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# Kinetic Investigation on the Reaction between Cu(II) and Excess D-penicillamine in Aqueous Media

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The kinetics and mechanism of reduction of Cu(II) with an excess D-penicillamine have been examined at pH = 6.2 and 0.60M in ionic strength. The reaction at the initial stage is biphasic with a rapid complexation process to give "red" transient complex of $[Cu(II)(pen)_2]^{2-}$ that is partially reduced to another transient "brown" intermediate. The "brown" intermediate is finally reduced to diamagnetic "yellow" complex, $[Cu(I)(Hpen)]_n$. The final reduction process is pseudo-first order in ["brown" transient] disappearance with $k = \{k_{3a} + k_{3b}[pen]^{2-}\}$, where $k_{3a} = (5.0 \pm 0.8) \times 10^{-3}\,\text{sec}^{-1}$ and $k = (0.14 \pm 0.02)$ $M^{-1}\text{sec}^{-1}$ at 25 °C. The activation parameters for the $[H_2pen]$-independent and $[H_2pen]$-dependent paths are $\Delta H^* = (52 \pm 5)\text{kJmol}^{-1}$, and $\Delta S^* = (-27 \pm 3)\text{Jk}^{-1}\text{mol}^{-1}$, and $\Delta H^* = (56 \pm 2)\text{kJmol}^{-1}$ and $\Delta S^* = (-18 \pm 0.7)\text{Jk}^{-1}\text{mol}^{-1}$ respectively. The nature of "brown" intermediate is not clearly identified, but this intermediate seems to be in the mixed-valence state, judging from the kinetic and spectroscopic informations.

## Introduction

D-penicillamine, $HS(CH_3)_2CH(NH_2)COOH$ ($H_2pen$) has been used as a medicinal chelating agent[1] and the oral administration of D-penicillamine to patients with Wilson's disease promotes the urinary excretion of excess copper[2,3], but the reaction between copper(II) and D-penicillamine has not been well characterized.

Unusual complications have been observed by previous workers[2,4-6] as D-penicillamine reacts with copper(II) to cause partial or complete reduction to produce paramagnetic "purple" complex anion, $[Cu(II)_6Cu(I)_8(pen)_{12}Cl]^{5-}$ or diamagnetic "yellow" complex, $[Cu(I)(Hpen)]_n$, depending on concentration ratio of Cu(II) to D-penicillamine[4]. Moreover, the presence of halide ions ($Cl^-$ or $Br^-$) is reported to be essential for the formation of "purple" complex ion in the mixed valence state[4].

The reduction of copper(II) with an excess thiol such as D-penicillamine is known to produce the appropriate disulfide[7] and it has been suggested on the basis of an investigation employing polarography and electronic absorption spectroscopy that the stoichiometry is as in the following reaction[8].

$$Cu(II) + 2\,RSH \longrightarrow Cu(I)(SR) + 1/2\,RSSR + 2\,H^+$$

Although the stoichiometry of this type of reaction is relatively well established, there are controversies about the nature of transient intermediates produced in the initial stage of the reaction and the reaction mechanism for the formation of Cu(I) complexes which has not been identified with certainty.

In this study, we reexamined the reduction of Cu(II) with an excess D-penicillamine in the acetate buffer (pH = 6.2) to elucidate the reaction mechanism for the formation of "yellow" complex.

## Experimental Section

**Materials.** Doubly distilled water was further purified by a passage through anion and cation resins (Dowex-1-hy-

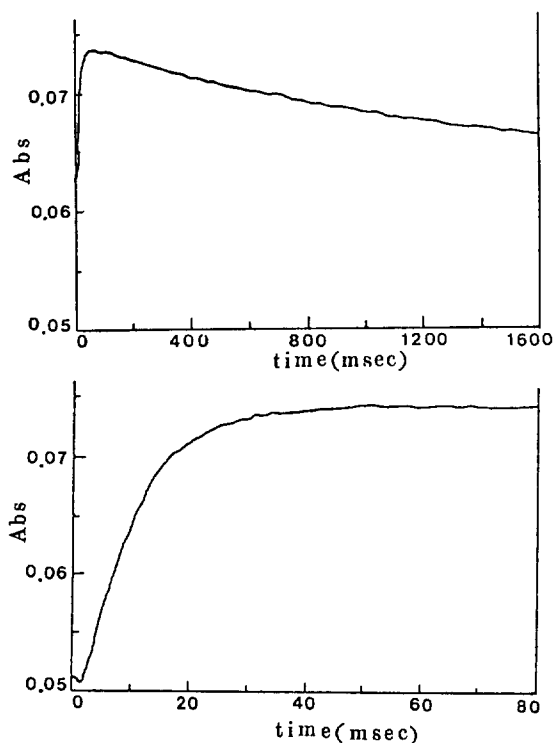282 *Bull. Korean Chem. Soc., Vol. 11, No. 4, 1990*

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**Figure 1.** The typical absorbance *vs.* time curve observed at 520 nm at the initial stage of the reaction in which $[Cu(II)(pen)_2]^{2-}$ is produced (a) and then $[Cu(II)(pen)_2]^{2-}$ is reduced (b).



