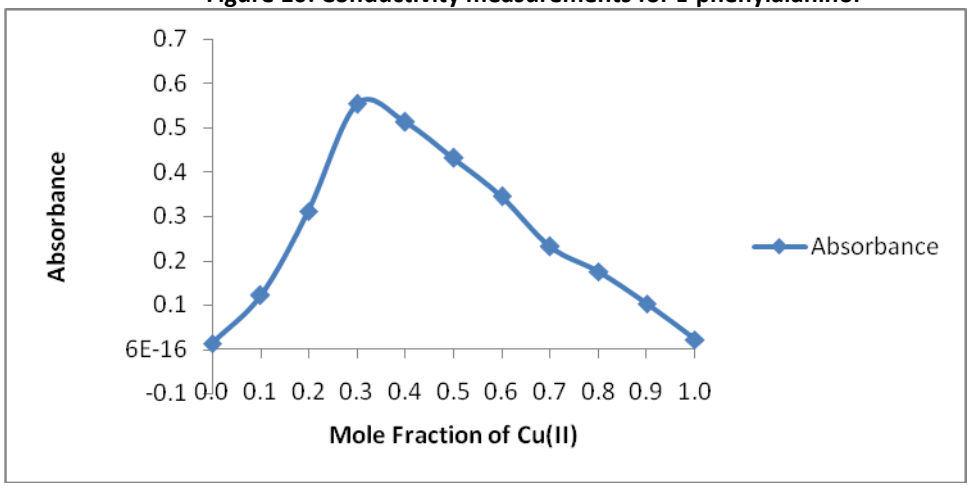

Figure 11: Job's Plot for Cu(II)-L-Phenylalaninol Complex

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A possible hypothetical structural interaction between *L*-phenylalaninol and copper (II) ions is shown in figure 12 where the aromatic rings possibly stack over each other via increased π-π stacking which would aid in fixing the ligands in position as well as provide electrons to the copper (II) ion via induction effect from the electron donating aromatic ring, which would help increase the K_f value.

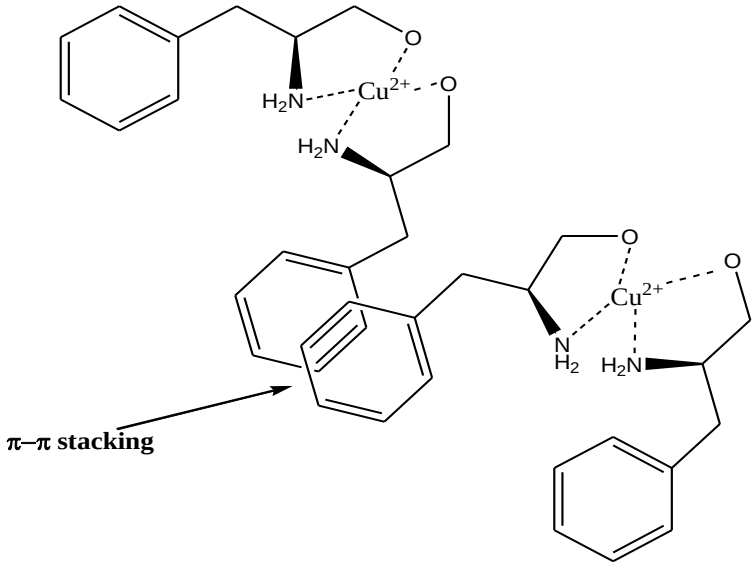

Figure 12: Possible structure of L-Phenylalaninol chelating with copper (II) ions

When investigating the chelation of (**1**) with copper (II) ions, it was observed that the K_f value obtained from the Job's plot and equation 1 was found to be 7.11 x 10^{11}. This value was lower than its analogue ethylene diamine (**3**) which has no ethyl groups attached to the nitrogen moiety. A stoichiometric ratio of 2:1 was obtained between (**1**) and the copper (II) ions as confirmed by both conductivity and the Job plot.

