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Thermochemical data on adducts of cyclic ureas and copper chloride: the resemblance to biological systems

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Abstract

Adducts of the general formula $CuCl_2{\cdot}4L$ (L: ethyleneurea (eu), ethylenethiourea (etu) and propyleneurea (pu)) were synthesized and characterized by elemental analysis, infrared spectroscopy, thermogravimetry and calorimetry. The infrared results showed that eu and pu coordinate through carboxylic oxygen atoms, whereas etu uses the nitrogen atom to bond the cation. Thermal degradation of adducts starts at 130, 160 and 140°C, respectively, and is reflected by a one stage mass loss. Decomposition temperatures correlate, to some extent, with metal–ligand bond strength. The standard enthalpies of the reaction: $CuCl_2(c) + 4L(c) = CuCl_2{\cdot}4L(c)$ in the condensed phase ($\Delta_r H^\theta_m$) were determined by reaction–solution calorimetry. The following values were obtained: -42.50 ± 0.92; -48.76 ± 0.66 and -43.64 ± 0.51 kJ mol^{-1} for eu, etu and pu adducts, respectively. Using $\Delta_r H^\theta_m$ values and auxiliary enthalpies of sublimation of copper chloride and adducts, the enthalpies of decomposition ($\Delta_D H^\theta_m$), lattice enthalpies ($\Delta_M H^\theta_m$), enthalpies of reaction in the gaseous phase ($\Delta_g H^\theta_m$) and the mean metal–ligand bond enthalpies (D⟨M–L⟩) were calculated to be: $\Delta_D H^\theta_m = 377.3 \pm 7.7; 518.0 \pm 8.4; 400.8 \pm 10.0$; $\Delta_M H^\theta_m = 552.0 \pm 7.7; 692.7 \pm 8.5; 575.5 \pm 10.1$; $\Delta_g H^\theta_m = 468.3 \pm 8.0; 575.4 \pm 8.8; 486.2 \pm 10.4$ and $D\langle M{-}L\rangle = 117.1 \pm 2.0; 143.8 \pm 2.2; 121.6 \pm 2.6$, for eu, etu and pu adducts, respectively.

Keywords: Copper chloride; Cyclic amides; Thermochemistry

1. Introduction

Amides and cyclic amides constitute a particular class of compounds of great interest for coordination chemistry. These molecules display the active moiety –(CO)–N= which is found in many important biological polymers such as polypeptides and proteins [1]. In attempting to understand the energetic of interactions between cations and ligands that can mimic the biological systems some thermochemical data were recently obtained [2,3]. Other investigations concerning thermochemistry of adducts containing similar cations to the above-mentioned molecules, such as cyclic amides [4–6], cyclic amide derivative [7], amide [8] or thioamides [9–11], have also been reported. Moreover, attention was focused on the determination of the metal–ligand bond enthalpy [12].

Metal cations play an important role in biological systems. One of them is copper(II) cation, whose properties and behavior were intensively explored in the past [13,14]. The purpose of these investigations was to synthesize compounds that present similarity to the biological systems, i.e. complexes containing copper and thiourea derivatives of α-amino acids

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[15], tetrapeptides containing cysteinyl or histidinyl residues [16] or amino acids [17].

Copper complexes containing thioligands such as dithiooxamide [18] or multidentate, sulfur–nitrogen chelating agents attached to the same molecule, such as 2,6-bis-(*N*-methyl-*S*-methyldithiocarbazato)pyridine [19], were also investigated. Another aspect to be emphasized is related to the self-redox reaction within the coordination compound in which the sulfur–copper occurs [20].

This publication reports the synthesis and characteristics of adducts of the general formula $CuCl_2{\cdot}4L$ (L: ethyleneurea (eu), ethylenethiourea (etu) and propyleneurea (pu)), the constitution of ligands is shown in Fig. 1. Special attention is focused on the determination of thermochemical parameters by solution–reaction calorimetry.

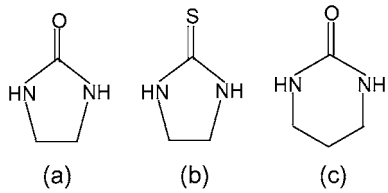

Fig. 1. Schematic representation of the chemical structures of eu (a); etu (b); and pu (c).

