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Copper(II) Complexes of Glycylglycine and Glycylsarcosine and Their Methyl Esters

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Received January 10, 1973

Infrared and potentiometric pH studies of aqueous solutions of Cu(II) with glycylglycine methyl ester (GGOMe), glycylsarcosine (GS), and glycylsarcosine methyl ester (GSOMe) provide evidence for a variety of complexes. Among those identified are $Cu(GGOMe)^{2+}$, $Cu(GS)^{+}$, and $Cu(GSOMe)^{2+}$ in which the ligands chelate to the metal *via* the terminal amino group and the amide carbonyl oxygen atom. As had been previously established for the Cu(II) complex of glycylglycine (GG), the amide proton also ionizes from $Cu(GGOMe)^{2+}$ to give $Cu(H_{-1}GGOMe)^{+}$ in which the ligand coordinates through the terminal amino group, the deprotonated amide nitrogen atom, and possibly also the ester group. The position of the ester group provides the opportunity for the metal ion to catalyze the hydrolysis of the ester to give the corresponding glycylglycine complex, $Cu(H_{-1}GG)$. Equilibrium constants have been determined for all of the complexes discussed above and related species.

Introduction

In a continuing investigation[2] of the catalytic properties of metal ions in the hydrolysis of amino acid esters, we turned to the copper(II) catalysis of glycylglycine methyl ester hydrolysis. Before conducting the kinetic studies it was necessary to investigate the nature of the complexes formed by copper(II) with glycylglycine methyl ester (GGOMe) and with the closely related glycylsarcosine methyl ester (GSOMe). In this paper are presented infrared data which suggest structures for these complexes and potentiometric results which provide stability constants for their formation.

Experimental Section

Reagents. The hydrochloride salt of glycylglycine methyl ester was purchased from Mann Research Laboratories and was of the highest purity available. Glycylsarcosine (GS) was purchased from Sigma Chemical Co. and was recrystallized three times from water–ethanol prior to use. The preparation and purification of glycylsarcosine methyl ester is described in a following publication.[3] Baker analyzed anhydrous $CuSO_4$ and $Cu(NO_3)_2 \cdot 3H_2O$ were used in the preparation of metal ion solutions.

Solutions of copper(II) and of the hydrochloride salts of GSOMe and GGOMe were standardized *via* ion-exchange techniques. Aliquots of the metal or hydrochloride salt solutions were passed through Dowex 50W-X8 strongly acidic cation-exchange resin, and the effluent solutions were titrated with standardized sodium hydroxide. Glycylglycine and glycylsarcosine solutions were standardized potentiometrically.

Infrared Spectral Measurements. Infrared spectra were obtained with a Perkin-Elmer 237B spectrophotometer. Irtran cells (Barnes Engineering, Stamford, Conn.) of 0.01 mm thickness were employed. The concentrations of ligand solutions were 0.2–0.5 *M* in 98% D_2O as solvent. The wave number values are estimated to be accurate to ± 3 cm^{-1}. The ionic strengths of all solutions were adjusted to 1.0 *M* by the addition of an appropriate amount of reagent grade KCl which does not absorb in the range of frequencies studied. Deuterium ion concentrations were measured with a Radiometer TTT1c pH meter fitted with Radiometer glass and calomel extension electrodes. The glass electrode was standardized using Beckman pH 4, 7, and 10 buffers. Using the following relationship, observed pH was converted to pD: $pD = pH_{obsd} + 0.41$.[4]

Copper(II) and ligand solutions were prepared by dissolving anhydrous $CuSO_4$ and ligand in 98% D_2O. The 2.5 *M* sodium deuterioxide (NaOD) solution was prepared by dissolving sodium metal in 98% D_2O.

A jacketed 10-ml titration cell was fitted with glass and calomel electrodes, a nitrogen inlet tube, and a microsyringe delivery tube. The solutions were stirred by means of a magnetic stirrer, and the temperatures of the solutions were maintained at 25.0° by passing thermostated water through the outer jacket of the titration cell. Appropriate amounts of sodium deuterioxide were added to the metal–ligand solutions; then a small portion of the solution was withdrawn, and the apparent pH and the infrared spectrum in the 1500–1800-cm^{-1} region were recorded.

Visible Spectra. Visible spectra of the 2:1 GGOMe–Cu(II) solutions used in the infrared studies were obtained with a Cary 14 spectrophotometer using a matched set of 1-cm glass cells. The visible spectra (400–800 nm) were recorded at every pD value that infrared spectra were recorded. At pD 2.3 an absorption band at ~780 nm was observed. As the pD was raised, the peak grew in intensity and shifted to lower wavelength. At pD 9.6 where hydrolysis of the ester to glycylglycine is rapid, one peak at ~628 nm was observed. This corresponds to the ~630 nm absorption reported by Kim and Martell[5] for 2:1 glycylglycine–Cu(II) solutions at this high pD. The predominant complex under these conditions is $Cu(H_{-1}GG)(GG)^{-}$ which contains two glycylglycinate ligands, only one of which has undergone amide proton ionization.[5]

Potentiometric Measurements. A Corning Digital 112 Research Model pH meter was used to determine hydrogen ion concentrations in all potentiometric titrations which were carried out in a double-walled titration cell of 50-ml capacity. The temperature of all solutions was maintained at 25.00 ± 0.05° by circulation of thermostated water through the outer jacket of the cell. The titration cell was fitted with Corning glass and calomel extension electrodes, a microburet delivery tube, and a nitrogen inlet tube. Ionic strengths of the solutions were maintained at 0.05 *M* by the addition of an appropriate amount of 1.0 *M* potassium nitrate. The solutions were stirred with a magnetic stirrer, and stirring was stopped prior to making pH readings. All titrations were performed in triplicate.