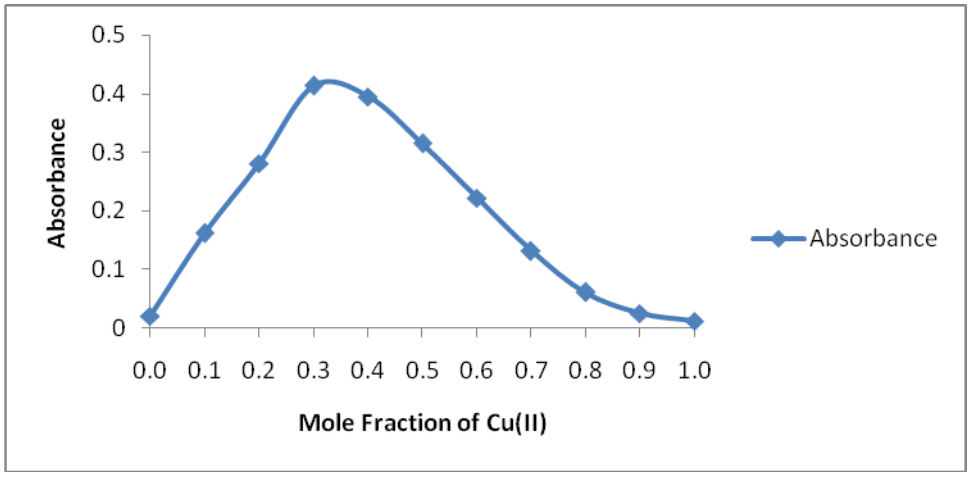

Figure 13: Job's Plot for Cu(II)-N,N'-Diethylethane diamine.

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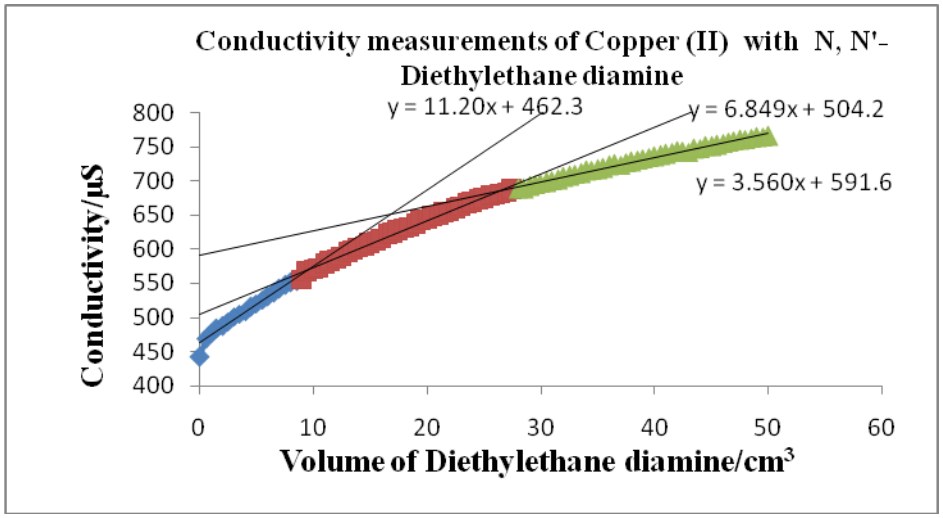

Figure 14: Conductivity measurements for N, N' Diethylethane

A possible structure of the interactions between the coordination of (**1**) and the copper (II) ions, is shown in figure 15. Like its analogue ethylene diamine, a possible coordinated square planar formation would be present where (1) acts as bidentate ligands coordinating to the copper (II) ion. A possible reason for the lower K_f value (7.11×10^{11}) may be due to possible steric hindrance between the ethyl groups as indicated in figure 15, causing a strain in the complex structure. Despite this the K_f value was encouraging enough and together with the fact that the presence of the attached ethyl groups to the nitrogen moiety make (**1**) increasingly amphiphilic in nature, this would make the ligand potentially useful. This is an important characteristic especially for chelation therapy to combat against metal poisoning and metal related diseases such as the Wilson disease. Increasing the ampiphilic nature of chelating ligands enables them to have access to intracellular and extracellular spaces in the body, and mobilize heavy metals from tissues, as they pass across the cell membrane and enhance metal decorporation [2].

