2 and 3) suggests that reactions 2 and 3 may contribute appreciable cyanogen to the products.

sion reaction of the type reported by Ogg and

Polanyi¹⁸

 $CN + CH_3CN \longrightarrow CH_3NC + CN - 15$ kcal.

The formation of some methylisonitrile in the methyl cyanide-nitrogen atom reaction is difficult to explain. It might arise from a reaction between CH₃ and CN radicals, or conceivably from an inver-

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FORMATION CONSTANTS OF SOME METAL DERIVATIVES: S-ALKYL CARBOXYLIC ACIDS

By Roger J. Irving¹ and W. Conard Fernelius

Contribution from The College of Chemistry and Physics, The Pennsylvania State University, University Park, Pennsylvania Received May 21, 1956

Formation constants are reported for the compounds $C_2H_5SCH_2COOH$, $C_2H_5SCH_2COOH$ and $o-C_2H_5SC_{6}H_4COOH$ with the following metals: Cu, Ni, Pb, Cd, Co, Zn, Mg. The order of stability for the metal derivatives of a given ligand is different in some respects from that previously established for coördination through oxygen and/or nitrogen. Fivemembered chelate rings are more stable than six-membered rings. For these sulfur-containing ligands log $K_2 > \log K_1$ with some metals, in contrast to the situation usually found for ligands coördinating through oxygen, nitrogen and oxygen, and nitrogen and sulfur. Difficulties encountered in the study of sulfur compounds are discussed.

Introduction

Since 1941 a good deal of information has accumulated on the relative stabilities of metal coördina-tion compounds.²⁻⁵ The data demonstrate the existence of several regularities among the properties of coördination compounds.⁵⁻⁸ However, if one lists the ligand molecules or anions for which data on formation constants exist, one sees that these ligands all coördinate through the atoms oxygen and nitrogen: oxygen only, β -diketones, ohydroxyaldehydes, tropolone, hydroxyquinones, kojic acid, etc.; nitrogen only, diamines, polyamines, o-phenanthroline, dimethylglyoxime, etc.; oxygen and nitrogen simultaneously, amines con-taining -O- and -OH, 8-quinolinol, amino acids, the "complexones," o-hydroxy azo dyes, etc. Although many familiar ligands coördinate through sulfur, very few data on formation constants exist for such ligands: sulfur only apparently none; sulfur and nitrogen simultaneously, amines containing -S- and -SH, 9,10 o-aminobenzenethiol11; sulfur and oxygen simultaneously, o-mercaptobenzoic acid.¹² Furthermore, these data are not suffi-

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ciently numerous to permit one to judge whether the same regularities which hold for coördination through oxygen and nitrogen, are valid for coordination through sulfur. The present report is a preliminary account of an investigation begun in an effort to furnish formation constant data for sulfurcontaining ligands.

Experimental

S-Ethylmercaptoacetic Acid, $C_2H_4SCH_2COOH$.—This compound was obtained by the action of ethyl mercaptan on monochloroacetic acid in alkaline solutions¹³: pale yellow liquid with an unpleasant odor; b.p. 117° at 11 mm., d^{20}_4 1.152; lit. values b.p. 117.8° at 11 mm., d^{20}_4 1.1518, 90% yield.

β-(S-Ethylmercapto)-propionic Acid, $C_2H_5SCH_2COOH$. —β-Chloropropionic acid (5.5 g.) was dissolved in 10 ml. of water containing 2.5 g. of sodium hydroxide. To the cooled solution (ice-bath) was added with constant stirring an icecold solution of 3.5 ml. of ethyl mercaptan and 2.5 g. of sodium hydroxide in 5 ml. of water. After the mixture was allowed to stand at room temperature for several hours, it was again cooled in ice and carefully made acid to litmus with 20% sulfuric acid. The solution was repeatedly extracted with ether, and the extract dried over calcium chloride. After removal of the ether, the oil was distilled *in vacuo* to yield a pale yellow oil soluble in water and readily soluble in dioxane; b.p. 127° at 12 mm., d^{20}_4 1.143, n^{25} D 1.482, yield 3.8 g. (68% based on chloropropionic acid), neut. equiv., 134.0 g., theoretical 134.2 g., molar refraction 3.46 cc., caled. 33.42 cc.

o-(S-Ethylmercapto)-benzoic Acid, $C_2H_bSC_eH_4COOH.$ — Thiosalicylic acid (7.2 g.) was added to a solution of 5 g. of sodium hydroxide in 10 ml. of water and 50 ml. of alcohol. This mixture was refluxed with 3.9 ml. of ethyl iodide for 2 hours. On cooling and acidification with dilute hydrochloric acid (litmus as indicator) the compound separated as a white powder.¹⁴ It was recrystallized twice from water; yield 95%, m.p. 135°; lit. value 134–135°. 2,3-Dimercaptopropanol was purchased from the Delta Chemical Works. Mercaptoacetic acid, cysteine hydrochloride, and methionine were obtained from Distillation Products Inductries Dioxano was purified by Eirepe

2,3-Dimercaptopropanol was purchased from the Delta Chemical Works. Mercaptoacetic acid, cysteine hydrochloride, and methionine were obtained from Distillation Products Industries. Dioxane was purified by Eigenberger's procedure¹⁵ and stored over activated alumina in a brown bottle to minimize the formation of oxidizing decomposition products on standing.

