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# Physico-chemical studies of the complexes of Hippuric acid with Cu(II), Ni(II), Zn(II), and Pb(II) ions in ethanol-water mixed solvent system

**Nabil Bader*, Aya Elmajbry, Zainab Al borki, Aziza Ahmida, and Abdalla Geath**

*Department of Chemistry, Faculty of Science, University of Benghazi, Benghazi, Libya*

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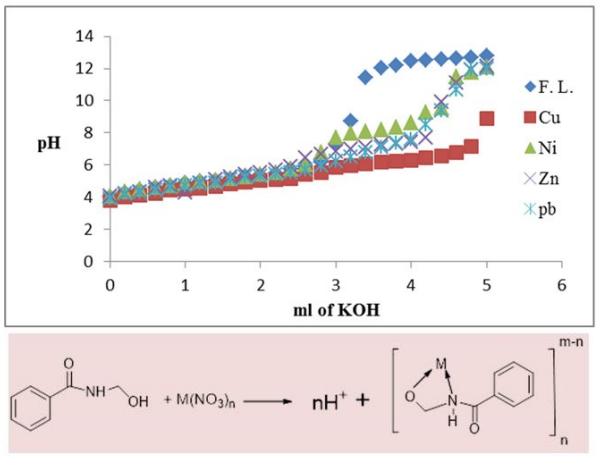
## GRAPHICAL ABSTRACT




## KEYWORDS

Hippuric acid
Metal complexes
Stability constant
Mixed solvent system

## ABSTRACT

Potentiometric titrations have been used to calculate the dissociation constants of Hippuric acid and its stability constants with Cu(II), Ni(II), Zn(II), and Pb(II) ions in ethanol-water mixed solvent system at different temperatures, and constant ionic strength of 0.1M solution sodium nitrate. The order of the stability constants of metal complexes at 298 K with respect to ligand was found to be Cu(II) > Pb(II) > Zn(II) > Ni(II). Effect of temperature on stability of hippuric acid complexes with Cu(II) and Pb(II) has been studied in order to calculate the Gibb`s free energy and enthalpy of the complex formation reaction, the results showed that coordination process is spontanous and exothermic. Effect of solvent ratio has been studied only for Cu(II) complex and the dissociation of hippuric acid at given added different ratios decreases on the following order 75% > 50%.

* Corresponding author: Bader, Nabil
Tel number: +218926622741, Fax number: +218926622741, E-mail: nabil.bader@uob.edu.ly
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## 1. Introduction

Hippuric acid, (N-benzoyl glycine, benzoyl amine acetic acid) is one of the important amino acids, which synthesised in the liver as a metabolite of benzoic acid urinary excretion [1].

Hippuric acid is one of the amino acids, present in the urine of herbivorous animals, also in small amount of human urine. Recently Subramanian et al. has isolated hippuric acid from buffalo urine and evaluated its antioxidant activities [2]. Hippuric acid is a mono carboxylic acid with three type of donor site the nitrogen and oxygen atom of the carboxylic group. The interest in hippuric acid is potentially capable of forming coordinate bonds with many metal ions through a carboxylic oxygen atom acting as a mono dentate ligand or bound through the carboxylic oxygen atom and nitrogen atom and acting as a bidentate ligand[3-5] or through the NH group [6]. Several binary and ternary metal complexes of hippuric acid and its derivatives have been reported [7, 8]. Hippuric acid can react with metal ions such as Cd(II), Hg(II), Zn(II), Mn(II), Co(II), Ni(II), Ag(I) to form coordinate bonds through carboxylic oxygen atom [9-13].

Many researches have measured the stability constant of amino acid complexes by Potentiometric technique such as L- Asparagine and L- Glutamine with $La^{3+}$. $Ce^{3+}$, $Pr^{3+}$, Nd $^{3+}$, and $Y^{3+}$ [14], also Tyrosine ,tryptophan and glycine derivatives with Cu(II) and also the stability constant of $Co^{2+}$, $Ni^{2+}$, and $Zn^{2+}$ complexes with glycyl amine methyl phosphinic acid have been reported [15-18]. Yahya et al. [19] have reported the stability constant of some metal ions with 4-amino hippuric acid in aqueous solution. This study is focusing on metal complexes of Ni(II), Cu(II), Zn(II), and Pb(II) with hippuric acid in mixed solvent system (Ethanol-Water) at different conditions.