The eu, etu and pu molecules chosen in this investigation present a close similarity not only from the structural point of view, but also due to the available

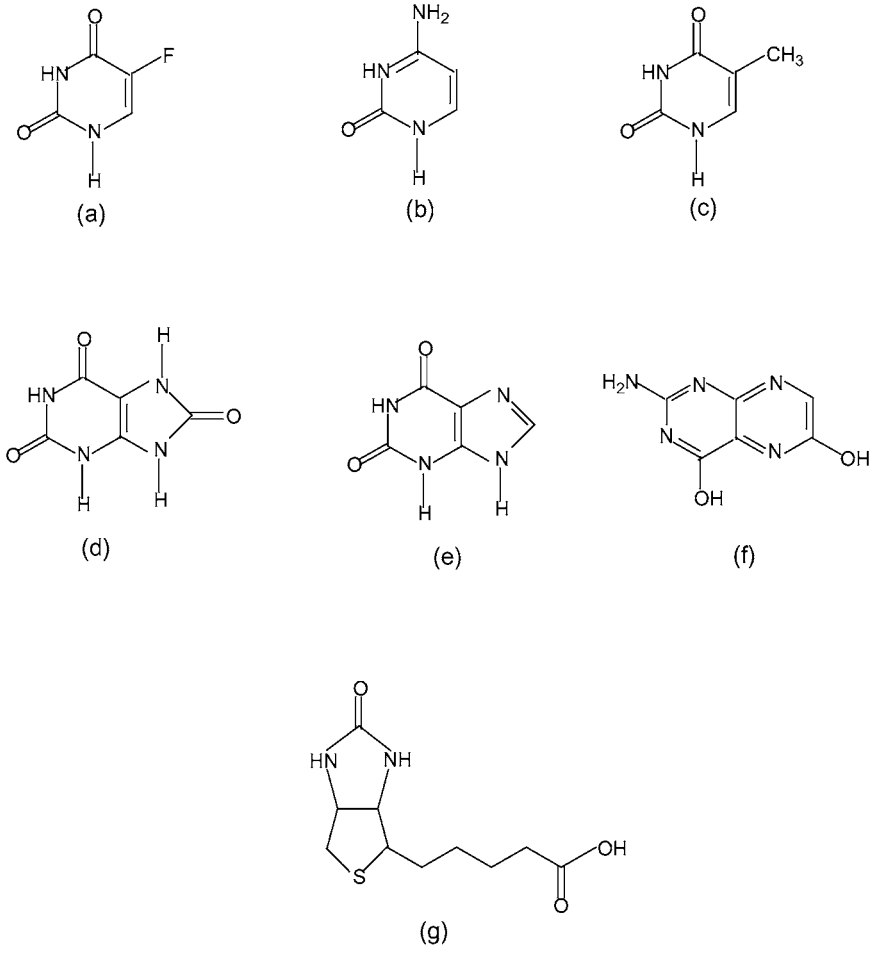

Fig. 2. Schematic representation of the chemical structures of 5-fluorouracil (a); cytosine (b); thymine (c); uric acid (d); xanthyne (e); xanthopterin (f); and biotin (g).

basic centers. These properties induce in many circumstances a variety of functional activities. In this series of molecules, part of the structure is inserted in more complex molecules, with prominent biological importance, such as 6-mercaptopurine used as a drug for leukemia [21] and 5-fluorouracil employed against breast and skin cancer [21]. The amino acid cycloserine [21], the pyrimidine base uracil, the purine bases guanine, xanthine and uric acid, the pyrimidine bases thymine, cytosine and biotin, a mobile carboxyl group carrier in a variety of enzymatic carboxylation reactions [22], are also illustrative examples.

Some of these relevant biological molecules are schematically represented in Fig. 2. Xanthopterin and leucopterin with pterin structure are biological pigments that occur widely in nature, giving color to many insect wings, fishes, and amphibian skins [22].

The aim of this investigation is to explore the interaction involving a selected series of molecules with a given cation. The energetics of the bonds formed can give relevant support to the understanding of structural similarities between the fragments investigated and those found in biological macromolecules.

2. Experimental

Ethyleneurea, ethylenethiourea and propyleneurea (Aldrich) were all analytical grade and used without purification. Copper chloride, $CuCl_2{\cdot}2H_2O$, was dehydrated as before [23]. The original method consisted of heating the compound in air at 110°C for 2 h [24], while in the present case, the temperature used was lower, 60°C, and the process lasted a longer time, 8 h under vacuum, to avoid any decomposition. The anhydrous yellow–brown compound was stored over phosphorus pentoxide and handled in a dry nitrogen atmosphere.