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TABLE I

Formation Constants of Metal Derivatives of Sulfur-Containing Acids in 50% Dioxane at 30°

	S-Ethylmercaptoacetic acid			β -(S-Ethylmercapto) - propionic acid			o-(S-Ethylmercapto)- benzoic acid		
Metal Ion	Max. \overline{n}	$\log K_1$	log Kı	Max. n	$\log K_1$	$\log K_2$	Max. \overline{n}	$\log K_1$	$\log K_2$
H+	-5.56			-6.34			-6.17		
Cu++	2	4.55	3.60	2.5	4.2	a	2.0	4 16	3.30
Pb++	1.7	3.97	2.90	2.2	4.34	3.57	2.0	4	d
Cd++	0.8	3.45		2.1	3.17	3.55	2.0	3.34	3.35
Zn++	1.0	3.14		2.0	3.02	3.22	2.0	2.87	3.52
Ni++	0.9	3.12		1.7	2.86	3.38	1.7	2.37	3.62
Co++	0.9	3.06		2.0	2.8b	2.0	2.0	3.1	e
Mg++				1.8	3.0 av. c		2.0	2.18	3 .29

^a When \overline{n} 0.7, a hydroxy species formed. ^b Likely, but not certain, value. ^c Value from formation curve because calculations from twelve sets of n values gave unreal roots in every case. ^d Even at small n values, hydroxy species formed. ^e Even at low pH values, hydroxy species formed.

The potentiometric titrations were performed at 30° by a modified form^{18,17} of the procedure described by Calvin and Wilson,⁶ with 0.1 mmole of metal ion as nitrate and 0.4 mmole of ligand present in 100 ml. of 50% dioxane. Calculations were made as described by Block and McIntyre.¹⁸

Results

The results are assembled in Table I. In several instances (EtSCH₂COOH with Cu, Pb, Cd; Et-SCH₂CH₂COOH with Cu, Pb, Cd, Co^{*}; *o*-Et-SC₆H₄COOH with Pb, Cd) doubling the concentration of ligand (0.8 mmole of ligand to 0.1 mmole of metal ion) resulted in higher \bar{n} values than those given in the table. (The variations were particularly large in the case marked^{*}). However, in such cases calculations at the higher concentration for the case N = 2 yielded the same values for log K_1 and log K_2 as calculations at the lower concentration for the case N = 2.

No calculations of formation constants is possible when the acid dissociation constants of the ligand acids are not known. Simple titration in aqueous solution is not suitable for determination of the dissociation constants of very weak acids. Nevertheless, worthwhile information can be obtained by titrating such acids in the presence of metal ions and observing the relative displacements of the titration curves from that of the weak acid alone.

With 2,3-dimercaptopropanol (BAL), the ions, Cu⁺⁺, Ni⁺⁺, Pb⁺⁺ and Zn⁺⁺ gave precipitates above pH 3 in water. The Pb⁺⁺ and Zn⁺⁺ compounds were insoluble in all mixtures of waterdioxane up to 75% dioxane. The complexes of BAL with Cu and Ni are quite stable as shown by the lowering of the pH of BAL in the presence of metal ions, while Mg shows no evidence of coordination. From a solution of pH 10 where the ratio of BAL to Ni⁺⁺ was 2:1, a soluble green compound was isolated. Calcd. for Ni(SCH₂CHSH-CH₂OH)₂: Ni, 19.4. Found: Ni, 20.6.

Although mercaptoacetic acid is essentially mono-

(16) L. G. Van Uitert and C. G. Haas, Jr., J. Am. Chem. Soc., 75, 451 (1953); L. G. Van Uitert, W. C. Fernelius and B. E. Douglas, *ibid.*, 75, 457 (1953).

(17) B. E. Bryant, W. C. Fernelius and B. E. Douglas, *ibid.*, 75, 3784 (1953).

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basic ($pK_{\rm D} = 5.3$, $pK_{\rm D2} = 11$) in titration with base, it is definitely dibasic when titrated in the presence of Ni⁺⁺ and the titration curve shows strong coördination. The mercapto acid oxidizes readily.

