Table V. Electrochemistry of Copper(II) Mercaptides

| compd | $E_{1/2}$, mV[a] | $N$[b] | $\Delta E_p$, mV |
|---|---|---|---|
| [Cu(1)(*p*-$ClC_6H_4S$)] (**2**) | −860 | 0.88 | 668 |
| [Cu(1)($C_6H_5S$)] (**3**) | −850 | 0.80 | 616 |
| [Cu(1)($OH_2$)]$BF_4$ (**4**) | −490 | 0.85 | 265 |
| ferrocene | 500 | 1.00 | 376 |

[a] All results reported were obtained at a scan rate of 100 mV $s^{-1}$ under the conditions described in the Experimental Section. $E_{1/2}$ values were calculated by taking $(E_{p,c} + E_{p,a})/2$. [b] Comparison of cathodic peak currents to that for ferrocene.

adjustment by the −0.100 V required to correct the ferrocene couple to the standard value of +0.400 V vs. the SHE. From the results shown, it appears clear that the binding of the mercaptide ligands is associated with a stabilization of the copper(II) state of approximately 350 mV. This stabilization must arise from the shift to the highly distorted five-coordinate geometry of **2** and **3**, compared to **4**. In addition, the greater donation of electron density to the metal by the more powerful mercaptide apical ligand should contribute to the observed shift in potential by making the copper(II) more difficult to reduce.

If the prominent bands observed in the visible spectra of **2** and **3** do indeed correspond to the $\sigma$(S)− and $\pi$(S)−Cu charge-transfer bands of the "blue" copper proteins, then the blue shift of ~11 000 $cm^{-1}$ between the characteristic 600-nm band of the type 1 copper and the higher energy band at 354 nm for **2** should be seen again in the difference in electrochemical potentials for these species. Indeed, if one takes a typical potential for type 1 copper to be +400 mV vs. SHE, the 0.1-V correction cited above for our reference electrode would place type 1 copper at +500 mV in our system. The separation in potentials between our complexes **2** and **3** and the type 1 site would then be 1.35 V, which corresponds to 10 850 $cm^{-1}$. These electrochemical results thus provide further confirmation of the assignment of these intense visible transitions for **2** and **3** as LMCT transitions. More details of the orbitals involved in these transitions are expected to arise from our planned theoretical studies of the electronic structures of **2** and **3**.

**Acknowledgment.** We thank the Research Corp. (Grant No. 8076) and the National Institutes of Health (Grant No. GM 25302) for generous support of this work. Additional support from a Colorado State University Biomedical Research Support Grant (NIH Grant No. 534613) and the NATO Research Council (travel grant to O.P.A.) is also gratefully acknowledged. The Nicolet R3/E diffractometer and computer system were purchased with funds provided by the National Science Foundation (Grant No. CHE 8103011). The authors also wish to thank Dr. C. M. Elliott for helpful discussions and generous blocks of time on his electroanalytical instruments.

**Registry No.** **2**, 84927-41-3; **3**, 84927-42-4; **4**, 84927-43-5; [Cu(**1**)($OH_2$)]$ClO_4$, 61114-06-5; [Cu(**1**)($OH_2$)]$PF_6$, 84927-44-6.

**Supplementary Material Available:** Tables VI–XIII, showing least-squares planes, anisotropic temperature factors, positional parameters and isotropic temperature factors for hydrogen atoms, and structure factors for **2** and **3** (36 pages). Ordering information is given on any current masthead page.

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Contribution from the Departments of Chemistry, Radford University, Radford, Virginia 24142, and Virginia Polytechnic Institute and State University, Blacksburg, Virginia 24061

# Interaction of Manganese(II) and Amino Acids with Emphasis on Cysteine and Penicillamine (β,β-Dimethylcysteine)

ROBERT K. BOGGESS,* JOHN R. ABSHER, SCOTT MORELEN, L. T. TAYLOR,* and JEFF W. HUGHES

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The interaction of manganese(II) with bidentate and tridentate ligands containing nitrogen, oxygen, and/or sulfur donor atoms has been investigated. The tridentate amino acids L-cysteine and D-penicillamine have proven to be the best chelators for manganese(II) on the basis of aqueous titration data. Mono and bis chelates of high-spin manganese(II) employing these amino acids have been prepared and characterized. Oxygen-uptake experiments in solution have been carried out both on the isolated complexes and on prepared solutions of differing L:Mn(II):$OH^-$ ratios. In each situation oxygen is rapidly consumed. Observations made during oxygenation experiments suggest that the sulfur-containing amino acid is oxidized to disulfide and that manganese catalyzes this reaction. An oxygenated manganese species is postulated as an intermediate with penicillamine.

## Introduction

Reports of amino acid complexes with manganese(II) compared to those with other transition metal ions are less abundant partly due to their relatively weak interaction. For example, the formation constant ($\beta_2$) of the bis(L-histidinato)manganese(II) complex is some 6–12 orders of magnitude less than for other first-row transition-metal ions.[1] A recent review of amino acids with chelatable side-chain donor atoms[2] and two reviews specifically dealing with cysteine and penicillamine[3,4] rarely mention manganese(II) although chromium, iron, cobalt, nickel, copper, zinc, and several second- and third-row transition metals are discussed at length. A report specifically dealing with the chemistry of biological manganese devoted one short section to its interaction with amino acids.[5]

* To whom correspondence should be addressed: R.K.B., Radford University; L.T.T., Virginia Polytechnic Institute and State University.

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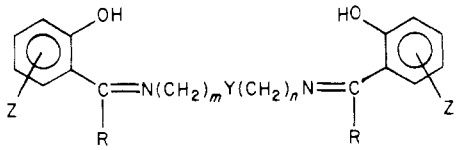
Several earlier reports from this laboratory[6] have dealt with a series of manganese(II) complexes that show chemical reactivity toward small molecules such as $O_2$ and nitric oxide (NO) and that might serve as models for biological molecules. The goals of this study have been to (1) determine the ligand parameters that enhance small-molecule reactivity and (2) ascertain the stoichiometry and nature of the manganese–small molecule interaction. The ligands investigated have been linear tetradentate and pentadentate Schiff-base ligands (I) whose




I

manganese(II) complexes react readily with dioxygen in solution or as a suspension. Reactivity toward dioxygen is a function of central donor atom (Y), aliphatic chain length ($n$, $m$), and aromatic substituent (Z). The oxidation Mn(II) → Mn(III) is observed in all complexes, but further oxidation of the metal and/or the ligand is a common feature. Reactivity with NO is likewise ligand dependent. Reversible coordination of NO is observed with some pentadentate ligands to produce manganese(I) nitrosyls, but manganese(II) associated with tetradentate ligands (Y = $CH_2$) exhibits no affinity for NO.

