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The Thermal Stability of Copper Cluster Ions of the Type $Cu(I)_8Cu(II)_6L_{12}Cl^{5-}$, where L is d-Penicillamine

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Abstract

Mixed valence copper cluster ions which form when Cu(II) reacts with d-penicillamine in the presence of chloride ion are relatively stable. The hydrated sodium salt of the copper cluster decomposed at 169 °C, based on differential scanning calorimetry. The analogous silver/nickel and silver/palladium clusters decomposed at 143 and 138 °C, respectively. In aqueous solutions the copper cluster undergoes an accelerated decomposition in the presence of counterion Cu(II), but this reaction may be prevented by sequestering Cu(II), which is released in the decomposition, with the resin Chelex-100. The cluster's stability is enhanced in the presence of Chelex-100, such that the reaction is 150-fold slower at 100 °C relative to a mixture containing 1.0×10^{-4} M Cu(II). In the absence of Cu(II) counterion the rate law is second order with respect to the cluster, with $k = 10^{23} \pm 10^{4} \exp(-40\,600 \pm 1000/RT)$; ($R$ = 1.987 cal/K mol)(E_a = 40.6 kcal/mol).

Introduction

d-Penicillamine reacts with aqueous cupric ion, forming a mixed valence, red–violet, anionic product [1]. The structure of this ion has been characterized by X-ray crystallography [2], and an independent crystallographic investigation of a red–violet cation formed from copper and 2,2-dimethylcysteamine (decarboxylated penicillamine) establishes that the two entities are clusters with the same framework structure [3], as shown in Fig. 1. They have the formula $Cu(I)_8Cu(II)_6L_{12}Cl^{5-}$. Later, it was shown that other metal ions form analogous structures with these kinds of ligands [4], e.g. $Ag(I)_8Ni(II)_6L_{12}Cl^{5-}$, which closely resembles the copper cluster electrophoretically but is orange-colored. The cluster of copper and d-penicillamine is stable enough to survive aziridine esterifications [5], but ligands related to penicillamine which lack the gem-dimethyl structure (cysteine, cysteamine) are inherently unstable. These only form a transient red–violet species. The cluster of copper and d-penicillamine may have a practical application since it appears to be non-toxic and experiments with animals have shown the feasibility of rapidly measuring an inulin-like renal clearance based on the cluster's copper atomic absorption [6]. Similarly the copper-64 labeled cluster is easily prepared [7] and it could be used to obtain positron images of renal dynamics [8]. There is essentially no literature on the stability of these compounds, and in view of the potential applications cited here, such information is needed. We report here our

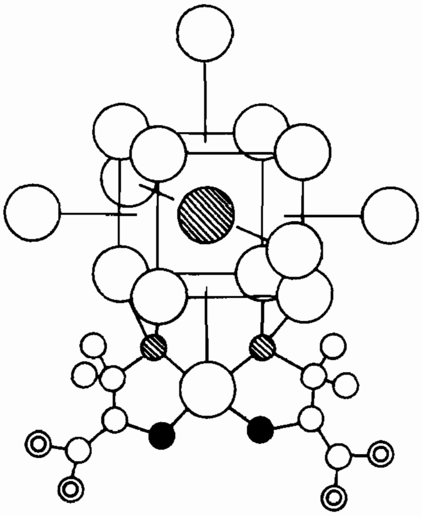

Fig. 1. Partial framework structure of the cluster of copper and penicillamine showing the heavy atoms (large circles) and two of a total of twelve ligands (small circles). A chloride ion (shaded) is at the center of a cube of eight Cu(I) ions. Six Cu(II) ions above the cube faces form an outer octahedron. The twelve ligands are arranged pairwise in approximately square planar geometry around each Cu(II) ion with nitrogen and sulfur coordinating. Each sulfur atom bridges between two Cu(I) ions and one Cu(II) ion. Legend for the ligand atoms: carbon (plain), sulfur (shaded), nitrogen (black), oxygen (concentric). For simplicity, the hydrogen atoms (nine per ligand) are not shown.

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preliminary findings for the cluster anion of copper and d-penicillamine.

Experimental

Detailed methods for preparing and purifying the cluster of Cu(I)/Cu(II) and d-penicillamine, including the radiolabeled version, have been published [5. 7]. The analogous compounds containing Ag(I)/Ni(II) and Ag(I)/Pd(II) were prepared according to reported methods [4] but these were isolated as sodium salts from Chelex-100 columns. Thermal studies were performed with a Perkin-Elmer DSC-4 differential scanning calorimeter (DSC) using TADS software and a Varian series 634 spectrophotometer was used for absorbance measurements. All kinetic data reported here for aqueous solutions were obtained by the method of initial rates, and the values are given as the mean plus or minus the standard deviation. In the case of the copper cluster, rates were based on a decrease of its absorption at 520 nm, for which the molar extinction coefficient is 28 000. Product absorption was found to be minimal at this wavelength. Similar measurements of the Ag(I)/Ni(II) cluster were obtained at 450 nm, but in this case an absorption increase due to the formation of a pyrolysis product was observed. These substances obey Beer's law [4, 5]. Reactions were carried out in thoroughly clean glass containers, with stirring, and temperature control was achieved by means of an oil thermostat. Some of the samples (e.g. those which were degassed or exposed to oxygen) were prepared in fire-sealed ampules using vacuum line methods.

