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Ternary Complexes in Solution. XIII. Mixed-Ligand Complexes of Copper(II) or Zinc(II) with 2,2'-Bipyridyl and Thioether Carboxylates or Some of the Sulfoxide or Sulfone Derivatives [1,2]

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Received February 10, 1972

The stability constants of ternary Cu^{2+} and Zn^{2+} complexes, each of which contained 2,2'-bipyridyl and a second ligand of carboxymethyl alkyl *or* aryl *sulfide or the sulfoxide or sulfone derivative, were determined by potentiometric titration in 50% aqueous dioxane ($I = 0.1$, $NaClO_4$; 25°). A comparison of the stability of these ternary complexes with those formed with simple carboxylates indicates that the thioether (or sulfoxide or sulfone) groups participate in complex formation in all the mixed-ligand cases. This is different from the results obtained recently for the binary complexes of Cu^{2+} and Zn^{2+} with thioether carboxylates: chelate formation is definite only for the binary complexes with carboxymethyl* alkyl *sulfides, while with carboxymethyl* aryl *sulfides, the stability constants are of an order that can be explained by the formation of simple carboxylate complexes alone.*

Introduction

The ternary complexes investigated so far in solution have had mainly ligands with O and/or N atoms as binding sites.[1-7] The most striking qualities were observed in systems containing Cu^{2+}, an aromatic amine, and a further ligand coordinating through O atoms: the resulting mixed-ligand complexes are very stable.[7] For example, the ternary complex, 2,2'-bipyridyl-Cu^{2+}-pyrocatecholate (eq 1),[8] is more stable than the corresponding binary one, Cu^{2+}-pyrocatecholate (eq 2).[6] In other words, positive values are obtained for the stability difference, ΔlogK, as defined by equation 3. For the mentioned example, $\Delta \log K_{Cu} = +0.43$.[6] This result may seem surprising, since usually $K^{Me}_{MeL} > K^{MeL}_{MeL_2}$,[9] due to the fact that more coordination positions are available for bonding of the first ligand to a given metal ion than for the second ligand. Clearly, the difference, Δlog K, which results from subtraction of the logarithms of two constants, is also a constant; this is due equilibrium 4.

$$\mathrm{Me(bipy)} + \mathrm{L} \rightleftharpoons \mathrm{Me(bipy)L}$$

$$K^{\mathrm{Me(bipy)}}_{\mathrm{Me(bipy)L}} = \frac{[\mathrm{Me(bipy)L}]}{[\mathrm{Me(bipy)}][\mathrm{L}]} \tag{1}$$

$$\mathrm{Me} + \mathrm{L} \rightleftharpoons \mathrm{MeL} \qquad K^{\mathrm{Me}}_{\mathrm{MeL}} = \frac{[\mathrm{MeL}]}{[\mathrm{Me}][\mathrm{L}]} \tag{2}$$

$$\Delta \log K_{\mathrm{Me}} = \log K^{\mathrm{Me(bipy)}}_{\mathrm{Me(bipy)L}} - \log K^{\mathrm{Me}}_{\mathrm{MeL}} \tag{3}$$

$$\mathrm{Me(bipy)} + \mathrm{MeL} \rightleftharpoons \mathrm{Me(bipy)L} + \mathrm{Me} \tag{4}$$

The recent systematic studies of ligands containing O and/or N as donors have shown that the stability of the mixed-ligand complexes is strongly dependent on the kind of donor atoms available and the possibility of π bond formation.[1,2,6,7] Since S is one of the more important donor atoms *in vitro* as well as *in vivo*,[10] being able to form both, σ and π bonds, it is of considerable importance to learn something about the binding behavior of this atom in ternary complexes. The strongest and most common binding site in this respect is proffered by the thiol group (R-SH) so frequently encountered in cysteinyl residues, but redox reactions between the sulfide anion ($R\text{-}S^-$) and certain metal ions such as Cu^{2+} preclude the determination of stability constants.[11] To overcome this problem and because of the importance of such natural thiothers as methionine, thioether carboxylates were used in the present work. The presence of a carboxylate group as a second binding site in these ligands, allows the determination of the stability constants by potentiometric titrations and guarantees a certain minimal stability of the complexes. *Alkyl*

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(1) Part XII: H. Sigel, R. Griesser, and B. Prijs, *Z. f. Naturforschung*, *27b*, 353 (1972).

