

Contribution from the Institute of Inorganic Chemistry,
University of Basel, CH-4056 Basel, Switzerland**Stability of Metal Ion/Alkyl Thioether Complexes in Solution. Ligating Properties of "Isolated" Sulfur Atoms**

HELMUT SIGEL,* VOLKER M. RHEINBERGER, and BEDA E. FISCHER

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The stability constants for a number of the 1:1 complexes between 2,2'-thiodiethanol (tde), tetrahydrothiophene (tht), or diethyl sulfide and alkaline earth ions, 3d transition-metal ions, Zn^{2+} , Cd^{2+} , Hg^{2+} , or Ag^+ ($=M^{n+}$) have been determined in water or mixed aqueous solvents. The interaction between Cu^{2+} and the ether sulfur is connected with an absorption band in the near-UV region; hence it is possible to determine spectrophotometrically the stability of the Cu^{2+} complexes: e.g., for $Cu(tht)^{2+}$ $\log K_{Cu(tht)}^{Cu} = 0.02 \pm 0.04$ in 50% ethanol ($I = 1.0$) as solvent. Upon addition of another metal ion to a Cu^{2+} /thioether system the absorption decreases due to the competition between Cu^{2+} and the other M^{n+} for coordination at the ether sulfur. From this decrease in absorption it is possible to calculate also the stability constants of the M^{n+} complexes. The outstanding advantage of this method is that small differences in absorption can be measured very exactly, so that it is possible to measure the stability of very weak complexes like $Ca(tht)^{2+}$ ($\log K_{Ca(tht)}^{Ca} = -0.30 \pm 0.13$) or $Mn(tht)^{2+}$ (-0.31 ± 0.11) as well as of rather stable species like $Ag(tht)^+$ (3.51 ± 0.14) (these three latter constants were determined in 50% ethanol; $I = 1.0$). With $Cu(tde)^{2+}$ the influence of the solvent on complex stability was studied; the change from water to 80% ethanol or dioxane promotes the stability by a factor of about 2. The general importance of the ligating properties of thioether moieties toward the biologically important metal ions is briefly discussed.

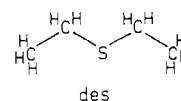
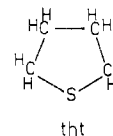
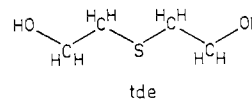
The thioether group is rather abundant in nature and recognized as a potential binding site for metal ions.¹ One important type of compound in which the thioether group is found is an α -amino acid.² The naturally occurring L-methionine and S-methyl-L-cysteine are aliphatic, asymmetrical sulfides. L-Methionine occurs in most proteins, and S-methyl-L-cysteine has been isolated from several plant sources. Other examples of biologically important compounds with a thioether function are d-biotin, a vitamin and coenzyme, and penicillin, an antibiotic.¹

Though the thioether group does often not contribute remarkably to the stability of complexes formed between amino acids containing this soft group and hard or borderline³ metal ions like Mg^{2+} and Mn^{2+} or Cu^{2+} and Zn^{2+} , there are suggestions that such metal ions may interact weakly or part of the time with the ether sulfur.^{1,2} Recently, the copper-thioether interaction has received special interest,^{4,5} as such an interaction was assumed to occur in the "blue" copper proteins, and indeed very recently by X-ray crystal structure analysis for plastocyanin a Cu^{2+} -thioether bond with a methionine residue was demonstrated.⁶ The corresponding observation was also made for the heme iron in cytochrome *c*^{7,8} as well as for cobaltocytocrome *c*,⁹ where the thioether function of a methionine residue is one of the axial ligands. Furthermore, with Mn^{2+} and Cu^{2+} a weak ether sulfur interaction with the tetrahydrothiophene part of d-biotin has been observed.^{1,10,11}

However, so far all the determinations of stability constants of complexes with hard or borderline metal ions have been done with polyethers¹² or with ligands containing in addition to the thioether moiety at least one proton-basic site,¹³⁻¹⁹ while solids of the Cu^{2+} complexes with 2,5-dithiahexane and 3,6-dithiaoctane have been isolated.²⁰ Certainly, soft metal ions³ like Cu^+ , Ag^+ , or Hg^{2+} have a pronounced coordination tendency toward the soft thioether group,^{1,2} and stability constants have been determined for a number of complexes formed by thioethers and such soft metal ions.²¹⁻²⁶

The reasons for the complete lack of stability data on the interaction between the biologically important hard or borderline metal ions³ like Mg^{2+} , Mn^{2+} , Cu^{2+} , or Zn^{2+} and simple thioethers are twofold: (i) such complexes are very weak² and (ii) a pH-metric determination of stability constants is not possible, as these ligands are very poor proton acceptors.²⁷ In fact, the ether sulfur is an extremely weak base,² $pK_a = -6.8$,²⁸ and as a consequence only thioether ligands containing an additional binding site, like an amino or a carboxylate group, have been studied.¹³⁻¹⁹

We now report on the stability of the complexes formed between alkaline earth ions, 3d transition-metal ions, Zn^{2+} , Cd^{2+} , Hg^{2+} , or Ag^+ , and the simple sulfur ligands tde, tht, and des.²⁹ The determination of these stability constants is based



on the following reasoning: Cu^{2+} is known to exhibit upon a multiple thioether interaction an intense absorption in the 340-450-nm spectral region;^{4,5} this is also true for simple Cu^{2+} -thioether 1:1 complexes; though in these cases the absorption is less pronounced, it does still allow one to determine the stability constant of the Cu^{2+} -thioether complex. This is of course a rather unstable species but it has the advantage that metal ions like Mn^{2+} can compete for the coordination at the ether sulfur in a system which contains both Cu^{2+} and Mn^{2+} . As a consequence, in the presence of Mn^{2+} the absorption of the Cu^{2+} -thioether system will be less than in a Mn^{2+} -free system, and from this decrease in absorption one can obviously calculate the stability constant of the Mn^{2+} -thioether complex. Hence, this procedure allows one to determine the stability of metal ion-thioether complexes which by themselves exhibit no absorption. The outstanding advantage of this method is that small differences in absorption can be measured very exactly, so that it is possible to determine the stability of very weak complexes like $Mn(thioether)^{2+}$ as well as of rather stable species like $Ag(thioether)^+$.

