Surfactants are chemical compounds that are amphiphilic in nature because of their dual nature of being both hydrophobic (due to their long hydrocarbon chains) and hydrophilic (due to their polar head groups). Because of their dual nature, they can have partial solubility in both organic and aqueous media. This paper will outline and review the role that surfactants play in environmental chemistry. As well as being good cleaning agents and lubricants, our work has demonstrated that they can act as good catalysts in aqueous media where they have several advantages over conventional solvents in terms of yields and rate enhancement. This is of particular interest since organic reactions generally rely on using toxic solvents and reagents, so a more environmentally friendly technology in chemistry is required to run organic reactions in aqueous media. Our research work has made use of a range of different natural product derivatives as catalysts. We are currently investigating the role of the amino acid phenylalanine since previous work using this backbone as a catalyst has been successfully reported. We will present our preliminary studies where we have used analogues of phenylalanine as catalysts in aqueous media. In addition, we will also outline the role of surfactants in reducing heavy metal toxicity since they can act as good chelating agents. As we are aware, heavy metal exposure in the 21st century is a global health concern. Metals such as mercury, lead and copper have been found to be prevalent in seawater and landfills. Hence new ways are being developed to remove heavy metal toxicity. We will therefore demonstrate the use of our synthetic analogues derived from phenylalanine to investigate their binding effect with a view to synthesise good chelating ligands derived from surfactants which can coordinate and dispose of the metal. The fact that the surfactants are amphiphilic means that this would be an advantage in the removal of toxic metals.

**Key Words**: Micelles, Critical micelle concentration, Catalysis, Heavy metal pollution, Heavy metal toxicity, Metal coordination

**INTRODUCTION**

Micellar media is becoming an integral part of environmental chemistry. It is formed by the aggregation of surfactant molecules at or above a certain concentration known as the critical micelle concentration (CMC). Surfactants are by definition amphiphilic molecules that contain both hydrophilic (water loving) and hydrophobic (water hating) characteristics (Fig. 1).

The use of micellar solutions as reaction media has provided a cleaner alternative to carrying out organic reactions since they can be done in an aqueous environment due to their amphiphilic nature. Micelles exist depending on the solvent used. For example the formation of normal micelles exist in a water medium (Fig. 2) where the polar head group points towards the aqueous exterior and the hydrophobic chain is positioned away from the aqueous region as indicated in Fig. 2.

Chemical industries are now undergoing an important transition period where there is public pressure to reduce the use of volatile organic solvents (VOC). Thus chiral micellar media can offer a cleaner alternative to more traditional
organic chemistry methods since they have the potential to solubilise substrates as well as concentrate and preorientate reactants, within the micellar core. As a result the yield and selectivity of reactions can be controlled by a number of effects namely concentration, cage, preorientation, microviscosity, polarity and charge effects. It is interesting to note that in the past there are relatively few reported applications of chiral micellar media.\(^5\)\(^6\)

In 1983 Grieco et al. carried out initial investigations using aqueous micellar media for Diels-Alder reactions (which was one of the first organic reactions to be carried out in water in the early 1930’s) and examined the intermolecular Diels-Alder reaction shown in Scheme 1.\(^7\)

![Fig. 2: Formation of miscelles](image)

**Scheme 1**: Diels-Alder reaction

When the reaction was carried out in toluene, moderate yields (of up to 46%) were generated. However in water, an improvement in yields (of up to 85%) were observed. The use of the sodium salt of the diene, accelerated the reaction further. Grieco concluded that the reason behind the acceleration was due to the diene molecule aggregating in a “micellar” manner and solubilising the dienophile.

