Thermochemical data on adducts of copper chloride with the amino acids lysine and glycine

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Abstract

Adducts of the general formula $CuCl_2 \cdot n$lys ($n = 1, 2, 4$; lys = lysine) and $CuCl_2 \cdot n$gly ($n = 2, 4$; gly = glycine) were prepared by reacting the ligands with $CuCl_2$ in solid state. The adducts were characterized by elemental analysis, infrared spectroscopy and thermogravimetry. In all cases, the cation is coordinated to the amino acids via amino and carbonyl groups. The standard molar enthalpy of reaction in the condensed phase: $CuCl_2(c) + xL(c) = CuCl_2 \cdot xL(c)$; $\Delta_r H_m^\circ$, was determined in aqueous solution by the ampoule-breaking method. From $\Delta_r H_m^\circ$ and the standard enthalpies of formation of copper chloride and the ligands, the standard molar enthalpies of formation of the adducts were calculated. The decomposition, lattice and reaction enthalpies and the mean ligand–metal bond enthalpy were also determined through appropriate thermodynamic cycles.
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1. Introduction

Proteins constitute one of the most common classes of substances present in biological systems. Their chemical properties are of fundamental importance to understand cell mechanisms as membrane transport, secretion or digestion. Twenty naturally occurring amino acids, joined together by peptide bonds, form the common protein structures. The understanding of the complexity of protein action in biological systems, the interaction of forming blocks between the set of amino acids and the species in living organisms is of essential interest. Amino acids have two principal potentially active sites in the formation of the peptide bonds, the acid carboxyl group and the basic amino group. However, natural amino acids can also include other functional groups in the chain during the peptide bond formation with sites for chemical activity in the peptide chains [1].

When cations are incorporated in proteins, these molecules manifest catalytic activity over countless reactions involving biomolecules, such as enzymes, whose action depends on metal complexation. This feature calls attention to the importance in following the interaction between cations with amino acids [2–4] or some peptides [5,6].

In attempting to explore some aspects connected to this interaction, a thermochemical study on adduct conduct to a significant contribution to the understanding of the energetics of the metal–ligand bond.

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Adducts of cadmium–glycine [7,8], copper–arginine and copper–alanine [9] have been recently published.

The present study is focused on copper, a metal of particular importance in cell function, due to its action in cellular nutrient absorption, transport, tissue distribution, excretion and toxicological activity [1]. The thermochemistry study is based on adducts: $CuCl_2 \cdot n$lys ($n = 1$, 2 and 4) and $CuCl_2 \cdot n$gly ($n = 2$ and 4). A set of thermochemical parameters was obtained through isothermic calorimetry, from which metal–amino bond enthalpy has been calculated.

2. Experimental

Reagent grade $CuCl_2 \cdot 2H_2O$, lysine and glycine were used. Anhydrous halide can be dehydrated from $CuCl_2 \cdot 2H_2O$ [9,10], which original method consisted in heating this compound in air at 110 °C for 2h [11]. However, in the present case, dehydration was carried out under reduced pressure at 60 °C for 2 h. A brownish powder was obtained, which was kept over phosphorus pentoxide and handled in dry nitrogen atmosphere.

The adducts were prepared in a dry-box under a dry nitrogen atmosphere. In a typical synthetic procedure the desired stoichiometry of the reactants was mechanically induced by grinding the solids in a mortar for 1 h. In each case, the end of any reaction was checked through absence of free amino bands in the infrared spectrum. The synthesized adducts were dried under vacuum at 50 °C for 8 h, before storage.

All adducts were characterized by means of a series of techniques [12]. Carbon, nitrogen and hydrogen contents were determined using a Perkin-Elmer microelemental analyzer. IR spectra were recorded on a FTIR Bomem MB series apparatus in the range 4000–400 cm^{-1}, with a resolution of 4 cm^{-1}. The spectra were obtained from powders in KBr discs. Thermogravimetric curves were obtained in a Shimadzu TGA 50 apparatus in an argon atmosphere with a heating rate of 1.67×10^{-1} K s^{-1}.

All calorimetric measurements were performed with a LKB 2250 isothermal instrument by using the ampoule-breaking procedure [13,14]. All measurements were obtained at 298.15 ± 0.02 K, using a 0.10 dm^3 reaction vessel charged with distilled water, which was used as calorimetric solvent. For

each enthalpic determination, at least four individual ampoules were broken and the complete thermal effects were recorded over 300 s. This period was enough to bring the baseline to the steady-state equilibrium condition. Ampoules containing masses varying from 5 to 100 mg of copper chloride, glycine, lysine and the respective adducts were prepared under anhydrous conditions in a dry-box under nitrogen atmosphere. Uncertainty intervals associated with the variation of the enthalpies of solution are quoted as twice the standard deviation of the mean.