Experimental Section

Materials. The metal perchlorates (purum or purissimum) were from Fluka AG, Buchs, Switzerland, with the exception of zinc and strontium perchlorate which were obtained from K&K Laboratories, Cleveland, Ohio. Silver nitrate was from BDH-Chemicals Ltd., Poole, England, and all the other metal nitrates (pro analysi) were from

Merck AG, Darmstadt, Germany. The concentrations of the metal stock solutions were determined by titration with EDTA.

The ligands, 2,2'-thiodiethanol (pro analysi; from Merck AG), tetrahydrothiophene (pro analysi; from Merck-Schuchardt, Hohenbrunn, Germany), and diethyl sulfide (purum, Fluka AG), were distilled twice before use over a Raschig-column under N_2 and then stored also under N_2 . The sulfoxide of 2,2'-thiodiethanol was prepared by the method of Reichstein and Goldschmidt³⁰ and recrystallized from methanol/acetone; mp 112–113 °C.

The solvents, ethanol (for spectroscopic use) and dioxane ("reinst"), were from Merck AG. The dioxane used for the spectrophotometric experiments was additionally purified over sodium³¹ (under N_2) in the additional presence of a trace of benzophenone.

The pH was measured with a Metrohm potentiometer E 353 or E 353B using an EA 121 or a micro-EA 125 Metrohm glass electrode. Calibration was done with commercial aqueous buffers (pH 4 and 7, from Metrohm AG, Herisau, Switzerland) and the direct readings for pH were used.

Spectrophotometric Measurements. Absorbance spectra were recorded with a Beckman spectrophotometer DB connected to a W+W Electronic Hi-Speed recorder 202 or on a Varian Techtron spectrophotometer (Model 635) connected to a Honeywell recorder (Model 196). Measurements at constant wavelength were done on a Bausch & Lomb Spectronic 88 photometer. Depending on the conditions, 1- or 4-cm quartz cells were used. Difference spectra were always taken in 1-cm quartz cells; one cell in the reference beam contained Cu^{2+} (and possibly also M^{2+}) and the other the sulfur ligand, whereas one cell in the sample beam contained the mixed system and the other the solvent; the ionic strength was maintained constant throughout (25 °C).

In the measurements at $I = 1.0$ of the $Cu^{2+}/2,2'$ -thiodiethanol system $[tde] = 5 \times 10^{-3}$ M and $[Cu(ClO_4)_2] = 0.02\text{--}0.30$ M or $[Cu(NO_3)_2] = 0.04\text{--}0.30$ M; the ionic strength was adjusted with $NaClO_4$ or $NaNO_3$, respectively (see Figures 1 and 2). In these experiments, e.g., with $Cu(ClO_4)_2/NaClO_4$, the concentration of ClO_4^- varies from 0.98 to 0.70 M but the changes in the activity coefficients are small:^{32–35} e.g., for $NaClO_4$ the change is less than 3%.³⁴ For the measurements in mixed solvents at $I = 0.4$ ($NaClO_4$) $[Cu(ClO_4)_2] = 0.02\text{--}0.13$ M was used.³⁶ The conditions of the competition experiments were $[tde] = 5 \times 10^{-3}$ M, $[Cu^{2+}] = 0.05\text{--}0.25$ M, and $[M^{2+}] = 0.05\text{--}0.25$ M, but the sum of $[Cu^{2+}] + [M^{2+}]$ was always ≤ 0.3 M (so that $I = 1.0$ could be adjusted); in the case of Ag^+ and Hg^{2+} the concentrations were 0.005–0.008 M. In all these experiments the pH was adjusted to about 3, except in the presence of Hg^{2+} where pH ~ 2 was used.

The experimental conditions with tetrahydrothiophene as ligand (see also Figure 4) were exactly the same as with 2,2'-thiodiethanol, but all experiments were done in 50% aqueous ethanol as solvent which corresponds to 0.24 mole fraction of ethanol, while with diethyl sulfide (also in 50% ethanol) the experimental conditions were in three experiments $[des] = 2.5 \times 10^{-2}$ M and $[Cu(ClO_4)_2] = 0.04\text{--}0.30$ (or 0.40) M and in five experiments $[des] = 5 \times 10^{-2}$ M and $[Cu(ClO_4)_2] = 0.075\text{--}0.30$ (or 0.40) M ($I = 1.0$, $NaClO_4$; 25 °C).