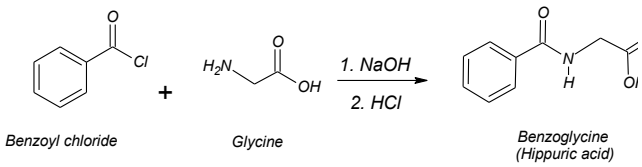
## Experimental

### *Reagents and solutions.*

All materials and reagents used in the work were of analytical grade or the highest Available purity.

### *Preparation of hippuric acid*

Hippuric acid was prepared according to following reaction [20] as shown in Scheme 1.




**Scheme 1.** Synthesis of hippuric acid

An appropriate amount of the prepared Hippuric acid was dissolved in absolute ethanol and distilled water to give a solution of 0.01M concentration. A 0.1M solution of potassium hydroxide was prepared by dissolving the amount of KOH in 75% (v/v) ethanol-water.

0.10M solutions of the divalent metal ions were prepared by dissolving the appropriate Weight of the metal nitrate salt in total volume of 250 mL distilled water.

## Results and Discussion

Potentiometric titration curves of the free ligand and mixtures of (metal ion–ligand) with alkali solution are shown in Fig. 1 which indicates clearly the formation of complexes which represent the equilibrium in the solution.

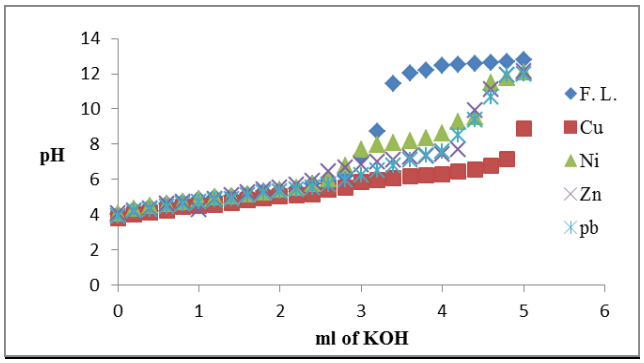
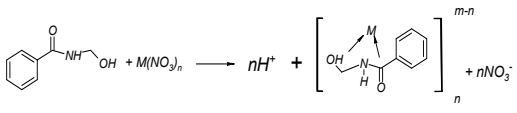



**Fig. 1.** Titration curve of hippuric acid and its metal complexes in 75% ethanol-water mixed solvent at 298K.

The results shows that as pH value of the ligand solution decreases when a neutral salt solution of metal ions were added is clear indication of complex formation, the bonding may occur through oxygen atom of the carboxylate ion and the lone pair electrons of the amido nitrogen atom, as seen in equation 1.




(eq.1)

The large decrease in pH for the metal titration curves relative to ligand titration curves in Figure1 in pHs indicate formation of strong metal complexes.

The titration curves of the Ni(II), Cu(II) and Zn(II)–L complexes are lowered from that of the (HL) curve, which indicates formation of Ni(II),Cu(II),Zn (II) and pb(II)–L complexes by displacement of protons.

The metal ligand stability constants were calculated by Irving and Rossotti equation 2 [21].

$$Log[\bar{n}/(1-\bar{n})] = \log K - pL \qquad \text{(eq.2)}$$

It has been observed that $\bar{n}$ values less or equal to 2 which indicates formation of 1:1and 1:2 complexes.

The dissociation constant and the stability constants of L1 with Ni(II), Cu(II), Zn (II) and Pb(II) in 75% (v/v) ethanol-water have been studied at 25 °C (298 K) and Cu and Pb at three different temperatures 288, 298, 308 K at constant 1.0 M ionic strength and the data are listed in Table 1. The results in Table 2 shows that the dissociation constant values increase with increase in temperature and this indicates that, the acidity of the ligand increases with increasing of temperature. Also the stability constant log K for the complexes decrease with increasing temperature and complexation process is more favourable at low temperatures.