The glass extension electrode was calibrated in terms of $-\log [H^+]$ (*i.e.*, pH_c) according to the procedure of Rajan and Martell[6] using HCl and acetic acid solutions. For the acetic acid titration, the actual hydrogen ion concentrations ($-\log [H^+]$) were calculated from values tabulated by Harned and Owen.[7]

Standardized perchloric acid was added to solutions of glycylglycine and glycylsarcosine (5×10^{-3} *M*) in order to determine the second protonation constant for these ligands. In the case of GSOMe the potentiometric titrations were performed as rapidly as possible due to the fairly rapid hydrolysis of the ester moiety. Only points from the region of 20–60% complete titration, where ester hydrolysis was negligible, were used in calculating protonation and metal chelate formation constants.

Calculations. All calculations were performed on an IBM 360-65 digital computer. All protonation constants of the ligands and the formation constants of the GS and GSOMe chelates of Cu(II) were calculated using Bjerrum's method.[8] The stability constant

(1) Fellow of the Alfred P. Sloan Foundation, 1970–1972.
(2) R. J. Angelici and J. W. Allison, *Inorg. Chem.*, 10, 2238 (1971), and references cited therein.
(3) R. Nakon and R. J. Angelici, *J. Amer. Chem. Soc.*, submitted for publication.
(4) A. K. Covington, M. Paabo, R. A. Robinson, and R. B. Bates, *Anal. Chem.*, 40, 700 (1968).
(5) M. K. Kim and A. E. Martell, *Biochemistry*, 3, 1169 (1964).
(6) K. S. Rajan and A. E. Martell, *J. Inorg. Nucl. Chem.*, 26, 789 (1964).
(7) H. S. Harned and B. B. Owen, "Physical Chemistry of Electrolytic Solutions," 3rd ed, Rheinhold, New York, N. Y., 1958, pp 635, 752.
(8) J. Bjerrum, "Metal Ammine Formation in Aqueous Solution," P. Haase and Son, Copenhagen, 1957.

for the reaction, $Cu(H_{-1}GG) + GGOMe \rightleftarrows Cu(H_{-1}GG)(GGOMe)$, from titration data on solutions containing equimolar Cu(II), GG, and GGOMe was calculated similarly.

The calculation of the formation constants of GG and GGOMe chelates of Cu(II) was performed using iterative programs. The 1:1 GG–Cu(II) system was solved using equations derived by Kim and Martell.[5] The 1:1 GGOMe to Cu(II) (5×10^{-3} *M*) data were treated by assuming that the only chelates present were CuL^{2+} and $Cu(H_{-1}L)^{+}$ in which the GGOMe ligand had a protonated and deprotonated amide nitrogen, respectively. By combining equations for the total concentration of metal species (TM), the total concentration of ligand species (TL), and charge balance, the following relationship was derived

$$K_1 = \left\{TL + CS + (B + D)\left(\frac{C \cdot TL + CS \cdot A}{B \cdot D + A \cdot D}\right)\right\} \Big/ \left\{\left(\frac{C \cdot TL + CS \cdot A}{B \cdot D + A \cdot D}\right)^2 \cdot B\right\}$$

where $A = 1 + K_{1a}[H^+]$, $B = 1 + K_H/[H^+]$, $C = [H^+]/K_{1a}$, $D = K_{1H}[H^+]$, $CS = [Cl^-] + [OH^-] - [Na^+] - [H^+]$, $K_{1a} = [Cu(H_{-1}L)^+] \cdot [H^+]/[CuL^{2+}]$, $K_{1H} = [LH^+]/[L][H^+]$, and $K_1 = [CuL^{2+}]/[Cu^{2+}] \cdot [L]$. Iterative programs including other possible species such as $[CuL_2^{2+}]$, $[CuLOH^+]$ and $[Cu_2L_2(OH)_2^{2+}]$, or $[Cu(H_{-1}L)OH]$ and $[Cu_2(H_{-1}L)_2(OH)_2]$ did not converge. Possibly such hydrolytic equilibria exist in higher pH ranges, but due to hydrolysis of the ester, the potentiometric data above pH 6.0 could not be used.