**Figure 2.** Maximal absorbance change observed at 520 nm as a function of the D–penicillamine to copper ratio $[H_2pen]/[Cu(II)]$ and the mole fraction, $X_{H_2pen}$.

droxide form and Dowex–50W–hydrogen form). D–penicillamine was purchased from Fluka Chemical Co. and used as received. Reagent grade cupric chloride, cupric nitrate, sodium acetate and sodium perchlorate were purified by recrystallization.

A stock solution of Cu(II) was standardized by the titration with standard $Na_2EDTA$ solution using PAN as an indicator[9]. Buffer solution (pH = 6.2) were prepared from 0.50M sodium acetate solution and 0.025M acetic acid.

Yellow precipitate formed as a reaction product was isolated, washed with water–ethanol, and dried in vacuum over $P_2O_5$ for the elemental analysis. Anal. Calcd for the $[Cu(I)(Hpen)H_2O]_n$: Cu, 27.78; C, 26.25; N, 6.12; H, 5.36. Found: Cu, 26.66; C, 27.66; N, 6.18; H, 4.85.

**Kinetic Measurements and Estimation of Specific Rate.** Reactions were monitored by following absorbance change at 520 nm on a Union Giken RA–401 stopped–flow spectrophotometer or on a Shimazu M–240 UV–Visible spectrophotometer. In most instances, total ionic strength was maintained at 0.60M by addition of $NaClO_4$ and pH values were maintained at 6.2 using acetate buffer solutions. Pseudo–first Order conditions were maintained by using ten–fold or more excess of D–penicillamine over Cu(II) for each run. Rate constants given in the tables are averaged from three or more measurements.

To avoid air oxidation, test solutions were thoroughly purged with nitrogen gas before each run.

## Results and Discussion
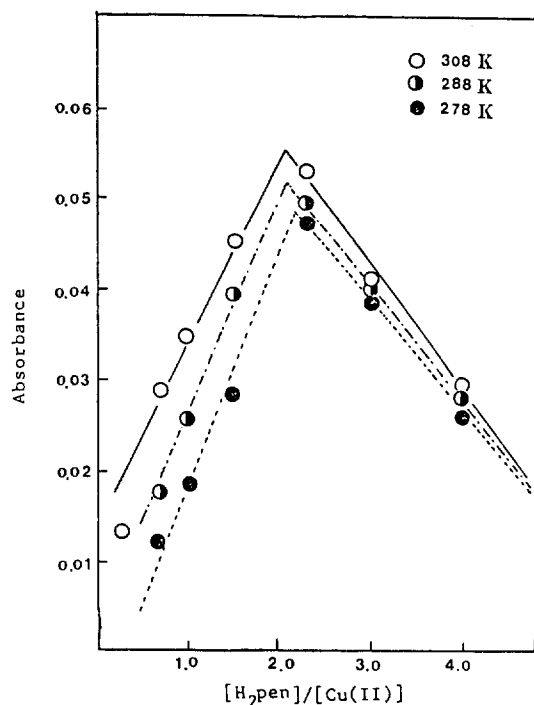
**The Formation and Decay of Transient Copper(II)**

**Complex.** When Cu(II) and D–penicillamine are mixed and stopped in a flow system, a very rapid increase followed by a slow decrease in absorbance at 520 nm was exhibited (see Figure 1). The principal observation at the initial stage of the reaction was the formation of red transients. The strong absorption at 520 nm for Cu(II) complex with D–penicillamine has been considered by previous workers[10] to be arisen from the charge transfer $(S(\sigma)-$ Cu(II)) and the increase in absorbance at 520 nm is definitely attributed to the formation of Cu(II)–S bondings. The maximal absorbance changes as a function of the [D–penicillamine]/[Cu(II)] ratio (see Figure 2 and Table 1). The results show a sharp peak at a [D–penicillamine]/[Cu(II)] ratio of 2, indicating that the stoichiometry for the formation of this red transient is two D–penicillamine for one Cu(II) and the formation of red transients can be described by reaction (1).

$$Cu\ (II) + 2H_2pen \rightarrow [Cu\ (II)\ (pen)_2]^{2-} + 4H^+ \qquad (1)$$
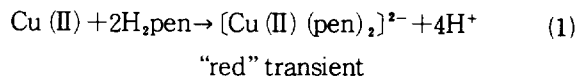
"red" transient

The existence of a series of copper(II) complexes $[CuL_2]$ of thiolate derivatives of types $CuS_4$, $CuS_2N_2$ and $CuS_2O_2$ is well established at high pH condition and copper(II)–thiol complexes of these types are also suggested to be existed transiently even at low pH condition[11].