Results and Discussion

The hydrated sodium salt of the cluster of copper and d-penicillamine, $Na_5Cu(I)_8Cu(II)_6pen_{12}Cl\cdot 56H_2O$, was examined by DSC. A broad endotherm peaking at 125 °C (onset at 60 °C), 78.9 cal/g or 303 kcal/mol based on the above formula is due to dehydration, while a second, sharper endotherm peaking at 169 °C (onset at 160 °C), 20.8 cal/g or 79.8 kcal/mol (based on the formula) marks decomposition. The red–violet chromophore is lost during the latter temperature interval.

The sodium salt is water soluble to the extent of 183 mg/ml [6], but if Cu(II) counterion is added, a red–violet precipitate forms immediately. The original sodium salt may be regenerated by slurrying the precipitate with Chelex-100 (sodium form). The pK_{sp} of the cupric counterion/cluster solubility equilibrium was found to be in the order of 24, but this value is difficult to measure accurately since counterion copper also causes the cluster to decompose. Aqueous solutions of the sodium salt thus pyrolize in an accelerated fashion since cupric ion accumulates as the cluster decomposes.

The rate law and activation energy of the latter reaction were obtained from the effects of concentration and temperature on initial reaction rates. Concentrations of cluster and cupric ion were varied around micromolar and 0.1 millimolar, respectively, with pH at 8.5, while the effects of temperature were observed in the range 40–80 °C. Least-squares analysis of log rate *versus* log concentration yielded an exponent of 1.23 ± 0.08 (18 ordered pairs) for cupric ion concentration and 1.08 ± 0.11 (18 ordered pairs) for the cluster's concentration. The rate law is thus approximately first order in both reactants. The reaction's temperature dependence yielded an apparent activation energy of 27.1 ± 3.7 kcal/mol (12 ordered pairs), and the empirical expression for the rate constant was found to be $k = 10^{17} \pm 10^2 \exp(-27\,100 \pm 3700/RT)$ in reciprocal molar-seconds ($R = 1.987$ cal/K mol).

The rate of this reaction is independent of dissolved oxygen concentration even though Cu(I) is present in the cluster. Significant differences were not observed between reaction mixtures which had been degassed, sealed under air or sealed under pure oxygen (respectively). It should be noted that all of these measurements were obtained with concentrations within an order of magnitude of the solubility limit, but precipitates were strictly avoided.

The rate law for cluster pyrolysis in aqueous solutions is substantially altered in the absence of aqueous cupric ion. This condition was achieved by stirring reaction mixtures with Chelex-100, which sequesters cupric ion as the cluster decomposes. In these experiments, the cluster concentration was varied in the 3–60 micromolar range (pH = 8.5), and the temperature dependence was observed between 90 and 110 °C in sealed vessels. A least-squares analysis of log initial rate *versus* log cluster concentration yielded an exponent of 1.93 ± 0.12 (24 ordered pairs; see Fig. 2). The apparent activation energy of this net second order process was found to be 40.6 ± 1.0 kcal/mol, and the empirical rate constant is $k = 10^{23} \pm 10^4 \exp(-40\,600 \pm 1000/RT)$ in reciprocal molar-seconds ($R = 1.987$ cal/K mol). As would be expected of a reaction involving the association of like-charged ions, the rate increases with increasing ionic strength [9]. It is noted that when pyrolysis was attempted with the cluster concentration above 80 micromolar and the temperature above 100 °C, the decomposition was rapid, and a brown product was formed.

In an earlier paper it was reported [10] that the unlabeled cluster slowly accumulates added copper-67 radiolabel (added as aqueous cupric ion). The inverse experiment was tried in the current study, *i.e.* the copper-64 labeled cluster was allowed to