The 2:1 GGOMe to copper(II) (2.5×10^{-3} *M*) system was solved using iterative programs and the K_1 and K_{1a} values obtained from the corresponding 1:1 system. The only series of equilibria which converged (fit the potentiometric data) included the following species ($n > 1$, moles of base per mole of ligand): $[CuL^{2+}]$, $[Cu(H_{-1}L)^+]$, $[Cu(H_{-1}L)L^+]$, and $[Cu(H_{-1}L)_2]$. Iterative programs attempting to fit the data to include $[CuL_2^{2+}]$ did not converge to reasonable values. While the infrared data (Table I) indicate that $[CuL_2^{2+}]$ is probably present in solutions at 0.5 *M* concentration below pD 6.4, the potentiometric data at 0.005 *M* suggest that $[CuL_2^{2+}]$ is not a major component of the solution in the pH range 6.3–7.1. The small amount of this species in solution below $n = 2$ precludes direct calculation of the stability constant for the following equilibrium

$$[CuL^{2+}] + L \rightleftarrows [CuL_2^{2+}]$$

By combining equations for TM, TL, and charge balance, the following equation was derived

$$K_{2a} = [TM - (B \cdot L/A) \cdot [1 - K_{1a}/[H^+] - K_2' \cdot L]][H^+]/[L^2 \cdot K_2' \cdot B/A]$$

where L is obtained from the following quadratic

$$L^2[K_2' \cdot K_{1a} \cdot B/([H^+] \cdot A)] + L[D + B + B/A] - [TL + CS] = 0$$

and

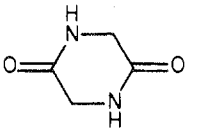
$$K_{2a} = [Cu(H_{-1}L)_2][H^+]/[Cu(H_{-1}L)L^+]$$

$$K_2' = [Cu(H_{-1}L)L^+]/[Cu(H_{-1}L)^+][L]$$

A, B, C, D, K_{1a}, TL, and TM are defined above.

Results and Discussion

Infrared Studies. Glycylglycine Methyl Ester (GGOMe). Infrared spectra of aqueous solutions of GGOMe at several pH values are shown in Figure 1. The frequencies of the absorption maxima (1600–1800 cm^{-1}) corresponding to various forms of GGOMe are given in Table I. At low and neutral pD values two carbonyl absorption bands are found at 1740 and 1686 cm^{-1}, corresponding to absorption by the ester and amide moieties, respectively. In the basic region the ester carbonyl band begins to disappear as a result of hydrolysis and cyclization to 2,5-piperazinedione (I);[9] the amide carbonyl band increases in intensity and shifts to a lower wavelength. The new broad band at high pD values at 1660 cm^{-1} is precisely in the region reported for the amide band of the glycylglycine anion (1683 cm^{-1})[10] and the amide band of 2,5-piperazinedione (1632 cm^{-1}).[11] Further support for the assignment of the 1660-cm^{-1} band to these two species comes from the known reaction of GGOMe to give these products in the neutral-basic pH region.[9] Although a shift in the amide band would be expected[10] as the ammonium group is deprotonated with an increase in pH, the concomitant hydrolysis and cyclization reactions at this pH obviate any chance of observing the deprotonated ester. Upon complete hydrolysis of the ester group, two carbonyl bands at 1660 (broad) and 1595 cm^{-1} are observed at pD 11.7, corresponding to the amide carbonyls and ionized carboxylate absorptions, respectively.



I

Table I. Infrared Spectra of Glycylglycine, GGOMe, and Their Cu(II) Complexes in D_2O

$M_{Cu^{2+}}$	M_L	pD	$-C(=O)OCH_3$	$-C(=O)NH-$	$-C(=O)O^-$
			Glycylglycine		
0[a]	0.29	4.31		1675 (vs)[b]	1595 (vs)[b]
0[a]	0.29	8.77		1665 (m),[b] 1630 (w)[c]	1595 (vs)[b,c]
0[a]	0.29	10.29		1632 (vs)[c]	1595 (vs)[c]
0.23[a]	0.23	3.58		1670 (m),[b] 1625 (m)[d]	1595 (m)[b,d]
0.23[a]	0.23	4.24		1625 (m)[d]	1598 (m)[d]
0.23[a]	0.23	5.18		1622 (m),[d] 1610 (vs),[e] 1610 (vs)[e]	1590 (m)[d]
0.23[a]	0.23	10.65		1610 (vs)[e]	1610 (vs)[e]
			Glycylglycine Methyl Ester		
0	0.25	6.71	1740 (vs)[f]	1686 (vs)[f]	
0	0.25	8.72	1740 (s)[f]	1685 (s),[f] 1660 (s),[g] 1630 (w)[c]	1595 (w)[c]
0	0.25	11.71		1660 (vs)[c,g]	1595 (m)[c]
0.25	0.25	2.89	1737 (vs)[f]	1685 (vs)[f]	
0.25	0.25	4.42	1737 (vs)[f,h]	1683 (s),[f] 1636 (s)[h]	
0.25	0.25	5.41	1740 (vs)[h]	1633 (vs)[h]	1594 (w)[d]
0.25	0.50	2.42	1736 (vs)[f]	1685 (vs)[f]	
0.25	0.50	4.54	1740 (s)[f,h]	1685 (s),[f] 1631 (s)[h]	
0.25	0.50	5.94	1742 (s)[h]	1629 (vs)[h]	1594 (w)[d]
0.25	0.50	7.04	1742 (s),[h] 1722 (s)[i]	1633 (s),[h] 1618 (s)[d,i]	1592 (m)[d]
0.25	0.50	7.95	1744 (w),[h] 1724 (s)[i]	1633 (s),[h] 1618 (s)[d,i]	1591 (s)[d]
0.25	0.50	8.99	1725 (w)[i]	1611 (vs)[e,i]	1611 (vs)[e]
0.25	0.50	9.66		1611 (vs)[e]	1611 (vs)[e]

[a] Taken from ref 5 and 10. [b] $^+NH_3CH_2CONHCH_2CO_2^-$. [c] $NH_2CH_2CONHCH_2CO_2^-$. [d] VI. [e] VII. [f] $^+NH_3CH_2CONHCH_2CO_2CH_3$. [g] I. [h] II. [i] III.