Calculation of Stability Constants from Spectrophotometric Measurements. The stability constants K_{CuL}^{Cu} of the complexes CuL^{n+} were determined by the Benesi-Hildebrand method.³⁷ Under experimental conditions with $[Cu^{2+}]_{tot} \approx [Cu^{2+}]_{free}$, i.e., $[Cu^{2+}]_{tot} > [L]_{tot}$, the following equation holds:

$$\frac{1}{[Cu^{2+}]_{tot}} = A_{max} K_{CuL}^{Cu} \frac{1}{A} - K_{CuL}^{Cu} \quad (1)$$

Plots of $1/[Cu^{2+}]$ vs. $1/A$ resulted in straight lines (see Figure 2) which were calculated by a least-squares procedure. From the intercept with the y axis one obtains the stability constant K_{CuL}^{Cu} (M^{-1}) of the complex CuL^{2+} ($\nu_0 = -K_{CuL}^{Cu}$) and from the intercept with the x axis one obtains $1/A_{max}$ ($x_0 = 1/A_{max}$), from which the extinction coefficient ϵ ($M^{-1} \text{ cm}^{-1}$) of this complex may be calculated ($\epsilon = A_{max}/d[L]_{tot}$).

The calculation of the stability constants K_{ML}^M of all the other metal ion complexes, i.e., aside from CuL^{2+} , is based on the competition of M^{n+} and Cu^{2+} for the coordination at the ligand L. Hence, two sets of experiments had to be carried out: (i) one in the absence of M^{n+} , i.e., CuL^{2+} will form undisturbed and an absorption $A_{(i)}$ will be measured; (ii) one in the presence of M^{n+} , i.e., now also ML^{n+} will form and therefore $[CuL^{2+}]_{(ii)} < [CuL^{2+}]_{(i)}$ and thus $A_{(ii)} < A_{(i)}$. Under experimental conditions where the total metal ion concentration is significantly higher than the total ligand concentration (we usually

had a ratio of 60:1) only 1:1 complexes, i.e., CuL^{2+} and ML^{n+} , will form. Therefore it holds as follows (charges are omitted): (i) in the absence of a second metal ion M^{n+}

$$A_{(i)} = \epsilon_{CuL} [CuL]d \quad \text{and} \quad [CuL] = A_{(i)} / (\epsilon_{CuL}d)$$

$$[Cu]_{tot} = [Cu]_{free} + [CuL]$$

$$[L]_{tot} = [L]_{free} + [CuL]$$

and also

$$[L]_{tot} = \frac{A_{(i)}}{\epsilon_{CuL}d} + \frac{A_{(i)}}{K_{CuL}^{Cu}(\epsilon_{CuL}d[Cu]_{tot} - A_{(i)})} \quad (2)$$

(ii) in the presence of a second metal ion M^{n+}

$$A_{(ii)} = \epsilon_{CuL} [CuL]d \quad \text{and} \quad [CuL] = A_{(ii)} / (\epsilon_{CuL}d)$$

$$[Cu]_{tot} = [Cu]_{free} + [CuL]$$

$$[M]_{tot} = [M]_{free} + [ML]$$

$$[L]_{tot} = [L]_{free} + [ML] + [CuL]$$

and also

$$[L]_{tot} = [ML] + \frac{A_{(ii)}}{\epsilon_{CuL}d} + \frac{A_{(ii)}}{K_{CuL}^{Cu}(\epsilon_{CuL}d[Cu]_{tot} - A_{(ii)})} \quad (3)$$

If the conditions in experiments i and ii are such that $[L]_{tot(i)} = [L]_{tot(ii)}$, from eq 2 and 3 $[L]_{tot}$ may be eliminated and $[ML]$ can be calculated:

$$[ML] = \frac{A_{(i)} - A_{(ii)}}{\epsilon_{CuL}d} + \frac{A_{(i)}}{K_{CuL}^{Cu}(\epsilon_{CuL}d[Cu]_{tot} - A_{(i)})} - \frac{A_{(ii)}}{K_{CuL}^{Cu}(\epsilon_{CuL}d[Cu]_{tot} - A_{(ii)})} \quad (4a)$$

The knowledge of $[ML]$ allows one to calculate for experiment ii also

$$[M]_{free} = [M]_{tot} - [ML] \quad (4b)$$

and

$$[L]_{free} = [L]_{tot} - [ML] - A_{(ii)} / (\epsilon_{CuL}d) \quad (4c)$$

Equations 4a–c give with the mass action law

$$K_{ML}^M = [ML] / ([M]_{free}[L]_{free}) \quad (4d)$$

the stability constant K_{ML}^M of the complex ML^{n+} .

There is also a simpler way to calculate K_{ML}^M provided the experimental conditions are such that $[M^{n+}]_{tot} \approx [M^{n+}]_{free}$ and $[Cu^{2+}]_{tot} \approx [Cu^{2+}]_{free}$; then eq 5 holds:³⁸

$$K_{ML}^M = \frac{A_{(i)} - A_{(ii)}}{A_{(ii)}} \frac{[Cu]_{tot} K_{CuL}^{Cu} + 1}{[M]_{tot}} \quad (5)$$

The evident advantage of eq 5 compared with eq 4 is that the extinction coefficient, ϵ_{CuL} , is not necessary to calculate K_{ML}^M . This means errors inherent in ϵ_{CuL} , which had to be determined by different kinds of experiments and to be calculated from Benesi-Hildebrand plots, are not carried over to K_{ML}^M . This may be of importance because generally the difference in absorption, $A_{(i)} - A_{(ii)}$, can be determined very exactly. For the present series of experiments it turned out that for all metal ion systems, with the exceptions of Ag^+ and Hg^{2+} , the agreement of the results obtained with eq 4 and 5 is excellent, and this shows that the determined values for ϵ_{CuL} are reliable. With Ag^+ and Hg^{2+} eq 4 must be used, because the experimental assumptions inherent in eq 5 do not hold for these systems. All the values listed in the tables have been calculated with eq 4 for the sake of uniformity.