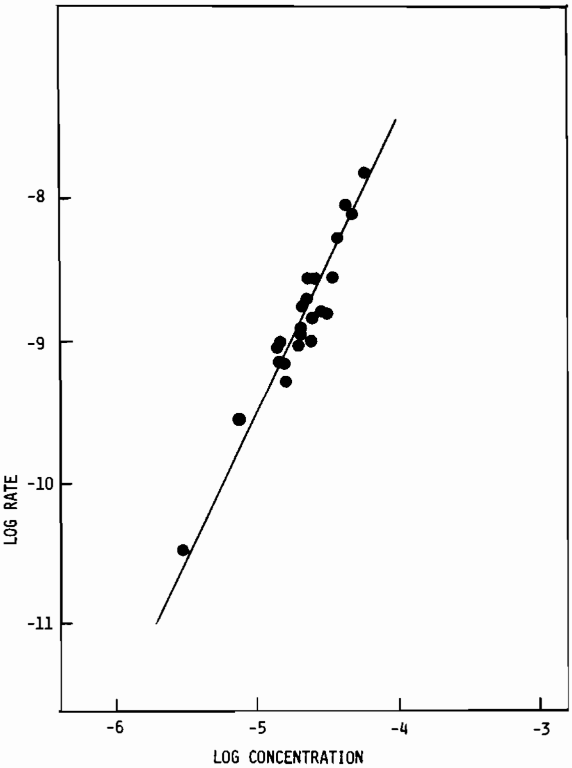

Fig. 2. The rate law for copper cluster pyrolysis in the presence of Chelex-100 is approximately second order. The concentration and rate units are molar and molar per second, respectively. These are based on colorimetrically measured cluster concentrations.

equilibrate with unlabeled cupric ion. In these measurements, the cluster and cupric ion concentrations were respectively 4.0×10^{-7} M and 4.0×10^{-4} M and thus similar to those described for the decomposition reaction, but the temperature was maintained at 25 °C under air, pH = 8.5. Decay corrected counts of activity remaining in the cluster fraction were obtained by sequestering the aqueous cupric ion with Chelex-100 and removing it by centrifugation (the cluster does not adsorb on Chelex-100). Under these conditions, the exchange rate was observed to be about 1.5% per hour or 2×10^{-11} M/s. It is noted that since Chelex-100 does not remove Cu(II) from the cluster, the exchange mechanism apparently depends on the presence of counterion Cu(II). Counterion Cu(II)-induced decomposition was not significant under the conditions of the exchange measurements (about 0.004% per hour).

We confirm a reported visible light photodecomposition of the cluster anion [11] and further note that at 0 °C the decomposition rate is not influenced by added Chelex-100. The available evidence thus defined at least three routes of decomposition (photochemical, cupric ion catalyzed and an intrinsic second order pyrolysis mode). Detailed insight into the mechanistic processes behind each of these modes is not possible at this time, but some general observations may be made. First, there are two sources of instability in the series of analogous copper clusters since they contain Cu(I), which is unstable with respect to molecular oxygen, and they also contain the thiolate ligand penicillamine (or an analog), which is also reactive with molecular oxygen or the Cu(II) ions present in the cluster. Nearly all who have published studies of these clusters (including the authors) have speculated that ligands which lack the gem-dimethyl group form unstable clusters because molecular oxygen is able to access and oxidize the sulfur atom or Cu(I). While this may be true for the transient clusters of cysteine and cysteamine, such a view does not explain the relatively long-term stability observed of mixed ligands clusters containing one or two cysteamine or cysteine methyl ester ligands [5]. Similarly, our current finding that molecular oxygen does not influence the penicillamine cluster's pyrolysis rate suggests that the rate limiting step precedes any events involving molecular oxygen. The reaction may instead be driven by an internal redox between Cu(II) and the thiolate ligand. This view is consistent with our observation that the transient cysteine and cysteamine clusters remain transient in degassed solutions. It is thus possible that clusters which lack the rigidity imposed by the gem-dimethyl group's bulk experience low internal barriers, and a reaction may be favored in which cupric ions are reduced and a pair of coordinating ligands are converted to a disulfide product, thus disrupting the structure.

The processes of precipitation, isotope exchange and cupric ion catalyzed decomposition are probably closely related, involving cupric ion interactions with peripheral carboxylate groups. It is noted that isotope exchange places two cupric ions in proximity to a pair of thiolate ligands, and stoichiometry for disulfide production is thus satisfied. Photochemical decomposition also could involve internal redox processes [12]. The second order rate law observed in the absence of aqueous cupric ion suggests a decomposition mechanism involving pairwise cluster ion encounters, and the nature of this process seems obscure. It has the largest activation barrier observed thus far and appears to define the intrinsic stability of the cluster.

The clusters of silver and nickel and of silver and palladium decomposed at lower temperatures. In DSC measurements the former presented a single, moderately broad endotherm with a maximum at 143 °C (onset at 119 °C), 188 cal/g or 726 kcal/mol, based on the approximate formula $Na_5Ag(I)_8Ni(II)_6$-$pen_{12}Cl \sim 40H_2O$. The palladium-containing analog behaved similarly with an endotherm peaking at 138 °C (onset at 127 °C), 159 cal/g or 660 kcal/mol, based on the approximate formula $Na_5Ag(I)_8Pd(II)_6$-

pen$_{12}$Cl ~ 40H$_2$O. Studies of these structures were limited by the small quantities available. The cluster of silver and nickel pyrolyzed in aqueous solutions at 70 °C (pH = 8.5; these contained suspended Chelex-100), and a more intensely absorbing product formed with a first order dependence on the cluster's concentration (the slope of a plot of log $\Delta A_{450}/\Delta t$ *versus* log cluster concentration was 0.943 ± 0.078 based on 11 ordered pairs).

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