(2) Part XI: R. Griesser and H. Sigel, *Inorg. Chem.*, *10*, 2229 (1971).

(3) D.D. Perrin, I.G. Sayce, and V.S. Sharma, *J. Chem. Soc.*, A, 1755 (1967); 446 (1968); 2060 (1969).

(4) G.A. L'Heureux and A.E. Martell, *J. Inorg. Nucl. Chem.*, *28*, 481 (1966).

(5) H. Sigel, *Chimia* (Aarau), *21*, 489 (1967).

(6) R. Griesser and H. Sigel, *Inorg. Chem.*, *9*, 1238 (1970).

(7) P.R. Huber, R. Griesser, and H. Sigel, *Inorg. Chem.*, *10*, 945 (1971).

(8) Abbreviations used: general metal ion, Me; general ligand, L; 2,2'-bipyridyl, bipy.

(9) L.G. Sillén and A.E. Martell, « Stability Constants of Metal-Ion Complexes », Special Pubblication No. 17, The Chemical Society, London, 1964.

(10) H. Sigel and D.B. McCormick, *Accounts Chem. Res.*, *3*, 201 (1970).

(11) G.R. Lenz and A.E. Martell, *Biochemistry*, *3*, 745 (1964).

an *aryl* substituted carboxymethyl sulfides were used as ligands to examine the influence of different electron densities on the sulfur. The systems studied contained Cu^{2+} or Zn^{2+}, 2,2′-bipyridyl, and as a second ligand, carboxymethyl *alkyl* sulfide, carboxymethyl *aryl* sulfide, or sulfoxide or sulfone derivative thereof.

Experimental Section

Materials and Synthesis. 2,2′-Bipyridyl, the metal perchlorates, and D_2O (99.75%) were purchased from Fluka AG, Buchs, Switzerland; dioxane was from Merck AG, Darmstadt, Germany. A solution of NaOD war prepared by dissolving NaOH in D_2O. This solution was used to adjust the pD of the solutions used for the NMR experiments. *p*-Nitrophenyl mercaptan was obtained from Aldrich Chemical Co., Milwaukee, Wisconsin. Iodoacetic acid was from Eastman Organic Chemicals, Rochester, New York.

Carboxymethyl *p*-nitrophenyl sulfide was synthesized as described.[12,13] The elemental composition was calculated for $C_8H_7NO_4S$: C, 45.06; H, 3.32; N, 6.57; O, 30.01; S, 15.04. Found: C, 45.20; H, 3.32; N, 6.57; O, 30.05; S, 14.91. All other thioether derivatives were the same as used recently.[12,13]

Apparatus and Determination of Constants. All experimental conditions were exactly the same as described recently.[13] The evaluation of the experimental data was done as before.[5,13] In the calculations of the stability constants due to the mixed-ligand complexes (eq 1), it was assumed that complex formation between Cu^{2+} or Zn^{2+} and 2,2′-bipyridyl is complete. The correctness of this assumption has been repeatedly proven,[4-7] but additionally it was checked potentiometrically for the present cases. These titrations revealed that the release of protons due to the complexing between Me^{2+} and bipy is completely finished before the reaction between $Me(bipy)^{2+}$ and L occurs. Hence, the curves that resulted from the titration of a solution containing only $HClO_4$ and those containing also Me^{2+} and bipy are superimposable. Of course this is true only at lower pH values (and in the pH region used for the calculation of the stability constants); at higher pH values, the curves are different due to hydrolysis of the Me^{2+}-2,2′-bipyridyl 1:1 complexes.