The results of the Cu^{2+} systems are the average of 4–8 independent series of measurements. The competition experiments were done between 11 to 25 times for each metal ion. The errors given throughout this paper are twice the standard deviation.

Results and Discussion

2,2'-Thiodiethanol Complexes. From the thioether ligands shown, 2,2'-thiodiethanol is the only one soluble enough to allow studies in aqueous solution. Actually this property was the reason that this ligand was selected. Some orienting

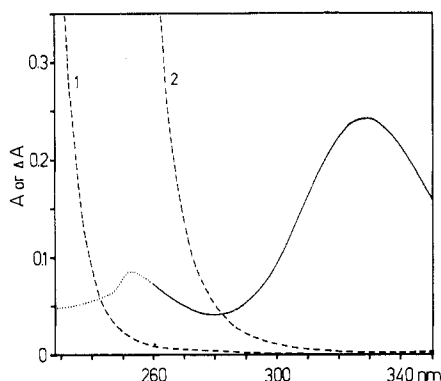


Figure 1. Broken lines: Absorption spectra of 2,2'-thiodiethanol (1) (5×10^{-3} M) and $\text{Cu}(\text{ClO}_4)_2$ (2) (0.20 M) in aqueous solutions at pH 3, $I = 1.0$ (NaClO_4), and 25°C measured in 1-cm quartz cells. Solid line: Absorption of the $\text{Cu}^{2+}/2,2'$ -thiodiethanol system under the above conditions measured as a difference spectrum; i.e., the reference beam contained one cell with 2,2'-thiodiethanol and a second one with $\text{Cu}(\text{ClO}_4)_2$, while the sample beam contained one cell with the mixed system and one with the solvent (cf. ● in Figure 2). The dotted line portion of the difference spectrum indicates uncertainty due to the large absorption of $\text{Cu}(\text{ClO}_4)_2$ at $\lambda < 260$ nm.

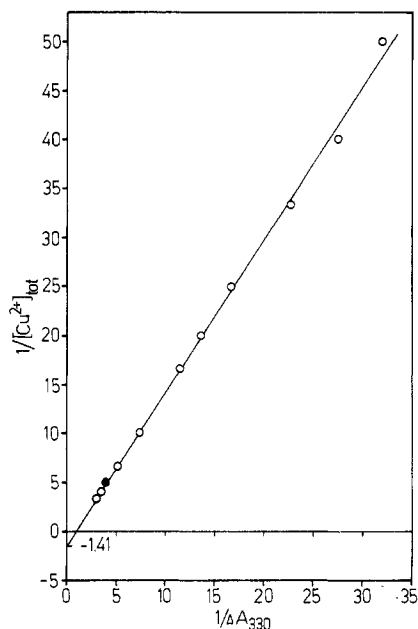


Figure 2. Graphical determination of the stability constant, $K^{\text{Cu}}_{\text{Cu}(\text{tde})}$ (M^{-1}), of the $\text{Cu}^{2+}/2,2'$ -thiodiethanol 1:1 complex in aqueous solution by plotting $1/[\text{Cu}^{2+}]_{\text{tot}}$ vs. $1/\Delta A_{330}$; $[\text{Cu}(\text{ClO}_4)_2] = 0.02\text{--}0.30$ M; $[\text{tde}] = 5 \times 10^{-3}$ M; $I = 1.0$, NaClO_4 ; 25°C ; pH about 3. The point ● is the evaluation of the difference spectrum shown in Figure 1. The straight line was drawn according to the least-squares method (regression). The intercept with the y axis corresponds to $-K^{\text{Cu}}_{\text{Cu}(\text{tde})} = -1.410 \pm 0.408 \text{ M}^{-1}$ and the intercept with the x axis to $1/A_{\text{max}} = 0.904 \pm 0.247$; i.e. $\epsilon_{330\text{nm}} = 221 \pm 60 \text{ M}^{-1} \text{ cm}^{-1}$ (see eq 1).

spectrophotometric experiments in the presence of HClO_4 (up to 9.9 M) indicated that the proton affinity of this ligand is as expected very low, i.e., $\text{p}K_a < -0.7$. This upper limit is in accordance with the acidity constant of protonated ethanol,³⁹ $\text{p}K_a = -1.9$, which still has a much higher proton basicity than ether sulfur, $\text{p}K_a = -6.8$.²⁸ This fact should be considered as an indication that with certain metal ions the ethanol moieties of 2,2'-thiodiethanol might participate in complex formation (vide infra).

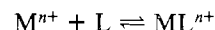
According to the concept outlined in the introduction, we used the absorption at 330 nm of the $\text{Cu}^{2+}/2,2'$ -thiodiethanol system (cf. Figure 1) to study its properties. As thioethers show often some sensitivity toward a slow oxidation by O_2 to

Table I. Logarithms of the Stability Constants of $\text{M}^{n+} 1:1$ Complexes (Eq 6) with 2,2'-Thiodiethanol or Tetrahydrothiophene²⁹ in Aqueous or 50% Aqueous Ethanol (Corresponding to 0.24 Mole Fraction of Ethanol) Solutions, Respectively, at $I = 1.0$ ($\text{NaClO}_4/\text{NaNO}_3$) and 25°C^{a-c}