Manganese(II) complexes of amino acids should be better models for biological systems, since it is generally believed that manganese porphyrins are not found in manganese-containing chloroplast and superoxide dismutase. This report is concerned with the coordination affinity of various amino acids and similar oxygen–nitrogen donor compounds with manganese(II). In addition, the preparation and $O_2$ sensitivity of several manganese–amino acid complexes containing sulfhydryl ligands are described.

## Experimental Section

**Materials.** All amino acids were obtained from Sigma Chemical Co., St. Louis, MO, and used without further purification. Other materials were reagent grade from common commercial suppliers.

**Titrations.** Titrations were performed under an argon atmosphere. In a typical experiment, 0.25 mmol of manganese(II) perchlorate (hexahydrate) was added to the deaerated solvent, followed by the ligand in an appropriate ratio, and the solution titrated with 1.00 M sodium hydroxide. Titrations were done in either water or an ethanol–water (1:1, v/v) mixture at $\mu$ = 0.10 (0.10 M $KNO_3$ or 0.10 M KCl).

**Equipment.** pH measurements were made with a Beckman Zeromatic pH meter equipped with a Fisher microcombination electrode; all pH values are reproducible to within ±0.10 unit. Standardization of the electrode was by commercial buffer solutions at pH 4.00 and 7.00. All experiments were performed at room temperature, 26 °C (±2 °C). Spectrophotometric measurements were made with a Perkin-Elmer Model 552 double-beam recording spectrophotometer. Infrared spectra were recorded with a Perkin-Elmer Model 283 double-beam recording spectrophotometer. Magnetic moments were measured by the Faraday method.

**Synthesis.** The preparation of manganese(II) complexes followed the method of Guntner and Schwarzhaus.[7] The ligand was added to methanol or ethanol (ca. 125 mL), and the solution heated near reflux under nitrogen for 0.5 h before an appropriate amount of NaOH or KOH pellets was added. If a precipitate formed, small quantities of water were added until the precipitate dissolved. A solution of hydrated manganese(II) chloride or perchlorate in 30–50 mL of deaerated methanol was then added to the solution at room temperature over a 30-min period. Precipitation in most syntheses was evident prior to the addition of half of the manganese(II). The reaction vessel was closed in a nitrogen atmosphere and transferred to an argon-filled drybox. The precipitate was filtered, washed with deaerated solvent, dried under vacuum, and stored in a drybox. A typical reaction used 12.5–25.0 mmol of manganese(II) with the appropriate stoichiometric amount of ligand and base.

**Oxygen-Uptake Measurements.** A constant-pressure Warburg apparatus described previously[6a] was used. Appropriate quantities of the ligand and base were dissolved in water and added to the reaction flask. After the system was charged with $O_2$, the manganese(II) solid (generally 0.50 mmol) in a small container was spilled into the solution and $O_2$-uptake monitored for several hours.

Table I. Amino Acids and Related Ligands Titrated with Base in the Presence of Manganese(II)

| amino acid | donor set |
|---|---|
| alanine | N,O |
| aspartic acid | N,O,O |
| *o*-tyrosine | N,O,O |
| arginine | N,O,O |
| L-3,4-dihydroxyphenylalanine (L-DOPA) | N,O,O,O |
| histidine | N,O,N |
| cystine | N,O,O,N |
| cysteine | N,O,S |
| penicillamine ($\beta,\beta$-dimethylcysteine) | N,O,S |
| anthranilic acid | N,O |
| *o*-aminophenol | N,O |
| *o*-aminothiophenol | N,S |
| glycolic acid | O,O |
| 2-mercaptoethanol | S,O |
| 3-mercaptopyropylamine | S,N |

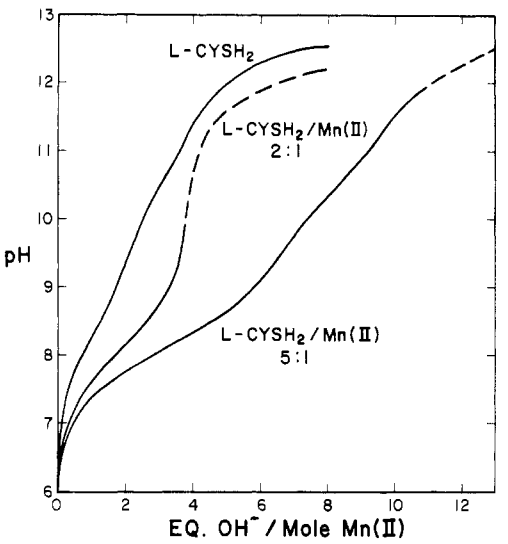



**Figure 1.** Titration of L-cysteine in the presence of Mn(II) (in 0.10 M $KNO_3$, $H_2O$). Abscissa is the equivalents of base per mole of Mn(II) at the ligand-to-metal ratio indicated.