3. Results and discussion

All prepared adducts appeared as blue powders. The elemental carbon, nitrogen and hydrogen analyses are in acceptable agreement with the proposed formula established for these adducts, as shown in Table 1.

The main infrared bands affected by cation coordination are those related to the carboxyl groups of the amino acid molecules for the five synthesized compounds, as shown in Table 2. As can be observed, all

Table 1
Percentages of experimental (exp) and calculated (calc) values for elemental analysis of carbon (C), nitrogen (N) and hydrogen (H) for copper chloride adducts with lysine and glycine

Adduct	C (%)		N (%)		H (%)	
	Exp	Calc	Exp	Calc	Exp	Calc
$CuCl_2 \cdot$lys	25.9	25.67	9.5	9.98	5.1	4.99
$CuCl_2 \cdot$2lys	33.5	33.76	12.6	13.13	6.1	6.56
$CuCl_2 \cdot$4lys	39.1	40.08	14.9	15.59	7.1	7.79
$CuCl_2 \cdot$2gly	17.0	16.87	10.1	9.84	3.7	3.51
$CuCl_2 \cdot$4gly	21.5	22.09	12.0	12.89	4.7	4.60

Table 2
Infrared bands (cm^{-1}) for lysine, glycine and their respective adducts with copper(II) chloride

Compound	$v_{as}(COO^-)$	$v_{as}(N–H)$	$v_s(COO^-)$	$v_s(N–H)$
Lysine	1578	2930	1406	2845
$CuCl_2 \cdot$lys	1623	3255	1375	3150
$CuCl_2 \cdot$2lys	1624/1663	3245	1393/1380	3140
$CuCl_2 \cdot$4lys	1655	3020	1393	2925
Glycine	1610	3471	1412	3410
$CuCl_2 \cdot$2gly	1655		1408	
$CuCl_2 \cdot$4gly	1652/1615		1408/1418	

synthesized adducts exhibit a positive shift of the antisymmetric and a negative shift of the symmetric stretching mode vibrations, in comparison to the free ligands. This fact is in agreement with a ligand coordination through the amidic nitrogen and an oxygen atom of the COO$^-$ group, leaving the unco-ordinated C=O group [7,8,15]. For CuCl$_2$·2lys and CuCl$_2$·4gly adducts, splitting of the symmetric and antisymmetric bands are observed, suggesting a stron-ger metal–amino acid interaction for these com-pounds. In case of lysine–copper adducts, it was proposed a non-participation of ω-NH$_2$ terminal group in the metal–amino acid bond, from spectroscopic and thermodynamic studies [16]. The symmetric and anti-symmetric nitrogen–hydrogen bands are also listed in Table 1 for lysine compounds, but it was difficult to locate them on those very broad bands in glycine compounds. Then, for adduct containing four lysine molecules it is expected that part of them are not bidentated to copper, because the coordination number 8 is most unlike. In fact, these shifts in N–H bonds are lower for such compounds, in agreement with the existence of monodentate ligand to establish the coor-dination number 6 for copper. On the other hand, when heated the thermogravimetric curves did not distin-guish this behavior.

The thermogravimetric curves for the adducts of copper chloride involving lysine show a mass loss related to the release of the ligand molecules, a loss which occurred in a single step, suggesting that all ligand molecules are bonded to the metal with iden-tical strengths. The observed mass loss percentages are in agreement with the (calculated) ones, such as: 55.0 (52.0), 68.0 (65.0) and 81.0 (78.0), for 1:1, 1:2 and 1:4 adducts, respectively.

The compound CuCl$_2$·2gly presented a main step of mass loss that occurred between 180 and 400 °C and represents 48.0% of the total mass of the adduct, due to the release of the glycine ligands. A new step between 400 and 700 °C represents 42.0% of the total mass of the adduct and is due to the sublimation of the metal halide.