The rate of formation of red transient was evaluated by use of the initial rate method. The initial slope, $\Delta[A]/\Delta t$ was obtained graphically and was assumed to be the same as the initial rate $\Delta[A]/\Delta t$ and the reaction was followed only for the first 5% of the reaction. The second–order rate constant $k$ for the reaction (1) at 25 °C was determined to be $(8 \pm 2) \times 10^6$ $M^{-1}sec^{-1}$. Kinetic results for the formation of

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**Table 1.** Maximal Absorbance Change Observed at 520 nm as a Function of the *D*-penicillamine to Copper Ratio [H$_2$pen]/[Cu(II)] and the Mole Fraction, $X_{H_2pen}$

| $T(°K)$ | $X_{H_2pen}$ | [H$_2$pen]/[Cu(II)] | Absorbance |
|---|---|---|---|
| 278 | 0.40 | 0.67 | 0.012 |
| 278 | 0.50 | 1.00 | 0.019 |
| 278 | 0.60 | 1.50 | 0.028 |
| 278 | 0.70 | 2.33 | 0.047 |
| 278 | 0.75 | 3.00 | 0.037 |
| 278 | 0.80 | 4.00 | 0.026 |
| 288 | 0.40 | 0.67 | 0.017 |
| 288 | 0.50 | 1.00 | 0.026 |
| 288 | 0.60 | 1.50 | 0.039 |
| 288 | 0.70 | 2.33 | 0.049 |
| 288 | 0.75 | 3.00 | 0.040 |
| 288 | 0.80 | 4.00 | 0.028 |
| 298 | 0.20 | 0.25 | 0.013 |
| 298 | 0.40 | 0.67 | 0.029 |
| 298 | 0.50 | 1.00 | 0.035 |
| 298 | 0.60 | 1.50 | 0.045 |
| 298 | 0.70 | 2.33 | 0.052 |
| 298 | 0.75 | 3.00 | 0.041 |
| 298 | 0.80 | 4.00 | 0.029 |

**Table 2.** Kinetic Results for the Formation of [Cu(II)(pen)$_2$]$^{2-}$ at 25 °C

| [CuCl$_2$] (mol/l) | D-penicillamine (mol/l) | initial rate $M/$ $t$, (Msec$^{-1}$) | $k$ (M$^{-1}$sec$^{-1}$) |
|---|---|---|---|
| 1.00 × 10$^{-3}$ | 1.00 × 10$^{-2}$ | 82.3 | |
| 1.00 × 10$^{-3}$ | 1.50 × 10$^{-2}$ | 132 | 8(± 2) × 10$^6$ |
| 1.00 × 10$^{-3}$ | 2.00 × 10$^{-2}$ | 154 | |
| 1.00 × 10$^{-3}$ | 2.50 × 10$^{-2}$ | 156 | |

"red" transient are summarized in Table 2.

The visible spectra of "red" transient was obtained utilizing multi-channel photodiode detector system attached to the stopped-flow spectrophotometer (see Figure 3). The spectra exhibits two strong absorption peaks at 465 nm ($E = 2700$ mol$^{-1}$dm$^3$cm$^{-1}$) and 540 nm ($E = 2500$ mol$^{-1}$dm$^3$cm$^{-1}$) and these results also strongly indicate one or more Cu(II)–S bonding interactions exist in red transient.