As earlier,[13,18,20,22] the potentiograph was calibrated with comercial aqueous buffers (pH 4 and 7, from Metrohm AG) and the direct readings for pH were used in the calculations. No "corrections" were applied for the change in solvent (50% aqueous dioxane; I = 0.1, $NaClO_4$; 25°).

Results

The acidity constants of the ligands according to eq 5 and the stability constants of the binary complexes, MeL (eq 2), and the ternary complexes, Me(bipy)L (eq 1), were determined by potentiometric titrations in 50% aqueous dioxane (I = 0.1, t = 25°). This mixed solvent was used for solubility reasons. For stability constants, measurements were made in the presence of an excess of metal ions, or an excess of metal ions and 2,2′-bipyridyl in a 1:1 ratio, with respect to the concentration of the thioether derivatives.

$$HL \rightleftharpoons H + L \qquad K^{H}_{HL} = \frac{[H][L]}{[HL]} \tag{5}$$

For the systems with carboxymethyl isopropyl sulfide or carboxymethyl phenyl sulfide, the results of such titrations are shown in Figure 1, where the pH of the solution is plotted against the neutralisation degree. The formation of complexes shifts the buffer region of the ligands to lower pH values. Thus, it may be concluded from Figure 1 that the stability of

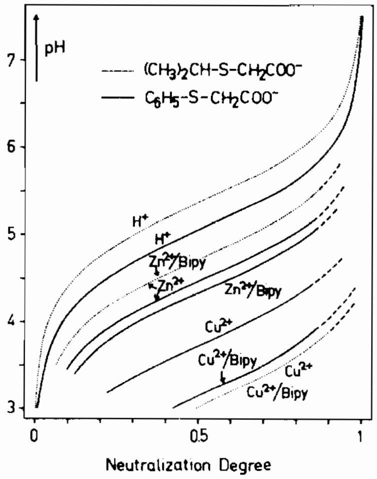

Figure 1. Variation of neutralization degree with pH during potentiometric titration with 0.1 *M* NaOH of thioether carboxylic acids (1.2×10^{-3} *M*) with and without metal ion (2.4×10^{-2} *M*), or metal ion and 2,2′-bipyridyl (each 2.4×10^{-2} *M*) in 50 ml of 50% aqueous dioxane (I = 0,1, $NaClO_4$; 25°). Portions of lines (- - -) extended toward higher degrees of neutralization indicate uncertainty due to hydrolysis. For the carboxymethyl isopropyl sulfide, the titration curves due to the binary and ternary systems are practically identical.

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(12) Y.-C. Lee, M.G. Joiner Hayes, and D.B. McCormick, *Biochem. Pharmacol.*, *19*, 2825 (1970).

(13) R. Griesser, M.G. Hayes, D.B. McCormick, B. Prijs, and H. Sigel, *Arch. Biochem. Biophys.*, *144*, 628 (1971).

(14) From NMR studies of different types of ligands, it is known that predominately the signal of the proton(s) neighboring the binding site of the paramagnetic cupric or manganous ion is broadened.[15,16] The observation of an effect with small amounts of the metal ion compared with those of the ligand is due to a high exchange rate of the metal ion.

(15) M. Cohn and T.R. Houghes, Jr., *J. Biol. Chem.*, *237*, 176 (1962).

(16) T.J. Swift and R.E. Connick, *J. Chem. Phys.*, *37*, 307 (1962).