**Table 1.** stability constants of metal complexes at 0.1M ionic strength in 75%(v/v) ethanol-water mixture

| Temp K | $pK_a$ | Log K | | | |
|---|---|---|---|---|---|
| | | Ni(II) | Cu(II) | Zn (II) | Pb(II) |
| 288 | 4.81 | | 3.31 | | 3.08 |
| 298 | 4.46 | 2.27 | 3.18 | 2.06 | 3.01 |
| 308 | 4.27 | | 2.93 | | 2.09 |

From the measurement the order of the stability constants of metal complexes at 298 K with respect to ligand was found to be Cu(II) > Pb(II) > Zn(II) > Ni(II), which is also in agreement with Irving and Williams order Fe(III) > Cu(II) > Zn(II) > Ni(II) > Co(II) > Cd(II) [22].

### *Gibb`s free energy*

Gibb`s free energy for complex formation has been calculated for each temperature in order to evaluate the spontaniety of the reaction. The values of ΔG of the formed complexes have been calculated using the following formula;

$$\Delta G = -2.303RT \log K \quad \text{(eq. 3)}$$

Were T is the temperature in kelvin (K) and R=8.314J/k.mol. The values of ΔG for Cu and Pb complexes at different temperatures are listed in Table 2.

**Table 2**. Gibb`s free energy for Cu and Pb complexes in 75% Ethanol-water solvent

| T (K) | Cu, ΔG (KJ/mol) | Pb, ΔG (KJ/mol) |
|---|---|---|
| 288 | -2.87 | -2.69 |
| 298 | -2.86 | -2.73 |
| 308 | -2.75 | -1.89 |

All values of ΔG for complexation are negative, indicating the spontaneity of the coordination process. The complex formation with Cu is more sponteous than Pb complexes.

### *Effect of Ethanol-water ratio*

Effect of Ethanol-water ratios on the dissociation of the organic ligand and its chelate compounds.

The titration curves of the ligand (Hippuric acid) in presence and absence of Cu(II) ion in 50% and 75% (v/v) ethanol-water solvent at 25 °C and 0.1M KNO3 ionic strength are shown in Fig. 2.

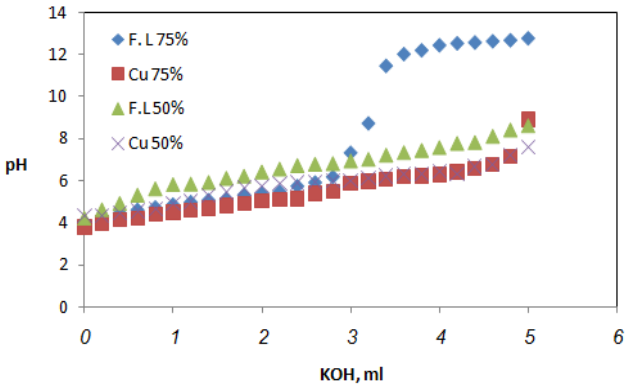



**Fig. 2**. Titration curve of Hippuric acid and its copper complexes in 75% and 50% ethanol-water mixed solvent at 25 °C.

The values of acid Dissociation constant pKa of hippuric acid and stability constants for Cu(II) complexes in different ratios of ethanol – water at 25 °C and 0.1M ionic strength are shown in Table 3.

The results showed that the complexation is affected by the composition of the mixed solvents. The dissociation of hippuric acid at given added different ratios decreases on the following order 75% > 50%.

**Table 3**. Effect of solvent ratio

| Ethanol–water Ratio | $pK_a$ | Log K Cu(II) |
|---|---|---|
| 50 % | 5.16 | 3.62 |
| 75 % | 4.46 | 3.18 |

## Conclusion

The results of the potentiometric studies on hippuric acid and its complexes with Cu(II), Ni(II), Zn(II), and Pb(II) in 75% v/v ethanol-water medium using pH titration technique indicates that the order of stability is Cu(II) > Pb(II) > Zn(II) > Ni(II). The negative free energy change in case of Cu and Pb complexes indicates the spontaneity of the complex formation process. The complexation of hippuric acid with Cu(II) ion is affected with ethanol-water ratio.

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