The thermogravimetric curve for CuCl$_2$·4gly adduct showed three mass loss steps as illustrated in Fig. 1. The first one is due to the release of two thirds of the ligand molecules in the range 200–370 °C. The third portion of the glycine molecule is released in the 370–600 °C interval, followed by sublimation of the metal halide in the last stage. The complete release of glycine molecules represent 67.0% of total mass, in good agreement with the calculated amount of 68.0%. This total glycine mass loss in distinct stages are in
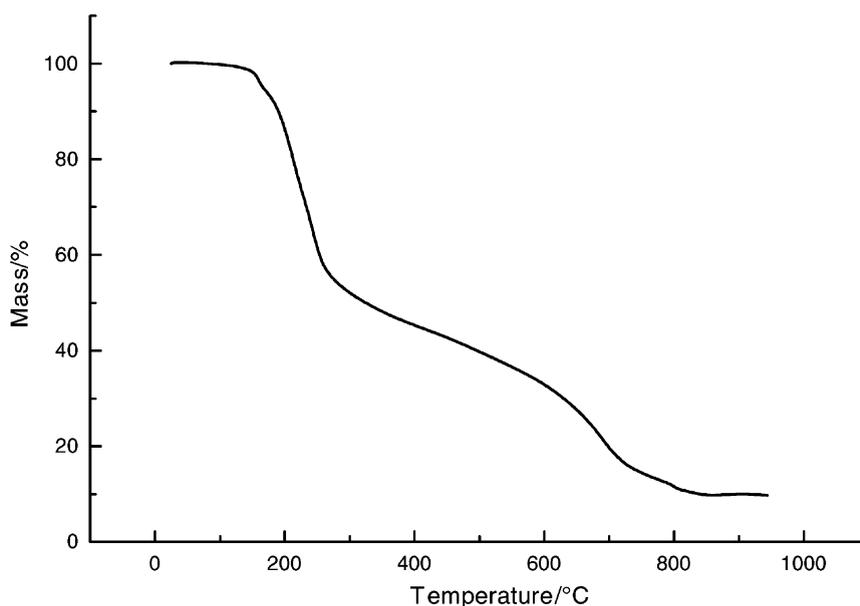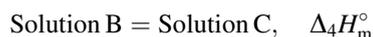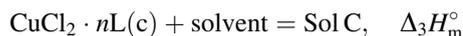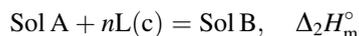

Fig. 1. Thermogravimetric curve of CuCl$_2$·4gly, adduct, obtained under argon atmosphere.

agreement with the infrared data, demonstrating that the four glycine molecules are coordinated to copper. However, part of them should be coordinated as monodentated way, and consequently, affects more strongly the profile of the thermogravimetric curve.

To obtain the energetic information about the amino acids, represented generically by L, with copper in a typical acid–base interactive process, a complete set of thermochemical parameters was calculated. All these data can be obtained from the standard molar enthalpy of reaction in the condensed phase [7,8,14,17] and the collected data which are based on the general equation:

$$CuCl_2(c) + nL(c) = CuCl_2 \cdot nL(c), \quad \Delta_r H_m^\circ$$
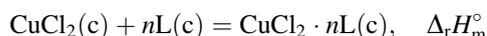
The standard molar enthalpic value might be obtained from a sequence of dissolutions of reagents and products in the calorimetric solvent, which was distilled water. In each calorimetric reaction a strict control of stoichiometry was maintained to ensure an equivalence of the initial and final stages of the reactions [18], as represented in the following thermochemical cycle:

$$CuCl_2(c) + solvent = Sol\,A, \quad \Delta_1 H_m^\circ$$

$$Sol\,A + nL(c) = Sol\,B, \quad \Delta_2 H_m^\circ$$

$$CuCl_2 \cdot nL(c) + solvent = Sol\,C, \quad \Delta_3 H_m^\circ$$

$$Solution\,B = Solution\,C, \quad \Delta_4 H_m^\circ$$

A null enthalpy $\Delta_4 H_m^\circ$ value was obtained when ampoules of mixtures of reactants were broken into a solution of the product of each reaction. From these values $\Delta_r H_m^\circ$ can be calculated by using Hess' law, through the equation:

$$\Delta_r H_m^\circ = \Delta_1 H_m^\circ + n\Delta_2 H_m^\circ - \Delta_3 H_m^\circ$$

Table 3
Standard molar enthalpies of dissolution ($\Delta_{sol}H_m^\circ$) of lysine, glycine, copper chloride and adducts in appropriate solvents at $T = 298.15 \pm 0.02$ K

