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Metal Chelates of Biologically Important Compounds. I. Complexes of DL-Ethionine and S-Methyl-L-cysteine

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Complexes of DL-ethionine, $CH_3CH_2SCH_2CH_2CH(NH_2)COOH$ (ethH), and S-methyl-L-cysteine, $CH_3SCH_2CH(NH_2)$-COOH (SmcH), have been prepared with manganese(II), cobalt(II), nickel(II), copper(II), zinc(II), palladium(II), platinum(II), cadmium(II), and mercury(II). The infrared spectra of the amino acids and of the metal complexes were measured in the range 4000–200 cm^{-1}. The diffuse reflectance spectra of the cobalt, nickel, and copper complexes were measured in the range 25,000–7000 cm^{-1}. Spectral and magnetic data indicate that the complexes are of four types, as follows. (a) ML_2 (L = eth, Smc; M = Mn, Co, Ni, Cu, Zn, Cd) complexes are polymeric in the solid state with carboxyl bridges. The metal atom is six-coordinate and the amino acid is bound to one metal atom *via* the nitrogen and one oxygen and to another metal atom *via* the second oxygen. (b) $M(LH)X_2$ (M = Pd, Pt; X = Cl, Br) complexes in which the amino acid is bound to the four-coordinate metal atom *via* the nitrogen and sulfur atoms only. (c) $[Hg(ethH)_2](ClO_4)_2 \cdot H_2O$ in which ethionine is possibly bound *via* the nitrogen only. (d) $[AgCu(Smc)_2]NO_3$ in which the amino acid residue is coordinated to the copper *via* nitrogen and oxygen and to silver *via* the sulfur atom.

Introduction

The use of chelating agents in biology and medicine has been said to have only just begun.[1] It has been observed recently that metal chelation apparently plays a definite role in the cause and treatment of cancer but just how is still a matter for conjecture.[2] There are indications that some metal chelates of ligands which have anticancer activity are more carcinostatic than the free ligands.[3]

We have commenced a study of the metal complexes formed by a number of chelating agents which are known to have a biological function or are likely to possess antiviral or carcinostatic activity. In order to gain information concerning these metal complexes and their possible mode of action, it is of importance, first, to isolate and characterize the complexes and, second, to investigate their structures and the type of bonding present.

DL-Methionine, $CH_3SCH_2CH_2CH(NH_2)COOH$ (mthH), is required in mammalian metabolism and, since it cannot be synthesized in the body, it is an essential amino acid which must be present in the diet. An important function of methionine in the body is its role in the synthesis of cysteine, and dietary methionine is by far the major source of methyl groups in the animal economy.[4]

Ethionine, $CH_3CH_2SCH_2CH_2CH(NH_2)COOH$ (ethH), is a methionine antagonist[5,6] and inhibits the metabolism of the latter. Ethionine can be metabolized in the rat[7] and inhibits the incorporation of methionine sulfur and glycine into the proteins of rats;[8] it also inhibits the conversion of methionine to cysteine by producing a decrease in the transmethylation from methionine to choline in rats. Ethionine also inhibits the growth of microorganisms[6] and has been found to inhibit leukemia in mice.[9]

S-Methyl-L-cysteine, $CH_3SCH_2CH(NH_2)COOH$ (SmcH), which differs from methionine by having one less methylene group, is a naturally occurring amino acid which has been isolated from beans (*Phaseolus vulgaris*) and may be present in many other plants.[10]

These three sulfur-containing amino acids are chelating agents which must compete with other ligands for metal ions in the body. The antibacterial activity of metal chelates of methionine can be explained as a fat solubilization of metal ions which then become effective at bacterial cell walls or within the cell itself.[11] Lenz and Martell[12] reported that the stability constants (log β_2) of the metal chelates of DL-ethionine are approximately 2 log units higher than those of the analogous DL-methionine chelates. These authors suggest that the greater stability of the ethionine chelates allows ethionine to compete successfully with methionine at an enzyme surface when metal coordination is involved in the enzyme reaction. The order of stabilities of the metal chelates $M(eth)_2$ and $M(Smc)_2$ (M = Mn, Co, Ni, Cu, Zn, Cd, Hg, Pb) led Lenz and Martell to the conclusion that there is little or no involvement of the thioether sulfur atom in chelation in these complexes. Similarly Li and Manning[13] concluded that the sulfur is not involved in coordination in the methionine complexes of zinc, cadmium, and mercury, whereas it is involved in coordination in the corresponding complexes of cysteine, $HSCH_2CH(NH_2)COOH$. Shindo