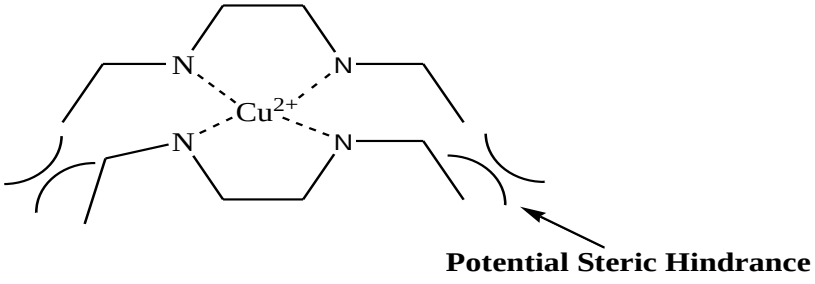

Figure 15: Possible structure of the interaction between N,N'-Diethylethane chelating with copper (II) ions

Finally we tested the chelation of our synthesized ligand (**2**) on copper (II) ions. Incoorporation of an aliphatic amide to the *L*-phenylalaninol structure (**5**) resulted in an increase in the K_f value (1.44×10^{15}) when chelated with copper (II) ions. Conductivity measurements showed a stoichiometric value of 2.4:1 between ligand (**2**) and copper (II) ions.

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However results from the Job's plot confirmed a stoichiometric ratio of 3:1 (figure 16 and figure 17).