	Reagent	Solvent	Solution	$\Delta_{sol}H_m^\circ$
1	$CuCl_2(c)$	H_2O	A_1	-50.01 ± 0.19
2	lys(c)	A_1	A_2	-29.16 ± 1.36
3	$CuCl_2 \cdot lys(c)$	H_2O	A_2	8.10 ± 0.40
4	2lys(c)	A_1	A_4	-60.38 ± 1.69
5	$CuCl_2 \cdot 2lys(c)$	H_2O	A_5	26.95 ± 0.72
6	4lys(c)	A_1	A_6	-101.60 ± 0.38
7	$CuCl_2 \cdot 4lys(c)$	H_2O	A_7	46.13 ± 1.42
8	2gly(c)	A_1	B_1	33.73 ± 0.82
9	$CuCl_2 \cdot 2gly(c)$	H_2O	B_2	14.68 ± 0.54
10	4gly(c)	A_1	B_3	65.83 ± 0.36
11	$CuCl_2 \cdot 4gly(c)$	H_2O	B_4	57.78 ± 0.51

The enthalpic values for all dissolution processes employed in the thermodynamic cycle are listed in Table 3. Each enthalpic value of dissolution is a mean value derived from at least five independent measurements. By using the resulting $\Delta_r H_m^\circ$ value, as well as the corresponding auxiliary data, a complete set of thermochemical parameters were calculated and the values are summarized in Table 4. Thus, the standard molar enthalpy of formation of each adduct in condensed phase was calculated by considering the respective enthalpy of reactions, given by: $\Delta_r H_m^\circ = \Delta_r H_m^\circ(product) - \Delta_r H_m^\circ(reagent)$. The enthalpy of decomposition ($\Delta_D H_m^\circ$) and lattice enthalpy ($\Delta_M H_m^\circ$) are related to the following reactions: $CuCl_2 \cdot 4L(c) = CuCl_2(c) + 4L(g)$ and $CuCl_2 \cdot 4L(s) = CuCl_2(g) + 4L(g)$ [18], respectively. These enthalpy values were calculated by using the equations:

$$\Delta_D H_m^\circ = -\Delta_r H_m^\circ + n\Delta_{cr}^g H_m^\circ(L)$$

$$\Delta_M H_m^\circ = \Delta_D H_m^\circ + \Delta_{cr}^g H_m^\circ(CuCl_2)$$

Table 4
Standard molar enthalpy values (kJ mol^{-1}) for reaction in condensed phase ($\Delta_r H_m^\circ$), enthalpy of formation ($\Delta_f H_m^\circ$), enthalpy of decomposition ($\Delta_D H_m^\circ$), lattice enthalpy ($\Delta_M H_m^\circ$), enthalpy of reaction in gaseous phase ($\Delta_g H_m^\circ$) and the mean value of enthalpy of the copper–ligand bond, $\langle D \rangle$(M–L), for the adducts

	$CuCl_2 \cdot lys$	$CuCl_2 \cdot 2lys$	$CuCl_2 \cdot 4lys$	$CuCl_2 \cdot 2gly$	$CuCl_2 \cdot 4gly$
$-\Delta_r H_m^\circ$	87.30 ± 1.43	137.30 ± 1.85	197.7 ± 1.48	30.70 ± 1.00	41.96 ± 0.65
$-\Delta_f H_m^\circ$	818.4 ± 1.9	1456.1 ± 3.8	2950.5 ± 6.3	1242.3 ± 1.7	2370.0 ± 2.3
$\Delta_D H_m^\circ$	326 ± 20	615 ± 40	1154 ± 80	306.9 ± 9.3	594.4 ± 18.4
$-\Delta_M H_m^\circ$	501 ± 20	790 ± 40	1327 ± 80	481.6 ± 9.4	769.1 ± 18.4
$-\Delta_g H_m^\circ$	262.0 ± 1.7	551 ± 20	1089 ± 60	343.5 ± 4.9	631.0 ± 13.9
$\langle D \rangle$(M–L)	262.0 ± 1.7	276 ± 10	272 ± 15	171.8 ± 2.5	157.8 ± 3.5

Based on the acid–base reaction in the gaseous phase, $\Delta_g H_m^\circ$, the corresponding enthalpy values are related to the reaction:

$$CuCl_2(g) + 4L(g) = CuCl_2 \cdot 4L(g)$$
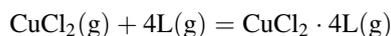
The expression to calculate these enthalpy values is

$$\Delta_g H_m^\circ = \Delta_r H_m^\circ - \Delta_{cr}^g H_m^\circ(CuCl_2) - (n-1)\Delta_{cr}^g H_m^\circ(L)$$

