A calorimetric investigation into copper–arginine and copper–alanine solid state interactions

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Abstract

Complexes of formula $CuCl_2 \cdot 2arg$ and $CuCl_2 \cdot 4ala$ (arg = arginine; ala = alanine) were prepared at room temperature by a solid state route. The metal–amino acid solid state interactions were studied by i.r. spectroscopy and solution calorimetry. For both complexes, participation of the carboxylate group as well as nitrogen in coordination are inferred, based on the i.r. data. For the copper–arginine compound, the calculated thermochemical parameters are: $\Delta_r H_m^\theta = -114.9 \pm 1.42$ and $\Delta_f H_m^\theta = -1608.3 \pm 11.6$ kJ mol^{-1}. For copper–alanine compound, a complete set of thermochemical parameters were calculated: $\Delta_r H_m^\theta = -18.0 \pm 0.9$; $\Delta_f H_m^\theta = -2490.4 \pm 4.3$; $\Delta_D H_m^\theta = 597.2 \pm 17.7$; $\Delta_M H_m^\theta = 771.9 \pm 18.7$; $\Delta_g H_m^\theta = 627.1 \pm 22.3$ and $\langle D \rangle$ (Cu–L) $= 156.8 \pm 5.7$ kJ mol^{-1}. Based on $\Delta_r H_m^\theta$ and dissolution enthalpy values, a stronger intermolecular solid state interaction can be inferred for the arginine complex, than for the alanine one complex, probably due to the formation of intermolecular hydrogen bonds in the former.

Introduction

In order to understand the complexity of protein action in biological processes, investigations on the interaction of their building blocks, the amino acids, with other common species present in living organisms, such as metal cations, is of essential interest [1, 2]. In this context, thermogravimetric and calorimetric investigations of the cadmium–glycine [3, 4] or cadmium–hystidine and cadmium–cysteine [5] interactions have been performed, paying special attention to the non-isothermal kinetic parameters for their solid state thermal degradation and the estimate of metal–amino acid bond dissociation enthalpies. Thermogravimetric and calorimetric studies of metal compounds involving cyclic amides related to molecules of biological importance, such as those with zinc [6] copper [7] or cobalt [8] have also played a major role in such bioinorganic studies.

The aim of this paper is to describe the synthesis, characterization and a thermal study of copper–arginine and copper–alanine adducts, with special attention focused on the thermal study of the solid state metal–amino acid interactions. Arginine and alanine structures are shown in Figure 1.

Experimental

Reagent grade $CuCl_2 \cdot 2H_2O$ (Aldrich), arginine (Aldrich) and alanine (Aldrich) were used. $CuCl_2 \cdot 2H_2O$ was dried at 90 °C under vacuum for 48 h, in order to obtain the anhydrous halide as a brown powder. The adducts were prepared by a mechanically induced solid state reaction between reactants by grinding stoichiometric amounts in a mortar for 70 min under a dry N_2 atmosphere. Samples of the adducts thus prepared were taken at 10 min intervals, and the reaction was considered to be complete when the free amino bands were absent from the i.r. spectra. The adducts were dried under vacuum at 50 °C for 48 h.

C, N and H contents were determined using a Perkin-Elmer microelemental analyzer. I.r. spectra were recorded on a Bomem apparatus in the 4000–400 cm^{-1} range (resolution 4 cm^{-1}). Spectra were obtained from powders in KBr discs.

All calorimetric measurements were performed on an LKB 2250 isothermic instrument, using the ampoule-breaking procedure, at 298.15 ± 0.02 K, using a reaction vessel (0.10 dm^3) charged with deionized H_2O, as the calorimetric solvent. For each enthalpy determination, at least four individual ampoules were broken and the complete thermal effects were recorded during 300 s. This period was sufficient to bring the baseline to the
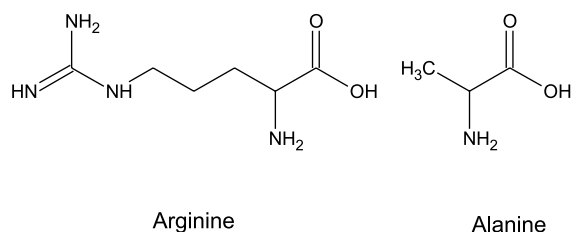
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Fig. 1. Structural formulae for (a) arginine and (b) alanine.

steady state equilibrium condition. Ampoules containing masses varying from 5 to 100 mg of $CuCl_2 \cdot 2H_2O$, arginine and alanine and the respective adducts were prepared under anhydrous conditions in a dry box under a N_2 atmosphere. Uncertainty intervals associated with the variation of the enthalpies of solution are quoted as twice the standard deviation of the mean.