M^{n+}	$\log K^{\text{M}}_{\text{M}(\text{tde})}$	$\log K^{\text{M}}_{\text{M}(\text{tht})}$
Mg^{2+}	-0.28 ± 0.06	
Ca^{2+}	-0.09 ± 0.07	-0.30 ± 0.13
Sr^{2+}	-0.11 ± 0.04	
Ba^{2+}	-0.08 ± 0.05	
Mn^{2+}	-0.22 ± 0.06	-0.31 ± 0.11
Co^{2+}	-0.20 ± 0.03	
Ni^{2+}	-0.16 ± 0.03	
Cu^{2+}	0.18 ± 0.08^e $0.10 \pm 0.12^{d,f}$	0.02 ± 0.04^g
Zn^{2+}	-0.18 ± 0.05	-0.21 ± 0.09
Cd^{2+}	-0.32 ± 0.04^d	
Ag^+	3.8 ± 0.2^h 3.43 ± 0.07^d	$3.51 \pm 0.14^{d,44}$ $>3.6^{d,44}$
Hg^{2+}	$>3.85^d$	

^a The constants of the Mn^{2+} , Cu^{2+} , and Ag^+ complexes with tde⁴² and tht⁴³ have also been mentioned in preliminary reports. ^b The constants of the Cu^{2+} complexes have been obtained from Benesi-Hildebrand plots; all the others are from competition experiments (see Experimental Section). The given range of error is throughout twice the standard deviation. ^c \log (stability constants) for $\text{Cu}(\text{tde})^{2+}$ have also been determined in mixed solvents (v/v) at $I = 0.4$ (NaClO_4) and 25°C (cf. Figure 3): in water/ethanol (values in parentheses are the extinction coefficients, $\epsilon_{330\text{nm}}$, $\text{M}^{-1} \text{ cm}^{-1}$) 100/0, $\log K^{\text{Cu}}_{\text{Cu}(\text{tde})} = 0.15 \pm 0.07$ (133 ± 21); 75/25, 0.31 ± 0.07 (170 ± 22); 50/50, 0.31 ± 0.08 (234 ± 33); 20/80, 0.48 ± 0.03 (474 ± 25); in water/dioxane ($\epsilon_{330\text{nm}}$, $\text{M}^{-1} \text{ cm}^{-1}$) 100/0, 0.15 ± 0.07 (133 ± 21); 85/15, 0.31 ± 0.03 (115 ± 6); 70/30, 0.35 ± 0.03 (123 ± 8); 50/50, 0.41 ± 0.05 (133 ± 12); 30/70, 0.41 ± 0.03 (191 ± 7); 20/80, 0.47 ± 0.02 (271 ± 11). ^d Measured in nitrate solutions; all the other values refer to perchlorate solutions. ^e $\epsilon_{\text{Cu}(\text{tde})/330\text{nm}} = 199 \pm 36 \text{ M}^{-1} \text{ cm}^{-1}$. ^f $\epsilon_{\text{Cu}(\text{tde})/350\text{nm}} = 116 \pm 22 \text{ M}^{-1} \text{ cm}^{-1}$. ^g $\epsilon_{\text{Cu}(\text{tht})/350\text{nm}} = 93 \pm 9 \text{ M}^{-1} \text{ cm}^{-1}$. ^h This large error is due to solubility problems as AgClO_4 precipitates.

the sulfoxide,⁴⁰ we flushed a $\text{Cu}^{2+}/\text{tde}$ solution for 1 h with O_2 but the difference spectrum was not altered by this treatment. In addition we prepared 2,2'-thiodiethanol sulfoxide³⁰ and took difference spectra in the presence of Cu^{2+} : there was no absorption at all in the 330-nm region. Therefore we measured difference spectra at constant concentrations of tde and increasing concentrations of Cu^{2+} and plotted $1/[\text{Cu}^{2+}]_{\text{tot}}$ vs. $1/\Delta E_{330}$.³⁷ As depicted in Figure 2, straight lines did result, thus showing that eq 1 (see Experimental Section) is valid and that 1:1 complexes are formed; i.e., the stability constant of $\text{Cu}(\text{tde})^{2+}$ corresponding to equilibrium 6 could be calculated for aqueous solutions at $I = 1.0$ (maintained with NaClO_4) and 25°C .



$$K^{\text{M}}_{\text{ML}} = [\text{ML}]/([\text{M}][\text{L}]) \quad (6)$$

As the addition of $\text{M}(\text{ClO}_4)_n$ to a $\text{Cu}(\text{ClO}_4)_2/\text{tde}$ system leads to a decrease in absorption at 330 nm due to the formation of $\text{M}(\text{tde})^{n+}$, we measured this decrease and calculated from such "competition" experiments the stability constants of the complexes $\text{M}(\text{tde})^{n+}$ (cf. Experimental Section). This was straight forward with the exception of a few cases where the perchlorate salts were not available or where the salts are relatively insoluble as with AgClO_4 . Therefore, the constant of $\text{Cu}(\text{tde})^{2+}$ was also determined in aqueous nitrate solution ($I = 1.0$, NaNO_3 ; 25°C), but the absorptions were now measured at 350 nm (i.e., not at the maximal absorption of $\text{Cu}(\text{tde})^{2+}$; Figure 1) because the absorption of nitrate at 330 nm is already considerable. Similarly, the competition experiments in the presence of nitrate were also done at 350 nm. The stability constants of all the $\text{M}(\text{tde})^{n+}$ complexes studied⁴¹ are listed in Table I together with the extinction coefficients