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(3) S. Kirschner, Y. K. Wei, D. Francis, and J. G. Bergman, *J. Med. Chem.*, **9**, 369 (1966).

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(13) N. C. Li and R. A. Manning, *J. Am. Chem. Soc.*, **77**, 5225 (1955).

and Brown[14] reported that in the complex $Zn(Smc)_2$ S-methyl-L-cysteine is coordinated *via* the nitrogen and one oxygen atom to give a four-coordinate species.

Recently McAuliffe, Quagliano, and Vallarino[15] isolated a number of complexes of DL-methionine with bivalent and trivalent metal ions. From infrared spectral data the authors concluded that in the complexes $M(mth)_3$ (M = Al, Cr, Fe, Rh, Bi) the ligand is coordinated through the nitrogen and carboxyl oxygen atoms and that the complexes $M(mth)_2$ (M = Mn, Co, Ni, Cu, Zn, Cd, Hg, Pb) are octahedral and polymeric with carboxylato bridges so that the ligand coordinates to one metal ion *via* the nitrogen atom and one oxygen atom of the carboxyl group and to a neighboring metal ion *via* the other oxygen atom of the carboxyl group. Subsequently McAuliffe[16] has reported that the infrared spectra of $Pd(mthH)Cl_2$ and $Pt(mthH)Cl_2$ indicate that in these complexes methionine is coordinated through the nitrogen and sulfur atoms and the compounds have a polymeric structure due to intermolecular hydrogen bonding between the free carboxylic acid residues.

In this paper we report some metal complexes of DL-ethionine and S-methyl-L-cysteine. Evidence concerning their structures was obtained from their infrared spectra, which were measured in the range 4000–200 cm^{-1}.

Experimental Section

Analyses.—Analyses for carbon, hydrogen, and nitrogen were carried out by Dr. E. Challen of the Microanalytical Laboratory, School of Chemistry, University of New South Wales.

Palladium and platinum were determined by direct ignition of the metal complexes. Other metals were determined by standard gravimetric procedures after the complex had been decomposed by fuming with a mixture of sulfuric, nitric, and perchloric acids.

Infrared Spectra.—The infrared spectra were obtained from Nujol and halocarbon mulls on a Perkin-Elmer 337 spectrophotometer in the range 4000–400 cm^{-1} and on a Perkin-Elmer 621 spectrophotometer in the range 600–200 cm^{-1}.

Visible–Ultraviolet Spectra.—The diffuse reflectance spectra were measured on a Zeiss PMQII spectrophotometer.

Preparation of the Metal Complexes.—The metal complexes were prepared by one of the methods listed below (see also Table I). The yields varied from 0.25 to 0.5 g.

Preparation I.—The amino acid, DL-ethionine or S-methyl-L-cysteine (0.005 mol), and sodium hydroxide (0.005 mol) were warmed together in water (25 ml). The pH of the solution was adjusted to ~8 with dilute hydrochloric acid. The metal nitrate hydrate (0.0025 mol) in water (10 ml) was added to the solution which was then stirred for 2 hr. The metal complex was then filtered off, washed with water, then with alcohol, and dried *in vacuo* over phosphoric oxide.

Preparation II.—The metal nitrate hexahydrate (0.0025 mol) in water (10 ml) was added to a solution containing the amino acid (0.005 mol) and sodium carbonate (0.0025 mol) in water (10 ml). The solution was warmed at 50° for 3 min and cooled, whereupon the metal complex deposited. In one instance the addition of a small amount of alcohol was necessary to bring about deposition of the complex. The complex was filtered off, washed with water, then with alcohol, and dried *in vacuo* over phosphoric oxide.