## Results and Discussion

**Titration–Synthesis.** Titration of a series of naturally occurring amino acids and related compounds in the presence of manganese(II) has been performed in order to observe the strength of complex formation and to determine the number of ligands coordinated to manganese(II). Titrations were carried out in water or in ethanol–water since several ligands or their complexes were insoluble in water alone. A variety of amino acids with different coordinating atoms or groups was studied (Table I). Typical titration curves wherein the donor atoms are exclusively nitrogen and oxygen show a depression of the $-NH_3^+$ $pK_a$ value when titrated solutions containing manganese(II) are compared to those without manganese(II). Titration of the –COOH groups is complete by a pH near 4. Complex formation, however, is not suffi-

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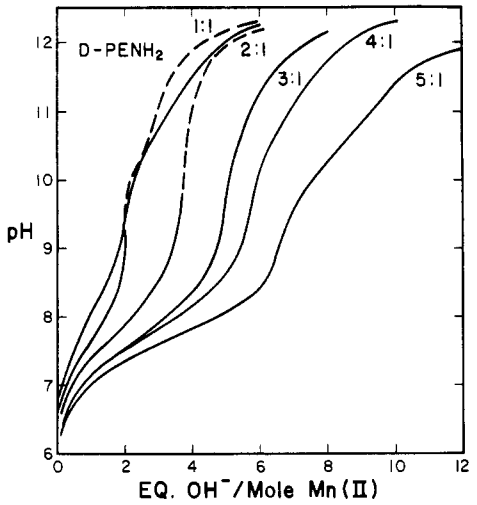



**Figure 2.** Titration of D-penicillamine in the presence of Mn(II) (in 0.10 M $KNO_3$, $H_2O$). Abscissa is the equivalents of base per mole of Mn(II) at the ligand-to-metal ratio indicated.

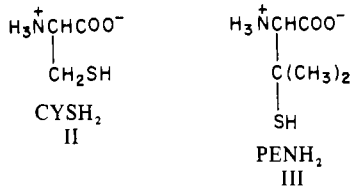
**Table II.** Macroscopic $pK_a$ Values for Cysteine and Penicillamine in Water

| ligand | $pK_1$ | $pK_2$ | $\mu$ | $T$, °C | ref |
|---|---|---|---|---|---|
| L-cysteine | $8.2_5$ | 10.5 | 0.10 (KCl) | 26 | *a* |
| | 8.31 | 10.47 | 0.10 ($NaClO_4$) | 20 | 10 |
| | 8.24 | 10.37 | 0.15 ($KNO_3$) | 25 | 8 |
| D-penicillamine | $8.0_5$ | 10.7 | 0.10 (KCl) | 26 | *a* |
| | 8.03 | 10.83 | 0.10 ($NaClO_4$) | 20 | 10 |
| | 7.95 | 10.45 | 0.15 ($KNO_3$) | 25 | 8 |
| | 8.09 | 10.55 | 0.10 ($KNO_3$) | 22 | 11 |

[a] This work.

ciently strong with these amino acids to prevent formation of manganese(II) hydroxide (pH ≥10). Limited stability constant data[1] support these findings: alanine, log $K_1$ = 3.4, log $K_2$ = 1.9; histidine, log $K_1$ = 3.24, log $K_2$ = 2.92.

Titration of two sulfur-containing amino acid ligands (cysteine (II) and penicillamine (III)) did not always yield




hydroxide formation. Titration of uncomplexed L-cysteine ($CYSH_2$) and D-penicillamine ($PENH_2$) (Figures 1 and 2, Table II) gave macroscopic $pK_a$ values in good agreement with literature values. The acidity constants for the ammonium and sulfhydryl groups are not well separated, and the first group is not fully titrated prior to the titration of the second group. The sulfhydryl group is more acidic in both ligands[8] so that the first $pK_a$ value refers to the predominant but not exclusive titration of the –SH proton. For titrations in the presence of manganese(II), a ligand-to-metal ratio in excess of 2 was required to prevent precipitation. In the case of the 2:1 cysteine titrations, precipitation occurs above pH 10 after 3.8 equiv of base has been added. (Dashed lines correspond to the onset of precipitation.) A further 2 equiv of base is consumed up to pH 12. For the 2:1 penicillamine titration, precipitation likewise occurs near pH 10 after 3.8 equiv of base has been added. An increase in the L:M ratio prevents hydroxide formation for both ligands. For the L:M ratio of 5:1,

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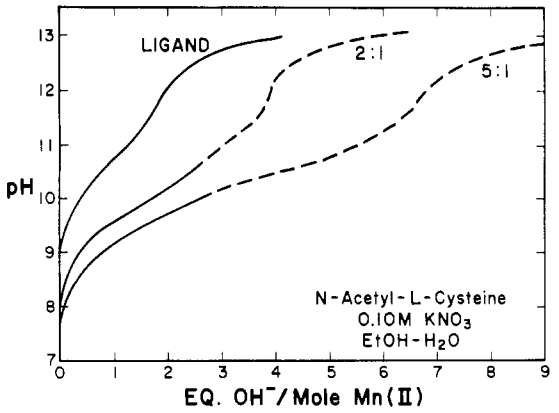



**Figure 3.** Titration of *N*-acetyl-L-cysteine in the presence of Mn(II) (in 0.10 M $KNO_3$, EtOH–$H_2O$). Abscissa is the equivalents of base per mole of Mn(II) at the ligand-to-metal ratio indicated.

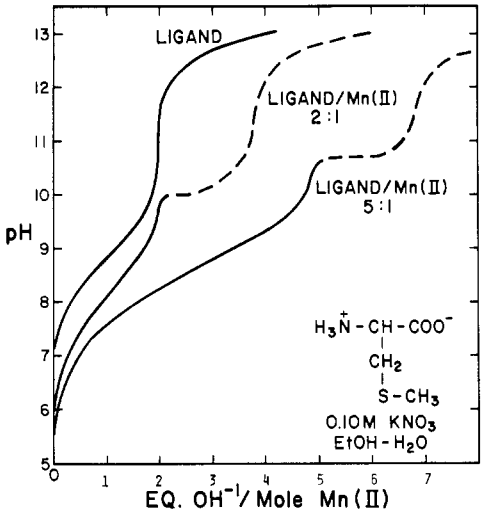



**Figure 4.** Titration of *S*-methyl-L-cysteine in the presence of Mn(II) (in 0.10 M $KNO_3$, EtOH–$H_2O$). Abscissa is the equivalents of base per mole of Mn(II) at the ligand-to-metal ratio indicated.