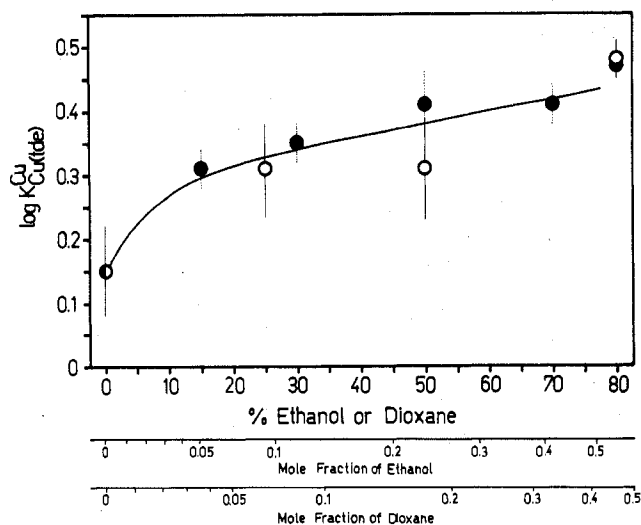


Figure 3. Logarithms of the stability constant, $\log K_{\text{Cu(tde)}}^{\text{Cu}}$ ($I = 0.4$, NaClO_4 ; 25°C), of the $\text{Cu}^{2+}/2,2'$ -thiodiethanol 1:1 complex in dependence on increasing concentrations of ethanol (O) or dioxane (●) (the second solvent component is always water; v/v). The solid and dotted lines indicate twice the standard deviation (cf. Table I, footnote c).

of Cu(tde)^{2+} obtained under the different experimental conditions.

As the stability of most of the complexes listed in Table I is rather small, one has to ask for the influence of the anions present in the experiments, i.e., ClO_4^- and NO_3^- , on the stability constants. For ClO_4^- an influence can be eliminated as an association between this anion and the metal ions used does not occur (or is extremely small),^{45,46} while with NO_3^- in some cases very weak complexes might exist,^{46,47} and the values listed for Cu(tde)^{2+} and Ag(tde)^+ might hint to this direction. However, these comparisons show at the same time clearly that the influence of NO_3^- , if present at all, is very weak indeed.

It is gratifying to note that the stability constant of Ag(tde)^+ , i.e., $\log K_{\text{Ag(tde)}}^{\text{Ag}} = 3.60 \pm 0.03$ ($I = 1.0$, KNO_3 ; 20°C), which was determined potentiometrically in a direct way by Widmer and Schwarzenbach²⁴ with an Ag electrode, is in excellent agreement with the results listed in Table I. This is a convincing proof that the competition experiments are reliable, especially as one is close to the limit of this method with the $\text{Ag}^+/\text{Cu}^{2+}/\text{tde}$ system as the decrease in absorption is in the order of 90% (or more), which is the result of the high stability of Ag(tde)^+ compared with the absorbing Cu(tde)^{2+} .⁴⁸

The stability constant of Hg(tde)^{2+} could not be determined by the competition method as the stability of this complex is too high compared with the one of Cu(tde)^{2+} ; i.e., the absorption decreased practically to zero. Therefore, only a lower limit of the stability constant could be calculated which is in accordance with the potentiometrically determined constant by Widmer:²⁴ $\log K_{\text{Hg(tde)}}^{\text{Hg}} = 5.65 \pm 0.05$ ($I = 1.0$, KNO_3 ; 20°C).

Somewhat surprising is the very low stability of Cd(tde)^{2+} , especially if compared with the stabilities of Ag(tde)^+ and Hg(tde)^{2+} (Table I). This was also observed by Widmer,²⁴ who had tried to make a rough guess with the aid of an Ag electrode about the stability of this complex and obtained $\log K_{\text{Cd(tde)}}^{\text{Cd}} \approx 0.3$. Hence, in agreement with an earlier conclusion,² the coordination tendency of Cd^{2+} toward the thioether moiety indicates that Cd^{2+} , classed as soft,³ is more aptly described as borderline.

As measurements of the other thioether ligands had to be done in mixed solvents for reasons of solubility, we were interested to see how a change in the solvent is reflected in the stability of the complexes. Therefore the $\text{Cu}^{2+}/\text{tde}$ system was

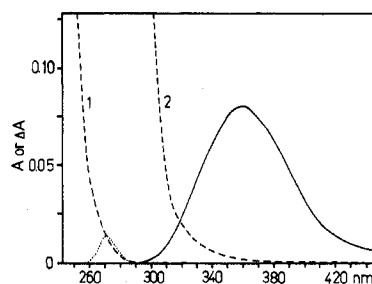


Figure 4. Broken lines: Absorption spectra of tetrahydrothiophene (1) (5×10^{-3} M) and $\text{Cu}(\text{ClO}_4)_2$ (2) (0.20 M) in 50% aqueous ethanol (v/v) at pH 3, $I = 1.0$ (NaClO_4), and 25°C measured in 1-cm quartz cells. Solid line: Absorption of the $\text{Cu}^{2+}/\text{tetrahydrothiophene}$ system under the above conditions measured as a difference spectrum; i.e., the reference beam contained one cell with tetrahydrothiophene and a second one with $\text{Cu}(\text{ClO}_4)_2$, while the sample beam contained one cell with the mixed system and one with the solvent. The dotted line portion of the difference spectrum indicates uncertainty due to the large absorption of $\text{Cu}(\text{ClO}_4)_2$ at $\lambda < 295$ nm.

also studied in mixtures of water/ethanol and water/dioxane. The poor solubility of NaClO_4 at higher dioxane concentrations limited the adjustment of the ionic strength to 0.4. The results (cf. Table I, footnote c) are shown in Figure 3 where $\log K_{\text{Cu(tde)}}^{\text{Cu}}$ is plotted vs. increasing concentrations of ethanol or dioxane. It is obvious that the influence of the two organic solvents on the stability of Cu(tde)^{2+} is comparable: The change in the solvent from water to 80% ethanol or dioxane (corresponding to 0.55 or 0.46 mole fraction, respectively) increases the stability constant by about 0.3 log unit; i.e., the stability of Cu(tde)^{2+} is enhanced by a factor of about 2. It may be added that the position of the maximal absorption of Cu(tde)^{2+} at 330 nm is not altered by the addition of ethanol or dioxane to the solvent but that the molar extinction coefficient increases somewhat (Table I, footnote c).