Results and discussion

The elemental analysis results are summarized in Table 1 and the main i.r. bands are summarized in Table 2.

For the alanine adduct, the observed increase in the $v_a(COO^-)$ band, as well as a decrease in $v_s(COO^-)$, are in agreement with coordination involving the amine nitrogen, as well as an oxygen atom of the carboxylate group [3, 4, 9]. For free alanine, the Δv difference (asymmetric–symmetric) is 171 cm^{-1}, whereas for its compound it is 211 cm^{-1}. This parameter could be used as a measure of the M-ligand bond strength [9].

For the arginine adduct, a decrease in both the asymmetric and symmetric carboxylate bands are observed. Furthermore, the NH_2 band at 2300 cm^{-1} in the free amino acid does not appear in the complex. This fact strongly suggests coordination involving the amino group, as well as participation of the carboxylate group, in a bidentate form, as observed for iron(II) djenkolate

complexes [10]. The Δv values for free arginine and its complex are 206 and 211 cm^{-1}, respectively.

To obtain energetic information about the copper–amino acid interactive process, a complete set of thermochemical parameters were calculated. The standard molar enthalpy of reaction in condensed phase is based on the general equation:

$$CuCl_{2(c)} + nL_{(c)} = CuCl_2 \cdot aL_{(c)}; \quad \Delta_r H_m^\theta$$
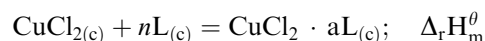
where n is the number of amino acid molecules and L is a given amino acid. The standard molar enthalpy value might be obtained from a sequence of dissolution of reagents and products in the calorimetric solvent. In each calorimetric reaction strict control of stoichiometry was maintained to ensure an equivalence of the initial and final stages of the reactions, as represented in the following thermochemical cycle:

$$CuCl_{2(c)} + solvent = Sol\ A; \quad \Delta_1 H_m^\theta$$

$$Sol\ A + nL_{(c)} = Sol\ B; \quad \Delta_2 H_m^\theta$$

$$CuCl_2 \cdot nL_{(c)} + solvent = Sol\ C; \quad \Delta_3 H_m^\theta$$

$$Solution\ B = solution\ C; \quad \Delta_4 H_m^\theta$$

A null enthalpy $\Delta_4 H_m^\theta$ was obtained when ampoules containing stoichiometric reactant mixture solutions were broken into a solution of the product. Form these values, $\Delta_r H_m^\theta$, can be calculated by Hess's law:

$$\Delta_r H_m^\theta = \Delta_1 H_m^\theta + \Delta_2 H_m^\theta - \Delta_3 H_m^\theta$$

The enthalpy values for all dissolution processes employed in the thermodynamic cycle are listed in Table 3. Each enthalpy value of dissolution is a mean value of at least five independent measurements. By using the $\Delta_r H_m^\theta$ value, as well as a set of auxiliary data, a complete set of thermochemical parameters were calculated and are summarized in Table 4. The thermochemical parameters and the equations employed for their calculations are:
1. Enthalpy of formation:

$$\Delta_f H_m^\theta(adduct) = \Delta_r H_m^\theta + \Delta_f H_m^\theta(CuCl_2)$$
$$+ n\Delta_f H_m^\theta(ligand)$$

2. Decomposition enthalpy:

Table 1. Elemental analysis results for arginine and alanine copper adducts

Compound	Found (calcd.)%	N	H
$CuCl_2 \cdot 2arg$	29.10 (29.7)	22.85 (23.1)	5.79 (6.2)
$CuCl_2 \cdot 4ala$	28.95 (29.4)	11.97 (11.4)	5.54 (5.7)

*Table 2.* Main i.r. bands (cm^{-1}) for arginine, alanine and their $CuCl_2$ adducts

Compound	NH_2[a]	NH_2[b]	$v_a(COO^-)$	$v_s(COO^-)$
Arginine	2300	1683	1618	1412
$CuCl_2 \cdot 2arg$	–	1642	1600	1389
Alanine	2110	1617	1579	1408
$CuCl_2 \cdot 4ala$	1983	1658	1605	1394

[a] Prominent band, assigned to a combination of asymmetrical NH_2 bonding and the torsional oscillation of the same group.
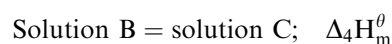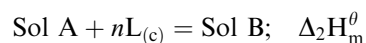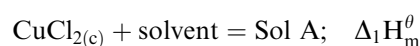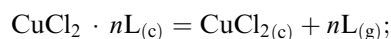[b] Asymmetric ($-NH_2$) N–H bond.