In the same year, Breslow made studies on the reaction between cyclopentadiene and methacrylate (R=CH\(_3\)) (Scheme 2) in the presence of either sodium dodecyl sulphate (SDS) or cetyltrimethylammonium bromide (CTAB).\(^8\)
Scheme 2: The reaction between Cyclopentadiene and methylacrylate

Breslow concluded that these detergents had little effect compared to when using water on the product ratio N/X (endo/exo). However Saur observed that the use of CTAB did enhance the reaction rate as well as selectivity. Saur’s observations were confirmed by Singh using different substrates where yields of up to 86% were observed at ambient temperatures (3 hours at 30 °C) compared to using the conventional Diels-Alder conditions (where toluene was used as solvent and heated at reflux for 10-12 hours), where yields of up to 50% were observed. In 1998, Diego-Castro and Hailes investigated the effects of aqueous surfactant solutions on Diels-Alder reactions using a series of acrylates ranging from methyl to nonyl. The use of methyl acrylate resulted in the observed selectivities being exactly what Breslow had reported. However when using CTAB, a higher endo/exo ratio was observed. This was attributed to the high concentrations above the CMC at which SDS and CTAB were used (2.4 and 770) in Breslow’s work. This clearly demonstrated that careful selection of the surfactant concentrations can affect product selectivity. Experiments using nonyl acrylate showed virtually no increase in the product yield when using water and surfactant solutions. It was postulated that this was due to the tendency of nonyl acrylate to self-aggregate.

The effects of pH were also investigated using CTAB, where it was observed that both the yields and selectivities were affected which depended on the pH of the solution. The highest yield and N/X ratio were generated at higher and lower acidity. It was rationalized that at low pH, the acrylate is readily protonated forming a mixed micelle.

At high pH, counterion effects were found to influence the aggregate shape or polarize the reacting substrates which could influence the yields and selectivities.

In 2005, Caumul and Hailes synthesised a surfactant derived from the alkaloid cinchonine as catalysts in the reaction between nonyl acrylate and cyclopentadiene.
which was used to successfully enhance the yields of a range of Baylis-Hillman reactions carried out in water.\textsuperscript{12}

This reaction which was first reported in the 1970’s was typically carried out in organic solvents using tertiary amine bases such as DABCO and DBU.\textsuperscript{13}

More recently the reaction was reported to be accelerated in the presence of water as well as using Lewis acid conditions which include the addition of lanthanide triflates with DABCO or the addition of TiCl$_4$.\textsuperscript{14-17} (Scheme 3)

\[
\begin{align*}
\text{R} & \quad \text{H} \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \\
\text{O} & \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \\
\text{CO}_2\text{Me} & \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \\
\text{H}_2\text{O, pH 1} & \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \\
\text{amine} & \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \\
\text{R} & \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \\
\text{CO}_2\text{Me} & \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \\
\end{align*}
\]

\textbf{Scheme 3 : Baylis-Hillman reaction between an aldehyde and methyl acrylate}

In recent years, modified cyclised cinchonine bases have been successfully used by Hatakeyama and co-workers in organic solvents.\textsuperscript{18}

We decided to therefore synthesise a surfactant (+)-cinchonine analogue (1) under basic conditions which would be isolated as the hydrochloride salt and which would be used as a catalyst to investigate how its amphiphilic nature can affect the reaction yields of Baylis-Hillman reactions. (\textbf{Scheme 4(a)} and \textbf{Scheme 4(b)})

\[
\begin{align*}
\text{HOH} & \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \\
\text{N} & \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \\
\text{O} & \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \\
\text{N} & \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \\
\text{H} & \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \\
\text{N} & \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \\
\text{CT} & \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \quad \text{\textbf{\&}} \\
\end{align*}
\]

\textbf{Scheme 4 (a)} : NaH, DMF, CH$_3$(CH$_2$)$_{15}$Br, 50%  \quad \textbf{Scheme 4 (b)} : HCl, dioxane 88%

The use of surfactant (1) as catalyst for the respective Baylis-Hillman reactions were carried out in the absence of DABCO and DBU using acidified water (the first of its kind) since it was envisaged that protonating the acrylate substrate would drive the reaction forward.\textsuperscript{12}

\begin{align*}
\text{Reaction between electron withdrawing aldehyde (2-nitrobenzaldehyde) and methyl acrylate resulted in the highest yield 54\% being generated when using compound (1) as catalyst. This catalyst was found to be just as successful as commercially available DBU using the same conditions. Compound (1) was most efficient under acidic conditions at 0 \degree C. The reactions were also performed using benzaldehyde over a pH range (0 \degree C and 25 \degree C) to confirm the effect of the acidity on the reaction. It was observed that the yield of the reaction increased with decreasing pH.}
\end{align*}