The color of the reaction solution changes into brown color at first and then finally into yellow color as this "red" transient disappears. The decay profile of absorbance at 520 nm against time reveals that two consecutive step reactions are involved. As shown in Figure 4, there is a sharp break point in the curve at around 50 seconds. The decrease in absorbance at 520 nm is definitely attributed to the reduction of copper(II) in the red transient and, in the first reduction process, the "brown" colored intermediate is transiently produced. This "brown" intermediate is further reduced into diamagnetic "yellow" complex, [Cu(I)(Hpen)H$_2$O]$_n$ which is reported to be polymeric[12]. The nature of this "brown" transient is not clearly identified, but we believe that this intermediate is in the mixed valence states. The absorbance of "brown" transient at 520 nm is about a half of that of "red"
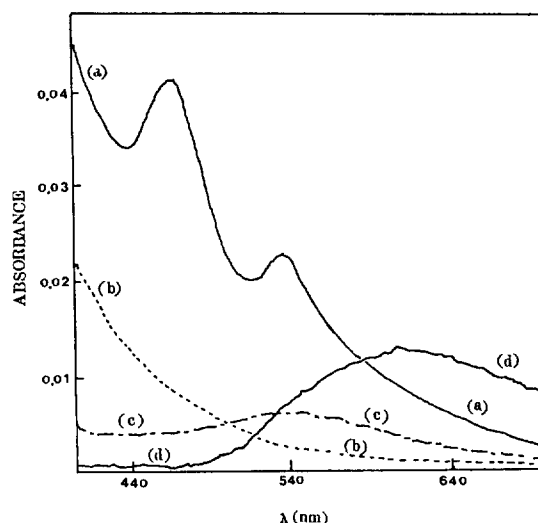


**Figure 3.** Electronic absorption spectrum of (a) [Cu(II)(pen)$_2$]$^{2-}$, (b) [Cu(I)(Hpen)]$_n$, (c) "brown" transients and (d) Cu(II)$_2$(pen–pen)$_2$. The absorbance unit used is arbitrary.
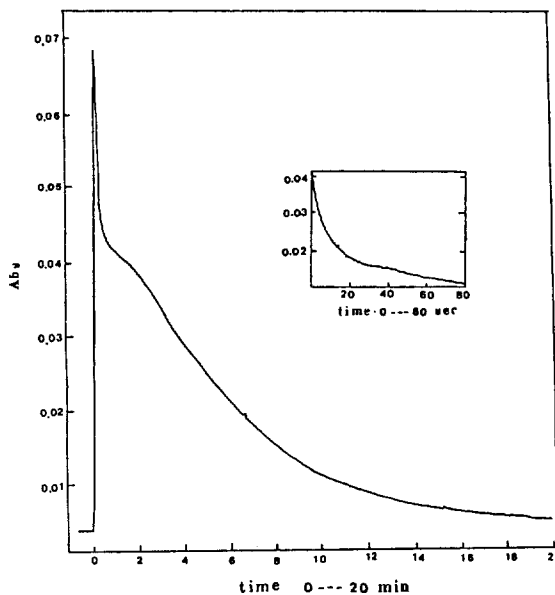


**Figure 4.** Kinetic profile observed at 520 nm for reaction of Cu(II) (1.0 × 10$^{-3}$M) with D–penicillamine (1.0 × 10$^{-2}$ M) at 25 °C. The supporting medium consists of 0.5 M sodium acetate and 0.025 M acetic acid; the pH was 6.2. Note the sharp break point in the curve at around 40 seconds after mixing. Kinetic profile shown in the box was obtained by the use of stopped-flow system.

transient and the visible spectra of "brown" transient is quite similar to that of mixed valence complex, [Cu(I)$_8$ Cu(II)$_6$(pen)$_{12}$Cl]$^{5-5}$ although the magnitude of absorbance in the region of 400 nm–600 nm is smaller (see Table 3). The first reduction process for "red transient can be described by reaction (2).
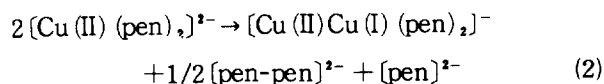
$$2\,[Cu\,(II)\,(pen)_2]^{2-} \rightarrow [Cu\,(II)\,Cu\,(I)\,(pen)_2]^-$$
$$+1/2\,[pen-pen]^{2-} + [pen]^{2-} \qquad (2)$$

**Table 3.** Spectral data for the Copper(II) and Copper(I) Complexes Formed During the Reaction Between Copper(II) and Excess D-penicillamine

| Species | $\lambda_{max}$ (nm) | $\varepsilon$ (mol⁻¹dm³cm⁻¹) | Band assignment | Reference |
|---|---|---|---|---|
| [Cu(II)(pen)₂]²⁻ | 465 | 2700 | S($\pi$)— Cu(II) | this work |
|  | 540 | 2500 | S($\sigma$)— Cu(II) |  |
| [Cu(II)Cu(I)- |  |  |  |  |
| (pen)₂]⁻ | 540 | 1000 | S($\sigma$)— Cu(II) | this work |
| [Cu(II)₈Cu(I)₆- | 430(sh) | 1000 | S($\pi$)— Cu(II) |  |
| (pen)₁₂Cl]⁵⁻ | 518 | 1700 | S($\sigma$)— Cu(II) | 10 |
| [Cu(II)₂-] |  |  |  |  |
| (pen–pen)₂] | 612 | 40 | $d-d$ | 5 |
| [Cu(I)(Hpen)]ₙ | 273 | 2500–3500 | S— Cu(I) |  |