The adducts of general formula $CuCl_2{\cdot}4L$ (L: eu, etu, pu) were synthesized in the solid state by grinding stoichiometric amounts of anhydrous chloride with the ligands in a mortar for 70 min in a dry box under a nitrogen atmosphere. With grinding, the adducts are formed, which is manifested in a progressive change in grain size and color. The adducts were again dried in vacuum for several hours before being stored.

Carbon, nitrogen and hydrogen contents were determined using a Perkin-Elmer microelemental analyzer. The infrared spectra of adducts dispersed in KBr were recorded on a Bomem apparatus, in 4000–400 cm^{-1} range, at a resolution of 4 cm^{-1}. Thermogravimetric (TG) curves were obtained on a Shimadzu TGA 50 apparatus. The differential scanning calorimetry (DSC) measurements were carried out on a DuPont 2000 apparatus. Both TG and DSC investigations were performed in an argon atmosphere at heating rate of 8.3×10^{-2}°C s^{-1}, by employing samples varying in mass from 5 to 30 mg.

All calorimetric measurements were carried out on a thermometric isothermal instrument, model LKB 2250. For each determination a thin glass ampoule was loaded with the desired solute and broken in the calorimetric solvent at 25.00 ± 0.02°C [3]. The ampoules for copper chloride and adducts were prepared under anhydrous conditions in a dry box with a dry nitrogen atmosphere. For all experiments the glass ampoules containing 5–60 mg of sample were broken in a 0.10 dm^3 reaction vessel filled with the calorimetric solvent. The enthalpy of reaction was obtained from at least six individual measurements. The completion of reaction required 240 s. Uncertainty intervals associated with the variation of the enthalpies of solution are quoted as twice that of the standard deviations.

The accuracy of calorimetric measurements was checked by measuring the thermal effect of dissolution of tris(hydroxymethyl)aminomethane (THAM) in standard hydrochloric solution. The value obtained was -245.85 ± 0.14 J g^{-1}, which conforms well to the recommended value [25,26].

3. Results and discussion

Results of elemental analyses are very close to those predicted for the assumed formula of the adducts, as shown in Table 1.

Table 1
Carbon, nitrogen and hydrogen content in the adducts $CuCl_2{\cdot}4L$ (L: eu, etu, pu); determined (calculated) values in percentages

Element	$CuCl_2{\cdot}4eu$	$CuCl_2{\cdot}4etu$	$CuCl_2{\cdot}4pu$
Carbon	29.70 (30.10)	24.68 (26.54)	35.21 (35.92)
Nitrogen	22.72 (23.41)	19.58 (20.65)	20.32 (21.00)
Hydrogen	5.52 (5.02)	4.74 (4.42)	6.13 (6.00)

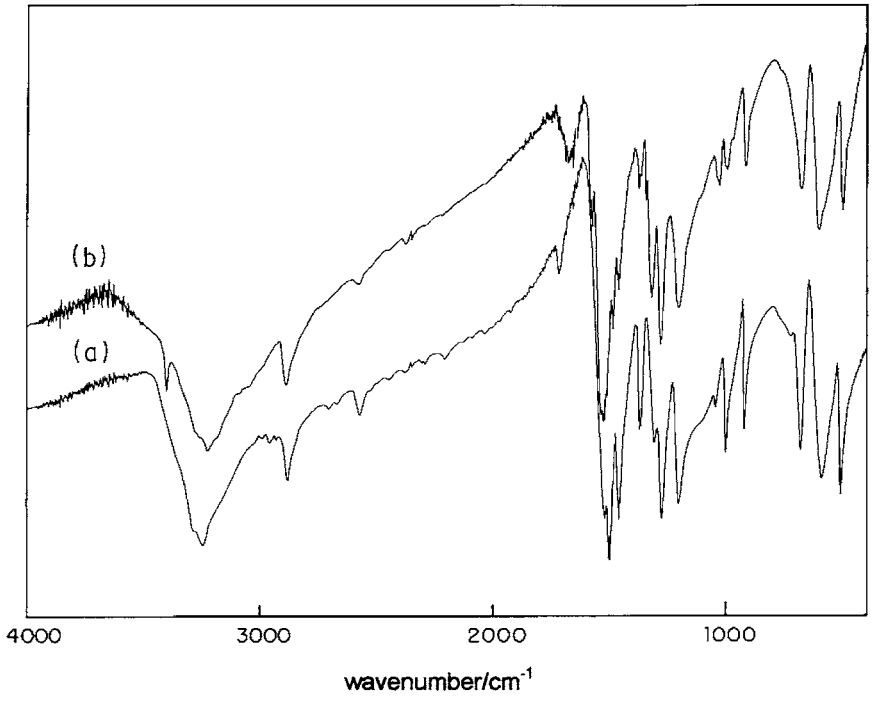

Fig. 3. Infrared spectra of etu (a); and $CuCl_2$·4etu (b) dispersed in KBr.

