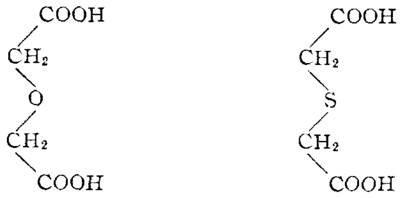

(I)

the carboxylate ions were bonding, one would expect smaller formation constants.

The log K_2 values increase in about the same order as log K_1. With the more basic ligands log K_1 − log K_2 for copper is greater than for other metals. This is a common type of behavior and is due to the fact that the copper, which normally has a coördination number of four, must, when combining with two ligand molecules, assume six coördination or else must not attach to all possible coördinating groups of the ligands.

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The Stabilities of Metal Complexes of Oxygen-containing Heterocyclic Compounds. Maltol[1]

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The stability constants of several bivalent metal ions with an oxygen-containing heterocyclic compound, maltol, have been measured in 50% by volume aqueous dioxane at 30° by the Bjerrum potentiometric titration technique. The Irving-Williams stability order of Mn < Co < Ni < Cu > Zn holds for the elements of the first transition series. The usual linear relationships between the logarithms of the stability constants and the acid dissociation constants of the chelating agents and the electronegativity and the second ionization potential of the metal ion are observed.

Among the naturally occurring compounds which are capable of forming metal complexes, there is a group which is characterized by the presence of an oxygen-containing heterocyclic ring. A large number of these are derivatives of the γ-pyrone flavonol and are widely distributed throughout the plant kingdom. These compounds can react with metals by the loss of a proton from the hydroxyl group on the heterocyclic ring. The carbonyl oxygen is then in position to form a five-membered chelate ring with the metal ion. Interest in these metal complexes has taken several forms recently. Quercetin and its glycoside rutin have been used for the treatment of capillary fragility; a number of their metal complexes have been synthesized in an attempt to find forms which are sufficiently soluble to increase the ease of administration.[2] Also, flavonol, quercetin, morin and myricetin have recently found use as analytical reagents.[3] The stabilities of several metal kojates have been measured by Bryant and Fernelius.[4]

It was felt that an investigation of the stabilities of the complexes which various metals form with chelating agents of this type was desirable. There are several complicating structural factors in the flavonols. Accordingly, maltol (3-hydroxy-2-methyl-4-pyrone), a simpler oxygen heterocyclic which is readily available, was chosen as a starting point.

Experimental

The maltol was kindly supplied by the Cliffs Dow Chemical Co. of Marquette, Michigan, and was used as received; m.p. 162–163°, literature[5] 162–164°. Dioxane was refluxed over metallic sodium for 6–8 hr. and then distilled through a four-foot bubble plate column.[6] Water was doubly distilled from alkaline permanganate solution. The tetramethylammonium hydroxide, obtained as a 1 *N* solution from Southwestern Analytical Chemicals, Austin, Texas, was diluted to approximately 0.1 *N* and standardized against primary standard potassium acid phthalate. Metal nitrate solutions were prepared by dissolving weighed quantities of the reagent grade salts in water and analyzing by standard quantitative methods. All other chemicals were reagent grade.

Stability constants were determined by potentiometric titration[7] in a 50% by volume dioxane–water solvent. The solution for titration contained about 0.15 g. of maltol (1.2×10^{-3} mole), 25 ml. of dioxane, 20 ml. of water and 5 ml. of the metal salt solution (0.03 *M*). In several experiments it was necessary to add a known amount of nitric acid to the solution to suppress chelation at the beginning of the experiment. Titrations were carried out at 30.00 ± 0.02° by addition of a standard solution of tetramethylammonium hydroxide from a microburet which could be read with a precision of ±0.002 ml. Titrations of Co(II) and Mn(II) were carried out in an atmosphere of nitrogen. Measurements were made with a Beckman model G *p*H meter with extension type calomel and glass (Beckman 1190–75) electrodes. The instrument was checked before and after each titration with standard buffers which covered the range of meter readings encountered during the titration.

Results and Discussion

The logarithms of the formation constants of the bivalent metal complexes of maltol are listed in Table I.

These are thermodynamic constants obtained by correcting the *p*H meter readings according to the data of Van Uitert,[8] as modified by Irving[9] and

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[1] Abstracted from a thesis submitted by N. Jack Clark in partial fulfillment of the requirements for the degree of Master of Science, Bucknell University, June, 1955. This work was supported by a grant from the Camille and Henry Dreyfus Foundation.