**Table 4.** Kinetic Results for the Reduction of [Cu(II)(pen)₂]²⁻ ᵃ

| $T$(°K) | [D-penicillamine] (mol/$l$) | $k$[M⁻¹sec⁻¹] |
|---|---|---|
| 288 | $1.00 \times 10^{-2}$ | 1.2 ($\pm$ 0.0) |
| 288 | $1.50 \times 10^{-2}$ | 1.9 ($\pm$ 0.2) |
| 288 | $2.50 \times 10^{-2}$ | 0.9 ($\pm$ 0.2) |
| 298 | $1.00 \times 10^{-2}$ | 2.8 ($\pm$ 0.1) |
| 298 | $1.50 \times 10^{-2}$ | 3.1 ($\pm$ 0.2) |
| 298 | $2.50 \times 10^{-2}$ | 2.7 ($\pm$ 0.2) |
| 308 | $1.00 \times 10^{-2}$ | 6.3 ($\pm$ 0.5) |
| 308 | $1.50 \times 10^{-2}$ | 6.7 ($\pm$ 0.8) |
| 308 | $2.50 \times 10^{-2}$ | 6.0 ($\pm$ 0.3) |
| 318 | $1.00 \times 10^{-2}$ | 11.8 ($\pm$ 0.7) |
| 318 | $1.50 \times 10^{-2}$ | 11.7 ($\pm$ 0.5) |
| 318 | $2.50 \times 10^{-2}$ | 12 ($\pm$ 3 ) |

ᵃ[Cu(II)] = 5.0 × 10⁻⁴ M, I = 0.60 M and pH = 6.2.



**Figure 5.** A typical [1/[A]ₜ-1/[A]ₒ] vs. time plot for the second-order decay for the reduction of [Cu(II)(pen)₂]²⁻. This plot is for the sixth experiment in Table 4.
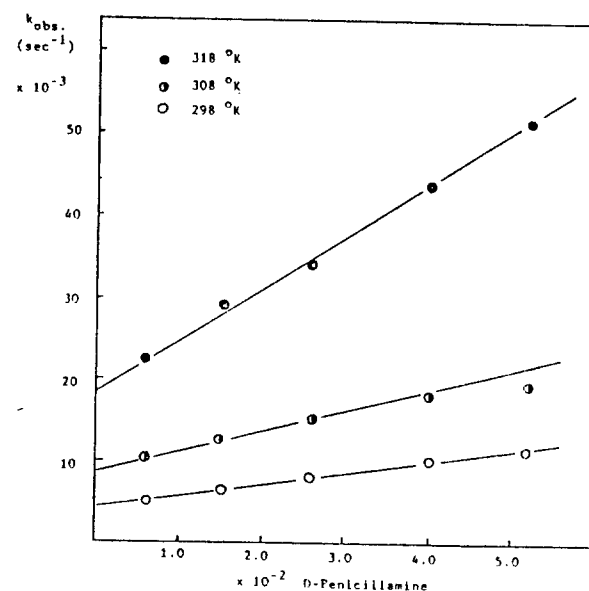


**Figure 6.** Dependence of the pseudo-first order rate constant ($k_{obs}$) on the concentration of D-penicillamine.

Kinetic runs for the reduction process in which the "red" transients decays to the "brown" transients were monitored at 520 nm as a function of time and for different D-penicillamine concentrations. The reduction follows apparent second-order kinetics as demonstrated by 1/[A] against time where [A] is the absorbance of "red" transients (see Figure 5). When relatively high concentration of D-penicillamine is employed ([D-penicillamine] > 10[Cu(II)]), the rate of decay is independent of the concentration of D-penicillamine. Kinetic results for the first reduction process are summarized in Table 4. For [Cu(II)] = 5.00 × 10⁻⁴M, and [D-penicillamine] = 10.0 × 10⁻²M, a second order rate constant of (2.8 ± 0.1) M⁻¹sec⁻¹ at 25 °C has been calculated.