\begin{align*}
\text{Finally, the use of LiCl (lithium chloride) as a salting out agent successfully raised the yields of products under identical conditions.}
\end{align*}

\begin{align*}
\text{Up to now the role of surfactants as a catalyst in aqueous media has been discussed. However the role of surfactants in reducing heavy metal toxicity because they can act as good chelating agents must also be mentioned since apart from its solubilising capabilities, micelles can chelate well with metals within their interior core.}
\end{align*}

\begin{align*}
\text{Heavy metal exposure has become an increasing health concern in the 21st century. These include lead (Pb), mercury (Hg) and copper (Cu). Human exposure to these metals have risen dramatically in the last 50 years as a result of an exponential increase in the use of heavy metals in industrial processes and products.}^5,6 \text{ Today exposure to heavy metals are increasing. For example their presence can be found in dental fillings in the form of mercury amalgam, lead in paints and tap water due to lead piping.}
\end{align*}

\begin{align*}
\text{Studies have confirmed that depending on the levels present, heavy metals can directly affect animal health by damaging mental and neurological functions and altering numerous metabolic body processes.}
\end{align*}

\begin{align*}
\text{Not only can this affect the health of living systems but the potential risk of metal toxicity is a major concern for terrestrial and aquatic ecosystems. Soil exposures to some metals induces significant toxicity to plants, causing a decrease in the number of plant growth.}^5,6
\end{align*}

\begin{align*}
\text{One of the ways of treating heavy metal pollution is by using chelating agents. However limited publications have shown the role of surfactants}
\end{align*}
in the chelation of metals. Despite this, reports have indicated that anionic surfactants such as sodium dodecyl sulphate, SDS in the presence of anionic ligands can extract specific toxic heavy metals from contaminated soils and from the sea. Presence of increased levels of heavy metals in the sea can occur as a result of oil leakage from ship vessels as well as dumping of industrial waste which can greatly affect aquatic systems. Selective sequential extraction is useful in identifying which fraction can be targeted by the surfactant-ligand agent. It has been observed that increasing the amount of ligands containing iodide anions (I⁻) coordinated with SDS can specifically remove higher levels of Cd but not Cu, Zn and Pb.

It was found that in the case of anionic micelles, the extracting ligand is preferentially located close to the surface of the surfactant aggregate, where it is held by hydrophobic interactions. In this position, it is accessible to the metal ion and so is readily coordinated.

An efficient technique has been reported which helps retard the movement or enhance the removal of contaminants which are present in soil and groundwater and contains hydrocarbons. This technique involves the use of a cationic surfactant (CTAB), coupled with electrokinetic treatment.

It is interesting to note that the contaminant hydrocarbons include organic solutions which are immiscible in water and are difficult to remove. This can be in the form of NAPL (Non-Aqueous Phase Liquids) which are found in contaminated soil and groundwater. Hence the use of surfactants can help clean up the NAPL by reducing the capillary pressure that traps them between the aquitard region of the sea or river bed. Surfactants can then be used to coordinate and remove these metals due to the amphiphilic nature of these surfactants.

More recently Larpent et al. designed an efficient surfactant capable of recognizing a range of metals known as Metal Chelating Thermo Responsive Surfactants (MCTS) which was synthesized with a di-block molecular structure by tethering non ionic alkylpolyoxyethylene surfactants with uranyl chelating groups. (Fig. 4)

**Fig. 4 : MCTS Chelation with metal**

The metal binding affinity of the surfactant was dependent on temperature. It was observed that the uranyl ligands shift equilibrium towards a complex having a bidentate metal coordination. MCTS was found to behave as a nonionic surfactant and exhibit a reversible temperature-dependent behaviour with clouding and phase separation when a micellar solution is heated above its cloud point (CP). The successfully trapped transition metal was extracted by cloud point separation.

In summary, attempts have been made to not make this mini review too exhaustive but to outline the importance of surfactants to the environment. We will now show some of our selected preliminary studies in this area.