Preparation III.—Copper acetate monohydrate (0.0025 mol) in water (10 ml) was added to a solution containing the amino acid (0.005 mol) and sodium acetate (0.1 g) in water (10 ml). The blue precipitate of the copper complex was filtered off, washed with water, then with alcohol, and dried *in vacuo* over phosphoric oxide.

Preparation IV.—The amino acid (0.001 mol) in warm water (25 ml) was treated with a solution of K_2MX_4 (M = Pd or Pt; X = Cl or Br) (0.001 mol) in water (5 ml). The solution was warmed on the steam bath for 20 min. On being cooled to 0°, the solution deposited the crystalline metal complex which was then filtered off, washed with a little water, then with alcohol followed by ether, and dried at 65°.

Preparation V.—The amino acid (0.005 mol) was added to a suspension of lithium hydroxide (0.005 mol) in alcohol (15 ml); this mixture was heated at 60° with stirring for 20 min and then filtered. To the filtrate was added a solution of mercuric perchlorate (0.0025 mol) in alcohol (10 ml), containing perchloric acid (0.5 ml). The precipitate of the mercury complex was filtered off and washed with alcohol and dried *in vacuo* over phosphoric oxide.

Preparation VI.—Bis(S-methyl-L-cysteinato)copper(II) (0.3 g) was warmed with a solution of silver nitrate (0.3 g) in water (25 ml) on the water bath for 15 min. The solution was cooled and alcohol (5 ml) was added. The deep blue complex was filtered off, washed with water, then with alcohol, and dried *in vacuo* over phosphoric oxide.

Preparation of Deuterated Compounds. DL-Ethionine.—Ethionine (0.2 g) was dissolved in hot deuterium oxide (5 ml) and the solution was kept at 70° for 15 min in a stoppered flask. On cooling, the solution deposited crystals of the amino acid which was filtered off and redissolved in deuterium oxide as described above. The doubly recrystallized ethionine was collected and dried at 100° for 15 min.

S-Methyl-L-cysteine.—S-Methyl-L-cysteine (0.2 g) was dissolved in hot deuterium oxide (5 ml). The solution was kept at 70° for 15 min in a stoppered flask, then cooled to 20°, when the amino acid was precipitated by the addition of acetone (3 ml). The process was repeated and the deuterated amino acid was collected and dried at 100° for 15 min.

Nickel Complexes.—The deuterated nickel complexes were prepared in deuterium oxide from the deuterated amino acids by the method described in preparation II.

Results and Discussion

The metal complexes which have been prepared, together with their method of preparation, analytical data, and room-temperature magnetic moments, are listed in Table I.

Because of the weak ligand fields of these two amino acids, the complexes of manganese(II), cobalt(II), and nickel(II) are high spin. The color of the cobalt complexes and the moments of the nickel complexes suggest an octahedral stereochemistry. Further evidence for this configuration was obtained from the infrared and visible–ultraviolet reflectance spectra.

The infrared spectra of DL-ethionine and S-methyl-L-cysteine were measured. The spectra of the deuterated compounds were also obtained in order to identify the bands due to the amino group.[17] Whereas the spectra of saturated aliphatic acids in the solid state display a carbonyl stretching frequency in the range

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[14] H. Shindo and T. L. Brown, *J. Am. Chem. Soc.*, **87**, 1904 (1965).

[15] C. A. McAuliffe, J. V. Quagliano, and L. M. Vallarino, *Inorg. Chem.*, **5**, 1996 (1966).

[16] C. A. McAuliffe, *J. Chem. Soc.*, *A*, 641 (1967).

[17] Tables listing the principal infrared bands and their assignments have been deposited as Document No. 9997 with the ADI Auxiliary Publications Project, Photoduplication Service, Library of Congress, Washington, D. C. 20540. A copy may be secured by citing the document number and remitting $1.25 for photoprints, or $1.25 for 35-mm microfilm. Advance payment is required. Make checks or money orders payable to: Chief, Photoduplication Service, Library of Congress.