The infrared spectra of etu and the respective adduct, $CuCl_2$·4etu, are shown in Fig. 3, while the main bands in the infrared spectra of all ligands and adducts are summarized in Table 2. The decrease in wave number of the carbonyl stretching mode and increase in wave number of both amide II and C–N stretching modes in the case of eu and pu adducts is typical for complexes in which coordination takes place through the carboxylic oxygen atom [6,7]. On the other hand, the increase in wave number of the thioamide I, $\gamma(C{=}S) + \delta(NCS)$ and $\gamma(C{-}N) + \delta(NCN)$, mode indicates that the nitrogen atom [27], and not sulfur [28], of etu is used to bond the cation in the adduct [27]. This unequivocal assignment is based on the property associated to sulfur donor atoms, which prefer to bond to copper soft acids, similar to platinum or palladium [28], in a typical acid–base interaction.

The acidic copper center [27] can be bonded by oxygen or nitrogen basic atoms from the ligands eu or etu, respectively, when the adducts are formed. From a simple inspection of the ligand structures in Fig. 4, it is possible to distinguish different features in coordination, based on properties associated with oxygen,

Table 2
Main bands (cm^{-1}) in infrared spectra of eu, etu, pu and the respective adducts

Compound	Amide I νC=O	Amide II N–H_{def}	νC–N
eu	1685	1508	1274
$CuCl_2$·4eu	1665	1525	1280
pu	1690	1542	1312
$CuCl_2$·4pu	1640	1548	1315
	Thioamide I	γ(C=S) + δ(NCS)	γ(C–N) + δ(NCN)
etu	1499	1276	1000
$CuCl_2$·4etu	1521	1278	1028

Fig. 4. Schematic representation of eu and etu showing increased electron density at oxygen (eu) or nitrogen (etu) atoms as a consequence of differences in electronegativity of O, N, S and C.

nitrogen, carbon and sulfur atoms, which are potentially basic centers that can bond to a cation. Thus, an important property to be considered is the electronegativity. According to the Pauling scale, the values of these atoms follow the order [29]: $O(3.44) > N(3.04) > S(2.58) > C(2.55)$. In this sequence, the higher electronegativity of elements implies an increase of electron density on carbonyl oxygen atom of eu or on the nitrogen atom of etu ligands, respectively, as is schematically presented in Fig. 4.

The thermogravimetric and derivative curves for $CuCl_2{\cdot}4etu$ are shown in Fig. 5. Identical behavior was observed for other adducts. Mass loss in a single step can be assigned to the release of ligand molecules. This experimental finding clearly suggests that all four molecules of ligands are identically bonded to the acidic metal center and implies that bond strength between metal and ligand coordination centers is similar in nature, as represented by the reaction $CuCl_2{\cdot}4L(c) \rightarrow CuCl_2(c) + 4L(g)$. The percentage of mass loss: 72, 75 and 76% for eu, pu and etu adducts, respectively, is close to that expected from the formulae, whose calculation was adjusted to a

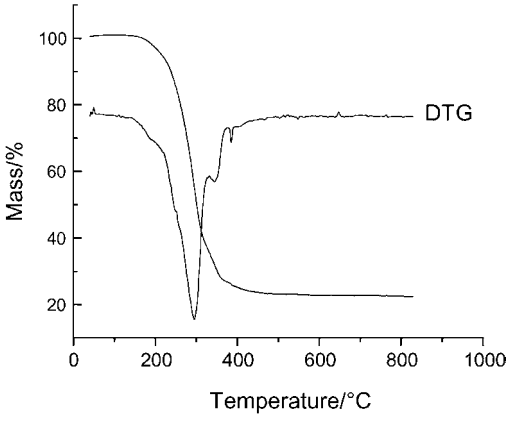

Fig. 5. TG and DTG curves for $CuCl_2{\cdot}4etu$ adduct.