**AIMS AND OBJECTIVES**

Our aims and objectives are two-fold:

1. First aim is to primarily use water as a reaction solvent with a view to investigate the efficacy of such reactions and monitor the influence of micellar catalysis.

Since previous studies have used â-amino alcohols as catalyst for a range of organic reactions showing good yields and selectivities, our aim was to therefore synthesise surfactants using the â-amino alcohol backbone made from amino acids. Phenylalanine was selected due to its aromatic moiety which can induce ð-ð interactions between the aromatic rings and help enhance reaction selectivity and yield. A range of phenylalanine surfactant intermediates were therefore synthesized and tested for their catalytic activity. This was done to investigate which functional group is responsible for reaction yield and/or selectivity enhancement.
These intermediates were tested on a specific Michael addition reaction in water. Interestingly limited work on the use of water as a solvent for Michael-type reactions have been reported. Those that have been reported such as the reaction between nitromethane and buten-2-one have indicated a rate acceleration compared to similar conditions in organic media such as dichloromethane, toluene and tetrahydrofuran. It was postulated that due to hydrophobic effects the reacting substrates aggregate in solution to reduce their hydrophobic interactions with water molecules.

Our investigations have therefore focused on the reaction between diethyl malonate and cyclopentenone. This paper will present some of our initial work.

2. Second aim is to design chelating agents to investigate their binding effects with metal ions, with a view to find solutions to the problem of metal toxicity and pollution. In this context, the complexation of a-amino alcohols (ethanolamine and phenylalaninol) with copper in aqueous solutions were examined using spectro-photometric techniques. The stoichiometric ratio between metal and ligand were determined using activity and conductivity measurements.

Copper was chosen specifically in order to study its interactions with ligands as the accumulation of copper in natural systems is becoming a real danger. In aquatic ecosystems, copper contaminates the marine life. While in agricultural land, it has been reported to cause a decrease in the number of vegetation growth.

MATERIAL AND METHODS

$^1$H NMR and $^{13}$C NMR analysis were carried out in 5 mm outer diameter tubes in CDCl$_3$ at room temperature using a FT Brucker 250 MHZ spectrometer. The chemical shift ($\delta$) of each peak was assigned relative to tetramethylsilane (TMS). Infrared spectra (IR) were recorded on an Avaral 320 FTIR spectrometer in the range of 4000 to 500 cm$^{-1}$. Chromatography “flash column” was performed over silica gel (70-230 mesh). Thin layer chromatography (TLC) was performed on a glass backed or on plates pre-coated with silica. Visualization was achieved by exposure to an iodine atmosphere.

The chemicals and reagents were of analytical grade and were purchased from Sigma-Aldrich Co. Ltd and Acros-Fisher Scientific, UK. All the chemicals were purified before use. THF was freshly distilled and dried using molecular sieves (4Å) prior to use. All reagents were distilled prior to use in column chromatography. All air and moisture sensitive reactions were carried out under an inert nitrogen atmosphere.

Optical rotation measurements were determined using an “optical activity polarimeter”. The substance to be analysed was dissolved in a solvent at a known concentration (g/100ml) and placed in an analysis tubing of a known length (1 dm = 10cm). The rotation observed is denoted with the Greek letter, $\alpha$. The specific rotation values [$\alpha$] were measured in degrees and were determined using the equation below:

$$[\alpha]_D = \frac{100 \ \alpha}{l \ c}$$

where $l$ is the sample path length in decimeters (1 dm = 10cm) and $c$ is the concentration of the substance in grams per 100ml of solution.

$(L)$-Phenylalanine Methyl ester

$(L)$-Phenylalanine (10.01g, 60.6mmol) was dissolved in methanol (AR grade-99%), (200ml) at -5°C. Thionyl chloride (10.1ml, 138mmol, 2.5 eq) was added dropwise until a clear solution was obtained. The pale yellow solution was left to stir for 18 hours at room temperature. Excess methanol was evaporated in vacuo to give the crude product.