Table I

Metal Chelates of dl-Ethionine and S-Methyl-l-cysteine

Compound	Color	Method of prepn	Magnetic moment, μ, BM	Analyses, %							
				Carbon		Hydrogen		Nitrogen		Metal	
				Calcd	Found	Calcd	Found	Calcd	Found	Calcd	Found
$Mn(eth)_2$	Colorless	I	5.89	38.0	38.5	6.4	6.4			14.5	14.8
$Co(eth)_2$	Pink	II	4.90	37.6	37.8	6.3	6.3			15.4	15.4
$Co(Smc)_2$	Pink	II	4.75	29.4	29.2	4.9	4.8			18.0	17.6
$Ni(eth)_2$	Blue	II	3.21	37.6	37.7	6.3	6.2	7.3	7.5	15.3	15.6
$Ni(Smc)_2$	Blue	II	3.24	29.4	29.5	4.9	4.9			18.0	18.2
$Pd(ethH)Cl_2$	Orange	IV	*a*	21.2	21.3	3.9	3.9			31.2	31.0
$Pd(ethH)Br_2$	Orange	IV	*a*	16.8	17.1	3.1	3.0			24.8	24.9
$Pd(SmcH)Cl_2 \cdot H_2O$	Orange	IV	*a*	14.6	14.8	3.4	3.4			32.3	33.3
$Pt(ethH)Cl_2$	Yellow	IV	*a*	16.8	17.0	3.1	3.3			45.5	45.4
$Pt(ethH)Br_2$	Yellow	IV	*a*	13.9	14.2	2.5	2.8			37.7	37.4
$Pt(SmcH)Cl_2 \cdot H_2O$	Yellow	IV	*a*	11.5	12.1	2.6	2.7			46.5	46.0
$Cu(eth)_2$	Blue	III	1.83	37.2	37.4	6.2	6.2			16.4	16.0
$Cu(Smc)_2$	Blue	III	1.95	29.0	29.0	4.9	4.9	8.4	8.3	19.1	18.9
$Zn(eth)_2$	Colorless	I	*a*	37.0	36.7	6.2	6.3	7.2	6.9		
$Zn(Smc)_2$	Colorless	I	*a*	28.8	28.1	4.8	4.6	8.4	8.6		
$Cd(eth)_2$	Colorless	I	*a*	33.0	33.0	5.5	5.5			25.8	25.4
$Cd(Smc)_2$	Colorless	I	*a*	25.2	24.0	4.2	4.1			29.5	27.8
$[Hg(ethH)_2](ClO_4)_2 \cdot H_2O$	Colorless	V	*a*	19.3	19.3	3.8	4.1	3.8	3.9		
$[AgCu(Smc)_2]NO_3$	Blue	VI	1.85	19.4	19.2	3.2	3.4			21.2[b]	20.7[b]

[a] Not measured; compound presumed to be diamagnetic. [b] Ag analysis.

1725–1700 cm^{-1},[18] the zwitterions of amino acids such as glycine, alanine, cysteine, and dl-methionine display $\nu_{as}(COO^-)$ at *ca.* 1600 cm^{-1} and $\nu_{sym}(COO^-)$ at *ca.* 1410 cm^{-1}.[14,15,19] The frequencies of the antisymmetric and symmetric carboxyl stretching modes for dl-ethionine and S-methyl-l-cysteine also occur in these regions, indicating that these two amino acids also exist as zwitterions in the solid state. The spectra of dl-ethionine and deuterated ethionine in the region 3500–1500 cm^{-1} are given in Figure 1.