(17) 2,2′-Bipyridyl is not pushed out of the coordination sphere of Cu^{2+} by the high excess of carboxymethyl phenyl sulfide, but most of Cu^{2+} exists under these conditions (*cf.* Table II) as the mixed-ligand complex, as the following estimations show. The constants for the carboxymethyl sulfide (L) system in water were estimated from the change observed for the constants with the acetate system[18] by replacing 50% aqueous dioxane as solvent by water: $pK^{H}_{HL} \simeq 3.6$; $\log K^{Cu}_{CuL} \simeq 1.3$; $\log K^{CuL}_{CuL_2} \simeq 0.7$; $\log K^{Cu(bipy)}_{Cu(bipy)L} \simeq 1.9$. Constants due to the 2,2′-bipyridyl system in water:[19] $pK^{H}_{H(bipy)} = 4.49$; $\log K^{Cu}_{Cu(bipy)} = 8.00$; $\log K^{Cu(bipy)}_{Cu(bipy)_2} = 5.60$. Using these constants, $[L]_{tot} = 0.2$ M, and $[bipy]_{tot} = [Cu^{2+}]_{tot} = 6.25\times10^{-5}$ *M* (*cf.* Table II), one obtains the following distribution of the species ($[Cu^{2+}]_{tot} \triangleq 100\%$): Cu(bipy)L, ~86%; Cu(bipy), ~11%; Cu, $Cu(bipy)_2$, CuL, and CuL_2, ~3%.

(18) R. Griesser, B. Prijs, H. Sigel, and D.B. McCormick, *Inorg. Nucl. Chem. Letters*, *5*, 951 (1969).

(19) G. Anderegg, *Helv. Chim. Acta*, *46*, 2397 (1963).

Table I. Negative Log Acidity Constants of Thioether Carboxylic Acids and Some of Their Sulfoxide and Sulfone Derivatives, and Log Stability Constants of the Corresponding Binary, MeL, and Ternary, Me(bipy)L, Cu^{2+} and Zn^{2+} Complexes, Determined in 50% Aqueous Dioxane (I = 0.1, $Na(ClO_4)$; 25°)

No.	Ligand	pK^{H}_{HL} [b]	$\log K^{Cu}_{CuL}$ [b]	$\log K^{Cu(bipy)}_{Cu(bipy)L}$	$\Delta\log K_{Cu}$	$\log K^{Zn}_{ZnL}$ [b]	$\log K^{Zn(bipy)}_{Zn(bipy)L}$	$\Delta\log K_{Zn}$
I	CH_3CH_2—S—CH_2COO^-	5.24	3.92	3.91	—0.01	2.22	2.18	—0.04
II	$CH_3CH_2CH_2$—S—CH_2COO^-	5.34	3.87	3.92	0.05	2.26	2.19	—0.07
III	$(CH_3)_2CH$–S–CH_2COO^-	5.37	3.93	3.94	0.01	2.22	2.22	0.00
IV	C_6H_5—CH_2—S—CH_2COO^-	5.32	3.40	3.82	0.42	2.19	2.16	—0.03
V	C_5H_5—S—CH_2COO^-	5.05	2.89	3.53	0.64	2.04	2.20	0.16
VI	p–CH_3–C_6H_4–S–CH_2COO^-	5.17	3.01	3.61	0.60	2.04	2.22	0.18
VII	p–NO_2–C_6H_4–S–CH_2COO^-	4.54	2.59	2.95	0.36	1.78	1.91	0.13
VIII	C_6H_5–CH_2–SO–CH_2COO^-	3.88	2.65	2.83	0.18	1.84	1.80	—0.04
IX	C_6H_5–SO–CH_2COO^-	3.90	2.53	2.72	0.19	1.96	1.89	—0.07
X	C_6H_5–CH_2–SO_2–CH_2COO^-	3.66	2.49	2.63	0.14	1.73	1.75	—0.02
XI	C_6H_5–SO_2–CH_2COO^-	3.85	2.61	2.87	0.26	1.87	1.83	—0.04

[a] The reproducibility of the stability constants was at least ±0.05; that for the acidity constants was smaller, *cf.* ref. 13. [b] These data are the same as those given in ref. 13, with the exception of VII; the constants due to the latter system were determined only now ($pK^{H}_{HL}=4.54\pm0.02$).

Table II. Line Widths[a] from PMR Spectra of Carboxymethyl Phenyl Sulfide (V) with Increasing Amounts of $[Cu(ClO_4)_2]_{tot}=[2,2'\text{-bipyridyl}]_{tot}$ (V was 0.2 *M* in D_2O; pD ~5.5; 37°)[17].

