hydroxyl group would account for a higher basicity in the pyridine tautomer than would be found in 2,6-pyridinedicarboxylic acid. If this is the case, then chelation has promoted a profound change in the chelidamic acid structure. The remarkable drop of from 4 to 6 in the pK value of the hydroxy group (pK_3) also may be explained by the presence of the pyridine tautomer in the chelates. The observed pK_3 of chelidamic acid does not represent a true dissociation constant of the phenolic hydroxy group, since it involves the tautomeric equilibrium constant as well. If the chelate is in the pyridine tautomer, then dissociation of the hydroxy group can be accomplished much more readily. The variation in the pK_3 of the chelates from metal to metal represents a smaller but significant effect of the variation in the electron-withdrawing ability of the metal ions. It is interesting to note in this regard that the order observed, Cu(II) > Co(II) > Zn(II) > Ni(II) > Mn(II), parallels the acid strengthening effect that metals have on coördinated water molecules, *i.e.*, on the ease of metal hydrolysis. This suggests the possibility for the metal to transmit its electronegative influence on an oxygen atom, through an aromatic ring. This ability of metal ions to exert an electronic influence over a distance certainly would have important biochemical implications. At the present time, a series of compounds which will serve to further test this hypothesis is under study.

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Metal Derivatives of Arylazopyrazolone Compounds. IV. Molarity Quotients of Azopyrazolone Compounds Containing *o*-Carboxymethoxy and *o*-Carboxythiomethoxy Groups

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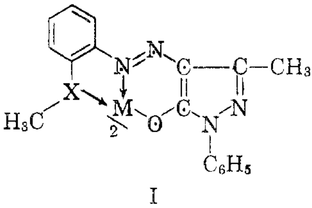
The relative stabilities of the metal derivatives of tetradentate azopyrazolone compounds containing an *o*-carboxymethoxy or an *o*-carboxythiomethoxy group have been measured potentiometrically in 75 volume % dioxane. Divalent copper, nickel, cobalt, and cadmium show a stronger affinity for sulfur than for oxygen. Divalent zinc, manganese, magnesium, calcium, strontium, barium, and the uranyl ion bond stronger to oxygen than to sulfur.

Introduction

Recently we reported[2] that arylazo compounds (I) which contained either an *o*-methoxy or an *o*-thiomethoxy group coördinated to metal ions as terdentate ligands. Divalent copper, nickel, cobalt, and cadmium formed more stable derivatives with the thiomethoxy compound, while zinc formed a more stable derivative with the methoxy compound.

Pfitzner[3] reports the possible coördination of an ether-like oxygen to copper(II) where the group *o*-substituted to the azo linkage is carboxymethoxy. Two compounds of this type, 1-phenyl-3-methyl-4-(2-carboxymethoxybenzeneazo)-5-pyrazolone (IIa) and 1-phenyl-3-methyl-4-(2-carboxythiomethoxybenzeneazo)-5-pyrazolone (IIb), were prepared in order to study the relative affinities



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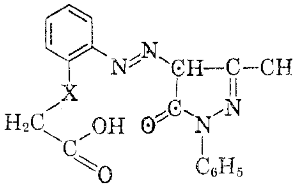

II

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(1) Summer Research Student (1958).

(2) F. A. Snavely, B. D. Krecker, and C. G. Clark, *J. Am. Chem. Soc.*, **81**, 2337 (1959).

(3) H. Pfitzner, *Angew. Chem.*, **62**, 245 (1950).

of a wider variety of metal ions for either sulfur or oxygen bonding.

Experimental

Preparation of the Azo Compounds.—The azo compounds were prepared by coupling the appropriate diazotized amines to 1-phenyl-3-methyl-5-pyrazolone.[4]

The lactam of *o*-aminophenoxyacetic acid was prepared by the method of Jacobs[5] from *o*-aminophenol and converted to the sodium salt of the free acid by boiling in concentrated sodium hydroxide solution.

The lactam of *o*-aminothiophenoxyacetic acid was prepared by the method of Unger[6] from *o*-aminothiophenol and converted to the sodium salt of the free acid by boiling in concentrated sodium hydroxide solution.