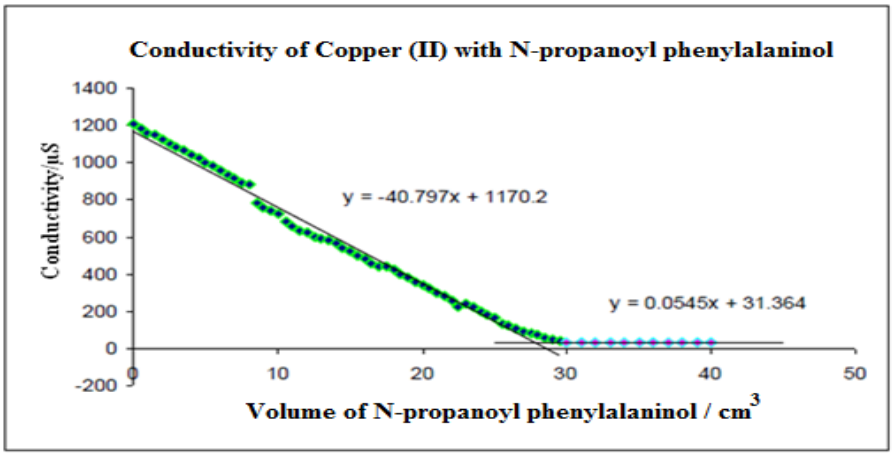

Figure 16: Conductivity measurements for N-propanoyl phenylalaninol

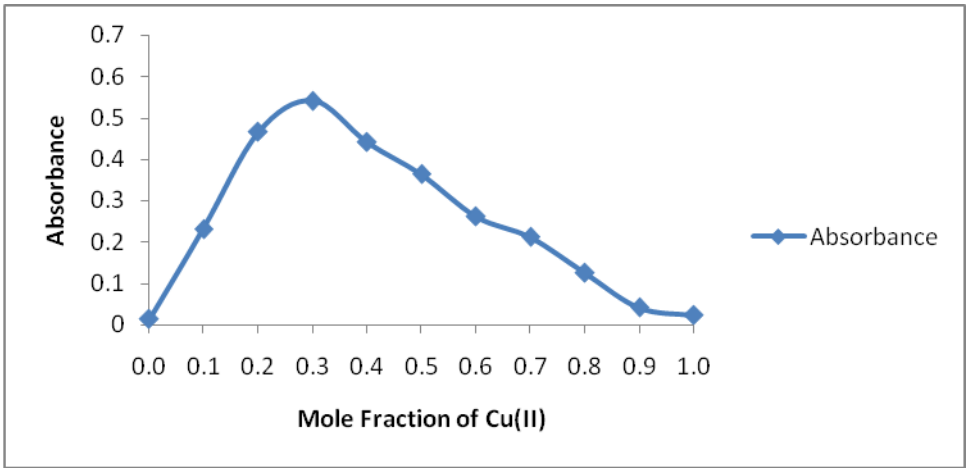

Figure 17: Job's Plot for Cu(II)-N-Propanoyl L-Phenylalaninol complex

The high K_f obtained maybe attributed to an increased number of binding sites available in the molecule (**2**) as indicated by a possible hypothetic structure shown in figure 18 as well as π-π stacking between the aromatic rings. The presence of the amphiphilic amide chain can potentially make our synthesized ligand more lipophilic as well as create binding sites on the amide moiety for the copper (II) ions to interact, as explained and postulated by Hu and co-workers [16] when they investigated the influences of peptide side chains on metal ion binding sites.

ISSN: 0975-8585

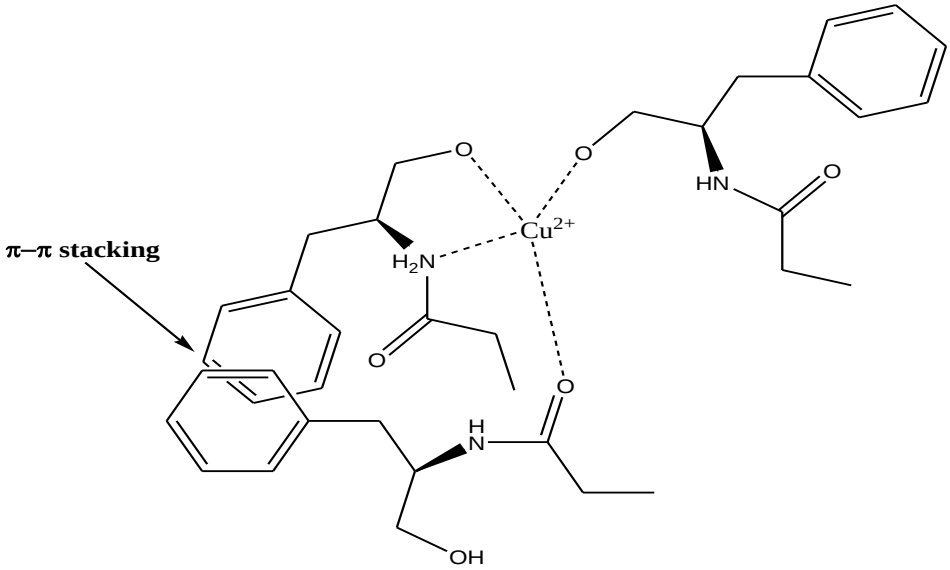

Figure 18: Possible structure of the interaction between N-propanoyl L-phenylalaninol and copper (II) ions

CONCLUSIONS

We have been able to successfully synthesise lipophilic ligands (**1**) and (**2**), one of which is derived from the amino acid L-phenylalanine and the other derived from ethylenediamine. Preliminary studies show that both ligands have shown promising binding strength, 7.11 x 10^{11} for (**1**) and 1.44 x 10^{15} for (**2**). We have also been able to carry out a comparative study of diamine and □-amino alcohol analogues, illustrating the importance of how functional groups and lipophilic nature of molecules affect their binding strengths as we look towards making useful chelating ligands in the field of medicine and environmental chemistry.

ACKNOWLEDGEMENTS

We are grateful to the following technical staff at the University of Mauritius: Miss S.L'Omlette for the running of NMR and Mr V. Ramsahye for assistance during the polarimetry and analytical studies.

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