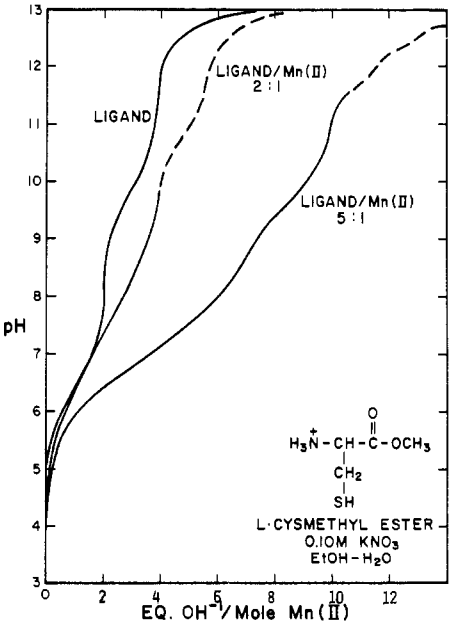



**Figure 5.** Titration of L-cysteine, methyl ester, hydrochloride in the presence of Mn(II) (in 0.10 M $KNO_3$, EtOH–$H_2O$). Abscissa is the equivalents of base per mole of Mn(II) at the ligand-to-metal ratio indicated.

there is an inflection point at 7.0 equiv in the titration curve and only a 2:1 complex is indicated, as 5.0 equiv of base is

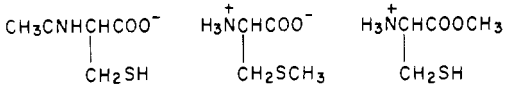
Table III. Acidity Constants of L-Cysteine Derivatives in Water and Ethanol-Water[a]

| ligand | titration reaction | water | ethanol-water[b] |
|---|---|---|---|
| *N*-acetyl-L-cysteine | $-COOH \rightarrow -COO^-$ | 3.1 | 4.05 |
| | $-SH \rightarrow S^-$ | 9.8 | 10.6 |
| *S*-methyl-L-cysteine | $-NH_3^+ \rightarrow -NH_2$ | 9.0 | 8.7 |
| L-cysteine, methyl ester | $-NH_3^+ \rightarrow -NH_2$ | 6.6 | 6.2 |
| | $-SH \rightarrow -S^-$ | 9.1 | 9.8 |
| L-cysteine, ethyl ester[12] | $-NH_3^+ \rightarrow -NH_2$ | 6.77 | |
| | $-SH \rightarrow -S^-$ | 7.45 | |
| L-cysteine[12] | $-COOH \rightarrow -COO^-$ | <2.5 | |
| | $-SH \rightarrow S^-$ | 8.53 | |
| | $-NH_3^+ \rightarrow -NH_2$ | 8.86 | |

[a] Conditions are $\mu = 0.10$ and 25 °C. [b] In order to obtain a measure of the hydrogen ion activity referenced to the standard state in the mixed solvent, 0.15 log unit was subtracted from the pH meter reading (Bates, R. G. "Determinations of pH"; Wiley-Interscience: New York, 1964; pp 222–224).

consumed by the more acidic group of the ligand and 2.0 additional equiv is consumed by the second coordinated donor group of two ligands. The remaining three unbound ligands then titrate with the same $pK_a$ as the free ligand. Ratios between 2:1 and 5:1 for penicillamine can be interpreted in a similar fashion. The hydroxide precipitate with cysteine but not with penicillamine (5:1 curves) at high pH is consistent with L-cysteine forming the weaker complex with manganese(II):[9] $CYS^{2-}$, $\log K_1 = 4.90$, $\log K_2 = 3.75$; $PEN^{2-}$, $\log K_1 = 5.80$, $\log K_2 = 4.52$.

Derivatives of L-cysteine (IV–VI) in which the three potentially coordinating groups are selectively blocked were titrated in the presence of manganese(II) (Figures 3–5). The $pK_a$ values for these free ligands in water and ethanol–water are given in Table III. The acidity constants in the mixed solvent compared to those in water are consistent with the higher dielectric solvent (water) stabilizing charged groups better; i.e., the constants are smaller in water when a charged species is formed ($-COO^-$ and $-S^-$) but larger when a neutral species ($-NH_2$) is formed. This interpretation requires an inversion in the relative acidity of the –SH and $-NH_3^+$ groups as the former is more acidic in L-cysteine but the latter is more acidic in the methyl ester derivative. The same inversion has previously been noted with L-cysteine and its ethyl ester.[12]



IV VI

Hydroxide formation is evident with all L-cysteine derivatives even with 5:1 ratios. The titration of L-cysteine methyl ester (5:1) (Figure 5) indicates the formation of a 3:1 complex since an inflection point at 8.0 rather than 7.0 equiv (as in L-cysteine, vide supra) is observed, and only two ligands titrate as if unbound. Although the $-COO^-$ group is normally regarded as a weak coordinator, its importance is clearly illustrated by the fact that cysteine forms only a 2:1 complex and hydroxide formation is prevented until a higher pH. For the remaining derivatives, it is not possible to infer the number of bound ligands as depression of the acidity constants is not sufficient to separate bound from unbound ligand. These results, however, again suggest the involvement of nitrogen, oxygen, and sulfur donor groups in the coordination of $CYS^{2-}$ and $PEN^{2-}$ to manganese(II) since the blocking of any donor atom gives rise to hydroxide precipitation. A crystal structure of $[Co(D\text{-pen})(L\text{-pen})]^-$[13] and a variety of mixed-ligand structures with histidine penicillamine and cysteine indicate that terdentate coordination by these ligands is possible.

Table IV. Elemental Analysis Data for Isolated Manganese Complexes

| | % calcd | | | % found | | | $\mu_{eff}$, $\mu_B$ |
|---|---|---|---|---|---|---|---|
| | C | H | N | C | H | N | |
| Mn(CYS) | 20.70 | 2.90 | 8.05 | 20.58 | 2.93 | 8.01 | 5.06 |
| $Mn(CYSH)_2]\cdot H_2O$ | 23.01 | 4.47 | 8.94 | 22.71 | 3.80 | 8.71 | 5.60 |
| $Na_2[Mn(CYS)_2]\cdot H_2O$ | 20.17 | 3.36 | 7.84 | 20.27 | 3.41 | 7.70 | 6.07 |
| $Mn(PEN)\cdot H_2O$ | 27.28 | 5.04 | 6.36 | 27.26 | 5.07 | 6.32 | 5.31 |
| $Mn(PENH)_2\cdot 1.5H_2O$ | 31.74 | 6.13 | 7.40 | 31.67 | 5.94 | 7.41 | 5.89 |
| $Mn(CYS\text{-}SCY)\cdot H_2O$ | 23.15 | 3.89 | 9.00 | 23.12 | 3.52 | 8.93 | 5.77 |
| $Mn(CYS\text{-}CH_3)_2$ | 29.72 | 4.99 | 8.66 | 29.55 | 4.99 | 8.60 | 5.92 |