The sodium salts of the *o*-amino acids were diazotized by the inverted method and coupled to the pyrazolone in an aqueous solution buffered with sodium acetate. The crude azo compounds were digested with dilute hydrochloric acid and recrystallized from chlorobenzene.

(IIa) 1-phenyl-3-methyl-4-(2-carboxymethoxybenzeneazo)-5-pyrazolone, orange crystalline fibers, m.p. 218–219°; (IIb) 1-phenyl-3-methyl-4-(2-carboxythiomethoxybenzeneazo)-5-pyrazolone, orange fibers, m.p. 206–207°. Each of the azo compounds was tested for colored impurities on a chromatographic column packed with silica gel. Determination of neutral equivalents gave values within 0.10% of calculated values.

Potentiometric Titrations.—The titrations were performed at 30.0 ± 0.1° in 75% dioxane as described previously.[7] Cobalt(II) and manganese(II) were titrated under a nitrogen atmosphere. The solutions were so adjusted that in 100 ml. of solution there was 0.700 mmole of azo compound, 0.997 mmole of nitric acid, and 0.200 mmole of metal nitrate. A 1.007 *N* solution of carbonate-free sodium hydroxide was used. The meter reading correction factor (log U_H) equals 0.45. The molarity quotients were calculated by the method of formation functions ($\bar{n}$) of Bjerrum[8] and Calvin[9] for the simple system $M^{2+} + Ch^{2-} \rightarrow MCh$.

The values reported are the average of at least four calculations from experimental data.

The average time per titration was about 2 hr. However, the rate of reaction of nickel(II) with the sulfur derivative, compound IIb, was extremely slow. About 4 to 5 hr. was required between each addition of sodium hydroxide to reach equilibrium.

Results

The dissociation constants of compound IIa, the *o*-carboxymethoxy compound, are $Q_1 = 3.63 \times 10^{-7}$ and $Q_2 = 2.14 \times 10^{-10}$; for compound IIb, the *o*-carboxythiomethoxy compound, the values are $Q_1 = 1.26 \times 10^{-7}$ and $Q_2 = 1.07 \times 10^{-11}$. The first constant is a measure of the dissociation of the carboxyl group while the second is the dissociation of the hydrogen from the pyrazolone group. The color of the two compounds in the undissociated form is a light orange. The dissociated forms are a more yellow-orange.

The stoichiometry of the titration curves shows that 1:1 complexes are formed with the divalent metal ions. That is, two hydrogen ions are liberated per metal ion coördinating, one from the carboxy group and one from the pyrazolone moiety. It is assumed that the carboxy group is bonded to the metal ion. (1) Mur[10] reports that a methylated carboxymethoxy group *ortho* to the azo linkage loses the methyl group upon coördination. (2) The alkaline earths coördinate with the *o*-carboxymethoxy derivative and do not coördinate in the absence of the carboxy group. (3) The same results are obtained if the titrations are carried out in a 1:1 ratio of metal to azo compound or when the azo compound is in excess. (4) Stereochemically this bonding is possible.

The molarity quotients of the metal derivatives are listed in Table I. The decreasing order of stabilities for the divalent metal derivatives of the *o*-OCH_2COOH compound is Cu > UO_2 > Ni > Zn > Co > Pb > Mn > Ca > Mg > Sr > Ba, for the sulfur compound Cu > Ni > Co > Zn > Cd > Pb > Mn > Mg. With but a few exceptions the stability order follows that of *o,o'*-dihydroxyazo compounds.[11]

TABLE I

MOLARITY QUOTIENTS OF SOME DIVALENT METAL IONS OF SUBSTITUTED AZOPYRAZOLONE COMPOUNDS IN 75 VOLUME % DIOXANE AT 30°

Metal ion	Chelating agent log Q_1 IIa	IIb	Metal ion	Chelating agent log Q_1 IIa	IIb
Cu	>14	>17	Pb	9.5	10.1
UO_2	11.92	...	Mn[a]	8.49	8.53
Ni	11.60	14.50	Mg	5.7	3.9
Co	10.66	13.44	Ca	7.23	...
Zn	10.77	11.72	Sr	4.8	...
Cd	9.96	10.87	Ba	3.9	...

[a] Manganese(II) chloride.

Discussion

From a consideration of the acid dissociation constants of the chelating agents one would expect

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[4] K. F. King, Senior Honors Dissertation, Franklin and Marshall College, 1954.