Titration curves of aqueous solutions of cysteine in the presence of Cu⁺⁺, Ni⁺⁺, Zn⁺⁺, Pb⁺⁺, Cd⁺⁺ and Co⁺⁺ give evidence of coördination while those in the presence of Mn⁺⁺ and Mg⁺⁺ do not. The curves in general follow a complicated pattern above pH 5 due to oxidation,¹⁹ precipitation, or formation of basic metal cysteinates. Cystine hydrochloride could not be studied, as it is insoluble in both water and water-dioxane mixtures.

Dissociation constants (pK_D) from the neutralization curve of methionine, CH₃SCH₂CH₂CHNH₂-COOH are 2.94 and 9.15.²⁰

Methionine in 50% dioxane coördinates strongly with several metal ions and from the titration curves the order of stability is Cu > Ni > Zn >Co > Cd.

Discussion

The choice of suitable ligands coördinating through sulfur for potentiometric study is not easy despite their wide use in analytical chemistry. Many of the most interesting compounds are not suitable for study because of (1) lack of solubility of ligand and/or metal derivatives, (2) ease of hydrolysis, and (3) ease of oxidation of -SH groups to disulfides. Further, those sulfur compounds which are neither weak acids or bases cannot be studied by potentiometric titration.

The results tabulated in Table I show that like the chelate rings containing nitrogen and oxygen, the five-membered chelate rings containing sulfur are more stable than six-membered rings:

The increase in \overline{n} values upon increasing the concentration of ligand is very unusual. If this increase in \overline{n} is real and if it can be assumed that >S and -COO⁻ are held with greatly different intensity, then it seems reasonable that the neutral species

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(20) O. H. Emerson, P. L. Kirk and C. L. A. Schmidt, J. Biol. Chem., 92, 449 (1931), give 2.28 and 9.21 at 25°.



III seems more likely because many compounds of Cu and Pt of this type with sulfur-containing ligands are known.

The most important conclusion to be drawn from Table I is that for the three ligands the strength of bonding as indicated by log K_1 values is Co < Ni < Cu > Zn which is the same order of stability as for ligands containing oxygen and/or nitrogen. Irving and Williams²¹ in a comprehensive study of the problem show that in the first transition series the stability order of the divalent metals is a direct consequence of their ionization potentials and ionic radii. The empirical order Cu > Ni > Pb > Co > Zn > Cd > Mg^{sb,22} holds with minor variations for many oxygen and nitrogen type ligands, but lead and cadmium fall out of line when the ligand contains sulfur: Cu > Pb > Cd > Zn > Ni.

For the great majority of cases of metal ion coordination studied so far $\log K_n > \log K_{n+1}$. In several instances in Table I, $\log K_2 > \log K_1$. This situation is in direct contradiction to the view held by Bjerrum²³ that there is a statistical decrease in the numerical values of succeeding formation constants. Even though this may well be an over simplification omitting such factors as steric hindrance, type of hybrid orbitals formed, or possible rearrangement of orbitals, the instances where $\log K_2 > \log K_1$ are few in number

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 (22) D. P. Mellor and L. Maley, Nature, 159, 370 (1947); 161, 436

1948).

(23) Ref. 2, pp. 40-4.

Ag +-NH₂: log $K_1 = 3.19$; log $K_2 = 3.83^{24}$ Ag +-monoamines^{9,25}

Zn⁺⁺-NH₃: log $K_1 = 2.37$; log $K_2 = 2.44$; log $K_3 = 2.50$; log $K_4 = 2.15^{26}$ Fe⁺⁺-dipyridyl: log $K_1 = 4.26$; log $K_2 < 5$; log $K_8 > 7.3^{27}$

Fe⁺⁺-o-phenanthroline: $\log K_1 = 5.19$; $\log K_{1-3} = 21.3$

so that $\log K_2$ and $\log K_3$ are probably both greater than $\log K_{1.}^{28}$ The abnormally high second and third formation constants of ferrous ion with dipyridyl and *o*-phenanthroline have been explained on the basis of "orbital stabilization." The evidence of an electronic rearrangement lies in the change from paramagnetism to diamagnetism.²¹ No explanation of the reversal of order of formation constants in the case of Ag⁺ and Zn⁺⁺ has been proposed. The general reversal of order for these sulfur-containing ligands makes a study of these ligands particularly important.

Several earlier workers have studied the metal derivatives of cysteine.^{19,29–33} The Ni⁺⁺, Co⁺⁺, Co⁺⁺⁺ and Fe⁺⁺ derivatives have been definitely established (in some cases more than one for a given ion). The Ni⁺⁺ compound is stable; the Co⁺⁺ compound oxidizes readily to a substance which seems to contain Co⁺⁺⁺ and some cystine; the Fe⁺⁺ compound is stable but the Fe⁺⁺⁺ compound formed on oxidation is unstable so that cystine is the product.

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