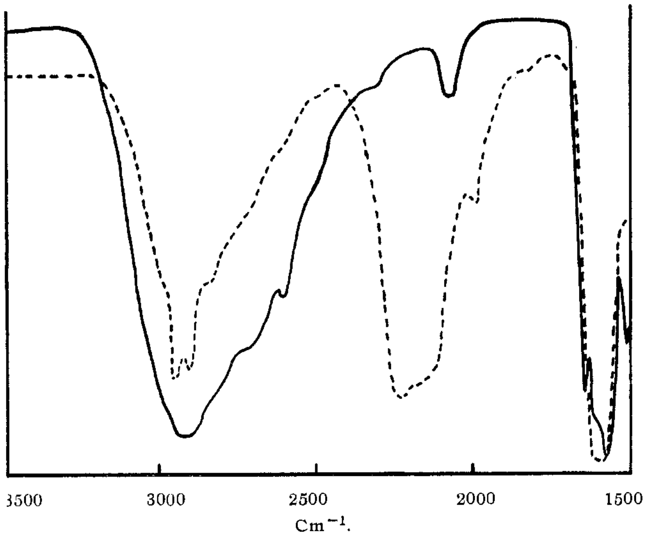

Figure 1.—Infrared spectra of dl-ethionine (———) and deuterated dl-ethionine (– – – –).

The infrared spectra of all the metal complexes, listed in Table I, were measured.[17] The spectra of the nickel complexes of the deuterated ligands were also measured in order to establish which band in the region of 1600 cm^{-1} is the antisymmetric carboxyl stretching mode; the NH_2 deformation occurs as a shoulder on the lower frequency side of the very strong $\nu_{as}(COO)$ band in the spectra of the metal complexes of the undeuterated ligands. The bands of interest in the spectra of the deuterated nickel complexes are listed in Table II.

Table II

Principal Infrared Bands (cm^{-1}) of Nickel Chelates of Deuterated dl-Ethionine and S-Methyl-l-cysteine

Compound	$\nu(ND)_2$	ν_{as} (COO)	ν_{sym} (COO)	δ (ND_2)
$Ni(eth)_2$ (deuterated)	2498 m, 2415 m	1590 s	1410 s	1180 m
$Ni(Smc)_2$ (deuterated)	2492 m, 2440 sh, 2415 m	1593 s	1408 sh 1398	1185 m

The spectra of the nickel complexes of ethionine and deuterated ethionine in the range 3500–2000 cm^{-1} are shown in Figure 2. These spectra, in contrast to the spectra of ethionine and deuterated ethionine (Figure 1), display the NH_2 and ND_2 stretching modes as well-resolved bands. The sharpness of these bands indicates the absence of hydrogen bonding between the amino and carboxyl groups in the complexes such as occurs in the free ligands. The spectra of the nickel complex of S-methyl-l-cysteine and of the manganese, cobalt, and cadmium complexes also display sharp $\nu(NH_2)$ bands. However, these bands are not quite as sharp in the spectra of the copper and zinc complexes but are by no means as broad as those of the free ligands. The frequencies of the NH_2 stretching modes (3360–3090 cm^{-1}) indicate that the amino group is coordinated[20] in all of the metal complexes. Primary amines usually display two bands in the region 3500–3300 cm^{-1}; the frequency of these bands is lowered by usually less than 100 cm^{-1} in the solid state.[21] The range of $\nu(NH_2)$ frequencies

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(18) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd ed, Methuen and Co. Ltd., London, 1958, pp 162, 167.

(19) (a) M. Tsuboi, T. Onishi, I. Nakagawa, T. Shimanouchi, and S. Mizushima, *Spectrochim. Acta*, **12**, 253 (1958); (b) K. Fukushima, T. Onishi, T. Shimanouchi, and S. Mizushima, *ibid.*, **14**, 236 (1959).

(20) G. F. Svatos, C. Curran, and J. V. Quagliano, *J. Am. Chem. Soc.*, **79**, 3313 (1957).

(21) See ref 18, pp 249, 253.