[5] W. A. Jacobs, *J. Am. Chem. Soc.*, **39**, 2190 (1917).

[6] O. Unger, *Ber.*, **30**, 608 (1897); O. Unger and G. Groff, *ibid.*, **30**, 2397 (1897).

[7] F. A. Snavely, W. C. Fernelius, and B. P. Block, *J. Am. Chem. Soc.*, **79**, 1028 (1957).

[8] J. Bjerrum, "Metal Ammine Formation in Aqueous Solution," P. Haase and Son, Copenhagen, 1941.

[9] M. Calvin and K. W. Wilson, *J. Am. Chem. Soc.*, **67**, 2003 (1945).

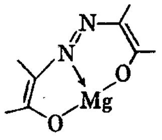
[10] V. I. Mur, *J. Gen. Chem. USSR*, **64**, 585 (1954).

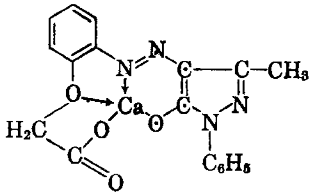
[11] F. A. Snavely, W. C. Fernelius, and B. E. Douglas, *J. Soc. Dyers Colourists*, **73**, 493 (1957).

that the *o*-carboxythiomethoxy compound, a slightly weaker acid, would form the more stable metal derivatives. However, the considerably greater stability of the copper, nickel, and cobalt derivatives with the sulfur compound (about 10^3 greater than their oxygen analogs) suggests a strong contribution from the ether-like sulfur. The zinc derivative with the sulfur compound is only 10 times more stable than its oxygen analog, while lead and manganese form derivatives of about equal stability with the sulfur and oxygen compounds.

Cadmium is reported[12] to bond more strongly to sulfur than to oxygen. This at first sight does not appear to be true with the above compounds. The ionic radius of cadmium(II) is about the same as calcium(II) and, as noted below, the calcium ion appears to be the proper size to form a compound of maximum stability with the oxygen chelating agent. Thus, due to the size effect, the cadmium derivative of compound IIa is probably more stable than would otherwise be found.

The fact that calcium forms a more stable derivative than magnesium with the carboxymethoxy derivative is not unique. Calcium generally forms more stable derivatives than magnesium with aminopolycarboxylic acids. Martel and Calvin[13] have pointed out that reagents with fewer donor groups and a less highly chelated structure generally give a more nearly normal order of stability. Magnesium forms more stable derivatives than calcium with the *o,o'*-dihydroxyazo compounds[11,14] in which two chelate rings are formed. However, with compound IIa (a tetradentate chelating agent) three rings are formed and calcium is more stable than magnesium. As stated above, it would seem that this is true selectivity in which the size of the calcium ion is the significant factor.





It is important to point out with respect to the above arguments on size effect that the beryllium ion did not coördinate with either of the chelating agents. Certainly it would seem that the beryllium(II) ion is much too small if the ideal size of an inert gas type ion is that of calcium(II), 0.99 Å.

The alkaline earths, calcium, strontium, and barium, all precipitated with the sulfur azo compound within the buffer zone of the first dissociation constant. Stoichiometry of the titrations shows that the precipitates were simple salts of the carboxylic acid group. The metal precipitates hydrolyzed at higher concentrations of sodium hydroxide to precipitate the respective hydroxides.

The above results are in agreement with the classification of Ahrland,[12] *et al.*, in which zinc(II) and the inert gas type ions are classified as "a" type elements (bond stronger to first members N, O, F, than to following members of the family) and copper(II), nickel(II), cobalt(II), and cadmium(II) are classified as "b" type elements (bond stronger to P, S, Cl, and the following members of their respective families than to the first members).

Acknowledgment.—The authors are indebted to the Research Corporation and the Du Pont Grant for financial support in carrying out this investigation.

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(12) S. Ahrland, J. Chatt, and N. R. Davies, *Quart. Rev.* (London), **12**, 265 (1958).

(13) A. E. Martel and M. Calvin, "Chemistry of the Metal Chelate Compounds," Prentice-Hall, New York, N. Y., 1952, p. 195.

(14) G. Schwarzenbach and W. Biedermann, *Helv. Chim. Acta*, **31**, 678 (1948).