The crude solid was purified via recrystallisation with ethyl acetate to yield the title compound as pale yellow crystals (11.50 g, 88%); m.p.155-156°C; $[\alpha]_D = +38^\circ$ (c=3 in ethanol at 24°C); $n_{d}$ (max/cm$^{-1}$) 3432, 1744, 1398, 741; $\delta_H$ (250 MHz; D$_2$O) 3.87 (3H, s, OCH$_3$), 3.26 (1H, s, OCH$_3$), 3.26 (1H, dd, $J = 10.5$ Hz), 3.29 (1H, dd, $J = 10.5$ Hz), 4.46 (1H, t, $J = 15.7$ Hz), 7.40 (2H, d, $J = 8.5$ Hz), 7.33 (2H, t, $J = 8.5$ Hz), 7.08 (H, t, $J = 6.5$ Hz); $\delta_C$ (75 MHz; D$_2$O) 36.3, 54.3, 54.8, 128.8, 130.1, 134, 170.7.

CHNS for C$_{10}$H$_{14}$O$_2$NCl

Theoretical % composition:

C, 55.68%; H, 6.5%; N, 6.497%
Experimental result:

C, 55.20%; H, 5.755%; N, 6.541%

(L)-Phenylalaninol

A 250ml two-neck round-bottom flask was equipped with a magnetic stirrer bar, a reflux condenser and a dropping funnel. The flask was charged with sodium borohydride (1.14g, 30.3mmol) and 40ml THF (freshly distilled and predried over sodium). L-Phenylalanine (2.01g, 12.11 mmol) was added in small portions and the flask was cooled to 0°C in an ice bath. The reaction was carried out under an inert nitrogen atmosphere. A solution of iodine (2.9g, 27.35mmol dissolved in 20ml THF) was poured into the dropping funnel and added dropwise slowly over 30 min resulting in vigorous evolution of hydrogen. After addition of iodine, the flask 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 4h and extracted with 4× 25 ml of DCM. The organic extracts were dried over anhydrous sodium sulphate, filtered and concentrated in vacuo to give a solid (1.270g, 8.41mmol). The crude solid was recrystallised from toluene (10ml) to yield the title compound as white crystals (1.2 g, 59.7%): m.p:89-90 °C; [\(\alpha\)]D = -22.8° (c=1.2, 1M HCl); \(n_{\text{max}}/\text{cm}^{-1}\) 3438, 3355, 2938, 1633, 1579, 1454, 753; \(d_\ell\) (250 MHz; CDCl3) (2H, t, \(J\) 6.0 Hz), 2.81 (1H, m), 2.83 (1H, m), 3.10 (1H, m), 3.63 (1H, m), 3.67 (1H, m), 7.17 (1H, t, \(J\) 6.0 Hz), 7.20 ( 2H, d, \(J\) 6.8 Hz), 7.26 (2H, t, \(J\) 7.0 Hz); \(d_c\) (75 MHz; D2O) 36.3, 54.3, 54.8, 128.8, 130, 130.1, 134, 170.7.

CHNS for C9H13ON

Theoretical % composition

C, 71.5%; H, 8.6%; N, 9.26%

Experimental result

C, 70.92%; H, 5.751%; N, 9.239%

Propanoyl Chloride

To a round bottom flask containing propionic acid (20 ml, 265.24mmol), thionyl chloride (20ml, 268mmol) was distilled prior to use and was added dropwise at room temperature. After evolution of fumes had ceased, the reaction mixture was refluxed for 3 hours. The resulting solution was then distilled to yield the title compound as a colourless solution (6.0g, 70%). m.p:80-81 °C; \(n_{\text{max}}/\text{cm}^{-1}\) 2990, 2945, 1791, 1408; \(d_\ell\) (250 MHz; CDCl3) (2H, t, \(J\) 7.0 Hz), 1.38 (3H, t, \(J\) 7.3 Hz), 3.08 (2H, q, \(J\) 7. 5 Hz); \(d_c\) (75 MHz; CDCl3) 9.4, 40.8, 174.6.