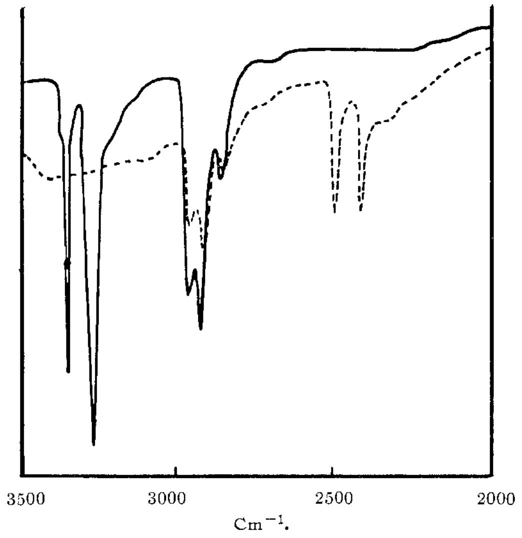

Figure 2.—Infrared spectra of the nickel complex of ethionine: ———, $Ni(eth)_2$; – – – –, $Ni(eth)_2$ (deuterated).

for the copper complexes is about 100 cm^{-1} lower than for the complexes of manganese, cobalt, nickel, zinc, and cadmium, indicating that the metal–nitrogen bond is strongest for copper(II); a similar result was reported for the copper(II) complex of methionine.[15]

Bivalent palladium and platinum yielded complexes of the type $MLHX_2$ (M = Pd, Pt; LH = ethH, SmcH; X = Cl, Br). The S-methylcysteine complexes were isolated as monohydrates, and the presence of water was confirmed by the occurrence of a strong OH stretching vibration at *ca.* 3500 cm^{-1} in the infrared spectra of these two complexes. The $\delta(NH_2)$ mode occurs at *ca.* 1570 cm^{-1}, while the $\nu_{as}(COO)$ mode occurs in the range 1737–1703 cm^{-1}, *i.e.*, about 120 cm^{-1} higher than in the spectra of the other metal complexes and of the free ligands. This high frequency denotes that the carboxylic group is neither coordinated to the metal nor hydrogen bonded, since saturated monobasic aliphatic acids which do not carry electron-attracting substituents display a strong band in the range 1725–1705 cm^{-1}.[18] The palladium and platinum complexes display a band in the range 385–378 cm^{-1}; this band is assigned as the metal–sulfur stretching vibration ν(M–S). This band is not present in the spectra of the other metal complexes. Metal–sulfur stretching vibrations have been reported to occur at 358–308 cm^{-1} for diethyldithiophosphato complexes,[22] 399–376 cm^{-1} for monothio-β-diketone complexes,[23] as a doublet at 373–338 and 359–333 cm^{-1} for some tris(1,2-dithiolato)-rhenium complexes,[24] and as a doublet at 320–317 and 310–305 cm^{-1} for *cis*-$\{PtX_2[(CH_3)_2S]_2\}$ (X = Cl, Br).[25] However, in thiourea complexes of transition metals ν(M–S) occurs in the range 298–205 cm^{-1}.[26]

The two bands at 331–321 and 305–288 cm^{-1} in the spectra of the chloro complexes are assigned as metal–chlorine stretching vibrations, since the bromo complexes do not absorb in this region but display a band at 240–230 cm^{-1}; however, this band was poorly resolved in the spectra which we were able to obtain. For palladium(II) and platinum(II) the ν(M–Cl) mode has been reported to occur in the range 370–315 cm^{-1}, and the ν(M–Br) mode, at 285–230 cm^{-1}.[25,27,28]

The infrared spectra clearly indicate that in the complexes of palladium and platinum the amino acid is acting as a bidentate chelating agent, being coordinated to the metal *via* the nitrogen and sulfur atoms, while the carboxyl group is not bound at all. From a study of the infrared spectra of the methionine complexes $M(mthH)Cl_2$ (M = Pd, Pt), McAuliffe[16] recently concluded that the amino acid is coordinated through the nitrogen and sulfur atoms and that the complexes have a polymeric structure due to intermolecular hydrogen bonding between the carboxyl groups. As the spectra were not measured below 620 cm^{-1}, no ν(M–S) was observed. McAuliffe's suggestion of intermolecular hydrogen bonding, based on the occurrence of the OH out-of-plane deformation as a narrow weak band at *ca.* 940 cm^{-1}, seems unlikely in view of the high frequency (1720 cm^{-1}) of the $\nu_{as}(COO)$. A recent X-ray study showed that the $Pd(mthH)Cl_2$ molecules pack together as dimers with hydrogen bonding between the carboxyl groups.[29]