GGOMe–Cu(II). Infrared spectra of 2:1 GGOMe–Cu(II) solutions are shown in Figure 2. Frequencies of the absorption maxima for the 1:1 and 2:1 ligand to metal ratios are summarized in Table I. In both the 1:1 and 2:1 systems at very low pD two carbonyl absorption bands at 1736 and

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(10) M. K. Kim and A. E. Martell, *J. Amer. Chem. Soc.*, 85, 3080 (1963).

(11) H. Lenormant, *Ann. Chim., Ser. 12*, 5, 459 (1950).

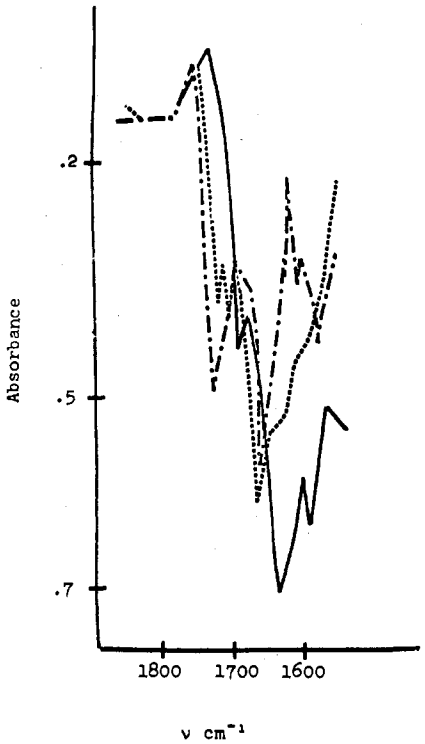


Figure 1. Infrared spectra of 0.25 *M* GGOMe in D_2O: —·—, pD 6.71; · · · · ·, pD 8.72; ——, pD 11.71.

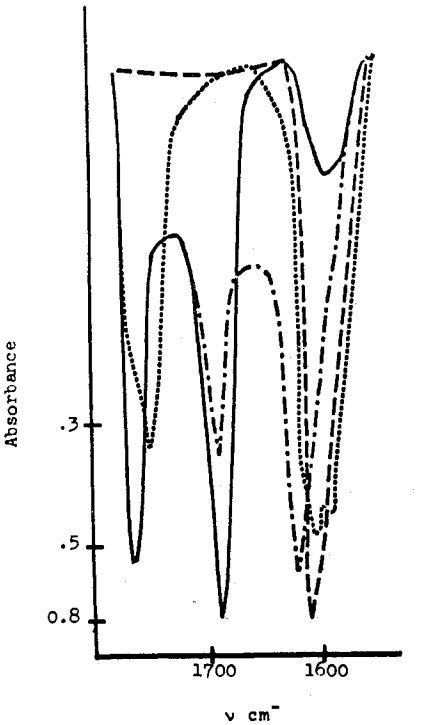
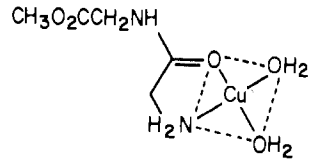


Figure 2. Infrared spectra of 0.25 *M* Cu(II) and 0.50 *M* GGOMe in D_2O: ——, pD 2.42; —·—·—, pD 4.54; · · · · ·, pD 7.95; – – – –, pD 9.66.

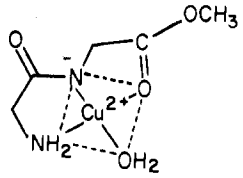
1685 cm^{-1} are observed, corresponding to the absorption of the uncomplexed ester and amide groups, respectively. As the pD is raised the intensity of the amide band at 1686 cm^{-1} decreases and a new band at 1634 cm^{-1} appears. The new band at lower wavelength is assigned to the amide carbonyl group complexed to copper(II) (structure II). There



II

is no change in the ester carbonyl frequency upon complexation of the amide carbonyl oxygen to copper(II). Continued addition of base results in the complete disappearance of the absorption band corresponding to the uncoordinated amide group and a continued increase in the band assigned to the complexed amide group. Unfortunately, in the 1:1 ligand to metal system, precipitation of copper(II) hydroxide occurs at pD 5.8. The infrared spectrum of the resultant solution is identical with that of the 2:1 solution at pD 5.8.

At about pD 6.60 in the 2:1 system the appearance of one shoulder on the ester carbonyl peak and two shoulders on the amide carbonyl peak indicates that amide proton ionization and ester hydrolysis are occurring. The shoulder at 1722 cm^{-1} increases as the pD is raised, and eventually the peak at 1738 cm^{-1} becomes a shoulder of the peak at 1722 cm^{-1}. The lower wavelength ester carbonyl band suggests coordination of the ligand as in structure III. It is not



III

possible to establish whether this shift indicates only amide proton ionization or also coordination of the ester to the Cu(II).

The carbonyl frequencies at 1633, 1618, and 1594 cm^{-1} are assigned to amide carbonyl oxygen bound to copper(II) as in II, the carbonyl of the ionized amide group bound to copper(II) as in III, and the ionized carboxylate group which is formed upon hydrolysis of the ester. As the pD is raised the carbonyl peaks assigned to the carboxylate ion and ionized amide group increase in intensity while the peak assigned to II decreases in intensity.