**The Formation of "Yellow" Complex, [Cu(I)(Hpen)]ₙ.** Unlike red transient, The "brown" intermediate is relatively stable in excess [Cu(II)] and in the absence of halide ions, but reacts with excess D-penicillamine to form diamagnetic "yellow" complex. It has been suggested on the basis of IR spectrum of "yellow" complex that the Cu(I) atoms are coordinated by the thiolate groups of ligand but not by the amino groups, and that the amino groups are in their protonated form[6]. Birker *et al.*[5] and other workers[12] suggested that the "yellow" complex is in the polymeric form since it is improbable that a monomeric species of Cu(I) would be stable in

solution, and they formulated for this Cu(I)-Hpen complex as [Cu(I)(Hpen)H₂O]ₙ. We isolated "yellow" complex from the reaction solution and performed elemental analysis. The result of elemental analysis is in accrordance with the formula as suggested by previous workers[6]. The second reduction process in which the "yellow complex is formed from "brown" intermediate obeys pseudo-first order kinetics. Plots of $k_{obs}$ vs. [D-penicillamine] are linear but do not pass through the origin at all temperatures (see Figure 6) leading to the following empirical rate law.
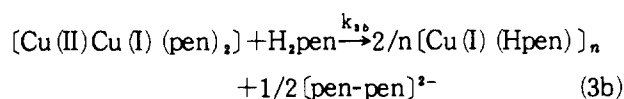
$$- d\,[Cu\,(II)Cu\,(I)\,(pen)_2]^-/dt = k_{obs}[Cu\,(II)Cu\,(I)\,(pen)_2]^-$$

$$k_{obs} = (k_{3a} + k_{3b}\,[H_2pen])$$

A plausible reaction Scheme for the formation of "yellow" compelx can be outlined in equation 3a and 3b with $k_{3a} = (5.0 \pm 0.8) \times 10^{-3}$sec⁻¹ and $k_{3b} = (1.37 \pm 0.02)$M⁻¹sec⁻¹ at 25 °C and I = 0.6 moldm⁻³.

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**Table 5.** Kinetic Results for the Formation of Diamagnetic "Yellow" Complex, $[Cu(Hpen)]_n$

| $T(^{\circ}K)$ | [D–penicillamine] (mol/$l$) | $k_{obs}$ (sec$^{-1}$) | $k_{cal}$ (sec$^{-1}$) |
|---|---|---|---|
| 298 | $5.00 \times 10^{-3}$ | $5.1(\pm 0.6) \times 10^{-3}$ | $5.18 \times 10^{-3}$ |
| 298 | $1.50 \times 10^{-2}$ | $6.5(\pm 0.3) \times 10^{-3}$ | $6.55 \times 10^{-3}$ |
| 298 | $2.50 \times 10^{-2}$ | $8.1(\pm 2) \times 10^{-3}$ | $7.92 \times 10^{-3}$ |
| 298 | $4.00 \times 10^{-2}$ | $10 (\pm 2) \times 10^{-3}$ | $9.98 \times 10^{-3}$ |
| 298 | $5.00 \times 10^{-2}$ | $11 (\pm 1) \times 10^{-3}$ | $11.4 \times 10^{-3}$ |
| 308 | $5.00 \times 10^{-3}$ | $10 (\pm 4) \times 10^{-3}$ | $10.6 \times 10^{-3}$ |
| 308 | $1.50 \times 10^{-2}$ | $13 (\pm 3) \times 10^{-3}$ | $12.7 \times 10^{-3}$ |
| 308 | $2.50 \times 10^{-2}$ | $15.3(\pm 0.2) \times 10^{-3}$ | $14.7 \times 10^{-3}$ |
| 308 | $4.00 \times 10^{-2}$ | $18.2(\pm 0.2) \times 10^{-3}$ | $17.8 \times 10^{-3}$ |
| 308 | $5.00 \times 10^{-2}$ | $19.6(\pm 0.0) \times 10^{-3}$ | $19.9 \times 10^{-3}$ |
| 318 | $5.00 \times 10^{-3}$ | $22.4(\pm 0.1) \times 10^{-3}$ | $22.2 \times 10^{-3}$ |
| 318 | $1.50 \times 10^{-2}$ | $29.1(\pm 0.7) \times 10^{-3}$ | $28.6 \times 10^{-3}$ |
| 318 | $2.50 \times 10^{-2}$ | $34.0(\pm 0.9) \times 10^{-3}$ | $35.0 \times 10^{-3}$ |
| 318 | $4.00 \times 10^{-2}$ | $44 (\pm 1) \times 10^{-3}$ | $44.5 \times 10^{-3}$ |
| 318 | $5.00 \times 10^{-2}$ | $52 (\pm 1) \times 10^{-3}$ | $50.9 \times 10^{-3}$ |