N-Propanoyl, (L)-Phenylalanine

Methyl ester

L-Phenylalanine methyl ester hydrochloride (1.01g, 4.55 mmol) was dissolved in THF (75 ml) at room temperature. Triethylamine (1.0 ml, 7.1 mmol) was added to the mixture and left to stir for one hour. Propanoyl chloride (0.4ml, 4.4mmol) was added dropwise over a period of 15 minutes. When the addition was completed, a catalytic amount of DMAP (0.35g, 2.86 mmol) was added to the mixture and the reaction was heated to reflux at 70°C 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 50 ml) and the combined organic extracts were washed with sodium hydrogen carbonate (5%, 50 ml). The organic layer was dried over anhydrous magnesium sulphate and the solvent was removed in vacuo and purified via flash chromatography (petroleum ether: ethyl acetate, 1:1) to yield the title compound as a pale yellow oil (0.75g, 77%). \(n_{\text{max}}/\text{cm}^{-1}\) (KBr plate): 3272, 2972, 1742, 1649, 1536, 745; \(d_\ell\) (250 MHz; CDCl3): 1.08 (3H, t, \(J\) 7.5 Hz), 2.16 (1H, dd, \(J\) 6.25), 2.25 (1H, dd, \(J\) 4.7), 3.12 (2H, q, \(J\) 8.0 Hz), 3.72 (3H, s), 4.90 (1H, m); 6.07 (1H, br), 7.09 (2H, m), 7.28 (3H, m); \(d_c\) (75 MHz; CDCl3) 12.5, 32.3, 40.7, 55.1, 55.9, 129.9, 131.4, 132.1, 138.9, 175.2, 176.4.

Preparation of Bis(ethoxycarbonylmethyl)cyclopentanone

Diethyl malonate (0.38 ml, 2.50 mmol), cyclopentenone (0.25 ml, 2.50 mmol) and potassium carbonate (0.11 g, 1.09 mmol) were stirred in the presence of the chosen catalyst (0.018M, 0.45, mmol) in distilled water (25 ml) and heated at reflux for 48 hours. The reaction mixture was subsequently cooled to room
temperature and extracted with ethyl acetate (3 × 25 ml). The combined organic extracts were dried over sodium sulfate and the solvent removed in vacuo. The crude product was purified by flash chromatography (hexane: ethyl acetate 1:1) to afford the desired product as a colourless oil (0.278 g, 45.9%).

\[ n_{\text{max}}/\text{cm}^{-1} (\text{nujol}) : 1730, 2983, 1372, 1465; d_1 (250 MHz; \text{CDCl}_3) 1.26 (6H, m), 1.60-2.00 (2H, m), 2.24-2.40 (4H, m), 2.85 (1H, m), 3.35 (1H, d, J 6.2 Hz), 4.20 (4H, m, 8-H); d_2 (75 MHz; \text{CDCl}_3) 13.3, 26.5, 35.7, 37.4, and 42.2, 55.6, 60.5 (2 x C), 167.2 and 167.3 (2 x C).

**Stoichiometric Determination of Copper Complexing with Ethanolamine by UV Spectroscopy**

Copper sulphate (25 cm$^3$, 0.6M) was diluted in water. Titration of the copper sulphate solution (10ìl) with ethanolamine (3cm$^3$, 0.03ml) was performed and the absorbance measured with water being used as the reference.

**Stoichiometric Determination of Copper Complexing with Ethanolamine by UV spectroscopy (using Borax buffer)**

The same procedure as described above was carried out but using a buffer of disodium tetraborate decahydrate (0.05M) in hydrochloric acid.

**Stoichiometric Determination of Copper Complexing with Ethanolamine by UV Spectroscopy (using potassium nitrate buffer)**

The same procedure as described above was carried out but using a buffer of potassium nitrate (0.05M) for copper sulphate.

**Stoichiometric Determination of Copper Complexing with Ethanolamine by conductivity measurements**

Ethanolamine (40 cm$^3$, 0.01M) was placed in a burette. Copper sulphate (50 cm$^3$, 0.0025M) was placed in a conical flask containing a platinum electrode. The solution was stirred to ensure uniform distribution of the mixture. A titration of the solutions were performed. The activity and conductivity measurements were recorded after each 0.5 cm$^3$ addition of ethanolamine using a calibrated ion analyzer. A calibration curve was obtained throughout the titration.