At pD 9.66 the ester carbonyl absorption band has decreased greatly in intensity, while the free carboxylate peak has grown. Within 10 min at pD 9.66 the carboxylate and amide carbonyl peaks are observed to coalesce and yield a single new peak at 1611 cm^{-1}, corresponding to the spectrum of bisglycylglycinatocopper(II).[5] The absence of an absorption at 1632 cm^{-1} in the final spectrum indicates that the 2,5-piperazinedione is not formed in the Cu(II)-containing solutions, in contrast to that found in the Cu(II)-free solutions.

Glycylsarcosine Methyl Ester (GSOMe). Infrared spectra of aqueous solutions of GSOMe are shown in Figure 3. The frequencies of the absorption maxima are listed in Table II. At low pD two carbonyl absorption bands appear at 1734 and 1662 cm^{-1}, corresponding to absorption by the ester and amide groups, respectively. As the pD is raised a new band appears at 1608 cm^{-1}; simultaneously the intensity of the ester band decreases. This new band may be assigned to an ionized carboxylate group of glycylsarcosine resulting from ester hydrolysis and/or to *N*-methyl-2,5-piperazinedione[11] resulting from cyclization of the ester. The closely related glycylglycine methyl ester has previously

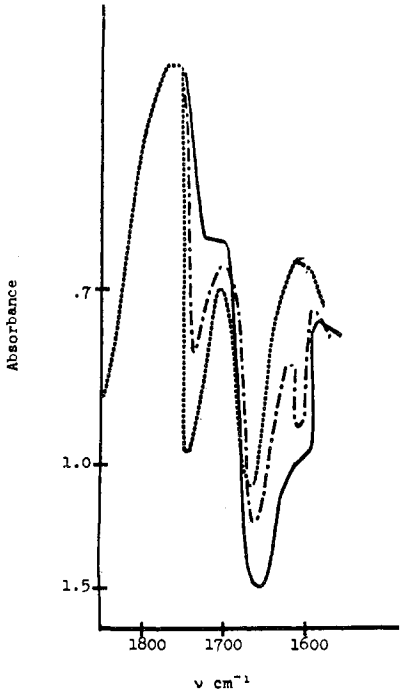
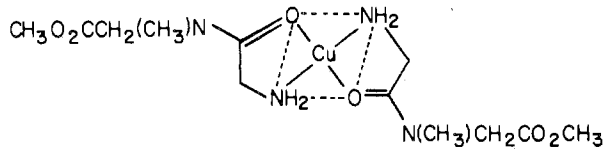


Figure 3. Infrared spectra of 0.26 *M* GSOMe in D_2O: · · · · ·, pD 4.12; –·–·–, pD 6.59; ——, pD 10.6.

been shown to form analogous products.[9] Further base addition results in eventual disappearance of the ester carbonyl peak, broadening and a shift to lower wavelength of the amide carbonyl peak, and broadening and growth of the 1608-cm^{-1} band. These changes indicate complete conversion of the ester to the hydrolysis and cyclization products.

GSOMe-Cu(II). Infrared spectra of 2:1 GSOMe-Cu(II) solutions are shown in Figure 4. Frequencies of the absorption maxima are give in Table II. At very low pD two absorption maxima are present at 1661 and 1732 cm^{-1} corresponding to uncoordinated ester and amide carbonyl bands, respectively. By pD 4.5 the absorption of the uncoordinated amide carbonyl band had decreased in intensity, and a new band appears at 1608 cm^{-1}, assigned to coordination of the amide carbonyl oxygen to copper(II) as in structure IV. No change was observed in the ester carbonyl



IV

frequency upon complexation of the amide group.

Upon addition of base the band corresponding to the uncomplexed amide group decreases in intensity, while the band assigned to the metal ion complexed amide group increases. Again no change was observed in the ester carbonyl frequency, but a decrease in intensity was observed. Since no other bands were observed in the carbonyl region as the ester group hydrolyzed, the resultant carboxylate group apparently absorbs at roughly the same frequency as does the metal-complexed amide group. (See Cu(II)-glycylsarcosine below.) At pD 10.2, a precipitate (presumably copper(II) hydroxide) separates leaving a solution which shows absorptions at 1665 and 1602 cm^{-1}. This spectrum is very similar to that observed for GSOMe in the absence of Cu(II)

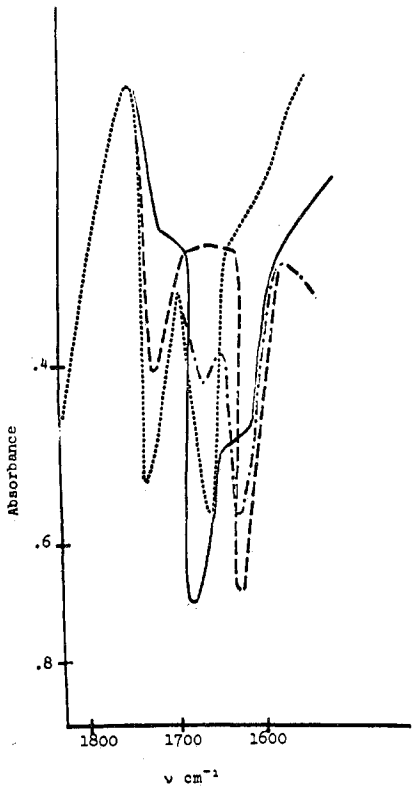


Figure 4. Infrared spectra of 0.26 *M* Cu(II) and 0.52 *M* GSOMe in D_2O: · · · · ·, pD 3.52; –·–·–, pD 4.55; – – – –, pD 8.35; ——, pD 10.2.