$[Cu^{2+}]=[bipy]$	C_6H_5—	—CH_2—
—	1.40	0.64
6.25×10^{-5}	1.96	2.78
1.25×10^{-4}	2.41	5.0
2.5×10^{-4}	3.27	9
5×10^{-4} (precipitation)		

[a] Given in cps; measured at the half height of the peaks on an expanded scale (100 cps); errors in line width determinations are within 10%.

the binary and ternary complexes formed with carboxymethyl isopropyl sulfide is about the same for both metal ions, *i.e.*, $\Delta\log K_{Cu}\simeq0$ and $\Delta\log K_{Zn}\simeq0$; and with carboxymethyl phenyl sulfide as ligand the stability of the ternary complexes is significantly greater than that of the binary ones, *i.e.*, $\Delta\log K_{Cu}>0$ and $\Delta\log K_{Zn}>0$. This different behavior with regard to the stability of the ternary complexes as exemplified by these two ligands is generally observed with carboxymethyl *alkyl* sulfides and carboxymethyl *aryl* sulfides, as can be seen from the results presented in Table I.

The high stability of the ternary complexes (compared with the binary ones) formed with carboxymethyl *aryl* sulfides prompted us to investigate the proton magnetic resonance spectra of carboxymethyl phenyl sulfide, V, in the presence of increasing amounts of Cu^{2+} (*cf.*[14]) and 2,2′-bipyridyl in a 1:1 ratio,[17] and to compare these data (*cf.* Table II) with the ones obtained earlier[13] in the presence of metal ion alone, *viz.* Mn^{2+} or Cu^{2+}. From such a comparison, we hoped to solve the question[13] about whether or not chelates are formed between Cu^{2+} (or Mn^{2+}) and carboxymethyl *aryl* sulfides. Such chelate formation is definite for the binary Cu^{2+}-carboxymethyl *alkyl* sulfides.[13]

An attempt to observe also a chemical shift[15] in the PMR spectrum of carboxymethyl phenyl sulfide, V, in the presence of Zn^{2+} and 2,2′-bipyridyl failed, due to solubility problems in 1:1:1 mixtures.

Discussion

The acidity constants of the ligands and the stabilities of the binary complexes, including those with Mn^{2+}, have already been compared and discussed recently.[13] Therefore, we can concentrate now on the stability of the mixed-ligand complexes.

Thioether Carboxylates. The most surprising point of the results given in Table I is that thioether carboxylates, I-VII, can be divided into at least two or even three classes according to the order of the $\Delta\log K_{Cu}$ values. The carboxymethyl *aryl* sulfide systems, V and VI, have $\Delta\log K_{Cu}\simeq0.6$; these results are of an order only very rarely observed.[6] In contrast, $\Delta\log K_{Cu}\simeq0.0$ for the carboxymethyl *alkyl* sulfide systems, I-III. Of course, even the latter value is still considerably greater than expected statistically, *i.e.* the ternary complexes are more stable than expected. A third, less clear-cut class may be formed with carboxymethyl benzyl sulfide, IV, and carboxymethyl *p*-nitrophenyl sulfide, VII, with intermediate values for $\Delta\log K_{Cu}$. As usually observed,[2,18,20] the stabilities of the Zn^{2+} complexes show the same general trend which is less pronounced than that of the Cu^{2+} complexes (*cf.* Table I).

Before discussing possible reasons that lead to these classes, it seems reasonable to consider the structure of these complexes, *i.e* does the thioether group actually participate in complex formation. An unequivocal answer is obtained when the stability of the thioether carboxylate complexes is greater than expected on the basis of the basicity of the carboxylate groups. Therefore, it is convenient to plot the stability constants against the acidity constants. For series of structurally related ligands, straight lines result.[21] The "reference" lines given in Figures 2 and 3 are due to simple carboxylate systems.[20,22] In Figure 2, the data due to the mixed-ligand Cu^{2+} systems are plotted; those due to the binary complexes are given for comparison. In Figure 3, only the data of the ternary Zn^{2+} complexes are shown.