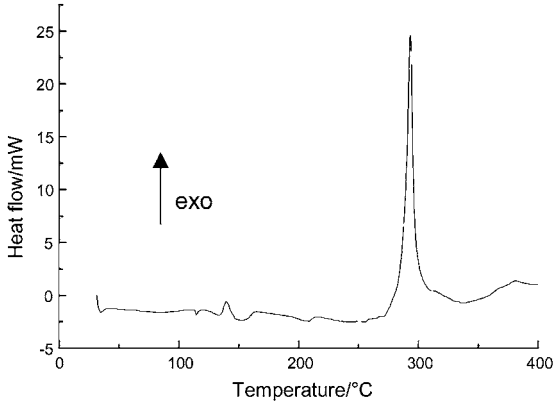

Fig. 6. DSC curve for $CuCl_2{\cdot}4etu$ adduct.

single decomposition process for the above equation. However, on heating, a rupture of the metal–ligand bond occurs and this event influences mainly the thermodynamics and kinetics of the thermal decomposition process [30].

The DSC curves for all adducts are similar, due to the fact that disruption of ligand–metal bonds occurs in an exothermic process. An example of such a behavior is shown for $CuCl_2{\cdot}4etu$ in Fig. 6. For eu adducts, two exothermic peaks with maxima at 160 and 265°C correspond to enthalpy values of −79.9 and −284.6 kJ mol^{-1}, respectively. In the case of pu adducts a couple of peaks at 205 and 315°C is associated with enthalpy values of −399.1 and −417.0 kJ mol^{-1}. Further, the etu adduct exhibits a single exothermic peak at 300°C, corresponding to −411.8 kJ mol^{-1}. The presence of two peaks is again seen on the DSC and DTG curves of $CuCl_2{\cdot}4eu$ and $CuCl_2{\cdot}4pu$, indicating the ligand molecules are released in two distinct steps.

The features associated with the energetic of cyclic ligand–copper interactive process might be determined by considering the collected set of the thermochemical data, obtained for a series of investigated compounds. Thus, the initial step consisted of determining the standard molar enthalpies of the general reaction in the condensed phase.

$$CuCl_2(c) + 4L(c) = CuCl_2 \cdot 4L(c); \Delta_r H^{\theta}_m$$

The standard molar enthalpy value might be obtained from a sequence of dissolution of reagents and products in the calorimetric solvent, due to its

Table 3
Values of enthalpy, kJ mol^{-1}, for all steps of dissolution

Adduct	$\Delta_1 H^\theta_m$	$\Delta_2 H^\theta_m$	$\Delta_3 H^\theta_m$
$CuCl_2$·4eu	−27.65 ± 0.29	16.91 ± 0.28	31.76 ± 0.56
$CuCl_2$·4etu	−27.63 ± 0.26	23.21 ± 0.34	44.34 ± 0.50
$CuCl_2$·4pu	−27.64 ± 0.24	16.72 ± 0.15	32.72 ± 0.42

capacity in easily dissolving both reagents and products. A 1.00 mol dm^{-3} hydrochloric acid solution was employed as calorimetric solvent. For each calorimetric reaction strict control of stoichiometry was maintained to ensure equivalence of the initial and final stages of the reactions, as represented in the following thermochemical cycle.

$$CuCl_2(c) + \text{solvent} = \text{Sol A}; \Delta_1 H^\theta_m$$

$$\text{Sol A} + 4L(c) = \text{Sol B}; \Delta_2 H^\theta_m$$

$$CuCl_2 \cdot 4L(c) + \text{solvent} = \text{Sol C}; \Delta_3 H^\theta_m$$

$$\text{Sol B} = \text{Sol C}; \Delta_4 H^\theta_m$$

Zero enthalpy values for $\Delta_4 H^\theta_m$ were obtained when ampoules of a mixture of reactants were broken into a solution of the product. From the values derived for each step, $\Delta_r H^\theta_m$ were calculated by employing Hess's law, using the following equation.

$$\Delta_r H^\theta_m = \Delta_1 H^\theta_m + \Delta_2 H^\theta_m - \Delta_3 H^\theta_m$$

The enthalpy values for all dissolution processes used in the thermodynamic cycle are listed in Table 3. Each enthalpy value of dissolution is the mean of at least five independent measurements and a complete set of thermochemical parameters is listed in Table 4. The values for the enthalpy of decomposition ($\Delta_D H^\theta_m$) and lattice enthalpy ($\Delta_M H^\theta_m$) are related to the following reactions: $CuCl_2$·4L(c) = $CuCl_2$(c) + 4L(g) and $CuCl_2$·4L(s) = $CuCl_2$(g) + 4L(g), respectively. These enthalpy values were calculated by using the following equations [5,6].