Table II. Infrared Spectra of Glycylsarcosine, GSOMe, and Their Cu(II) Complexes in D_2O

$M_{Cu^{2+}}$	M_L	pD	$-C(=O)OCH_3$	$-C(=O)N(CH_3)-$	$-C(=O)O^-$
			Glycylsarcosine		
0.00	0.28	6.81		1662 (vs)[a]	1598 (vs)[a]
0.00	0.28	9.71		1662 (vs),[a] 1628 (s)[b]	1598 (vs)[a,b]
0.00	0.28	11.86		1628 (s)[b]	1598 (vs)[b]
0.28	0.28	3.59		1662 (vs),[a] 1625 (s)[c]	1598 (s)[a,c]
0.28	0.28	5.07		1662 (w),[a] 1629 (vs)[c]	1598 (s)[a,c]
0.28	0.28	5.91		1629 (vs)[c]	1597 (s)[c]
0.28	0.56	3.74		1662 (vs),[a] 1604 (vs)[c]	1604 (vs)[a,c]
0.28	0.56	5.07		1662 (vs),[a] 1610 (vs)[c]	1610 (vs)[a,c]
0.28	0.56	9.01		1610 (vs)[c]	1610 (vs)[c]
0.28	0.56	10.02		1608 (vs)[c]	1608 (vs)[c]
			Glycylsarcosine Methyl Ester		
0.00	0.26	4.12	1734 (vs)[d]	1662 (vs)[d]	
0.00	0.26	6.59	1734 (vs)[d]	1662 (vs)[d], 1608 (m)[e]	1608 (m)[a]
0.00	0.26	8.51	1734 (m)[d]	1661 (vs),[a,d] 1608 (s)[e]	1608 (s)[a]
0.00	0.26	10.6	1734 (w)[d]	1658 (vs),[b,d] 1608 (s)[e]	1608 (s)[b]
0.26	0.52	3.52	1732 (vs)[d]	1661 (s)[d]	
0.26	0.52	4.55	1731 (vs)[d]	1659 (m),[d] 1608 (s)[f]	1608 (s)[c]
0.26	0.52	6.52	1730 (s)[f]	1608 (vs)[c,f]	1608 (vs)[c]
0.26	0.52	8.35	1730 (m)[f]	1609 (vs)[c,f]	1609 (vs)[c]
0.26	0.52	10.2		1665 (vs)[b,e]	1602 (m)[b]

[a] $^+NH_3CH_2CON(CH_3)CH_2CO_2^-$. [b] $NH_2CH_2CON(CH_3)CH_2CO_2^-$. [c] V. [d] $^+NH_3CH_2CON(CH_3)CH_2CO_2CH_3$. [e] *N*-Methyl-2,5-piperazinedione. [f] IV.

Table III. Stability Constants for the Reaction of Cu(II) with GG, GS, and Their Methyl Esters[a,b]

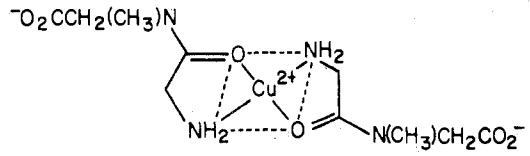
Ligand	Log K_{1H}	Log K_{2H}	Log K_1	Log K_2	Log K_2'	Log K_{1a}	Log K_{2a}
GG	8.18 ± 0.01	3.19 ± 0.01	5.26 ± 0.02[c]		2.92 ± 0.02[d]	−4.31 ± 0.02[d,e]	
GS	8.60 ± 0.01	2.92 ± 0.01	6.28 ± 0.01[f]	4.88[g]			
GGOMe	7.78 ± 0.01		4.11 ± 0.01		3.30 ± 0.03	−5.23 ± 0.01	−6.57 ± 0.03
GSOMe	8.01 ± 0.01		5.18 ± 0.01	3.91 ± 0.01			

[a] At 25.0° and 0.05 M (KNO_3) ionic strength. [b] Log K_2' for $Cu(H_{-1}GG) + GGOMe \rightleftarrows Cu(H_{-1}GG)(GGOMe)$ is 2.4 ± 0.1. [c] 5.42 ± 0.02 at $\mu = 1.0$ in ref 5. [d] 2.92 ± 0.02 at $\mu = 1.0$ in ref 5. [e] −4.38 ± 0.02 at $\mu = 1.0$ in ref 5. [f] 6.13 at $\mu = 0.16$ in ref 14. [g] 4.62 at $\mu = 0.16$ in ref 14.

at this pH; it suggests that the ester has either hydrolyzed to give glycylsarcosine and/or cyclized to *N*-methyl-2,5-piperazinedione.