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(20) R. Griesser, B. Prijs, and H. Sigel, *Inorg. Nucl. Chem. Letters*, 4, 443 (1968).
(21) A.E. Martell and M. Calvin, Chemistry of the Metal Chelate Compounds, Englewood Cliffs, N.J., Prentice-Hall, 1952.

It can be concluded from Figure 2 that all the ternary complexes, Cu(bipy)L, formed with the thioether carboxylates, I-VII, are significantly more stable than expected on the basis of the basicity of the corresponding carboxylate groups alone. This result shows clearly that $Cu(bipy)^{2+}$ reacts with these ligands by forming a 5-membered chelate which involves the thioether and the carboxylate groups. In contrast, in the case of the binary complexes, chelate formation is definite only with the carboxymethyl *alkyl* sulfides, I-IV, but not with the carboxymethyl *aryl* sulfides, V-VII.[13] This means the stabilities of the binary complexes formed with the latter ligands, V-VII, correspond with the reference line.

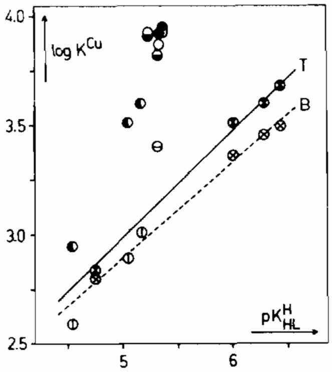

Figure 2. Relation between log K^{Cu} ($\hat{=}\log K^{Cu}_{CuL}$ or log $K^{Cu(bipy)}_{Cu(bipy)L}$) and pK^{H}_{HL} for the binary complexes, CuL (⊗, O, ⊖, ⦶), and the ternary complexes, Cu(bipy)L (⨂, ●, ◒, ◐), with *simple* carboxylates (⊗, ⨂), the carboxymethyl *alkyl* sulfides, I-III (O, ●), carboxymethyl *benzyl* sulfide, IV (⊖, ◒), and the carboxymethyl *aryl* sulfides, V-VII (⦶, ◐) (*cf.* Table I). The data on the monodentate carboxylates, which furnish the reference lines due to the binary (B) and ternary (T) Cu^{2+} complexes, are taken from earlier reports on formate, acetate, and propionate[20] and on valerate[22] (*cf.* also the data due to α-or β-substituted halogeno carboxylates[18]).

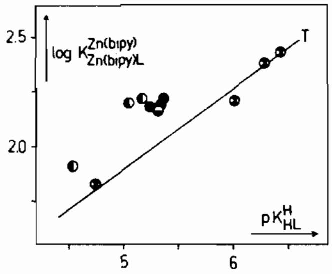

Figure 3. Relation between log $K^{Zn(bipy)}_{Zn(bipy)L}$ and pK^{H}_{HL} for the ternary complexes, Zn(bipy)L, with *simple* carboxylates (⨂), the carboxymethyl *alkyl* sulfides, I-III (●), carboxymethyl *benzyl* sulfide, IV (◒), and hte carboxymethyl *aryl* sulfides, V-VII (◐) (*cf.* Table I). The data on monodentate carboxylates, which furnish the reference line due to the ternary (T) Zn^{2+} complexes, are taken from earlier reports on formate, and propionate[20] and on valerate[22] (*cf.* also the data due to α- or β-substituted halogeno carboxylates[18]).

A rather similar situation is found in the series of Zn^{2+} complexes: in the ternary complexes, chelates are formed with all ligands, I-VII, (*cf.* Figure 3). Although the stability increase due to the coordination of the thioether group is less remarkable than with Cu^{2+}, it is still significant. Again, in the case of the binary Zn^{2+} complexes, chelate formation is definite only with the carboxymethyl *alkyl* sulfides, I-IV.[13]