$^a[CuCl_2] = 5.00 \times 10^{-4}$.
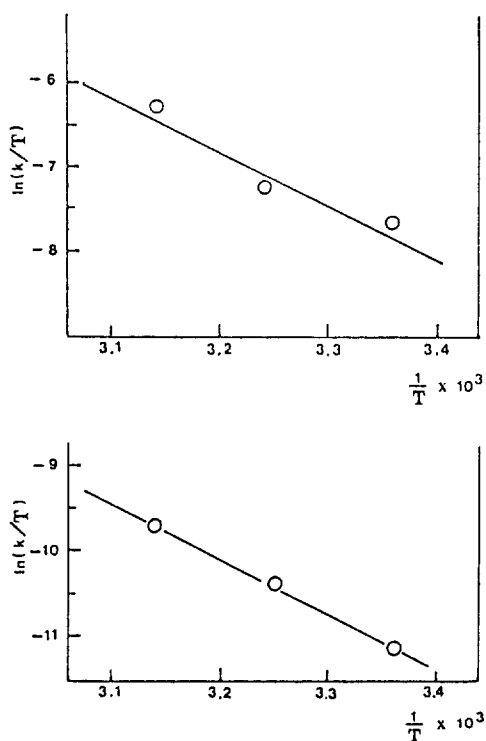




**Figure 7.** A plot of $\ln(k/T)$ vs. $1/T$ for the formation of diamagnetic "yellow" complex.

$$[Cu(II)Cu(I)(pen)_2] \xrightarrow[k_{3a}]{H^+} Cu(I) + 1/n[Cu(I)(Hpen)]_n$$

$$+ 1/2[pen-pen]^{2-} \qquad (3a)$$

$$Cu(I) + pen^2 \xrightarrow{H^+} 1/n[Cu(I)(Hpen)]_n \qquad (fast)$$

$$[Cu(II)Cu(I)(pen)_2] + H_2pen \xrightarrow{k_{3b}} 2/n[Cu(I)(Hpen)]_n$$

$$+ 1/2[pen-pen]^{2-} \qquad (3b)$$
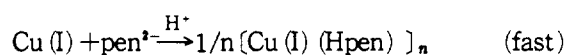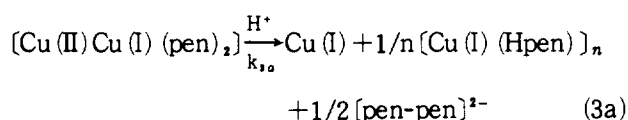
**Table 6.** Rate Parameters for the Reaction of the Formation Yellow Complex, $[Cu(I)(pen)]_n$

| Form of Rate terms | $k$ at 25 °C | $\Delta H^{\neq}$, kJ/mol | $\Delta S^{\neq}$ e.u. |
|---|---|---|---|
| $k_{3a}[Cu(II)Cu(I)(pen)]^-$ | $(4.5 \pm 0.8) \times 10^{-3}sec^{-1}$ | $52(\pm 5)$ | $-27(\pm 3)$ |
| $k_{3b}[Cu(II)Cu(I)(pen)]^-$ | | | |
| $[H_2pen]$ | $(0.14 \pm 0.02)M^{-1}sec^{-1}$ | $56(\pm 2)$ | $-18.1(\pm 0.6)$ |

Rate data for the formation of "yellow" complex are summerized in Table 5. Activation parameters were calculated from equation 4, where $k$ is $k_{3a}$ or $k_{3b}$ and $K$ and $h$ are the Boltzman and Planck constants

$$k = (KT/h)\exp(-\Delta H^{\neq}/RT)\exp(\Delta S^{\neq}/R) \qquad (4)$$

Plots of $\ln(k/T)$ against $1/T$ for reaction 3a and 3b are shown in Figure 7 and rate parameters calculated are listed in Table 6. The $\Delta S^{\neq}$ for the two paths are negative and this is consistent with the suggestion that the polymerization processes of Cu(I) species are involved in reactions 3a, 3b.

## Conclusion

The results of this study give convincing support to the suggestion that the formation of diamagnetic yellow complex, in our experimental conditions, proceeds *via* a rapid complexation process followed by consecutive two reduction processes.

The stoichiometry for the formation of the Cu(II) complex produced at the initial stage of reaction is two D–penicillamine for one Cu(II). This Cu(II) complex has been suggested to be 1:1 complex by previous workers[5,13] but our experiment results strongly indicate that this Cu(II) species is 1:2 complex although it exists only transiently at pH = 6.2.