Tetrahydrothiophene Complexes.⁴⁹ As the tetrahydrothiophene ring is a ligating part of *d*-biotin,^{1,10,11} it seemed worthwhile to include tht into the present study. The complex formation between Cu^{2+} and tetrahydrothiophene manifests itself also by a new absorption band, which has a maximum at 359 nm (Figure 4). At this wavelength the stability constant and the extinction coefficient of Cu(tht)^{2+} , as well as, by competition experiments, the stability constants of other M(tht)^{n+} complexes,⁴⁴ were determined in 50% aqueous ethanol solutions corresponding to 0.24 mole fraction of ethanol ($I = 1.0$; 25°C), as described for the $\text{M}^{n+}/2,2'$ -thiodiethanol systems. The results are assembled in Table I together with those of the M(tde)^{n+} complexes. Again, the stability of Hg(tht)^{2+} is so high that only a lower limit of its constant could be determined, but it is evident that to a first approximation the stability of the tde complexes formed with soft, borderline, or hard metal ions in aqueous solution is comparable with the stability of the corresponding tht complexes in 50% aqueous ethanol.

A more subtle comparison is made for the complexes of the hard and borderline metal ions in Figure 5, where the data are plotted for the 2,2'-thiodiethanol and tetrahydrothiophene complexes according to the extended Irving-Williams series.⁵² For the 3d transition ions complex stability follows for both ligands in the order predicted by Irving and Williams,⁵² but the tht complexes are somewhat less stable than the tde complexes. This stability difference becomes even more pronounced by taking into account that different solvents were used, the influence of which may be estimated from Figure 3. Moreover, the stability of the alkaline earth ion complexes with 2,2'-thiodiethanol is evidently too high; there can be no doubt that this is the result of the participation of the ethanol moieties of tde in complex formation which will of course be

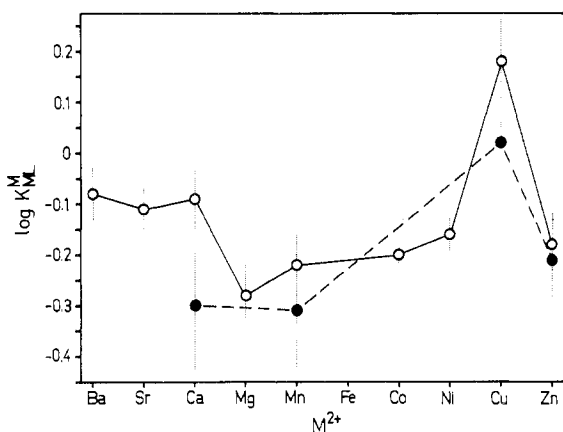


Figure 5. Plots of the stability constants, $\log K^{\text{M}}_{\text{ML}}$ (Table I; $I = 1.0$, NaClO_4 ; 25°C), of the M^{2+} 1:1 complexes with 2,2'-thiodiethanol (O/water) or tetrahydrothiophene (●/50% ethanol) according to the extended Irving-Williams series.⁵²

Table II. Logarithms of the Stability Constants of Some Cu^{2+} 1:1 Complexes (Eq 6) with Thioethers ($I = 1.0$, NaClO_4 ; 25°C)

ligand ²⁹	solvent	$\log K^{\text{Cu}}_{\text{CuL}}$
tde ^a	50% ethanol ^d	0.31 ± 0.08
des	50% ethanol ^d	-0.47 ± 0.19
tht ^b	50% ethanol ^d	0.02 ± 0.04
des ^c	96% dimethylformamide ^e	0.29 ± 0.11
tht ^c	96% dimethylformamide ^e	0.19 ± 0.05

^a $I = 0.4$, NaClO_4 ; see Table I, footnote c. ^b From Table I.

^c H. Sigel; details to be published in different context. ^d This corresponds to 0.24 mole fraction of ethanol. ^e This corresponds to 0.85 mole fraction of dimethylformamide.

especially pronounced with hard metal ions. These ethanol moieties either may directly substitute a solvent molecule in the coordination sphere of a metal ion, thus giving rise to an inner-sphere chelate formation, or can form hydrogen bonds with water molecules still coordinated to a metal ion (see also the following section).

The Cu^{2+} /Diethyl Sulfide System.⁵³ Ether sulfur occurs in nature in cyclic thioether moieties, e.g., in *d*-biotin and penicillin,¹ but also as a simple thioether group as in *S*-methyl-L-cysteine or L-methionine.^{1,2} For the latter cases diethyl sulfide seems to be a simple model and this is one reason we felt at least one complex should also be studied with this ligand. The other reason is that tetrahydrofuran is a better Lewis base than ether,^{54,55} and one might surmise the corresponding properties for tetrahydrothiophene and diethyl thioether.

The complex formation between Cu^{2+} and diethyl sulfide in 50% aqueous ethanol (v/v), which corresponds to 0.24 mole fraction of ethanol, is again connected with an absorption in the near-UV region (maximum at 349 nm): $\epsilon_{349} = 61 \pm 20 \text{ M}^{-1} \text{ cm}^{-1}$ ($I = 1.0$, NaClO_4 ; 25°C). The stability constant of $\text{Cu}(\text{des})^{2+}$ is given in Table II, together with the constants of some related complexes.