**Stoichiometric Determination of Copper Complexing with Phenylalaninol by conductivity measurements**

Phenylalaninol (40 cm$^3$, 0.01M) was placed in a burette. Copper sulphate (50 cm$^3$, 0.0025M) was placed in a conical flask containing a platinum electrode. The solution was stirred to ensure uniform distribution of the mixture. A titration of the solutions were performed. The activity and conductivity measurements were recorded after each 0.5 cm$^3$ addition of ethanolamine using a calibrated ion analyzer. A calibration curve was obtained throughout the titration.

**RESULTS AND DISCUSSION**

The synthesis of the surfactant intermediates (2) and (3) derived from L-Phenylalanine are outlined in Scheme 5.

Propanoic acid was used to make one of the surfactant chains. The acid was reacted with thionyl chloride and heated at reflux for 3 hours to give propanoyl chloride in 85% yield.

Phenylalanine was selected as the potential surfactant head group since the aromatic ring can induce δ-δ interactions between each other which can help enhance reaction selectivity and yield. Phenylalanine was esterified by reacting it with thionyl chloride in excess methanol to give the methyl ester as the hydrochloride salt in 90% yield. The conversion was confirmed by $^1$H NMR analysis showing the presence of the esterified OCH$_3$ peak at d 3.72.

The resulting ester was reacted with propanoyl chloride using a slight excess of triethylamine base to deprotonate the quaternised molecule and generate the free amine. Hence compound (3) was generated in 77% with the help of a catalytic amount of DMAP. Scheme 6.
Table 1: Results from Michael addition using varying surfactants or surfactants analogues

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>% Yield</th>
<th>[α]D</th>
<th>% e.e</th>
<th>Isomer</th>
</tr>
</thead>
<tbody>
<tr>
<td>-</td>
<td>5</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>CTAB</td>
<td>43</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>SDS</td>
<td>22</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>L-Phenylalanine</td>
<td>45.5</td>
<td>+13.5°</td>
<td>39</td>
<td>R</td>
</tr>
<tr>
<td>L-Phenylalanine methyl ester</td>
<td>5</td>
<td>+15.9°</td>
<td>46</td>
<td>R</td>
</tr>
<tr>
<td>N-Propanoyl</td>
<td>34</td>
<td>+14.6°</td>
<td>42</td>
<td>R</td>
</tr>
<tr>
<td>L-phenylalanine methyl ester</td>
<td>43</td>
<td>-10.5°</td>
<td>30</td>
<td>S</td>
</tr>
</tbody>
</table>

The synthesized analogues were subsequently tested for their catalytic ability together with some selected commercially available surfactants-CTAB and SDS on the Michael addition reaction between diethylmalonate and cyclopentenone. The results were compared when no catalyst was used.

The reactions were performed at a surfactant concentration of 0.018M. When using commercially available CTAB and SDS as catalyst, yield enhancement was clearly observed compared to when using no catalyst where very low yields were obtained (Table 1).
CTAB generated a better yield of product compared to SDS. In both these cases, this indicated that these surfactants were able to successfully solubilise the reacting substrates into the micellar core enhancing the catalytic activity of these materials and allow the reaction to take place in water.\textsuperscript{1, 11, 12}

When using the phenylalanine analogues as catalyst, esterifying the carboxylic group resulted in a rise in reaction selectivity to the \textit{R}-isomer but a drastic drop in yield. Addition of the propanoyl chain showed an increase in reaction yield and a marginal decrease in the reaction selectivity. However a good enantiomeric excess of 42\% was observed which was selective to the \textit{R}-isomer.

A predicted transition state was drawn to rationalize the preferential selectivity to the \textit{R}-isomer.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{fig5.png}
\caption{Aromatic ring}
\end{figure}

It was postulated that the cyclopentenone molecule sits above the aromatic ring of the phenylalanine analogue as indicated in Fig. 5, which will block the bottom face where the diethyl malonate can attack. Hence attack would take place at the top face. This is due to the p-p stacking between the two rings (cyclopentenone and the catalyst) and potential Van Der Waals interaction between the propanoyl chain to hold the substrate in place. Attack would take place away from the aliphatic chains which could cause steric hindrance. Hence the attack from the top face would preferentially generate the \textit{R}-isomer with high selectivity.