In contrast to the palladium and platinum complexes, the mercury complex $[Hg(ethH)_2](ClO_4)_2 \cdot H_2O$ does not display an M–S stretching vibration; consequently, the amino acid is not coordinated through the sulfur atom in this complex. The $\nu_{as}(COO)$ mode occurs at 1580 cm^{-1}, indicating that the carboxyl group is not free as in the palladium and platinum complexes. It seems likely that intermolecular hydrogen bonding occurs between the carboxyl groups of adjacent complex ions in the crystal. However, the complex behaves as an electrolyte in water (Λ_{1000}, 387 mhos at 25°). The presence of a strong, broad, unresolved band at 1090 cm^{-1} and a sharp band at 623 cm^{-1} indicates that the perchlorate groups are ionic[30] in the solid state also. It is suggested that in this complex the mercury atom is two-coordinate and the amino acid is bound through the nitrogen atom only. With nitrogen donors mercury(II) usually displays a coordination number of 2[31] and, being typically b class,[32,33] does not form strong bonds with oxygen.[23]

In order to obtain additional evidence that the thioether group of S-methylcysteine will coordinate to a b class metal such as silver(I), we prepared the complex $[AgCu(Smc)_2]NO_3$ by treatment of a solution of $Cu(Smc)_2$ with silver nitrate. The infrared spectrum of $[AgCu(Smc)_2]NO_3$ is similar to that of $Cu(Smc)_2$,

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(22) S. H. H. Chaston, S. E. Livingstone, T. N. Lockyer, V. A. Pickles, and J. S. Shannon, *Australian J. Chem.*, **18**, 673 (1965).

(23) S. H. H. Chaston and S. E. Livingstone, *ibid.*, **20**, 1065 (1967).

(24) G. M. Schrauzer and V. P. Mayweg, *J. Am. Chem. Soc.*, **88**, 3235 (1966).

(25) J. R. Allkins and P. J. Hendra, *J. Chem. Soc.*, *A*, 1325 (1967).

(26) D. M. Adams and J. B. Cornell, *ibid.*, *A*, 884 (1967).

(27) R. J. H. Clark and C. S. Williams, *Inorg. Chem.*, **4**, 350 (1965).

(28) D. M. Adams, and P. J. Chandler, *Chem. Commun.*, 69 (1966).

(29) N. C. Stephenson, J. F. McConnell, and R. Warren, *Inorg. Nucl. Chem. Letters*, **3**, 553 (1967).

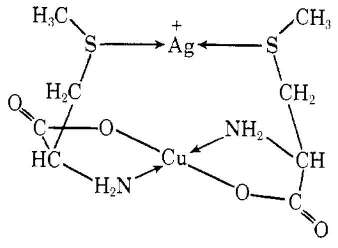
(30) B. J. Hathaway and A. E. Underhill, *J. Chem. Soc.*, 3091 (1961).

(31) D. Grdenić, *Quart. Rev.* (London), **19**, 303 (1965).

(32) S. Ahrland, J. Chatt, and N. R. Davies, *ibid.*, **12**, 265 (1958).

(33) S. E. Livingstone, *ibid.*, **19**, 386 (1965).

except that it shows a ν(Ag–S) band at 380 cm^{-1}, indicating that the amino acid residue is coordinated to copper through the nitrogen and one oxygen atom and to silver through the sulfur atom. The spectrum shows that the nitrate group is ionic.[34] In water the complex beahves as a uni-univalent electrolyte (Λ_{1000}, 102 mhos at 25°). A structure such as I seems more likely than



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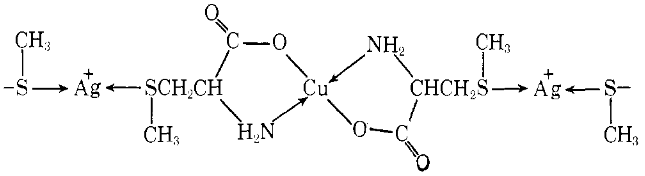
the polymeric structure II.