$$\Delta_D H^\theta_m = -\Delta_r H^\theta_m + 4\Delta^g_{cr} H^\theta_m(L)$$

$$\Delta_M H^\theta_m = \Delta_D H^\theta_m + \Delta^g_{cr} H^\theta_m(CuCl_2)$$

Based on the acid–base reaction in gaseous phase, $\Delta_g H^\theta_m$, 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

$$\Delta_g H^\theta_m = \Delta_M H^\theta_m - \Delta^g_{cr} H^\theta_m(L)$$

Using $\Delta_g H^\theta_m$ values, the mean metal–ligand bond dissociation enthalpy can be calculated using the expression

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

where n represents the number of ligands and $\Delta^g_{cr} H^\theta_m$ is the enthalpy of sublimation. The results are also listed in Table 4.

For these calculations the auxiliary data of the enthalpies of sublimation of $CuCl_2$, eu and pu were used: 174.7 ± 1.0 [31], 83.7 ± 1.9 [6] and 89.3 ± 2.5 [6] kJ mol^{-1}, respectively.

The missing enthalpy of sublimation of etu was calculated as 117.3 ± 2.1 kJ mol^{-1} by using the respective enthalpy of sublimation of the eu ligand. The procedure was based on the relation between enthalpies of sublimation of series of similar compounds, in present case, enthalpies of sublimation of amides and thioamides [32].

$$\Delta^g_{cr} H^\theta_m \text{ (thioamide)} = \Delta^g_{cr} H^\theta_m \text{ (amide)} \times 1.08 + 26.24$$

The enthalpy values listed in Tables 3 and 4 show that eu and pu gave very similar results, which can be expected due to the similarity in coordination that yields compounds very similar in structure and composition. Therefore, the mean copper–oxygen bond

Table 4
Standard molar enthalpies of reaction ($\Delta_r H^\theta_m$), decomposition ($\Delta_D H^\theta_m$), lattice ($\Delta_M H^\theta_m$), gaseous phase ($\Delta_g H^\theta_m$) and mean copper ligand–bond (D⟨M–L⟩), kJ mol^{-1}, for the adducts $CuCl_2$·4L (L: eu, pu and etu)

Adduct	$\Delta_r H^\theta_m$	$\Delta_D H^\theta_m$	$\Delta_M H^\theta_m$	$\Delta_g H^\theta_m$	D⟨M–L⟩
$CuCl_2$·4eu	−42.50 ± 0.92	377.3 ± 7.7	552.0 ± 7.7	468.3 ± 8.0	117.1 ± 2.0
$CuCl_2$·4etu	−48.76 ± 0.66	518.0 ± 8.4	692.7 ± 8.5	575.4 ± 8.8	143.8 ± 2.2
$CuCl_2$·4pu	−43.64 ± 0.51	400.8 ± 10.0	575.5 ± 10.1	486.2 ± 10.4	121.6 ± 2.6

enthalpy values derived by examining compounds containing these two molecules can be expected to be very close to those occurring in a copper–biotin complex, where the same coordination site is involved. For the set of similar molecules, such as those shown in Fig. 2, a proposed estimation for $\langle D \rangle$(Cu–L) can also be applied.

The mean copper–nitrogen bond enthalpy in the etu adduct is about 20% higher than the copper–oxygen bond enthalpy in eu or pu complexes. This fact can be explained by considering a resonance effect (Fig. 4), as well as electron density and the hardness of nitrogen atom, which favor coordination of the latter atom to the cation.

One more finding is important, namely, that temperatures of degradation (t_i): 130, 140 and 160°C for eu, pu and etu adducts, respectively, follow the order of D⟨M–L⟩ values.

4. Conclusion

The results obtained show that eu, pu and etu can be used as models to study the energetics of the interaction between metal cations (e.g. Cu^{2+}) and molecules of biological interest.

Taking into account that eu, pu and etu exhibit coordination centers similar to many biological molecules, the mean metal–ligand bond enthalpies obtained can serve as confident estimates to consider the thermodynamics of complexation of the latter. On the other hand, differences in electron displacement and metal–ligand bond strength cause that eu, pu and etu may behave differently when they constitute fragments of biological macromolecules. The importance of thermogravimetry and solution calorimetry in investigations of biological systems is further reinforced.

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