Using $\Delta_g H_m^\circ$ values, the mean metal–ligand bond dissociation enthalpy can be calculated using the following expression for a compound with n ligands:

$$\langle D\rangle(M-L) = \frac{\Delta_g H_m^\circ}{n}$$

In order to calculate these thermochemical data, the standard molar enthalpy of formation of copper chloride in the crystal phase of -218.0 ± 1.0 kJ mol^{-1} and that related to the gaseous phase of -43.3 kJ mol^{-1} [19], enabled the enthalpy of sublimation to be calculated as 174.7 ± 1.0 kJ mol^{-1}. Also needed are the standard molar enthalpies of formation in the condensed and in the gaseous phases for ligands used in forming these adducts. For glycine, two independent determinations are reported [20,21]: -527.5 ± 0.5 and -528.61 ± 0.34 kJ mol^{-1} for the condensed phase, and for gaseous phase [20], the value of -390.5 ± 4.6 kJ mol^{-1} is also reported. The standard molar enthalpy of sublimation is then 138.1 ± 4.6 kJ mol^{-1}. [22,23]: 130.5 ± 2.1 and 136.4 ± 0.4 kJ mol^{-1}. Based on these published results, and to maintain coherence in the collected values, then the couple for the crystalline phase and for sublimation [20] of -528.61 ± 0.34 and 138.1 ± 4.6 kJ mol^{-1}, respectively, were used in all calculations.

The standard molar enthalpy of formation of lysine in the condensed phase [20] of -678.7 ± 1.5 kJ mol^{-1} was also chosen. However, the standard enthalpy of formation of lysine in the gaseous phase was estimated by means of the group addition method [24] as -449 ± 20 kJ mol^{-1}. The deviation quoted was estimated from the maximum error found for similar amino acids: glycine, alanine, valine and leucine, for which experimental have been reported [25]. From these values the enthalpy of sublimation of lysine was estimated as 239 ± 20 kJ mol^{-1}.

In attempting to obtain information about the acid–base interactive process in gaseous phase, the enthalpies of sublimation for the adducts must be known. However, this class of compounds decomposes on heating and it was assumed that the enthalpy of sublimation of the adduct is equivalent to the enthalpy of sublimation of 1 mol of the corresponding ligands [18]. This previous hypothesis was then supported by a series of sublimable adducts [26]. The principle was based on the assumption that the intermolecular forces in the adduct and ligand are very similar, since the crystalline structure of the formed compound and ligand remain virtually unchanged [18].

By comparing the calculated thermochemical data, some features can be detected: (a) for lysine the $\Delta_r H_m^\circ$ data vary linearly with the number of ligands. However, this general tendency is not observed for $\langle D\rangle(Cu-L)$ values. This fact suggests that for these compounds the structural solid state features associated with coordination play a major role in the energetic behavior, and (b) considering $\langle D\rangle(Cu-L)$ values for adducts of lysine and glycine with the same stoichiometry, it is observed that the former ligand exhibits much higher metal–amino acid values, proving that the copper–lysine interaction is more effective than the copper–glycine one.

It is worth mentioning that, for the adducts of lys and gly with copper, each amino acid molecule is bonded to the cation through two distinct bonds, that are copper–oxygen and copper–nitrogen. Consequently, the mean metal–ligand bond $[\langle D\rangle(M-L)]$ values listed in Table 4 are, in reality, the sum of these two contributions. However, as reported for the chelate [27] $Cu(gly)_2$, there is no way of calculating the individual contributions of each individual bond. However, the calculation for cadmium–oxygen bond in a 1:2 glycine adduct [7] gave the value 82.3 ± 5.0 kJ mol^{-1}. Supposing there is a certain similarity in cadmium and copper bonds in these adducts, then the copper–nitrogen bond in the synthesized copper adduct, could be estimated as near to 70 kJ mol^{-1}. The mean values obtained of 163 kJ mol^{-1} for the adducts $CuCl_2 \cdot n$gly ($n = 1, 2$) are lower than the estimated value of 413 kJ mol^{-1} for the previously considered chelate [19]. This fact could be easily understood by considering that the observed difference in metal–amino acid interactions for each individual compound can be related to the nature of the bonds of the compound formed. Thus, a high value for the nitrogen and oxygen bonds in the chelate compound is expected due to their more pronounced covalent metal–amino acid bond character.

Acknowledgements

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