II

The magnetic moments of the cobalt and nickel complexes denote a high-spin state and thus preclude a square-planar structure. The pink color of the cobalt complexes points to an octahedral rather than a tetrahedral configuration. The diffuse reflectance spectra of the cobalt, nickel, and copper complexes were measured; the band maxima are listed in Table III. The spectra of the cobalt complexes are similar to the spectra of the aquated ion $Co(H_2O)_6^{2+}$ and other six-coordinated complexes[35-37] and differ from the spectra of tetrahedral cobalt(II) complexes.[38] The spectra of the nickel complexes are similar to the spectra of $Ni(H_2O)_6^{2+}$ and other six-coordinate nickel complexes.[39-41] The splitting of the band at *ca.* 1000 mμ into two components at *ca.* 900 and 1200 mμ indicates some tetragonal distortion from regular octahedral (O_h) symmetry.[42,43] The spectra of the copper complexes are consistent with a tetragonally distorted octahedral configuration.[37,44]

TABLE III

ELECTRONIC BANDS OF THE COBALT, NICKEL, AND COPPER COMPLEXES

Complex	Bands
	λ_{max}, mμ; ν, cm^{-1} in parentheses
$Co(eth)_2$	455 sh (22,000), 490 (20,400), 1060 (9450), 1195 (8350)
$Co(Smc)_2$	455 sh (22,000), 505 (19,700), 1075 br (8500)
$Ni(eth)_2$	655 (15,000), 875 (11,450), 1190 (8400)
$Ni(Smc)_2$	615 (16,250), 975 (10,250), 1190 sh (8400)
$Cu(eth)_2$	605 (16,500), *ca.* 700 sh (14,300)
$Cu(Smc)_2$	620 (16,100), *ca.* 725 sh (13,800)

It is apparent that the cobalt, nickel, and copper complexes are six-coordinate. Since their infrared spectra are similar, it is reasonable to assume that the manganese, zinc, and cadmium complexes are six-coordinate also. As the spectra of all of these complexes display no ν(M–S) band and since the sulfur atoms in $Cu(Smc)_2$ are available for coordination to a b class acceptor such as silver ion, the sulfur atom of the amino acid is not coordinated. Since the NH_2 stretching modes are well resolved, there appears to be no hydrogen bonding between the amino and carboxyl groups in the complexes. It seems then that these complexes are polymeric with the carboxyl group acting as a bridge between two metal atoms which are thereby six-coordinate. This polymeric carboxyl-bridged structure was proposed by McAuliffe, Quagliano, and Vallarino[15] for the methionine complexes $M(mth)_2$ which they prepared.

Conclusion

With bivalent metals, DL-ethionine and S-methyl-L-cysteine have been found to form complexes of the following types.

(a) **ML_2 (M = Mn, Co, Ni, Cu, Zn, Cd; LH = ethH or SmcH).**—These are polymeric in the solid state so that the metal ion is six-coordinate. The amino acid residue is coordinated to one metal atom *via* the nitrogen and one oxygen atom, while the other oxygen atom is coordinated to another metal atom.

(b) **$M(LH)X_2$ (M = Pd, Pt; X = Cl, Br).**—In these complexes the amino acid is coordinated *via* the nitrogen and sulfur atoms only and the carboxylic group does not form a bridge. The metal atoms have a square-planar coordination.

(c) **$[Hg(ethH)_2](ClO_4)_2 \cdot H_2O$.**—It is suggested that in this complex ethionine is bound *via* the nitrogen atom only. Intermolecular hydrogen bonding probably occurs between the carboxyl groups of adjacent complex ions in the crystal.

(d) **$[AgCu(Smc)_2]NO_3$.**—In this mixed-metal complex the amino acid residue is coordinated to the copper atom *via* the nitrogen and an oxygen atom and to the silver ion *via* the sulfur atom. It is likely that in the solid state the second carboxyl atom is coordinated to another copper atom as in the compounds of type a.

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