While isolation of manganese complexes of $CYS^{2-}$ and $PEN^{2-}$ from the titration experiments was not practical, syntheses in a nonaqueous medium were undertaken. Table IV lists those complexes that have been prepared and their elemental analyses. Although varying in metal:ligand ratio and the extent of ligand deprotonation, each manganese(II) complex is a pale white, semicrystalline solid. Each complex is prepared by judiciously choosing the appropriate metal:ligand:base stoichiometric ratio. Magnetic susceptibility measurements support a high-spin manganese(II) assignment in each case. The two complexes with an L:M ratio of 1:1 have low magnetic moments. If the Mn(II) is to be four- or six-coordinate, some polymerization must occur and the low magnetic moments may be the result of antiferromagnetic coupling through bridging ligands. Two additional complexes have been prepared from the thioether of cysteine and cystine both of which are high-spin complexes. Structural inferences from Nujol mull infrared spectra are suggestive but not definitive.[15] Those complexes that have been formulated with $H_2O$ show broad absorption in the 3300–3500-$cm^{-1}$ region. Superimposed on this feature in all cases are sharp bands typical of coordinated amino functions. In no case does absorption around 2500 $cm^{-1}$ appear, indicating that the thiol group has been deprotonated in each complex. $Mn(CYSH)_2\cdot H_2O$ and $Mn(PENH)_2\cdot 1.5H_2O$ yield poor-quality IR spectra; however, noncoordinated carboxyl groups are suggested, which may be the site of protonation. Alternatively, S–H stretching vibrational modes are known to be quite weak in intensity and may go unobserved.

**Oxygenation.** Oxygen-uptake experiments in a constant-pressure Warburg apparatus were carried out with cysteine and penicillamine as well as some derivatives of each. The addition of manganese(II) to the solutions caused an increase in both the rate and quantity of $O_2$ consumed in all cases. Ligand-to-metal ratios in excess of 3:1 were required to prevent initial precipitation of $Mn(OH)_2$, and $O_2$ consumption curves were similar regardless of whether the enantiomeric or the racemic form of the ligand was used. For $CYSH_2$:Mn(II):$OH^-$ in a 5:1:7 ratio (Figure 6), a precipitate at the solution–oxygen interface is evident during the initial 10 min of reaction and the original colorless solution acquires a light green color. Within the next 90 min, more precipitate forms and the solution begins to lose color. After ca. 2 h, the solution is colorless, a white precipitate (the major product) is suspended in solution, and a small amount of a dark precipitate is present

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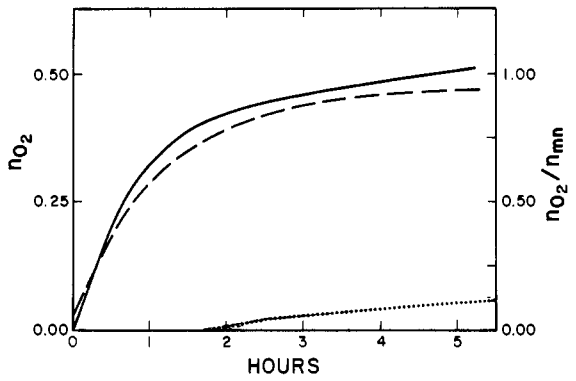


**Figure 6.** $O_2$ consumption as a function of time. Solution contains $CYSH_2$, Mn(II), and $OH^-$ in a 5:1:7 ratio (pH 10), near the first inflection point in the titration curve (Figure 3): D,L-$CYSH_2$ (—); L-$CYSH_2$ (---); L-$CYSH_2$ with no Mn(II) (···). In the experiment with no Mn(II) present, a full 2 equiv of base was added.

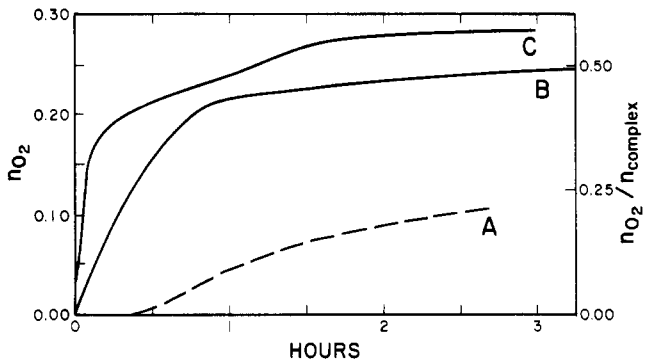


**Figure 7.** $O_2$ consumption as a function of time for Mn(CYS) (A), $Mn(CYSH)_2 \cdot H_2O$ (B), and $Na_2[Mn(CYS)_2] \cdot H_2O$ (C).

on the top of the solution. Final oxygen consumption is 0.5 mmol of $O_2$ or $n_{O_2}/n_{Mn} = 1.0 \pm 0.1$. Figure 7 also indicates that the free ligand is susceptible to oxygenation after a 1-h induction period under strongly basic conditions.

Guntner and Schwarzhaus[7] report that the Mn(II) complex $Mn(CYSH)_2$ ($CYSH^-$: bidentate via the N and O atoms, the thiol group remaining protonated) in methanol is green and that reaction with $O_2$ yields the white, dimeric complex (CYSH)Mn(CYSSCY)–Mn(CYSH) in which $CYSSCY^{2-}$ is coordinated cystine. We note the green color (vide supra) in our oxygen-uptake experiments but do not observe any color during the titration in which $O_2$ is rigorously excluded. In the preparation of the solid complexes, a very faint green is observed but colorless solids are obtained on filtration in an inert atmosphere. It is more likely, then, that the initial green color is the result of a Mn(III) species formed by the reaction of coordinated Mn(II) with $O_2$, which in turn oxidizes the cysteine to cystine (white solid) with reduction to colorless Mn(II).