Table 3. Standard molar enthalpies of dissolution $\Delta_{sol} H_m^\theta$ of arginine, alanine and their $CuCl_2$ complexes in deionized water at 298.15 ± 0.02 K

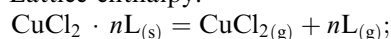| Reagent	Solvent	$\Delta_{sol} H_m^\theta$/kJ mol^{-1}
$CuCl_{2(c)}$	H_2O	-50.01 ± 0.19
$2Arg_{(c)}$	$CuCl_{2(aq)}$	-11.87 ± 0.06
$CuCl_2 \cdot 2arg_{(c)}$	H_2O	53.03 ± 1.17
$4Ala_{(c)}$	$CuCl_{2(aq)}$	38.54 ± 0.33
$CuCl_2 \cdot 4ala_{(c)}$	H_2O	6.48 ± 0.34

Table 4. Thermochemical parameters (kJ mol^{-1}) for copper–arginine and copper–alanine adducts

Parameter	CuCl$_2 \cdot$ 2arg	CuCl$_2 \cdot$ 4ala
$\Delta_r H_m^\theta$	-114.9 ± 1.4	-18.0 ± 0.9
$\Delta_f H_m^\theta$	-1608.3 ± 11.6	-2490.4 ± 4.3
$\Delta_D H_m^\theta$	–	597.2 ± 17.7
$\Delta_M H_m^\theta$	–	771.9 ± 18.7
$\Delta_g H_m^\theta$	–	627.1 ± 22.3
$\langle D \rangle$ (Cu–L)	–	156.8 ± 5.7

$$CuCl_2 \cdot nL_{(c)} = CuCl_{2(c)} + nL_{(g)};$$
$$\Delta_D H_m^\theta = -\Delta_r H_m^\theta + n\Delta_{cr}^g H_m^\theta(L)$$

3. Lattice enthalpy:
$$CuCl_2 \cdot nL_{(s)} = CuCl_{2(g)} + nL_{(g)};$$
$$\Delta_M H_m^\theta = \Delta_D H_m^\theta + \Delta_{cr}^g H_m^\theta(CuCl_2)$$

4. Gaseous phase reaction enthalpy:
$$CuCl_{2(g)} + nL_{(g)} = CuCl_2 \cdot nL_{(g)};$$
$$\Delta_g H_m^\theta = \Delta_M H_m^\theta - (n-1)\Delta_{cr}^g H_m^\theta(L)$$
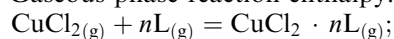
5. Mean metal–ligand bond dissociation enthalpy:
$$\langle D \rangle(M - L) = \Delta_g H_m^\theta / n$$

In order to calculate these parameters, the standard molar enthalpy of formation in the crystal phase and the sublimation enthalpy of copper chloride were used: -218.0 ± 1.0 and 174.7 ± 1.0 kJ mol^{-1} [11], respectively. The standard molar enthalpy of formation in the crystal phase and sublimation of alanine were taken as -536.6 ± 0.6 [12] and 144.8 ± 4.2 kJ mol^{-1}, respectively [13]. The standard molar enthalpy of formation in the crystal phase for arginine is -637.7 ± 3.2 kJ mol^{-1} [14]. A complete set of thermochemical parameters was not calculated for the arginine adduct, since the sublimation enthalpy of this amino acid is not available in the literature.

In general, $\Delta_r H_m^\theta$ values increase with the increasing number of ligands [6, 15]. So, based on the $\Delta_r H_m^\theta$ values for arginine and alanine adducts, a higher contribution of each arginine molecule to the condensed phase reaction enthalpy can be inferred. Furthermore, the $\Delta_r H_m^\theta$ values for CuCl$_2 \cdot$ 4ala lie well below the mean value, 45 kJ mol^{-1}, found for CuCl$_2 \cdot$ 4L adducts, where L is a cyclic amide such as ethyleneurea [7]. Such facts are probably due to the formation of hydrogen bonds in arginine and cyclic amide compounds, which are, presumably, absent in the alanine complex. A stronger intermolecular solid state interaction between arginine complexes, in comparison with alanine, can also be inferred, taking into account the dissolution enthalpy for both compounds, as shown in Table 3.

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