Keeping the above points in mind, one may conclude that the large Δ log K_{Cu} values found with the carboxymethyl *aryl* sulfides, V and VI (Table I), are not due to an exceptionally high stability of the ternary Cu^{2+} complexes, but rather to the low stability of the corresponding binary complexes. The difference in stability between the binary complexes of carboxymethyl *alkyl* sulfides and carboxymethyl *aryl* sulfides was attributed[13] to the smaller electron density of aromatically-substituted sulfur.[23] Hence, it is assumed that in the uncomplexed carboxymethyl *aryl* sulfides and in the corresponding *binary* complexes the electron density is delocalized from S toward the phenyl ring. In the present case, however, one is lead to postulate an electron delocalization in the opposite direction in the *ternary* complexes; taking into account the known π-acceptor qualities of 2,2'-bipyridyl[6,7] (which makes Cu^{2+} more electrophilic), this seems reasonable. As a matter of fact, it is suggested that the high stability of these mixed-ligand complexes is connected with a π-electron delocalization over the whole complex (such a cooperative effect was observed in other cases too[6,7]). In agreement with this hypothesis is Δ log $K_{Cu} = 0.36$ for the *p*-nitro derivative, VII, of carboxymethyl phenyl sulfide: due to the electron-withdrawing qualities of the nitro group, the electron density decreases at the sulfur atom and the Δ log K_{Cu} is about 0.25 units smaller than those with the two other aryl derivatives, V and VI. The value of Δ log $K_{Cu} = 0.42$ for the carboxymethyl benzyl sulfide system fits in the same picture: due to the methylene group between the phenyl ring and sulfur, the π-electron delocalization is rendered more difficult, *i.e.* the cooperative effect between the two ligands is weakened.

Metal Ion-Thioether Interaction and the PMR Results. The recent PMR results[13] from investigation of the binary Cu^{2+} and Mn^{2+} complexes with carboxymethyl ethyl sulfide, I, confirmed the conclusions from the stability studies: there definitely is chelate formation with Cu^{2+}, for which no hint could be observed with Mn^{2+} which evidences a simple Mn^{2+}-carboxylate complex. In other words, the different complexing abilities of these two metal ions are reflected in these PMR studies.

The binary Cu^{2+} complexes of the carboxymethyl *aryl* sulfides, V and VI, have a stability expected on the basis of the basicity of the carboxylate groups alone (*cf.* Figure 2; the same is true for the Mn^{2+} complexes[13]). Hence, no definite conclusion about the structure of these complexes can be drawn, as the sulfur atom may well coordinate about as strongly as did the dislodged water molecule, and then no visible gain of free energy (ΔG) would be observed. As already stated, chelate formation is definite with these ligands in the ternary complexes. Therefore, it is of interest to compare the influence of Cu^{2+} (or

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(22) H. Sigel, D.B. McCormick, R. Griesser, B. Prijs, and L.D. Wright, *Biochemistry, 8,* 2687 (1969).

(23) L.D. Pettit and C. Sherrington, *J. Chem. Soc.,* A, 3078 (1968).

Mn^{2+}) with the influence of Cu^{2+}-2,2′-bipyridyl[17] on the proton magnetic resonance spectra of carboxymethyl phenyl sulfide, V.[14]

In Figure 4, the line widths in the presence of increasing amounts of Mn^{2+} (6.25×10^{-5} to 10^{-3} *M*; ref. 13), Cu^{2+} (6.25×10^{-5} to 2.5×10^{-4} *M*; ref. 13), or Cu^{2+}-2,2′-bipyridyl (see TableII)[17] for the proton signals due to the phenyl group are plotted *versus* those of the methylene group of $-S-CH_2-COO^-$. There is no apparent difference between the influence of Mn^{2+} or Cu^{2+}, nor Cu^{2+}-2,2′-bipyridyl; the data due to the ternary complex fit within the experimental error on the line given by the two binary complexes. This result is rather surprising (one might have expected a stronger broadening of the proton signals due to the phenyl group in the presence of Cu^{2+}-2,2′-bipyridyl), but the uniform behavior (Figure 4) may be explained by assuming chelate formation also for the binary Cu^{2+} and Mn^{2+} complexes and not only for the ternary complex, Cu(bipy)L, for which it follows unequivocally from the thermodynamic results (Table I; Figure 2). Indeed, examples are known where chelate formation is not manifested in the stability of complexes.[24] However, it should be noticed that this kind of interpretation may be satisfactory for the Cu^{2+} complexes, but *not* for the Mn^{2+} complexes. In the latter cases, it leads to the suggestion of chelate formation between Mn^{2+} and carboxymethyl *aryl* sulfide, while such a chelate formation seems improbable, as mentioned,[13] with carboxymethyl *alkyl* sulfides.