We have indicated the oxidation reaction to be between $CYS^{2-}$ coordinated to Mn(II) (rather than $CYSH^-$) since substitution of cysteine by *S*-methyl-L-cysteine gives an oxygen-uptake curve similar to that of L-alanine (vide infra). A free sulfide group therefore is essential to the oxidation process. The principal reaction

$$4CYS^{2-} + O_2 + 2H_2O + 2CYSSYC^{2-} + 4OH^- \quad (1)$$

would require an $n_{O_2}/n_{CYS^{2-}}$ ratio of 0.25; the oxygen-uptake curve gives a value near 0.2 (0.50 mmol of $O_2$ consumed/2.50 mmol of $CYS^{2-}$). It appears plausible then that Mn(II) principally serves in a catalytic role. Both the light and dark precipitates, however, contain manganese as the characteristic absorption spectrum of $MnO_4^-$ was obtained after adding sodium bismuthate in an acid medium to the isolated solid. The light product is probably a cystine complex as it seems

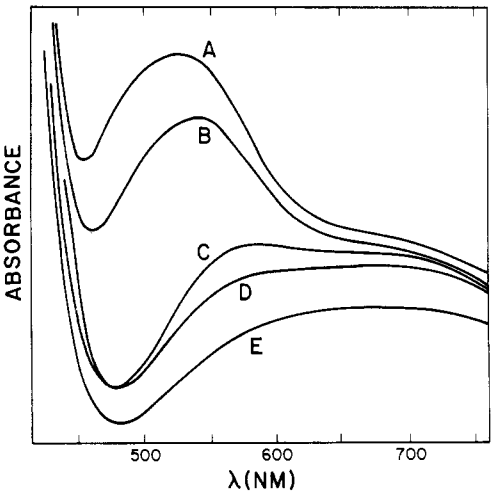


**Figure 8.** Absorption spectra of a solution of D-$PENH_2$, Mn(II), and $OH^-$ in a 5:1:7 ratio: (A) spectrum after a 2-min exposure to $O_2$; (B–E) spectra run at ca. 5-min intervals as the solution sat in a spectrophotometric cell.

unlikely that $CYSH^-$ (as indicated by Guntner and Schwarzhaus) would remain, given the oxygen-uptake data.

Oxygen-uptake experiments in the presence of Mn(II) were also carried out with two derivatives of cysteine, *S*-methyl-L-cysteine and *N*-acetyl-L-cysteine, and with L-alanine with similar results although the former cysteine derivative has a blocked sulfide group while the latter one does not. In all experiments, only a dark precipitate was formed, and $n_{O_2}/n_{Mn}$ ratios near 0.25 (0.22 and 0.24 for *S*-methyl-L-cysteine and *N*-acetyl-L-cysteine, respectively) were observed. This would indicate the principal reaction was

$$4Mn^{2+}(aq) + O_2 + 2H_2O \rightarrow 4Mn^{3+}(aq) + 4OH^- \quad (2)$$

with little ligand involvement, unlike the case of cysteine above.

The solid Mn(II) complexes $Mn(CYSH)_2 \cdot H_2O$, Mn(CYS), and $Na_2[Mn(CYS)_2] \cdot H_2O$ are only partially water soluble, and thus it was not possible to observe whether a precipitate formed during the $O_2$-uptake experiments. The total amount of $O_2$ consumed (Figure 7) was approximately half that of the 5:1 $CYS^{2-}$–Mn(II) mixture for $Mn(CYSH)_2 \cdot H_2O$ and $Na_2[Mn(CYS)_2] \cdot H_2O$ and less than one-fourth for Mn(CYS). The latter compound is likely polymeric in structure, and its smaller $O_2$ consumption may be the result of only partial solubility and reaction. Alternately, the coordination geometry and ligand field environment may be different in view of the fact that bridging donor groups may be required to complete the structure in the solid state. It should also be noted that no color changes were observed in these experiments. The two bis chelates appear to exhibit more $O_2$ activity. Pale brown oxygenated products were not seriously examined because of precursor contamination. No doubt, oxidation of Mn(II) has occurred along with mercaptide oxidation. The experimental ratio of $n_{O_2}/n_{CYS^{2-}}$ is 0.25 for both mono and bis chelates and is expected if manganese-catalyzed oxidation of the $CYS^{2-}$ is occurring.

In several previous reports in which the reaction of cysteine with a metal ion is rapid, substitution by penicillamine has inhibited the rate of oxidation–reduction reaction and polynuclear complex formation and allowed the characterization of intermediate and final products.[8,16] With Mn(II), titration data suggest the initial complexes are similar regardless of whether $CYSH_2$ or $PENH_2$ is the ligand. However, oxygen consumption and spectral development are quite different for the two ligands. A solution containing a $PENH_2$:Mn(II):$OH^-$

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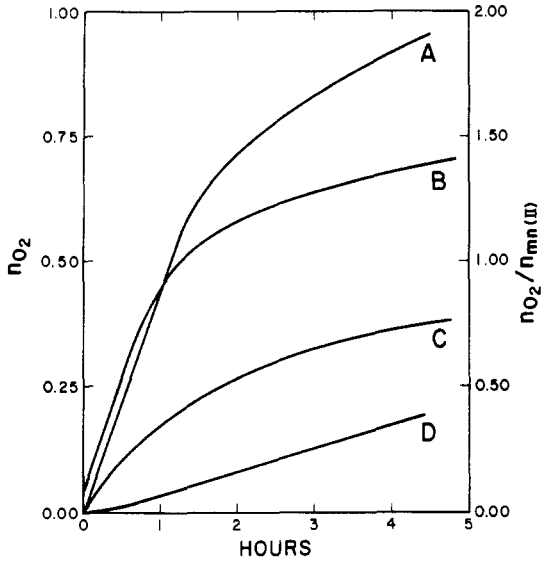


**Figure 9.** $O_2$ consumption as a function of time. Solution contains D-$PENH_2$, Mn(II), and $OH^-$ in ratios 5:1:7 (A), 4:1:7 (B), 2:1:7 (C), and 5:0:10 (D).