The reduction of Cu(II) complex occurrs in consecutive two–step reactions. Between two reduction steps, "brown" colored intermediate is formed. The nature of this intermediate is not cleary indentified but our experimental results lead to the conclusion that this "brown" intermediate is in the mixed–valence states and is tentatively formulated as $[Cu(II)Cu(I)(pen)_2]^-$. The knowledges on the nature and the structure of this "brown" intermediate seems to be very critical for the comprehensive understanding of the Cu(II)–thiol reactions. Several attempts to isolate this brown intermediate were made but were not successful.

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# Surface Enhanced Raman Spectroscopic Studies on Zn(II) and Mn(III) Tetrakis (4-N-Methyl Pyridyl) Porphyrins

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The surface enhanced Raman scatterings of Zn(II) tetrakis (4-N-methyl pyridyl) porphyrins were studied in silver sol. Zn(II) tetrakis (4-N-methyl pyridyl) porphyrin was found to be adsorbed on silver surface *via* flat-on geometry with some inhomogeneous distribution in the orientation of pyridyl groups. Both the selective enhancement of Raman modes depending on the mode character and the theoretical arguments of SERS are utilized to support the above conclusion. The surface induced substitution reaction of Mn(III) tetrakis (4-N-methyl pyridyl) porphyrin chloride to Ag(II) tetrakis (4-N-methyl pyridyl) porphyrin was detected *via* surface enhanced Raman spectrum.

## Introduction

Surface enhanced Raman scattering (SERS) spectroscopy has proven to be a very powerful method for investigating the structures of the molecules adsorbed on metal surface.[1,2] Not only the application of this distinct phenomena to molecular systems but also the elucidation of the strong Raman signal enhancement mechanism has attracted a great attention. In addition, SERS spectroscopy has been utilized to study the surface chemical reaction induced by the surface and/or the laser beam because the reaction provides direct changes in SERS spectra of the adsorbed molecule.[1] Indeed, some observations of a surface reaction *via* SERS spectra have been reported on small molecules.[3]

Some applications of SERS to hemoproteins revealed that a change in molecular structure or conformation may occur when they are adsorbed on a silver surface.[4,5] More specifically, the adsorption of hemoproteins on the silver surface can facilitate the separation of the porphyrin macrocycle from the hemoprotein into the $\mu$-oxo-bridged iron porphyrin dimer as a decomposition product from either thermally denatured or autooxidized hemoglobin.[4,5] For model compounds, Itoh *et al.*[6] reported that SERS on free-base TMPyP(4)H$_2$ in silver and copper mixed sol follows the formation of either Cu(II)TMPyP(4) or Ag(II)TMPy(4) through the metal insertion into the porphyrin core, depending on the ratio of the mixed sol and its pH.

In this paper, we examine the SERS of Zn(II)TMPyP(4) and Mn(III)TMPyP(4)Cl in silver sol to address the interaction between the metal surface and the adsorbed molecules. We found that no surface chemical reaction has occurred in

the SERS of Zn(II)TMPyP(4). However, in Mn(III)TMPyP (4)Cl, the surface induced substitution reaction has occurred and the formation of Ag(II)TMPyP(4) was observed by the SERS spectra.

## Experimental

Silver sols were prepared according to the literature. The distilled and purified water was used here. A 10 m*l* volume of silver nitrate solution ($6 \times 10^{-4}$ mol/*l*) was added dropwise slowly to a 30 m*l* sodium borohydride solution ($1.5 \times 10^{-3}$ mol/*l*) with continuous stirring. All the solutions were chilled in an ice-water during the preparation. The yellowish silver sol produced was stable at room temperature. After the addition of a small amount of Zn(II)TMPyP(4) and Mn(III) TMPyP(4)Cl (Porphyrin Product, Logan, UT, USA) into the silver sol, the color changed to red-orange and finally to blue-grey. The details of the Raman measurement system were described elsewhere.[7] Briefly, a sample solution was circulated at 2 m*l*/min with a peristaltic pump through a quartz capillary of 1.4 mm i.d. to avoid possible degradation. A 90° scattering geometry was employed. A Spectra-Physics 165 Ar$^+$ ion laser was used for sample excitation. A 1 m Jobin-Yvon Raman U-1000 double monochromator, a Hamamatsu R943-02 photomultiplier with a PMT cooler and a Hamamatsu C1230 photon counter/discriminator were used. For the intensity ratio measurement of SERS bands, two separate spectra were acquired, using scanning in both forward and backward directions with a fresh sample, keeping all the other conditions same. The two separate spectra were added to compensate the intensity