Glycylsarcosine (GS). Infrared spectra (not shown) of solutions of glycylsarcosine are summarized in Table II. At neutral pD where the amine group is protonated, two carbonyl peaks are observed at 1662 and 1598 cm^{-1}, corresponding to absorption by the amide and ionized carboxylate groups, respectively. As the pD is raised the peak at 1662 cm^{-1} decreases, and a new peak is observed at 1628 cm^{-1}. At pD 9.3 three peaks are present at 1658, 1628, and 1598 cm^{-1}. The peak at 1628 cm^{-1} is assigned to the glycylsarcosine anion amide carbonyl. At yet higher pD only two peaks at 1628 and 1598 cm^{-1} are observed corresponding to the amide and carboxylate carbonyl absorptions of the glycylsarcosine anion.

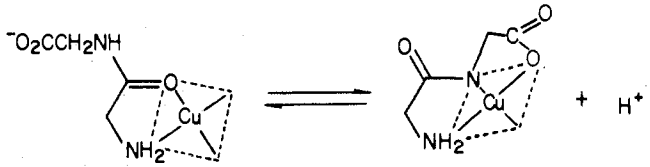
GS-Cu(II). Infrared spectra (not shown) of 1:1 and 2:1 GS-Cu(II) solutions at various pD values are listed in Table II. At low pD three carbonyl absorptions are found at 1662, 1625, and 1598 cm^{-1} corresponding to the uncomplexed amide carbonyl band, the metal-complexed amide carbonyl band, and the unprotonated carboxylate frequency, respectively. As the pD is raised, the uncomplexed amide carbonyl band decreases, while the other two peaks gain in intensity indicating further metal complex formation. At pD 5.5 the 1:1 ligand to metal ion system disproportionates to the 2:1 complex and copper(II), which precipitates as copper(II) hydroxide. The resultant solution yields a spectrum identical with that of the 2:1 GS-Cu(II) solution. Spectra of the 2:1 solutions at still higher pD show only one broad intense absorption at 1608 cm^{-1}, corresponding to both metal-coordinated amide carbonyl and ionized carboxylate groups as in V.



V

Stability Constants. Calculated stability constants for the Cu(II) coordination of glycylglycine and glycylsarcosine and their methyl esters are given in Table III. As noted in the Experimental Section, these calculations were straightforward except for the GGOMe-Cu(II) system. Datta and Rabin[12] had previously reported values of log K_1 and log K_2 ($K_2 = [Cu(GGOEt)_2^{2+}]/[Cu(GGOEt)^{2+}][GGOEt]$) of 4.66 and 4.58, respectively, for Cu(II)-glycylglycine ethyl ester (GGOEt) solutions. The unusual similarity of their K_1 and K_2 values contrasts with the ($\log K_1 - \log K_2$) difference of about 1.3 (Table III) for GSOMe-Cu(II) and also for the previously reported and related glycinamide-Cu(II) system.[13] Datta and Rabin assumed that no amide proton ionization occurred upon complexation of GGOEt. Making this assumption, we also found that our data yielded very similar constants ($\log K_1 = 5.30 \pm 0.02$ and $\log K_2 = 5.02 \pm 0.02$). However, the infrared results indicated that amide proton ionization does occur. Therefore, the deprotonated species, $Cu(H_{-1}GGOMe)^+$ (structure III), as well as Cu^{2+} and $Cu(GGOMe)^{2+}$ (structure II), was included in the calculations (using an iterative program) based on data from titrations of 1:1 GGOMe-Cu(II) solutions in the 5.5-6.0 pH range. This treatment gave very reasonable values (Table III) for K_1 and the amide deprotonation constant, K_{1a}. Unfortunately, the complexity of the equations prevented the possible evaluation of K_2 in a lower pH range in 2:1 GGOMe-Cu(II) solutions.

It has previously been shown[5] that glycylglycine first binds Cu(II) *via* its amino and amide carbonyl oxygen (structure VI) and then at higher pH loses its amide proton to go to $Cu(H_{-1}GG)$, structure VII. As noted above,



VI VII

GGOMe undergoes the analogous reactions to first form $Cu(GGOMe)^{2+}$ of structure II followed by amide proton ionization to give $Cu(H_{-1}GGOMe)^+$, structure III. In contrast, the amide *N*-methyl group eliminates the possibility of amide deprotonation from the initially formed complexes, $Cu(GS)^+$ and $Cu(GSOMe)^{2+}$, in which coordination occurs through the amino group and amide carbonyl oxygen atom.

It had been previously noted[14] that the stability constant (K_1) for the formation of $Cu(GS)^+$ is greater than that for $Cu(GG)^+$, presumably as a result of the electron-releasing character of the methyl group in GS. Likewise, log K_1 for $Cu(GSOMe)^{2+}$ is about 1 log unit larger than that for $Cu(GGOMe)^{2+}$.

The Cu(II) complexes of the methyl esters of both GG and GS have values of K_1 which are about 1.1 log units lower than that of the corresponding dipeptides. Since neither the $-CO_2^-$ groups of the dipeptides nor the $-CO_2-CH_3$ groups of their esters are coordinated to the metal ion, the enhanced stability of the Cu(II) dipeptide chelates is apparently due to the increased donor ability of the amino and amide oxygen groups, caused by the negative charge on the ligand. (This is also reflected by the higher pK_a of the dipeptides.) The same trend is also observed in K_2 values for $Cu(GS)_2$ as compared to $Cu(GSOMe)_2^{2+}$. Finally, the stability constant for $Cu(H_{-1}GG)$ binding of GG^- (log $K_2^1 = 2.92$) is greater than that for binding GGOMe (log $K_2^1 = 2.4$). All of these results indicate the reduced co-

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ordinating ability of dipeptide esters as compared to the dipeptides themselves.