ratio of 5:1:7 immediately darkens upon exposure to $O_2$ and, after a few minutes, has a deep purple color due to the appearance of an intense absorption band near 530 nm (Figure 8). Removal of $O_2$ from the solution results in a rapid decrease in intensity of the 530-nm band, and the solution becomes green due to the development of a broad absorption band between 500 and 800 nm (Figure 8, spectra B–E). Thirty minutes after removal of $O_2$, the solution has lost most of its color. Continued exposure (more than 2 min) of the original solution to $O_2$ produces a dark precipitate with gradual color loss to the solution. This reaction can be slowed considerably by exposing the solution to air rather than pure oxygen and can be nearly halted, though not reversed, by bubbling $N_2$ through the solution. The nature of the species producing the intense color is not known, but it seems apparent that a Mn(III) (or higher oxidation state) must be involved; a sulfur to Mn(III) charge-transfer band would be expected to produce an intense peak. Dioxygen coordination to the $[Mn(PEN)_2]^{2-}$ species followed by rapid oxidation to Mn(III) can be postulated. Loss of color is then speculated to occur via Mn(III) oxidation of $PEN^{2-}$ to the corresponding disulfide ($PEN–PEN^{2-}$). Although most likely due to coincidence, a $PENH_2$–Cu(II)–$OH^-$ mixture in a 1:1:2 ratio (pH 7) also produces an intense purple solution with an absorption band near 520 nm, and a species involving equipment amounts of Cu(II), Cu(I), and penicillamine was postulated to exist in solution.[8] A later report showed the species present was actually an anionic cluster, $[Cu^{II}_6Cu^{I}_8(D\text{-}PEN)_{12}Cl]^{5-}$.[17]

Oxygen-uptake studies show a rapid consumption of $O_2$ during the first 90 min (Figure 9) concomitant with the development of the intense color. The amount of $O_2$ consumed is dependent upon the $PENH_2$:Mn(II) ratio, increasing as the ratio increases, and upon the amount of base added to a fixed $PENH_2$:Mn(II) ratio. It appears certain that the ligand is being oxidized as evidenced by the oxidation of the free ligand within the same time span. Manganese undoubtedly catalyzes the oxidation since the rate of oxygen uptake is considerably enhanced in the presence of Mn(II). Further proof of ligand oxidation is supported by the observation that, while the experimental $n_{O_2}/n_{Mn}$ ratio varies, the $n_{O_2}/n_{PEN^{2-}}$ ratio is essentially constant (~0.35). A ratio greater than 0.25 ($n_{O_2}/n_{PEN^{2-}}$) indicates that the final state for manganese is more extensively

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**Table V.** Observed and Predicted $O_2$ Consumption (mmol) as a Function of D-$PENH_2$:Mn:$OH^-$ Mole Ratio[a]

| | 2:1:4 | 4:1:6 | 5:1:5 | 5:1:7 | 5:1:10 |
|---|---|---|---|---|---|
| observed | ca. 1.0 | ca. 1.5 | ca. 0.5 | ca. 0.75 | ca. 1.0 |
| predicted[b] | 0.375 | 0.625 | 0.625 | 0.75 | 0.75 |
| predicted[c] | 0.50 | 0.75 | 0.875 | 0.875 | 0.875 |

[a] Mn(II) content 0.50 mmol. [b] Based on reactions 3 and 4. [c] Based on reactions 3 and 5.

oxidized and/or some of the $O_2$ has become incorporated with the manganese. Solid products from the oxygen-uptake experiments are dark brown and contain manganese, presumably as Mn(III) or Mn(IV).

Reactions similar to those for $CYS^{2-}$ can be written as (3)–(5) for $PEN^{2-}$. In contrast to the $O_2$ reactions with Mn(II)

$$4PEN^{2-} + O_2 + 2H_2O \rightarrow 2PEN\text{–}PEN^{2-} + 4OH^- \quad (3)$$

$$4Mn^{2+}(aq) + O_2 + 2H_2O \rightarrow 4Mn^{3+}(aq) + 4OH^- \quad (4)$$

$$2Mn^{2+}(aq) + O_2 + 4OH^- \rightarrow 2MnO_2(s) + 2H_2O \quad (5)$$

and $CYS^{2-}$ in which slightly less $O_2$ is consumed than that required solely for reaction 1, the reaction of $O_2$ with Mn(II) and $PEN^{2-}$ consumes more $O_2$ than that required by reaction 3 (Table V). Experimental total oxygen consumption agrees with that predicted by considering oxidation of $PEN^{2-}$ to its disulfide and oxidation of Mn(II) to $MnO_2(s)$ for the 2:1 and 4:1 ligand:Mn(II) ratios. For the 5:1 ratio, however, even further oxidation of ligand and/or manganese is suggested. The products from these reactions are again dark solids that contain manganese.

The quantity of oxygen consumed and the composition of the products are also dependent upon the amount of base added. For a fixed $PENH_2$:Mn(II) ratio of 5:1, addition of 10.0 equiv of base resulted in a total oxygen consumption of 1.5 mmol of $O_2$ or 1.7 times that required for both reactions 3 and 5. The dark solid remaining after completion of the reaction contains manganese. When 7.0 and 5.0 equiv of base were added to the same amount of $PENH_2$ and Mn(II), identical oxygen-uptake curves were observed and ca. 1.0 mmol of $O_2$ was consumed. The products isolated, however, were not the same. With 7.0 equiv of base, a dark, manganese-containing solid was obtained while with 5.0 equiv of base, a white solid with *no* manganese was obtained.