Interestingly, when reducing phenylalanine methyl ester to phenylalaninol, an increase in reaction yield was observed but more importantly a reversal in the enantioselectivity was noted. This clearly indicated that the aliphatic OH has an effect on reaction selectivity.

Finally, we performed some analytical studies on our catalytic \textit{b}-amino acid analogues. The complexation of \textit{\textalpha{}}-amino alcohols, ethanolamine (which was chosen because it is the simplest \textit{b}-amino alcohol) and phenylalaninol with copper in aqueous solutions were examined using spectrophotometric methods.\textsuperscript{23}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{fig6.png}
\caption{Phenylalaninol with Copper}
\end{figure}
In the first attempt to study the interaction of ethanolamine with copper ions in a buffer solution, a titration was performed varying ligand concentration. Since a precipitation reaction had taken place when using Borax, a solution of KNO₃ was used as buffer instead. Measurements were recorded using UV-vis spectrophotometry indicating that a level of coordination was taking place between 650 nm and 800 nm as shown from the observed maxima. However the correct stoichiometry could not be determined, and so activity measurements were carried out. (Fig. 7)

After titration of copper sulphate solutions with ethanolamine, activity and conductivity measurements (Fig. 6 and Fig. 11) indicated that in both cases (L)-Phenylalaninol and ethanolamine gave a stoichiometry ratio of 1:2. Table 2 and Table 3 between metal and ligand showing that they act as bidentate ligands coordinating to copper ions. The coordination of Cu²⁺ ions was predicted to be a coordinated square planer as shown in Fig. 6 and Fig. 11.

**Table 2 : Stoichiometry of copper complexing with ethanolamine**

<table>
<thead>
<tr>
<th></th>
<th>Copper</th>
<th>Ethanolamine</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of moles</td>
<td>1.25 x 10⁻⁴</td>
<td>2.3 x 10⁻⁴</td>
</tr>
<tr>
<td>Ratio</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

**Table 3 : Stoichiometry of copper complexing with Phenylalaninol**

<table>
<thead>
<tr>
<th></th>
<th>Copper</th>
<th>Phenylalaninol</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of moles</td>
<td>1.25 x 10⁻⁴</td>
<td>2.12 x 10⁻⁴</td>
</tr>
<tr>
<td>Ratio</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

![Scan Graph](image)

**Fig. 7 : UV absorbance of copper ethanolamine complex**
**Activity of copper -ethanolamine complex**

\[ y = -2.8106x + 248.67 \]
\[ y = -299.41x + 5902.4 \]

![Graph showing activity of ions for ethanolamine](image1)

**Fig. 8**: Graph showing activity of ions for ethanolamine

**Conductivity of Copper-Ethanolamine Complex**

\[ y = -6.549x + 236.7 \]
\[ y = -2.307x + 280.0 \]
\[ y = -9.3091x + 306 \]

![Graph showing the conductivity of ions for ethanolamine](image2)

**Fig. 9**: Graph showing the conductivity of ions for ethanolamine

**Activity of phenylalaninol**

\[ y = -431.11x + 9740.1 \]
\[ y = -13.462x + 881.45 \]

![Graph showing the activity of phenylalaninol](image3)

**Fig. 10**: Graph showing the activity of phenylalaninol
CONCLUSION

Our preliminary results have confirmed that the use of surfactants in water enhances the reaction yields as indicated by the use of CTAB and SDS on our Michael reactions. We have attributed this to solubilisation and preorientation effects.

We have also shown that our surfactant analogues derived from phenylalanine has given us reasonable yields (up to 45%) and good selectivity (up to 46%). It was observed that the reaction yields and selectivity was due to the different functional groups attached and that the presence of aliphatic chains generates good selectivity.

Finally we have shown successful coordination of our β-amino alcohol analogues which will form the basis of making a range of surfactants used in metal chelation.

Hence future work will focus on completing our synthesis of surfactants derived from phenylalanine to be used in catalytic and complexation studies.

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