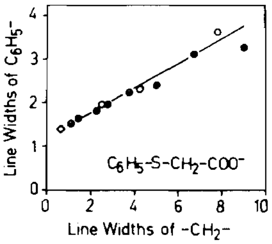

Figure 4. Correlation between the line widths of the protons due to C_6H_5- and $-CH_2-$ of carboxymethyl phenyl sulfide (V) without (◇) and in the presence of increasing amounts of Cu^{2+}/bipy (●, *cf*. Table II), Cu^{2+} (○, *cf*. ref. 13), or Mn^{2+} (⊗, *cf*. ref. 13).

The Sulfoxide and Sulfone Derivatives. For the binary Cu^{2+} and Zn^{2+} complexes, MeL, with the sulfoxides (VIII, IX) and sulfones (X, XI) of the carboxymethyl benzyl and carboxymethyl phenyl sulfides, it was concluded from thermodynamic data (using the stability of simple carboxylate complexes as a basis) that chelates are formed.[13] The same may be surmised for the ternary complexes, Me(bipy)L, which may be additionally evidenced by plots analogous to those of Figures 2 and 3.

In fact, the Δ log K_{Cu} Values (eq. 3) are positive for all four mixed-ligand systems, VIII-XI (Table I), which is in accord with the general behavior of ternary Cu^{2+} complexes containing 2,2′-bipyridyl and a second ligand with 0 as donors. Though usually Δ log $K_{Cu} \simeq 0.4$ for bidentate ligands with 0 donors,[5] the values in the present cases are only about $+0.2$ (*cf*. Table I). These smaller values are probably due to the decreased electron density on the oxygen (from the sulfoxides and sulfones) resulting from the p–d π back-donation from oxygen to sulfur.[13,25] The Δ log K_{Zn} values (Table I) are somewhat smaller than those of the corresponding Cu^{2+} systems, which is in agreement with earlier results.[2,18,20]

In Conclusion one may say that the thioether group is able to participate as a binding site in mixed-ligand complexes and exhibits interesting qualities therein. From the different behavior of *alkyl*- and *aryl*-substituted derivatives, it can be concluded that π bond formation is important for the stability of the complexes. Although the *aryl* substituted thioether carboxylates are not known to be naturally occuring ligands, these complexes can be considered as interesting models for one aspect of enzyme action: A dissoziation of the aromatic amine, 2,2′-bipyridyl, favors the simultaneous release of the thioether group from the coordination sphere of the metal ion. This is an interesting feature with regard to the recycling qualities of enzyme systems. This quality, especially evident with Cu^{2+}, arises from the significantly higher stability of the ternary 2,2′-bipyridyl-Me^{2+}-carboxymethyl *aryl* sulfide complex as compared with the binary Me^{2+}-carboxymethyl *aryl* sulfide complex. In this connection, it should be mentioned that the naturally occurring imidazole group has qualities in mixed-ligand complexes analogous to those of the pyridyl group.[1,7]

Acknowledgments. The measurements were performed with the skillful technical assistance of Miss R. Baumbusch and Miss M. Nicholson. This investigation was supported in part by a research grant from the Schweizerischen Nationalfonds zur Förderung der wissenschaftlichen Forschung, and by a grant from the CIBA-Stiftung (Basel), and in part by Research Grant AM-08721 from the National Institute of Arthritis and Metabolic Diseases, U.S.P.H.S., and by funds made available from the State University of New York.

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