Finally, *N*-acetyl-DL-penicillamine was investigated since the corresponding derivative of cysteine reacted very differently from cysteine. In contrast to *N*-acetyl-L-cysteine, *N*-acetyl-DL-penicillamine is very reactive toward $O_2$ in the presence of Mn(II), and the oxygen-uptake curve resembles that of $PENH_2$. Total oxygen consumption is ca. 1.2 mmol for 2.50 mmol of *N*-acetyl-DL-penicillamine, 0.50 mmol of Mn(II), and 3.50 mmol of $OH^-$ (5:1:7 ratio), or slightly more than that consumed in the corresponding experiment with $PENH_2$. The ligand alone is oxygen sensitive at high pH and consumes nearly 0.6 mmol of $O_2$/2.5 mmol of ligand in the same time period required for consumption of the 1.2 mmol. After 3 days, total $O_2$ consumption is 0.8 mmol in excess of that required for formation of the disulfide in reaction 3. An important difference between the $PENH_2$ and its *N*-acetyl derivative, however, is the absence of the intense purple color as the oxygenation reaction proceeds. Instead, a dark precipitate forms within a few minutes and the solution becomes yellow, reminiscent of the penicillamine reaction after nearly 60 min. Only a dark, manganese-containing solid is isolated at the conclusion of the reaction. Similar comparisons have been reported for Cu(II) with D-$PEN^{2-}$ and *N*-acetyl-DL-penicillamine. These results suggest that the final products in the reaction of Mn(II) with $PEN^{2-}$ or *N*-acetyl-DL-penicillamine may be the same, but the species imparting the intense purple

color is more stable with $PEN^{2-}$ than with *N*-acetyl-DL-penicillamine.

## Conclusions

Manganese(II) has been shown to complex more extensively with sulfur-containing amino acids than simple bidentate or other multidentate amino acids or other non amino acid ligands. Complexation is weak even with cysteine or penicillamine as evidenced by the tendency to form $Mn(OH)_2(s)$ during titrations. Mono and bis chelates of cysteine and penicillamine, which are sensitive to $O_2$, can be prepared and isolated. In the presence of $O_2$, both the sulfur-containing ligand and manganese(II) undergo oxidation but the extent of oxidation and products obtained are dependent upon the ligand, the ligand-to-metal ratio, and the pH of the solution.

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**Registry No.** II, 52-90-4; III, 52-67-5; IV, 616-91-1; V, 1187-84-4; VI, 2485-62-3; Mn(CYS), 84959-60-4; $Mn(CYSH)_2$, 60065-80-7; $Na_2[Mn(CYS)_2]$, 84944-32-1; Mn(PEN), 84944-33-2; $Mn(PENH)_2$, 84944-34-3; Mn(CYS–SCY), 78264-93-4; $Mn(CYS–CH_3)_2$, 84944-35-4.

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Contribution from the Department of Chemistry,
The University of Mississippi, University, Mississippi 38677

# Electrochemical Studies of Chloro Complex Formation in Low-Temperature Chloroaluminate Melts. 2. Silver(I)

T. M. LAHER and C. L. HUSSEY*

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A potentiometric titration procedure was used to study the coordination of silver(I) by melt chloride ion in the aluminum chloride–*N*-*n*-butylpyridinium chloride ($AlCl_3$–BPC) and aluminum chloride–1-methyl-2-ethylimidazolium chloride ($AlCl_3$–MEIC) melt systems. Analysis of data resulting from measurements on the cell Al|$AlCl_3$–RCl|fritted disk|$AlCl_3$–RCl,AgCl(dil)|Ag indicated that silver(I) forms very stable, mononuclear complexes of the type $AgCl_p^{1-p}$ ($2 \leq p \leq 4$) in the chloride ion-rich compositions of these melts. AgCl was insoluble in the equimolar $AlCl_3$–BPC and $AlCl_3$–MEIC melts. Stoichiometric formation constants for silver(I) chloro complexes in basic $AlCl_3$–BPC melt relative to the 66.7 mol % melt are as follows: $AgCl_2^-$, $3.5 \times 10^{19}$ (40.0 °C), $5.9 \times 10^{18}$ (60.0 °C); $AgCl_3^{2-}$, $3.2 \times 10^{20}$ (40.0 °C), $5.2 \times 10^{20}$ (60.0 °C); $AgCl_4^{3-}$, $1.6 \times 10^{23}$ (40.0 °C), $4.5 \times 10^{22}$ (60.0 °C). Stoichiometric formation constants in basic $AlCl_3$–MEIC melt relative to the 66.7 mol % melt are as follows: $AgCl_3^{2-}$, $1.8 \times 10^{20}$ (40.0 °C); $AgCl_4^{3-}$, $1.5 \times 10^{22}$ (40.0 °C).

## Introduction

The combination of aluminum chloride and certain organic chloride salts results in molten salts that remain liquid well below room temperature. Two classes of these ionic liquids have been recognized and found to be excellent solvents for many organic and inorganic solutes. These ionic liquids are based on *N*-alkylpyridinium chlorides, e.g., the aluminum chloride–*N*-*n*-butylpyridinium chloride ($AlCl_3$–BPC) melt system,[1,2] and dialkylimidazolium chlorides, e.g., the aluminum chloride–1-methyl-2-ethylimidazolium chloride ($AlCl_3$–MEIC) melt system.[3] Concentration cell measurements for both the $AlCl_3$–BPC[4,5] and $AlCl_3$–MEIC[3,6] systems indicate that the predominant chloroaluminate equilibrium reaction existent in these melts is

$$2AlCl_4^- \rightleftharpoons Al_2Cl_7^- + Cl^- \quad (1)$$

In addition, Raman spectral studies suggest that molecular $Al_2Cl_6$ and $AlCl_3$ are absent from melts that are formulated with 66.7 mol % or less $AlCl_3$.[7] Chloroaluminate melts that contain a molar excess of $AlCl_3$ over the organic chloride salt are termed "acidic" while those formulated with an excess of organic salt relative to $AlCl_3$ are denoted as "basic".

The large variation in chloride ion activity that can be achieved in these anhydrous, ionic liquids prompts them to be interesting solvents in which to study transition-metal coordination. In previous papers[8,9] we examined the coordination of cobalt(II), iron(II), iron(III), and nickel(II) by melt chloride ion in the $AlCl_3$–BPC system. Although a number of authors have discussed various aspects of silver(I) electrochemistry in molten chloroaluminates,[10–15] there is a paucity of data regarding the coordination of this metal species in these melts. The study reported herein concerns a potentiometric investigation of silver(I) chloro complex formation that was undertaken in both the $AlCl_3$–BPC and $AlCl_3$–MEIC systems.

## Experimental Section

**Instrumentation.** Melt preparation and subsequent titration experiments were conducted in a dry, oxygen-free nitrogen atmosphere

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