The higher K_1 value for coordination of GGOMe by $Cu(H_{-1}GGOMe)^+$ ($\log K_2^1 = 3.30$) as compared to $Cu(H_{-1}GG)$ reflects the availability of more coordination sites and a higher positive charge on the $Cu(H_{-1}GGOMe)^+$ complex.

Unlike the complexes of GS and GSOMe, the Cu(II) complexes of GG and GGOMe undergo amide proton ionization. Dissociation constants for this ionization in $Cu(GG)^+$ and $Cu(GGOMe)^{2+}$ are given in Table III as K_{1a}. As has been suggested by Kaden and Zuberbuhler[15] and by Nakon and Martell,[16] part of the driving force for this ionization is the formation of a second stable chelate ring as occurs when $Cu(GG)^+$ loses a proton to give $Cu(H_{-1}GG)$, as in eq 1. Thus, as compared to $Cu(GG)^+$ ($\log K_{1a} = -4.38$),[5] amide proton ionization occurs significantly less readily ($\log K_{1a} = -7.01$)[17] in Cu(glycinamide)$^{2+}$ in which no additional chelate ring is formed. The value of $\log K_{1a}$ (−5.23) for $Cu(GGOMe)^{2+}$ is intermediate between the above extremes, suggesting that the ester group is perhaps weakly coordinated to the Cu^{2+}, as in structure III. Whether the ester actually binds to the metal is not clear, but amide ionization and nitrogen coordination definitely place the ester group in a position near the metal ion where the metal ion may promote the hydrolysis of the ester, as will be discussed in a following paper.[3]

Registry No. 2:1 GGOMe-Cu(II), 38671-67-9; 1:1 GGOMe-Cu(II), 38671-68-0; 2:1 GSOMe-Cu(II), 38671-69-1; 2:1 GS-Cu(II), 38671-70-4.

Acknowledgment. This research was supported by the U. S. Public Health Service through Grant No. GM-12626 of the National Institute of General Medical Sciences.

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Heats of Reaction of Triphenylphosphine with Compounds of the Type Hexafluoroacetylacetonato(olefin)silver(I)

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Received November 15, 1972

Characterization of and heats of the following reactions are reported where hfacac is the conjugate base of hexafluoroacetylacetone, and the olefins are cyclopentene, cyclohexene, cycloheptene, *cis*-cyclooctene, 1,5-cyclooctadiene, and 1,3,5,7-cyclooctatetraene. Relative base-silver dissociation energies are found to be 18.4 ($P(C_6H_5)_3$), 8.6 (C_8H_{14}), 6.7 (C_6H_{12}), 5.1 (C_6H_{10}), 4.1 (C_7H_{12}), and 0.0 kcal/mol (C_5H_8) (ignoring solvation contributions). This ordering is in disagreement with all other available thermodynamic silver olefin data indicative of substantial solvation and entropic contributions in the previously reported data. Evidence is given for the formation of species of the type [Ag(hfacac)(olefin)$_2$]. The proton nmr spectra for these compounds are briefly discussed.

$$[Ag(hfacac)(olefin)] + P(C_6H_5)_3 \xrightarrow{CH_2Cl_2} [Ag(hfacac)(P(C_6H_5)_3)] + olefin \quad (1)$$

$$[Ag(hfacac)(P(C_6H_5)_3)] + P(C_6H_5)_3 \xrightarrow{CH_2Cl_2} [Ag(hfacac)(P(C_6H_5)_3)_2] \quad (2)$$

$$[Ag(hfacac)(olefin)] + olefin\ (excess) + P(C_6H_5)_3 \xrightarrow{CH_2Cl_2} [Ag(hfacac)(P(C_6H_5)_3)] + olefin \quad (3)$$

Introduction

We have been interested in preparing suitable metal-olefin compounds and obtaining relative metal-olefin dissociation energies by calorimetric studies on these compounds.[1] We previously have calorimetrically studied the interaction of dichlorobis(benzonitrile)palladium(II) with various chelating bases[2] and prepared a series of nonionic compounds of the type [Ag(hfacac)(olefin)] (hfacac is the anion of hexafluoroacetylacetonate) which are soluble in relatively nonpolar solvents.[1] We now wish to report the interaction of triphenylphosphine with the latter compounds and the enthalpic changes associated with these reactions.

Thermodynamic information regarding the metal-olefin interaction is significant for at least three reasons. Information regarding the metal-olefin bond can be gained by varying the electronic, steric, and strain characteristics of the olefin and observing the changes in the metal-olefin interaction. It can be used to test the various spectroscopic parameters that have been thought to reflect metal-olefin "bond strength," such as the decrease in the double-bond stretching frequency upon coordination of an olefin to a metal. Since heats of formation of compounds in the gas phase have been found to parallel closely heats of chemisorption on solids,[3] valuable information relatable to the catalytic activity of surfaces can be obtained.

Extensive thermodynamic information on silver-olefin compounds is available and has been reviewed.[4] Since that

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