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TABLE I

LOGARITHMS OF FORMATION CONSTANTS OF BIVALENT METAL COMPLEXES WITH MALTOL AND KOJIC ACID IN 50% DIOXANE-WATER AT 30°

	Maltol		Kojic acid	
	pK_1	pK_2	pK_1	pK_2
H^+	10.49	..	9.66	..
Cu^{++a}	10.05	8.34		
Pb^{++}	9.67	6.43		
Zn^{++}	8.24	6.60		
Ni^{++}	7.95	5.83	7.44	5.54
Co^{++}	7.67	5.62	7.11	5.07
Cd^{++}	7.44	5.54	7.00	5.17
Mn^{++}	6.81	5.00		
Ca^{++}	4.84	2.41		

[a] Acid added.

solving sets of simultaneous equations as described by Block.[10] Several sets of equations were used for each titration, and the agreement was always satisfactory. Corrections also were made for the increase in volume of the solution as the titration proceeded, the volumes being assumed to be additive. Activity coefficients used in the calculations were obtained by interpolation from the data of Harned and Owen[11] for HCl in dioxane-water solution and the assumption that these are valid for ions of the same charge type. Since activity coefficient data for doubly charged species in mixed dioxane-water solvents are lacking, they were calculated from the values for 1-1 electrolytes with the assumption that the Debye-Huckel limiting law holds true. There is undoubtedly some error involved in this. In none of the solutions did the ionic strength exceed 0.01, and the $\log(\gamma^4_{\pm 1-1}/\gamma^3_{\pm 2-1})$ term in all cases amounted to 0.30 ± 0.01. The values for the formation constants reported are average values for at least two titrations with each metal.

Also included in Table I are formation constants for three metals with kojic acid. These results differ slightly from those reported by Bryant and Fernelius[4]; this difference is principally due to the fact that these are thermodynamic constants whereas those previously reported are concentration constants.

The metals in Table I are listed in order of decreasing stability. For the elements of the first transition series the Irving-Williams[12] stability order Mn < Co < Ni < Cu > Zn is seen to hold for the maltol complexes. The order of stability of the Group II ions Ca < Cd < Zn is the same as observed for many other ligands. The stability of the complexes with Pb is greater than is usually observed. This is illustrated in Fig. 1, a plot of log K_1 as a function of the second ionization potential of the gaseous atoms[13] and of the electronegativity,[14] where the value for lead in each case lies considerably above the straight lines. It is interesting to note that the formation constants for the complexes of tropolone[15] with Pb and Zn show a behavior qualitatively similar to that of the maltol complexes.

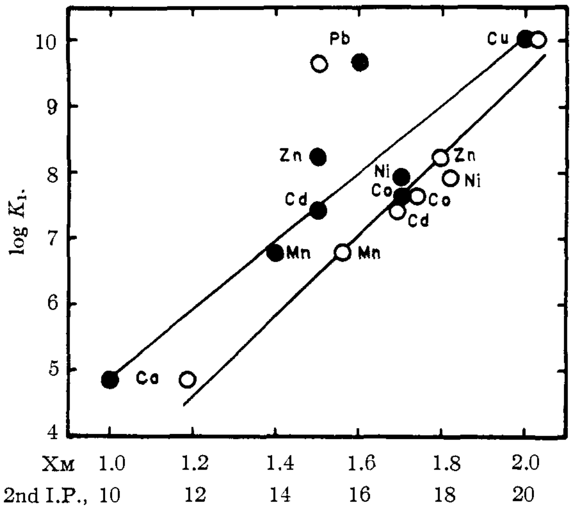

Fig. 1.—First formation constant of maltol complexes as a function of metal ion electronegativity and second ionization potential: open circles, second I.P. in e.v.; closed circles, electronegativities.

It was first pointed out by Calvin and Wilson[16] that a linear relationship exists between the logarithms of the acid dissociation constants of the chelating agents and the formation constants of the copper complexes. The different types of chelating agents (salicylaldehyde derivatives, β-diketones, etc.) gave a series of parallel lines. The formation constants of copper kojate[4] and copper maltolate, when similarly plotted, give a line parallel to and slightly below the β-diketone line. Similar plots show that the nickel and cobalt derivatives of the oxygen heterocyclics are somewhat more stable than the corresponding complexes of β-diketones of comparable acidity. Bryant and Fernelius[4] have also noted a slightly increased stability for zinc kojate.

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