The first two entries in Table II confirm unequivocally the conclusion of the preceding section that the ethanol moieties of tde may participate in complex formation. For Cu^{2+} it is evident that in 50% aqueous ethanol the stability of the complex increases by a factor of about 6 when des is replaced by tde as ligand.

More surprising is the increase in stability, by a factor of about 3, in going from $\text{Cu}(\text{des})^{2+}$ to $\text{Cu}(\text{tht})^{2+}$ (Table II) as here no additional binding sites can be involved. One is tempted to conclude from this result that the ether sulfur in tht is a better ligand or Lewis base than the sulfur in des due to a more pronounced sp^3 hybridization in tht, which would result in a higher electron density in a certain direction.

However, such a supposition would not be in agreement with the results of a crystal structure determination⁵⁶ which shows that the angle around the sulfur in the tetrahydrothiophene ring (of the biotinyl moiety) is 91° , i.e., is corresponding nearly perfectly to a simple p-like orientation of the sulfur orbitals. We feel that therefore an explanation should be sought along the following line of reasoning: des is certainly much more flexible than tht and hence less suitable for coordination. In other words, if a water molecule is replaced in the coordination sphere of a metal ion by tht, the steric interference with the neighboring coordinated water molecules will be less than if the more flexible, and hence more bulky, des coordinates. This conclusion is supported by the last two entries in Table II, which indicate within the experimental error the same stability of $\text{Cu}(\text{des})^{2+}$ and $\text{Cu}(\text{tht})^{2+}$ in 96% dimethylformamide corresponding to 0.85 mole fraction of DMF. In this solvent not enough water is present to fully aquate the ions; they are mainly solvated by the bulky dimethylformamide. The replacement of a dimethylformamide molecule in the coordination sphere of a metal ion by des or tht diminishes the steric differences between these two ligands, because dimethylformamide itself is rather bulky.

Conclusions

The ligating properties of the thioether group are rather pronounced toward soft metal ions, while their coordination tendency toward the biologically important hard or borderline metal ions is obviously weak. It may be pointed out, however, that such weak interactions still may occur stereospecifically as shown with the Mn^{2+} / and Cu^{2+} /*d*-biotin systems.^{1,10,11} In fact the present results obtained for the $\text{M}(\text{tht})^{n+}$ complexes give certainly a good estimate about the strength of the interaction between metal ions and the tetrahydrothiophene ring of the *d*-biotinyl moiety. Quite generally, the same may be concluded for other metal ion interactions with thioether groups which are a part of molecules occurring in living nature or elsewhere.

It should also be pointed out that an accumulation of several such weakly coordinating groups in the right steric conditions may lead to rather stable complexes.^{4a,12} Similarly, their presence in ligands together with other ligating groups is often—though not always—reflected in an enhanced complex stability; i.e., a thioether group may contribute remarkably to this stability especially if the steric conditions are favorable.^{13–15,19} In connection with the observed weak interactions with biologically important metal ions a recent remark of Chlebowski and Coleman⁵⁷ may be added: "Since the stability of metal-protein complexes may be expected to span a continuum just as the stabilities of model coordination complexes, many important enzymes may be metal ion activated in the sense that the metal is bound loosely enough to dissociate, at least partially, during rigorous isolation procedures. Aside from the difficulties this introduces in analytical procedures, activation may not be highly specific for a given metal ion species and thus it may be difficult to determine which among the several divalent metal ions which occur in significant concentrations in biological systems is the natural activator." In fact, considering the small differences in stability observed for the biologically important metal ions and their complexes with thioethers, it seems not even certain that there is a *single* natural activator in each case; it might rather be a whole group of metal ions as for example Mg^{2+} , Ca^{2+} , Mn^{2+} , and Zn^{2+} .

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Registry No. Mg, 7439-95-4; Ca, 7440-70-2; Sr, 7440-24-6; Ba, 7440-39-3; Mn, 7439-96-5; Co, 7440-48-4; Ni, 7440-02-0; Cu, 7440-

50-8; Zn, 7440-66-6; Cd, 7440-43-9; Ag, 7440-22-4; Hg, 7439-97-6; tde, 111-48-8; tht, 110-01-0; des, 352-93-2.

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Contribution from the Department of Chemistry, University of Cincinnati, Cincinnati, Ohio 45221

Infrared Matrix Isolation Studies of the $M^+SiF_5^-$ Ion Pair and Its Chlorine-Fluorine Analogues

BRUCE S. AULT

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The matrix isolation technique has been applied to the study of the $M^+SiF_5^-$ ion pair, as a model for possible intermediates in organosilicon reactions. This ion pair, formed through the reaction of an alkali fluoride salt and SiF_4 , showed six infrared bands, three in the Si-F stretching region and three in the deformation region. This spectrum is inconsistent with a strictly trigonal-bipyramidal D_{3h} geometry for the species, but a model in which the cation perturbs the anion axially yielding a C_{3v} species can account for the observed spectrum, although C_{2v} and C_{4v} structures are considered as well. The mixed chlorine/fluorine anions were synthesized also, by reaction of either MF or MCl with the appropriate precursor species. However, attempts to synthesize the $SiCl_5^-$ anion in this fashion were not successful.

Introduction

A large segment of synthetic organosilicon chemistry has been developed around the use of the fluoride anion, F^- , as a catalyst in these systems.^{1,2} It has been proposed that the mechanism of this catalysis proceeds through a penta-

coordinate silicon intermediate and then to products.³ Recently, pentacoordinate silicon anions have been synthesized and stabilized, but very little is known about the nature, geometry, and stability of these anions. Ion cyclotron resonance^{4,5} has been employed to give some heats of formation and the